

Aus dem Deutschen Diabetes-Zentrum
Leibniz Zentrum für Diabetes-Forschung
an der Heinrich-Heine-Universität Düsseldorf
Institut für Klinische Diabetologie
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**The influence of short-term exposure to air
pollution on cognitive and motor performance in
elderly women**

Dissertation

zur Erlangung des Grades eines Doktors der Medizin der Medizinischen
Fakultät der Heinrich-Heine-Universität Düsseldorf

vorgelegt von

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2026

Als Inauguraldissertation gedruckt mit der Genehmigung

der Medizinischen Fakultät der Heinrich-Heine-Universität Düsseldorf

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Für meine Familie.

Zusammenfassung

Hintergrund: Die Auswirkungen von Luftverschmutzung auf die Gesundheit älterer Menschen rücken zunehmend in den Fokus der Forschung. Insbesondere feine Partikel mit einem Durchmesser von weniger als $2,5\ \mu\text{m}$ ($\text{PM}_{2,5}$) gelten als kritisch, da sie tief in den Körper eindringen und verschiedene physiologische Prozesse beeinflussen können. Während die negativen Effekte einer langfristigen Exposition gegenüber $\text{PM}_{2,5}$ auf die kognitive Leistungsfähigkeit und die motorische Funktion bereits gut belegt sind, ist die Datenlage zu kurzfristigen Belastungen bislang uneinheitlich. Das Hauptziel dieser Arbeit ist es, den Zusammenhang zwischen kurzfristiger $\text{PM}_{2,5}$ -Exposition und kognitiven und feinmotorischen Funktionen zu untersuchen.

Methoden: In einer Querschnittsanalyse wurden 224 Frauen aus dem 2017/2018 Follow-up der SALIA-Kohorte untersucht. Die SALIA-Kohorte wurde ursprünglich zwischen 1985 und 1994 mit insgesamt 4756 Frauen im Alter von 51 bis 56 Jahren im Ruhrgebiet und dem südlichen Münsterland etabliert. Die kognitive Funktion wurde mithilfe des Montreal Cognitive Assessment (MoCA) erfasst, die feinmotorische Funktion durch die Zeit des 9-Hole-Peg-Tests (9HPT) gemessen. Die 9HPT-Zeiten wurden vor der Analyse logarithmisch transformiert, um eine approximativ normalverteilte Zielvariable zu erhalten. Die kurzfristige $\text{PM}_{2,5}$ -Exposition wurde wohnortbasiert für verschiedene Zeitfenster ermittelt, einschließlich der tagesaktuellen Belastung (Lag 0) sowie kumulativer Mittelwerte über mehrere Verzögerungsintervalle (Lag 0–1 bis Lag 0–28), um potenzielle verzögerte, kumulative Effekte abzubilden. Zur Untersuchung möglicher Assoziationen wurden lineare und logistische Regressionsmodelle unter Adjustierung für potenzielle Störfaktoren eingesetzt. Ergänzend wurden Subgruppenanalysen zur Prüfung der Ergebnisrobustheit durchgeführt.

Ergebnisse: Das durchschnittliche Alter der Teilnehmerinnen betrug 82,8 Jahre (Standardabweichung [SD] = 3,2). Der mittlere MoCA-Score betrug 22,2 (SD = 3,6) und lag damit unterhalb des üblichen Schwellenwerts für normale kognitive Leistungsfähigkeit bei älteren Personen (≥ 26 Punkte). Die geometrische Mittelzeit im 9HPT betrug 23 Sekunden (SD = 1,2) und lag damit etwa 1,5 Sekunden hinter dem Durchschnitt dieser Altersgruppe. Die Medianwerte der $\text{PM}_{2,5}$ -Belastung über die verschiedenen Verzögerungsintervalle hinweg lagen zwischen $10,9$ und $12,8\ \mu\text{g}/\text{m}^3$, mit Interquartilsabständen (IQR) von $2,7$ bis $7,7\ \mu\text{g}/\text{m}^3$. Für die kognitive Leistungsfähigkeit konnten keine statistisch signifikanten Zusammenhänge mit der $\text{PM}_{2,5}$ -Exposition festgestellt werden. Bezüglich der feinmotorischen Funktion ist der Anstieg der $\text{PM}_{2,5}$ -Konzentration um $6,13\ \mu\text{g}/\text{m}^3$ mit einer um $4,42\ \%$ verlängerten 9HPT-Zeit im Lag 0–7 assoziiert (95 %-Konfidenzintervall: $0,204$ – $8,816$; $p = 0,040$). Die Ergebnisse für die anderen Expositionszeiträume waren statistisch nicht signifikant, zeigten jedoch eine ähnliche Richtung.

Diskussion: Kurzfristige Exposition gegenüber PM_{2.5} zeigte keinen nachweisbaren Einfluss auf die kognitive Leistungsfähigkeit älterer Frauen. Die beobachtete Assoziation weist jedoch auf potenziell nachteilige Effekte auf die feinmotorische Funktion im höheren Alter hin. Gleichzeitig verdeutlichen die Ergebnisse, dass Einflussfaktoren wie Bildungsniveau, körperliche Aktivität, Rauchverhalten und Wohnumfeld differenziert berücksichtigt werden müssen, da sie kognitive und feinmotorische Fähigkeiten auf unterschiedliche Weise prägen. Um die komplexen Zusammenhänge zwischen Umweltbelastungen und altersbedingten neurodegenerativen Veränderungen umfassender zu verstehen, sind Studien mit größeren und heterogeneren Stichproben erforderlich.

Abstract (English)

Background: The health impact of short-term exposure to air pollution, including particulate matter with a diameter $\leq 2.5\mu\text{m}$ (PM_{2.5}) in the elderly, is of growing concern, particularly its influence on neurodegenerative diseases. While long-term exposure is well-documented to impact cognition and motor function, evidence on the specific neurobehavioral effects of short-term exposure remains limited and inconsistent. The primary objective of this work is to investigate the association between short-term PM_{2.5} exposure and cognitive and fine motor function in elderly women.

Methods: A cross-sectional analysis was conducted on 224 women from the 2017/2018 follow-up of the SALIA cohort, established between 1985 and 1994 in German Ruhrarea and south Muensterland, with 4756 women aged 51-56 at baseline. Cognitive function was assessed using the Montreal Cognitive Assessment (MoCA), and fine motor function was measured using the 9-Hole Peg Test (9HPT) time. Times for 9HPT were log-transformed before analysis to achieve approximately normality. Short-term exposure to PM_{2.5} was quantified in exposure windows using daily exposure (Lag 0) as well as averages of lagged exposure (Lag 0-1, Lag 0-7, Lag 0-14, Lag 0-21, and Lag 0-28) to identify delayed effects. Linear and logistic regression models were used to analyse the association between PM_{2.5} exposure and cognitive and motor performance, as well as declines, with adjustments for potential confounders. Additional analyses were performed to explore effect heterogeneity and assess the robustness of the findings.

Results: 224 women from the 2018 follow-up examination had a mean age of 82.8 years with a Standard deviation (SD) of 3.2. The mean MoCA score was 22.2 (SD = 3.6), which is below the normal cognition mean threshold of 26 in the elderly. The geometric mean time for motor function from 9HPT was 23 seconds (SD = 1.2). This is approximately 1.5 seconds slower than the average time for this age group. Median PM_{2.5} levels across exposure windows varied between 10.9 and 12.8 $\mu\text{g}/\text{m}^3$, with interquartile ranges (IQR) spanning from 2.7 to 7.7 $\mu\text{g}/\text{m}^3$. In adjusted models, 9HPT showed a positive association at Lag 07, with a 4.42% increase in 9HPT time per 6.13 $\mu\text{g}/\text{m}^3$ increase in PM_{2.5} exposure (95% CI: 0.204, 8.816, $p = 0.040$). At lag 07, a per IQR increase in PM_{2.5} exposure was associated with an average of 0.34 point increase in MoCA score (95% CI: -0.52 to 1.20); however, this effect was not statistically significant ($p = 0.43$). Effect estimates for other windows on 9HPT were directionally similar but not statistically significant.

Conclusion: While short-term PM_{2.5} exposure showed no significant impact on cognitive performance in the elderly, as measured by MoCA scores, it was associated with increased 9HPT times, particularly in Lag 07, suggesting potential adverse effects on fine motor function. Significant associations within subgroup analysis underscore the importance of addressing these confounders in environmental neuro-epidemiology. Future studies with larger sample sizes are needed to further explore the complex interaction between environmental exposure and neurodegenerative outcomes in the elderly.

List of abbreviations

9HPT: 9-Hole Peg Test
AD: Alzheimer's Disease
APHEA: Air Pollution and Health
APOE: Apolipoprotein E
BMI: Body Mass Index
CD: Cognitive decline
CI: Confidence Interval
CM: Centimetre
CERAD: The Consortium to Establish a Registry for Alzheimer's Disease
CNS: Central Nervous System
CT: Computed Tomography
DaTSCAN: Dopamine Transporter Scan
DSM-5: Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition
GCF: General Cognitive Function
IQ: Intelligence Quotient
IQR: Interquartile Range
L-DOPA: Levodopa
MCI: Mild Cognitive Impairment
MD: Motor dysfunction
MDS: International Parkinson and Movement Disorder Society
MMSE: Mini-Mental State Examination
MoCA: Montreal Cognitive Assessment
MRI: Magnetic Resonance Imaging
NA: Not available “missing data”
NC: Normal cognition
NMDA: N-Methyl-D-Aspartate
NMF: Normal motor function
OR: Odds Ratio
PD: Parkinson's Disease
PM: Particulate Matter
PM_{2.5}: Particulate Matter $\leq 2.5 \mu\text{m}$
SALIA: Study on the Influence of Air Pollution on Lung Function, Inflammation, and Ageing
SD: Standard Deviation
SPECT: single-photon emission computed tomography
TEWL: Transepidermal Water Loss
U.S.: United States
UBA: German environmental agency
 α : Alpha
 β : Beta
 μM : Micro-meter

Table of Contents

ZUSAMMENFASSUNG	I
ABSTRACT (ENGLISH)	III
LIST OF ABBREVIATIONS	IV
TABLE OF CONTENTS	V
1 INTRODUCTION	1
1.1 NEURODEGENERATION OVERVIEW	1
1.2 PREVALENT NEURODEGENERATIVE DISEASES AND THEIR RISK FACTORS	2
1.3 AIR POLLUTION'S INFLUENCE ON HEALTH	7
1.4 THE SHORT-TERM EFFECTS OF AIR POLLUTION	11
1.5 OBJECTIVES AND AIM OF THE STUDY	14
2 METHODS	16
2.1 STUDY POPULATION	16
2.2 THE MONTREAL COGNITIVE ASSESSMENT	18
2.3 THE NINE-HOLE-PEG-TEST	20
2.4 SHORT-TERM AIR POLLUTION ASSESSMENT	24
2.5 COVARIATES ASSESSMENT	24
2.6 STATISTICAL ANALYSIS	25
3 RESULTS	29
3.1 DESCRIPTIVE RESULTS	29
3.2 RESULTS FROM LINEAR REGRESSIONS	32
3.3 RESULTS FROM LOGISTIC REGRESSIONS	38
3.4 RESULTS FROM SUBGROUP ANALYSIS	43
4 DISCUSSION	50
4.1 STUDY AND RESULTS OVERVIEW	50
4.2 METHODS DISCUSSION	52
4.3 RESULTS DISCUSSION	54
4.4 STRENGTHS AND LIMITATIONS	59
4.5 FUTURE IMPLICATIONS AND CLINICAL IMPACT	60

4.6	CONCLUSION	61
5	REFERENCES	63
6	APPENDIX	72
6.1	DISTRIBUTION PLOTS	72
6.2	SALIA 2017 QUESTIONNAIRE (GERMAN)	75
	ACKNOWLEDGEMENTS (GERMAN)	83

1 Introduction

1.1 Neurodegeneration Overview

Neurodegenerative diseases are emerging as a major public health concern worldwide [1, 2]. Demographic shifts towards older populations have resulted in a rising burden of neurodegenerative diseases, leading to loss in quality of life, increased healthcare demand and premature deaths. Therefore, understanding and identifying modifiable risk factors plays a crucial role in developing effective prevention strategies.

Neurodegenerative diseases share the common pathology of neuronal loss in specific populations of neurons [3]. Neuronal loss in most cases involves anatomically and functionally related systems such as those governing motor or cognitive function [4]. Although the precise pathomechanism of neuron loss remains incompletely understood, several key pathological processes, including amyloidoses, tauopathies, and α -synucleinopathies, have been identified to contribute to the degeneration observed in various neurodegenerative conditions [5]. Neurodegenerative impairments are often classified based on their clinical manifestations, with mild cognitive impairment (MCI), dementia, and Parkinson's disease (PD) serving as the most common and classical examples, characterised by cognitive decline and motor dysfunction. They are highly prevalent in older age, and their prevalence increases as the population ages [1, 2, 6, 7]. Therefore, understanding the underlying risk factors involved is essential for prevention, early detection and disease management.

1.2 Prevalent neurodegenerative diseases and their risk factors

1.2.1 Mild Cognitive Impairment, Dementia, and Parkinson's Disease

Mild Cognitive Impairment

MCI is an evolving clinical concept, currently regarded as an intermediate stage between normal age-related cognitive changes and dementia [8]. According to the American Psychiatric Association's Diagnostic and Statistical Manual (DSM-5), Mild Neurocognitive Disorder, also known as MCI, is diagnosed based on modest cognitive decline in one or more cognitive domains identified through self-report, reliable informant accounts, or clinical observation and documented by objective cognitive assessment [9]. MCI should not interfere with daily independence, though tasks might require extra time, effort, or supportive strategies [9]. The prevalence of overall MCI in adults aged more than 60 years is found to be 21.4% in a population-based sample from Sweden [10]. Depending on the MCI criteria used and population studied, an average of 24.1% to 32.3% may progress to dementia [11]. To date, no pharmacological interventions have demonstrated efficacy in treating MCI; thus, management should prioritise the optimisation of vascular health and stroke prevention [12]. Non-pharmacological strategies such as regular aerobic exercise, cognitive engagement, and social interaction may offer benefits in slowing cognitive decline [12].

Dementia

The DSM-5 defines dementia as Major Neurocognitive Disorder, marked by a significant decline in one or more cognitive domains. This decline should be apparent based on concerns reported by the individual, a reliable informant, or observed clinically, and must be confirmed through objective cognitive assessment [9]. Unlike MCI, dementia involves a higher level of cognitive decline that interferes with independence in daily activities [9].

Patients with dementia often experience behavioural and psychological symptoms that are strongly correlated with cognitive decline [13]. These symptoms include abnormal motor behaviour such as increased and decreased motor function and agitation, anxiety, depression, hallucinations, and changes in sleep patterns [13].

In 2019, an estimated 57 million individuals worldwide were living with dementia. Due mainly to the ageing global population, this number is projected to rise to 152 million by 2050 [1]. Similar to MCI, dementia primarily affects older adults aged 65 and above [1]. The most common single cause of dementia is Alzheimer's disease (AD), which is characterised by cerebral atrophy with progressive loss of synapses and neurons, accumulation of amyloid plaques and neurofibrillary tangles, and significant deficits in cholinergic signalling [14, 15]. The second most common single cause is vascular dementia, which results from cerebrovascular disease, often associated with a history of stroke or transient ischemic attacks [14]. A major contributor to vascular dementia is cerebral small vessel disease (cSVD), a condition with multifactorial aetiology [16]. Recent studies have suggested that systemic inflammation may contribute to the pathogenesis of cSVD [17, 18]. A combination of AD and vascular dementia, referred to as "mixed dementia," represents the most prevalent overall cause of dementia [14].

The typical clinical presentation of AD is a gradually progressive memory decline, characterised predominantly by impaired ability to acquire new information, particularly autobiographical details such as recent personal events [19]. The clinical evaluation of suspected dementia follows a structured approach, beginning with a detailed medical history and a brief cognitive assessment, in alignment with DSM-5 criteria [9, 19]. The underlying aetiology should subsequently be determined through a combination of medical history, physical examination, laboratory investigations, and neuroimaging studies [19]. Management goals of dementia are to optimise quality of life by addressing cognitive and associated symptoms, as well as to delay the progression of cognitive decline [19]. Non-pharmacological management includes cognitive training and activities such as reading, engaging in cognitively stimulating games, physical exercise, social interaction, and long-term financial and medical planning [19]. Pharmacological treatments are more

personalised, requiring an understanding of the disease stage, aetiology, and accompanying neuropsychiatric and behavioural symptoms, and generally involve the use of acetylcholinesterase inhibitors, N-methyl-D-aspartate (NMDA) receptor antagonists, and drugs treating cerebrovascular risk factors such as hypertension, diabetes, hyperlipidemia, and atrial fibrillation [19-21].

Parkinson's disease

PD is the second-most common neurodegenerative disease after AD. PD primarily affects the elderly and has a prevalence of approximately 6.1 million people worldwide in 2016 [22]. It is considered the fastest-growing neurological condition [22, 23]. While this trend may be partly attributed to the global ageing population, age-adjusted data suggest that other factors, such as environment and exposure to toxic agents like air pollution, also play a role [22, 24, 25]. PD symptoms, which fall under the broader category of Parkinsonism, are primarily related to movement problems such as tremor, rigidity, and slowness of movement (bradykinesia), with postural instability and cognitive impairments appearing in some patients as the disease progresses [26]. PD is characterised by the progressive loss of dopaminergic neurons in the substantia nigra, accompanied by Lewy bodies composed of aggregated α -synuclein, which may result in striatal dopamine depletion [27, 28].

Diagnosis of PD is primarily based on medical history reporting PD symptoms and clinical and physical examination. According to the International Parkinson and Movement Disorder Society (MDS), the diagnosis of PD requires Parkinsonism based on three motor features (bradykinesia, rest tremor, rigidity) [29]. Additional diagnostic tools, such as the L-DOPA challenge test and neuroimaging techniques (including brain CT, MRI, and DaTSCAN with single-photon emission computed tomography (SPECT)), help distinguish typical PD caused by Lewy bodies from secondary forms of Parkinsonism [26, 30, 31]. Currently, no pharmacologic therapies prevent or delay PD progression [32]. Therefore, the PD therapy strategy mainly involves modifying the motor symptoms with dopamine-based medications, including Levodopa formulations, dopamine agonists, and monoamine oxidase-B inhibitors [32]. In addition, PD individuals may benefit from diverse exercise

interventions like high-intensity treadmill and advanced therapies such as deep brain stimulation and MRI-guided focused ultrasound [26, 32, 33].

1.2.2 Risk and protective factors of neurodegenerative diseases

Since no causal therapeutic strategies have yet been identified for MCI, dementia, or PD, understanding the role of risk and protective factors remains crucial in developing prevention strategies.

Ageing is a significant risk factor for neurodegenerative diseases, including MCI, dementia, and PD [34]. Besides increased age as a risk factor, the prevalence of dementia is consistently higher among women; this might be due to longer life expectancy in women [35]. Lower educational attainment is associated with a higher prevalence and risk of dementia [36]. Smoking has been identified as a potential risk factor for dementia [37]. Several genetic factors, most importantly the Apolipoprotein E (APOE)*4 allele, which is associated with higher risks of cardiovascular disease, were also associated with dementia [38]. Vascular conditions, including heart disease, hypertension, inflammation, elevated body mass index (BMI), stroke, and diabetes, are associated with an increased risk of both vascular and degenerative forms of dementia [39]. In addition, depression has also been identified as a risk factor for the development of dementia[40].

Despite the presence of numerous risk factors, several protective factors have been associated with a reduced incidence of dementia. Higher levels of education and engagement in cognitive activities are linked to a lower prevalence of the disease [41]. Participation in cognitively stimulating activities appears to confer both protective and enhancing effects on cognitive function [42]. Additionally, lifestyle factors, such as adherence to a Mediterranean diet, are generally associated with a lower rate of cognitive decline and a reduced risk of developing dementia [43, 44].

Highly evident risk factors for PD include a family history of PD, exposure to toxic substances such as pesticides, and exposure to general anaesthetics [24]. Smoking,

although identified as a potential risk factor for dementia, is conversely regarded as a protective factor for Parkinson's disease [24, 37]. Similarly, coffee consumption and physical activity are also considered protective factors for PD [24].

Over the past years, increasing evidence has established a link between air pollution and adverse effects on the brain (compare Section 1.3.3). Consequently, chronic air pollution is now recognised as a modifiable significant risk factor for both dementia and parkinson's disease [45]. This study will focus on exploring the effects of air pollution on cognitive and fine motor function, while also taking into account a broad range of risk and protective factors. **Figure 1** illustrates a summary of risk and protective factors associated with MCI, dementia, and PD.

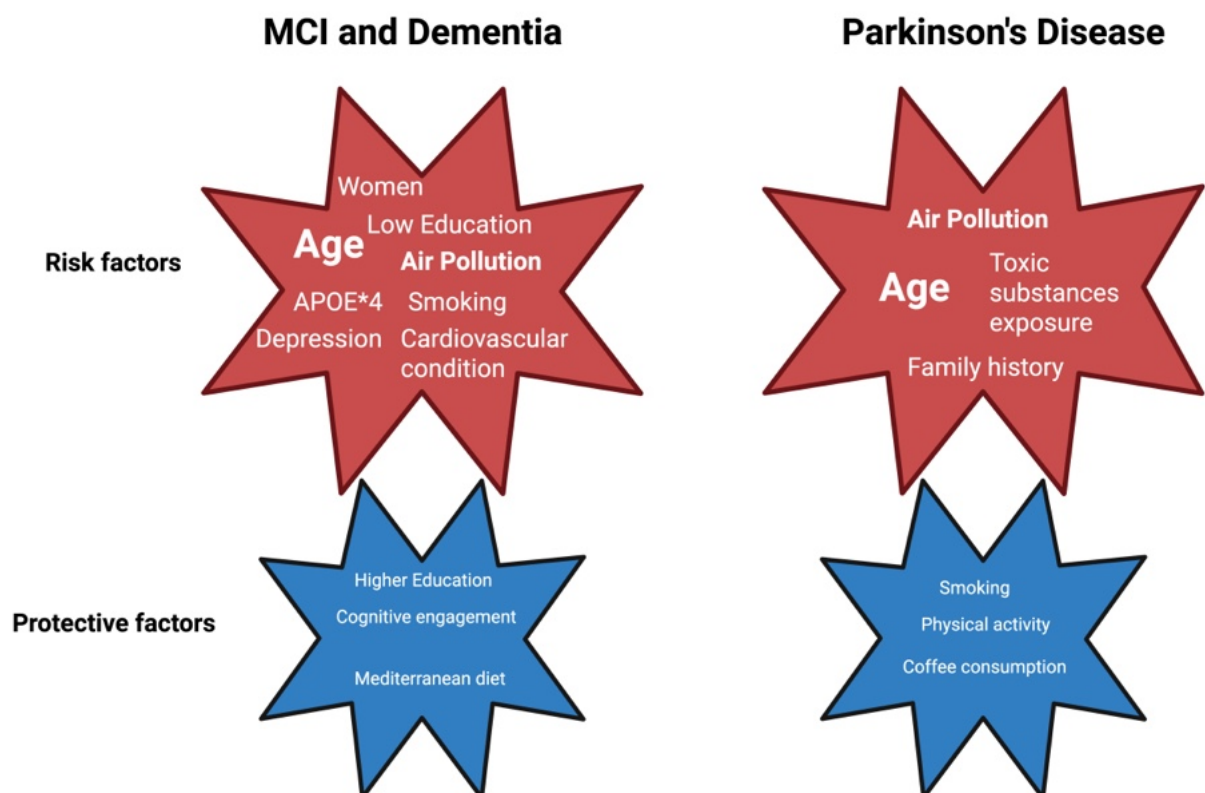


Figure 1: Summarised risk and protective factors of MCI, dementia, and Parkinson's Disease [46].

1.3 Air pollution's Influence on health

1.3.1 Overview and risks of ambient air pollution

Ambient (outdoor) air pollution is one of the most significant environmental risks to health. According to the World Health Organisation, in 2019, 99% of the world's population lived in areas where recommended air pollutant safe limits were not met [47]. Ambient air pollution is estimated to have caused 4.2 million premature deaths worldwide in 2019 [47]. PM originates from the combustion of fossil fuels, along with industrial, residential, and agricultural activities, which are primarily related to human activities [48]. The polluted air is a mixture rich in harmful components, such as respirable fine particles, carbon monoxide, lead, nitrogen dioxide, ozone, and sulfur dioxide, of which respirable fine particle matter (PM_{2.5}) is the leading environmental cause of premature mortality and a primary indicator of concern. PM is classified by aerodynamic diameter: coarse particles (PM₁₀) are 10 µm or less, fine particles (PM_{2.5}) range from 0.1 to 2.5 µm, and ultrafine particles (UFP, or PM_{0.1}) are smaller than 0.1 µm. Visual size comparisons are presented in **Figure 2**. PM_{2.5} has received significant attention as a human health concern, where effects associated with PM_{2.5} include cardiopulmonary, cardiovascular, and central nervous system (CNS) damage and disease.

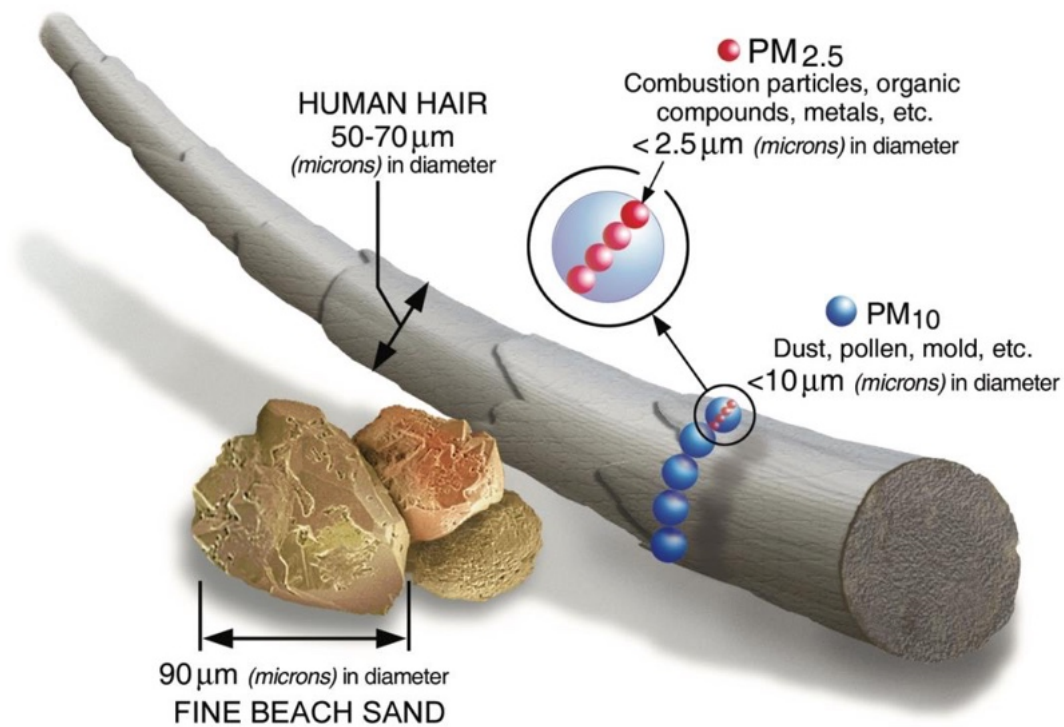


Figure 2: Size comparisons for PM particles.

Source: United States Environmental Protection Agency (epa.gov)

1.3.2 PM_{2.5} pathways into the brain

A key advance in understanding the pathways linking air pollution to the brain dates back to a dog experimental study from 2002, which compared dogs from the Mexico City Urban region, where fine PM and other pollutants reach very high levels, with control dogs from a less polluted region [49]. Its findings summarised an earlier expression of inflammatory markers in brain endothelial cells and subsequent brain damage through neuroinflammation in dogs from highly polluted Mexico City, providing insights into underlying potential pathophysiological mechanisms responsible for neurodegeneration in highly polluted areas [49]. Due to its small size, fine PM is hypothesised to enter the brain either directly via the olfactory bulb or indirectly through the bloodstream after passing through the respiratory tract [50, 51]. It induces systemic inflammation, increasing circulating inflammatory markers, which in turn may lead to neuroinflammation and

potentially damage the blood-brain barrier [51]. Damage to the blood-brain barrier can then allow both fine PM and inflammatory markers to accumulate in the brain's tissues, causing oxidative stress and neurodegeneration [51]. Moreover, recent findings indicate that PM_{2.5} may also reach the intestines and negatively impact the "brain-gut axis"—a novel area of investigation that continues to gain increasing scientific attention [51]. Exposure to urban air pollution from an early age also results in the accumulation of A β 42 (a component of amyloid plaques) and α -synuclein (a component of Lewy bodies) in brain areas associated with dementia and PD [52]. **Figure 3** demonstrates an illustration of potential pathways and pathogenesis related to PM_{2.5} on the CNS.

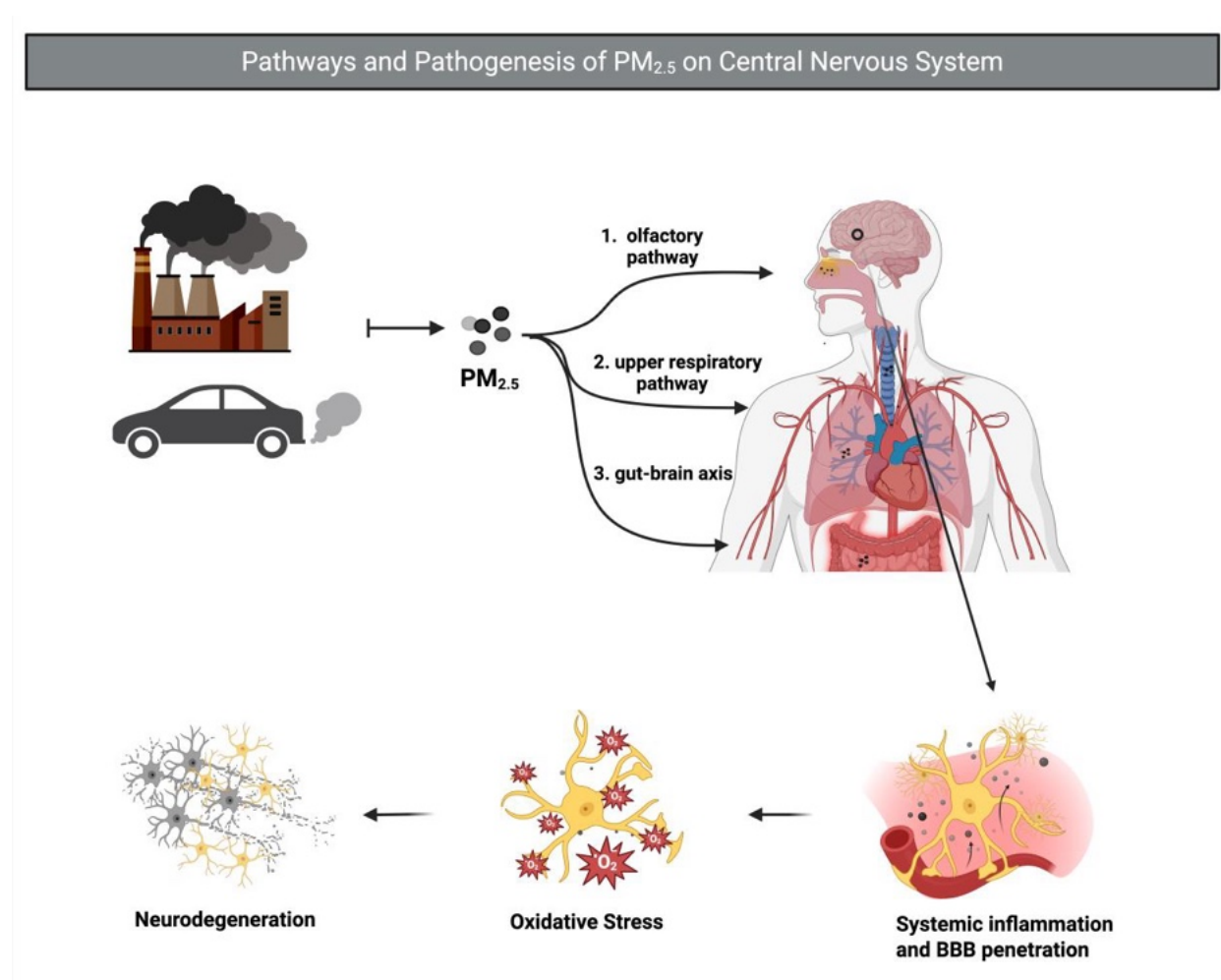


Figure 3: Potential pathways and the pathogenesis of PM_{2.5} on the central nervous system [53].

BBB: Blood-Brain-Barrier.

1.3.3 Impact of PM_{2.5} on cognitive and motor function

Exposure to air pollution, including PM_{2.5}, is considered a risk factor for MCI and dementia [54]. Cognitive decline is the main symptom observed in individuals diagnosed with MCI and dementia that has a direct influence on patients' quality of life and independence [9]. Chronic exposure to high levels of PM_{2.5} was associated with faster cognitive performance decline in older women from the Nurses' Health Study [55]. Previous results from the SALIA cohort (Study on the influence of Air pollution on Lung function, Inflammation and Ageing) suggest that chronic exposure to air pollution is associated with cognitive impairment and may be involved in the development of MCI [56, 57]. Kulick et al. also investigated the long-term effects of multiple pollutants, including PM_{2.5}, on cognitive decline in two cohort studies from Northern Manhattan, New York [58]. They identified a significant association between ambient air pollution and cognitive functioning in one cohort, with more evidence supporting the hypothesis that elevated exposure to PM_{2.5} and other pollutants accelerates cognitive decline over time [58]. Global cognitive decline was also slightly accelerated among participants with higher long-term PM_{2.5} exposure in the French Three-City prospective cohort [59].

Besides MCI and dementia, long-term exposure to PM_{2.5} is considered a significant risk factor for developing Parkinson's disease [60]. A population-based cohort study conducted in Ontario, Canada, found that each 3.8 µg/m³ (representing one interquartile range) increase in PM_{2.5} was associated with a 4% increase in PD incidence [61]. In addition, Brittany et al. investigated, in a population-based case-control study, whether air pollution is associated with an increased risk of PD and its clinical characteristics [62]. Findings indicated that higher exposure to PM_{2.5} was associated with an increased risk of PD in the elderly and urban areas, as well as a greater likelihood of developing the akinetic-rigid presentation and dyskinesia among PD patients [62].

1.4 The short-term effects of air pollution

While the effects of long-term exposure to air pollution on human health are well documented, particularly on the cardiovascular, respiratory, and central nervous systems [54, 60, 63, 64]. Growing evidence suggests that even short-term exposure — spanning from just days to weeks — may also have significant adverse health impacts. Samet et al. (2000) conducted a key study across 20 U.S. cities between 1987 and 1994, finding that a $10\text{ }\mu\text{g}/\text{m}^3$ increase in daily PM_{10} was associated with a 0.51% increase in all-cause mortality and a 0.68% increase in cardiovascular and respiratory deaths [65]. Another critical study from the APHEA project in Europe, published by Katsouyanni et al. (1997), found that a $50\text{ }\mu\text{g}/\text{m}^3$ increase in PM_{10} was associated with a 2% increase in daily mortality in Western European cities [66]. Although both studies focused on PM_{10} , which contains varying amounts of $\text{PM}_{2.5}$, they did not directly measure $\text{PM}_{2.5}$, mainly because monitoring was limited at the time. Their findings, however, were groundbreaking in demonstrating a significant foundational link between short-term exposure to ambient air pollution and increased daily mortality [65, 66].

To investigate the impact of short-term exposure to air pollution on cognitive performance, Shehab and Pope (2018) conducted an experimental study involving mainly young, healthy adult participants. The researchers assessed the effects of indoor air pollution, generated from candle burning and outdoor air pollution encountered during road commuting. Cognitive function was evaluated using the Mini-Mental State Examination (MMSE), Stroop Test, and Ruff 2 & 7 Selective Attention Test, administered before and after exposure. Within 1–2 hours of elevated $\text{PM}_{2.5}$ exposure, MMSE scores declined significantly in both exposure scenarios, and $\text{PM}_{2.5}$ from road commuting also reduced selective attention speed, as measured by the Ruff 2 & 7 test [67]. These findings were consistent with results from a second study conducted by Gao X., et al. (2021) in an older white male population, which found that higher outdoor $\text{PM}_{2.5}$ levels at each exposure window were associated with lower Global Cognitive Function (GCF) and MMSE scores, and greater odds of a low MMSE score [68]. Findings from both studies suggest that even

short-term exposure to fine PM may acutely impair global cognitive functioning and attention.

Increased average PM_{2.5} over the 2 days before evaluation was also associated with increased hospital admissions for PD in the elderly in the U.S. [69]. A South Korean cohort study found that the risk of PD aggravation, defined as emergency hospital admission for PD, significantly increased during exposure to higher short-term concentrations of air pollutants, including PM_{2.5} [70]. These findings suggest that short-term exposure to fine PM may influence the progression of neurodegenerative disease symptoms, leading to worse cognition or motor symptoms. A Summary of relevant studies on the effects of short-term air pollution is presented in **Table 1**.

Table 1: Summary of pertinent studies on short-term exposure to air pollution.

Study	Location	Study Design	Study Group (Sex/Age)	Main Findings
Samet et al. (2000)	20 U.S. cities	Time-series analysis	General population (mixed gender, all ages)	Short-term exposure to PM was significantly associated with increased daily mortality rates.
Katsouyanni et al. (1997)	12 European cities	Multicenter time-series study (APHEA project)	General population (mixed gender, all ages)	PM exposure was associated with increased daily mortality, with variability across cities.
Shehab & Pope (2019)	United Kingdom	Experimental human study	92 adults (mixed gender, mean age ~28)	Short-term PM _{2.5} exposure was associated with reduced cognitive performance.
Gao et al. (2021)	United States (Normative Aging Study)	Longitudinal panel study	954 adults (only male, age ≥65)	PM _{2.5} exposure correlated with lower cognitive performance; NSAID use attenuated the effect.
Zanobetti et al. (2009, 2014)	United States (nationwide, Boston)	Case-crossover study	General population (mixed gender, all ages)	Short-term PM _{2.5} exposure led to increased hospitalizations and mortality in high-risk groups.
Lee et al. (2017)	South Korea	Population-based cohort study	Parkinson's disease patients (mixed gender, mean age ~ 75)	Short-term PM _{2.5} exposure worsened Parkinson's symptoms and increased hospital visits.

1.5 Objectives and Aim of the Study

Although recent research has advanced our understanding of the effects of air pollution exposure, the impact of short-term exposure on cognitive and motor functions remains insufficiently investigated. For instance, while associations between short-term exposure to PM_{2.5} and cognitive function have been examined in younger adults and older white men, the effects on elderly women have, to our knowledge, not been evaluated. Similarly, despite emerging evidence linking short-term air pollution exposure with increased hospital admissions for PD, no studies have specifically assessed its short-term impact on motor function—PD’s hallmark symptom. Furthermore, existing studies on short-term air pollution and neurological outcomes have primarily been conducted in the United States and South Korea, with a notable lack of research in European populations. Across all previously conducted studies on short-term air pollution, addressing potential confounding factors remains a persistent methodological challenge. Several studies lacked detailed individual-level data, preventing adjustment for important factors such as smoking, socioeconomic status, and relevant health conditions, thereby leaving the possibility of residual confounding possible.

Therefore, this study aims to investigate the influence of short-term PM_{2.5} exposure on cognitive decline and fine motor dysfunction in German elderly women aiming to answer the following research question:

“What is the effect of short-term outdoor PM_{2.5} exposure on cognitive and motor performance, as well as cognitive decline and fine motor dysfunction, in elderly women?”

The study objectives are:

- I. To examine the association between short-term outdoor PM_{2.5} exposure and cognitive performance, assessed through the Montreal Cognitive Assessment (MoCA), and fine motor function, assessed through the Nine-Hole Peg Test (9HPT), in elderly women.

- II. To determine the association between short-term outdoor PM_{2.5} exposure and cognitive decline and fine motor dysfunction, defined through MoCA and 9HPT, in elderly women.
- III. To evaluate whether the association between short-term outdoor PM_{2.5} exposure and cognitive and fine motor performance, as well as cognitive decline and motor dysfunction, differs across stratified subgroups.

To address these objectives, the following hypotheses were formulated:

First Hypothesis:

H₀: Short-term exposure to PM_{2.5} does not affect MoCA and 9HPT scores in elderly women.

H₁: Higher short-term exposure to PM_{2.5} negatively affects MoCA and 9HPT scores in elderly women.

Second Hypothesis:

H₀: Short-term exposure to PM_{2.5} is not associated with cognitive decline or motor dysfunction in elderly women.

H₁: Higher short-term exposure to PM_{2.5} contributes to cognitive decline and motor dysfunction.

Third Hypothesis:

H₀: Short-term exposure to PM_{2.5} has no differential effects on cognitive decline and motor dysfunction among subgroups of elderly women.

H₁: Higher short-term exposure to PM_{2.5} affects cognitive decline and motor dysfunction differently across subgroups of elderly women.

The methodological approach used to test these hypotheses is described in the following Methods section.

2 Methods

2.1 Study Population

2.1.1 SALIA Cohort Study

The Study on the Influence of Air pollution on Lung function, Inflammation, and Ageing (SALIA) was initiated in the early 1980s by the State Government of North Rhine-Westphalia, Germany, and was part of the Environmental Health Surveys introduced as part of the region's Clean Air Policy. Its primary aim was to investigate the health effects of air pollution exposure on women, with a focus on lung function, inflammation, and ageing. The study population consisted of women residing in two distinct types of areas within North Rhine-Westphalia. These included the industrialised Ruhr Area (Dortmund, Duisburg, Herne, Gelsenkirchen, and Essen), characterised by high levels of air pollution due to coal mining, steel production, and heavy traffic, as well as two non-industrialised rural reference areas north of the Ruhr Area (Borken and Dülmen). These reference areas were chosen to serve as a contrast to the industrialised sites.

Baseline examinations were conducted consecutively between 1985 and 1994. Eligible participants included all women aged 54 to 55 years residing in the selected areas at the time of recruitment. Men were excluded from the study to avoid confounding bias due to their high occupational exposure to pollutants from mining and steel production industries, which were predominant in the region during the study period. This exclusion ensured that the study results primarily reflected the influence of ambient rather than occupational air pollution. In total, 4,874 women participated in the baseline examinations. The study and examinations were all conducted in German, and all women enrolled in the study were native speakers. The examinations included standardised questionnaires and clinical assessments to evaluate respiratory health, inflammation, and other ageing-related outcomes. In addition to the baseline surveys, several follow-up examinations have been conducted to track the health effects of air pollution exposure and ageing in this cohort. Details of the SALIA study cohort have been reported previously [64, 71, 72].

2.1.2 SALIA 2018 Follow-up

The follow-up study was conducted during 2018/2019 and involved 224 women from Dortmund, Duisburg, Essen, Gelsenkirchen, Herne, Borken, and Dülmen who agreed to participate again. All examinations took place in participants' home environments in order to minimise participant burden and ensure the validity of the performance measures. The primary focus was on evaluating neurological functions, particularly cognition and motor coordination.

The Montreal Cognitive Assessment (MoCA) was used as a cognitive screening tool, while the Nine-Hole Peg Test (9HPT) assessed participants' fine motor coordination and dexterity skills. Additionally, interviews gathered information about physical health, medical care usage, medication intake, respiratory diseases, sleep, allergies, and nutrition.

2.1.3 Ethical Approval

A valid ethics approval was obtained from the Ethics Committee of Heinrich Heine University Düsseldorf (Registration Number: 2017064332; Study Number: 6016R). All study-related investigations comply with the statutes of the Declaration of Helsinki of the World Medical Association. Written consent from all participants for their participation in the study and the use of their data was also obtained. The collected data were pseudonymized.

2.2 The Montreal Cognitive Assessment

2.2.1 Definition and purpose

The Montreal Cognitive Assessment, commonly known as “MoCA”, “MoCA Test” or “MoCA Cognition”, is a validated cognitive screening tool developed by Dr Ziad Nasreddine to identify MCI and early-stage dementia [73]. Over the years, it has gained widespread acceptance in clinical and research settings due to its high sensitivity and effectiveness in detecting both MCI and AD [74, 75].

The MoCA is a 30-point test designed to be administered in approximately 10 minutes, providing an in-depth assessment of a patient's cognitive health [73]. It evaluates several cognitive domains essential to daily functioning. These include tasks that assess visuospatial and executive function, such as planning, problem-solving, and spatial reasoning. The test also evaluates naming abilities, attention, language, abstraction, memory, and orientation. The domains cover different aspects of cognition, including language fluency and memory recall, as well as attention, reasoning, and spatial awareness.

A score of 26 or higher is considered normal, while scores below this threshold suggest potential cognitive impairment [73]. The test also adjusts for educational disparities, adding an extra point for individuals with 12 or fewer years of education. If a subject scores 30/30, the point is not added. This adjustment enhances the MoCA's diagnostic accuracy across different populations.

2.2.2 Task Description

The MoCA was administered with Test-Version 2017, currently available online at (www.mocatest.org), following standardised protocols to comprehensively evaluate participants' cognitive performance. Detailed instructions were provided for each task, with clarifications repeated once when necessary to ensure comprehension. The test tasks were conducted stepwise as in **Table 2**.

Table 2 Tasks description of Montreal Cognitive Assessment

Cognitive Skill	Task Description	Points
Alternating Trail Making	Draw a continuous line alternating between numbers and letters in ascending order (1-A-2-B, etc.), ensuring no crossing lines.	1
Visuoconstructional Skills	1. Copying a 3D cube: Correct alignment and proportionality were evaluated (1 point). 2. Clock-drawing task: Set hands to indicate 10:05 with points for contour (1), number placement (1), and hand positioning (1).	4
Naming	Identify three animal images.	3
Memory	Five unrelated words read aloud at a rate of one per second. Recall tested after two learning trials (no points allocated during trials) and reassessed later for scoring.	5
Attention	1. Forward & Backward Digit Span: Repeat numbers in same and reverse orders (2 points). 2. Vigilance: Tap hand whenever letter "A" is heard (1 point). 3. Serial Subtraction: Continuously subtract 7 from 60 (3 points).	6
Language	1. Sentence Repetition: Repeat two complex sentences exactly as spoken (2 points). 2. Verbal Fluency: Generate as many words starting with "B" in 60 seconds, excluding proper nouns (1 point).	3
Abstract Reasoning	Identify conceptual similarities between pairs: hammer-screwdriver (tools) and matches-lamp (light sources). One prompt allowed for concrete responses.	2
Delayed Recall	Recall five previously presented words without cues. Points awarded for spontaneous recall, category cues, or multiple-choice cues.	5
Orientation	Provide current date (year, month, exact date, and day) and name and location of the testing site.	6
Total	Maximum possible score for all tasks combined.	30

2.2.3 Cognitive Assessment

In this Study, MoCA was utilised as the primary tool for cognitive assessment. Due to the SALIA study methodology, only household educational attainment, defined as the educational level of the participant or her life partner, was available from the baseline assessment. Therefore, the educational correction recommended in the MoCA manual was applied using household education. Participants or their life partner with 12 or more years of education received an additional point to their total score. Two evaluation approaches were employed: (1) analysing the total MoCA scores of participants after educational correction to examine cognitive variability, and (2) categorising participants based on a cutoff score of 26 points, which is highly sensitive for detecting Mild Cognitive Impairment (MCI). Participants scoring 26 or higher were classified as cognitively intact, while those below 26 were identified as potentially cognitively impaired.

2.3 The Nine-Hole-Peg-Test

2.3.1 Definition and Purpose

The Nine-Hole Peg Test is a standardised, quantitative measure used to assess fine motor function and manual dexterity in clinical and research settings. The task is timed, with the total duration recorded as the primary outcome metric. This test is simple, non-invasive, and widely utilised for evaluating hand function in both neurologically intact individuals and those with conditions such as multiple sclerosis, stroke, and Parkinson's disease.

The 9HPT is considered a reliable and valid tool for assessing upper limb motor performance. According to Mathiowetz et al. (1985), the test demonstrated excellent test-retest reliability and has become a gold standard in motor function evaluation due to its sensitivity to subtle changes in manual dexterity [76-78]. The bilateral nature of the assessment allows for comparative analysis between hands, offering insights into lateralized deficits.

2.3.2 Task description

The administration of 9HPT followed standardised procedures as outlined by Mathiowetz et al. (1985). The test was conducted to assess fine motor coordination and dexterity of both the dominant and non-dominant hands [76]. To ensure familiarity with the task, each participant was provided with a practice trial for both arms before the timed assessments commenced.

The 9HPT setup (**Figure 4**) included a square pegboard with nine holes, each spaced 3.2 cm (1.25 inches) apart and 1.3 cm (0.5 inches) deep. Nine wooden pegs were used, each measuring 0.64 cm (0.25 inches) in diameter and 3.2 cm (1.25 inches) in length.

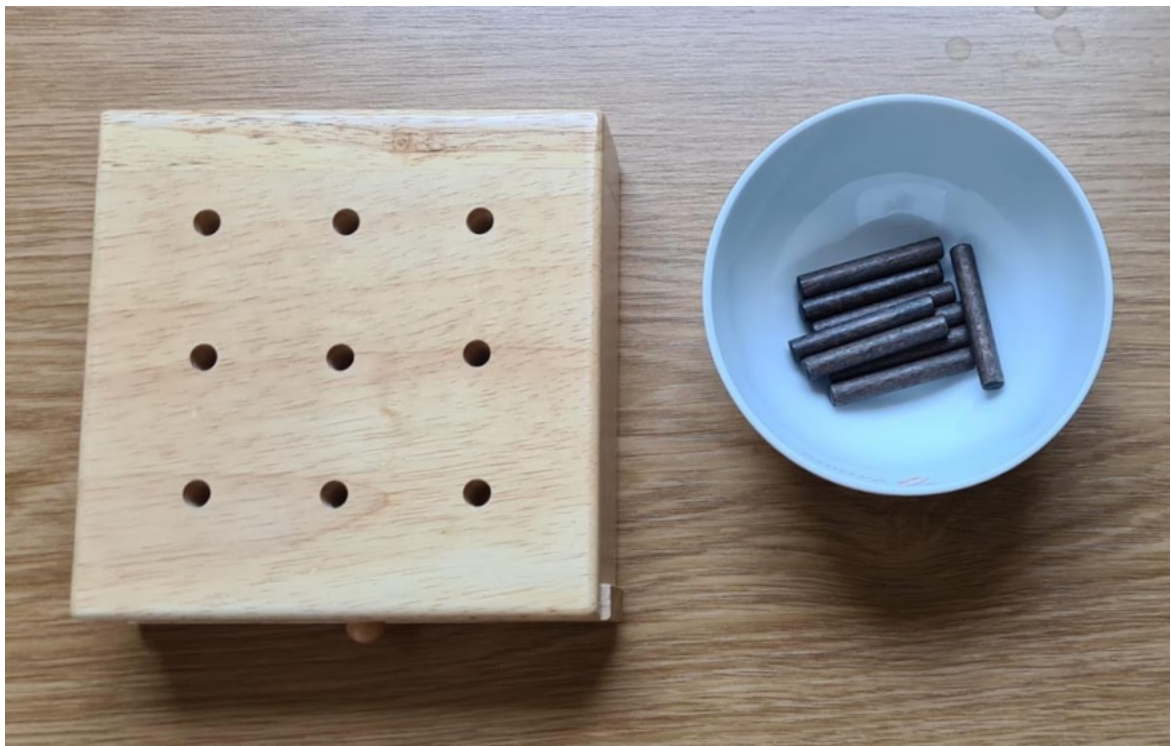


Figure 4: 9-Hole-Peg-Test setup. Photograph by the author.

Participants were seated with the pegboard placed directly in front of them on a stable surface. A container holding the pegs was positioned on the side of the hand being tested. Instructions were provided while demonstrating the activity. The dominant arm was tested

first. Participants were instructed as follows: “Pick up the pegs one at a time, using your right (or left) hand only, and put them into the holes in any order until all the holes are filled. Then remove the pegs one at a time and return them to the container (Demonstration in **Figure 5**). You can stabilise the pegboard with your left (or right) hand. This is a practice test. See how fast you can put all the pegs in and take them out again. Are you ready? Go!”

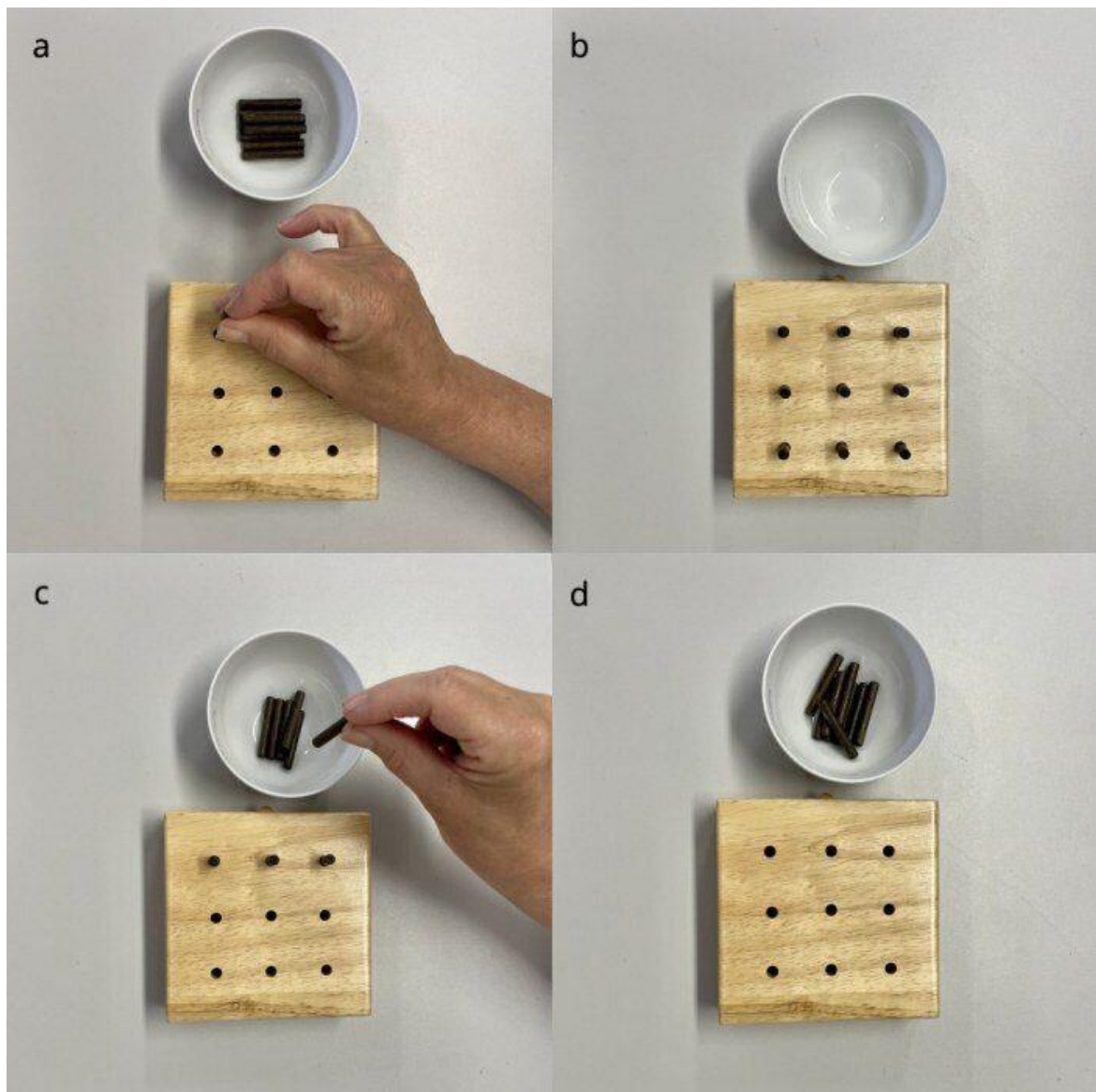


Figure 5: Demonstration of the 9-Hole Peg Test. Photograph by the author.

- a) The participant begins by placing pegs into the holes one at a time.
- b) All nine pegs are successfully inserted.

- c) The participant then removes the pegs from the holes.
- d) The test is completed once all pegs have been removed.

Following the practice trial, participants proceeded to the actual test. The instructions remained the same: “This will be the actual test. The instructions are the same. Work as quickly as you can. Are you ready? Go!” The stopwatch was started when the participant touched the first peg and was stopped when the last peg was placed back into the container. Verbal encouragement was provided during the task by prompting participants with phrases such as “Faster” while inserting the pegs and “Out again... faster” during peg removal.

After completing the test with the dominant hand, the container was repositioned to the opposite side of the pegboard, and the same instructions were given for the non-dominant hand. Timing and verbal prompts followed the same procedure to ensure consistency.

The recorded completion times, measured in seconds, were used for further analysis to assess motor performance. This standardised approach ensured reliability and validity in the administration of the 9HPT across all participants.

2.3.3 Motor function assessment

Upper extremity dexterity in healthy females aged 75 years and older has been normatively assessed using the Nine-Hole Peg Test (9HPT). The test completion times for this population were reported as 21.5 seconds (SD 2.9) for the right hand and 24.6 seconds (SD 4.3) for the left hand [76]. However, these normative values do not distinguish between dominant and non-dominant hand performance, which may introduce variability in the assessment of manual dexterity.

In this study, reduced upper extremity dexterity was evaluated using two distinct approaches. First, the shortest completion time recorded by each participant was identified to provide an individualised benchmark for dexterity. Second, a cutoff threshold of 21.5 seconds was employed, representing the mean right-hand completion time for healthy 75-and-older female adults. This approach, similar to the method used in the Montreal

Cognitive Assessment (MoCA), allowed participants to be categorised into healthy and potentially impaired groups based on their performance.

2.4 Short-term Air Pollution Assessment

Short-term exposure to fine particulate matter (PM_{2.5}) was estimated using data obtained from monitoring stations operated by the German environmental agency (UBA) and assigned to participants based on their residential address coordinates. A series of lagged exposure metrics was evaluated to investigate potential delayed and cumulative effects of PM_{2.5} exposure on cognitive and motor performance outcomes. Daily exposure (Lag 0) and averaged lagged exposures (Lag 0-1, Lag 0-7, Lag 0-14, Lag 0-21, and Lag 0-28) were quantified to capture exposure windows ranging from immediate (same-day) to prolonged short-term exposure over several weeks. Lag 0 corresponded to PM_{2.5} exposure on the same day participants performed the tests, while Lag 0-1 represented the mean exposure on the same day and the preceding day. Extended exposure metrics, including Lag 0-7, Lag 0-14, Lag 0-21, and Lag 0-28, reflected the average PM_{2.5} concentration over 7, 14, 21, and 28 days, respectively. This approach was similar to the study conducted by Gao et al. in 2021 [68].

2.5 Covariates assessment

Potential risk factors for neurodegenerative disease influencing motor and cognitive functions were identified based on previous literature and similar studies [57, 79, 80]. In this study, detailed information regarding participants' age, body mass index (BMI), smoking history (current or former smoking), passive smoking exposure, education level, physical activity, residential setting (rural vs urban), and comorbidities was gathered and included. Comorbidities included impaired respiratory conditions (chronic cough, hay fever, bronchial asthma, chronic bronchitis and chronic obstructive pulmonary disease (COPD)), depression, and myocardial infarction. Smoking history, passive smoking, and

comorbidities were each categorised into two groups: negative or not exposed as reference and positive or exposed.

Education level of participants or their life partner was dichotomised as low (reference; fewer than 10 years of education) and high (10 years or more of education). Physical activity status was categorised as frequently physically active (reference) or not frequently physically active. Residential setting was distinguished as rural (reference) and urban. Covariate data were collected through SALIA baseline assessments and were regularly updated during follow-up and questionnaire assessments.

2.6 Statistical analysis

Descriptive analyses were performed to summarise the characteristics of the study population, including MoCA and 9HPT scores and short-term exposure to PM_{2.5}. The primary outcome measures, MoCA and 9HPT scores, were treated as continuous variables. The distribution of both outcomes was assessed graphically using histograms and Q-Q plots (**Supplementary Figure 1-4**). 9HPT scores in seconds were then log-transformed to achieve an approximately normally distributed dependent variable (**Supplementary Figure 5-6**).

To evaluate the association between short-term PM_{2.5} exposure and cognitive and motor function, stepwise linear regression models were employed with MoCA and log (9HPT scores) as the dependent variables. Linear regression is used for quantifying the linear relationship between a dependent variable Y and one or more independent variables X . In its simplest form, the model is expressed as

$$Y = \beta_0 + \beta_1 \cdot X + \varepsilon$$

(β_0 : intercept, β_1 : slope coefficient of X , X : PM_{2.5}, ε : error term).

The models were structured as follows:

1. **Crude Model:** A basic regression model without adjustments for confounders.
2. **Main Model:** Adjusted for age, body mass index (BMI), ever smoking, passive smoking, education level, and physical activity.
3. **Extended Model:** Further adjusted for residential setting (urban vs. rural) and the presence of comorbidities, in addition to the variables included in the main model.

To assess dichotomised impaired outcomes, MoCA and 9HPT scores were stratified into two categories based on previously explained cutoffs. Logistic regression analyses were then performed to evaluate the association between PM_{2.5} exposure and the risk of cognitive dysfunction or motor decline. Logistic regression is used to model the relationship between a categorical dependent variable and one or more independent variables. For a binary outcome, the model is expressed as

$$\text{logit}(p) = \ln\left(\frac{p}{1-p}\right) = \beta_0 + \beta_1 \cdot X,$$

where p is the probability that the dependent variable equals 1, β_0 is the intercept, and β_1 represents the association between X and the log-odds of the outcome (*the effect of X*). The exponential of the coefficient, e^{β_1} , represents the odds ratio (OR), which quantifies the change in the odds of the outcome being 1 associated with a one-unit increase in the predictor. Similar to the linear regression, logistic regression models were conducted stepwise through crude, main, and extended models.

Sensitivity analyses were conducted to test the robustness of the findings. Participants were stratified into two subgroups for each confounder: ever vs never smoking, ever vs never passive smoking, frequent vs infrequent physical activity, high vs low education level, urban vs rural residency, and the presence vs absence of comorbidities. All regression models were reevaluated within each subgroup.

All analyses were conducted using a complete-case approach, whereby only participants with complete information on the outcome, exposure, and covariates included in the model

were retained for analysis. **Figure 6** illustrates the study workflow, including missing data, and outlines the sequence of steps involved in the analysis.

Consistent with standard practice in regression modelling, statistical inference was based on hypothesis tests of the regression coefficient associated with PM_{2.5} exposure (β_1). The null hypothesis ($\beta_1 = 0$) states that there is no association between PM_{2.5} exposure and the respective outcome, whereas the alternative hypothesis ($\beta_1 \neq 0$) indicates the presence of an association. Statistical significance was defined as a p-value < 0.05 . All statistical analyses were performed using R software (version 4.2.2).

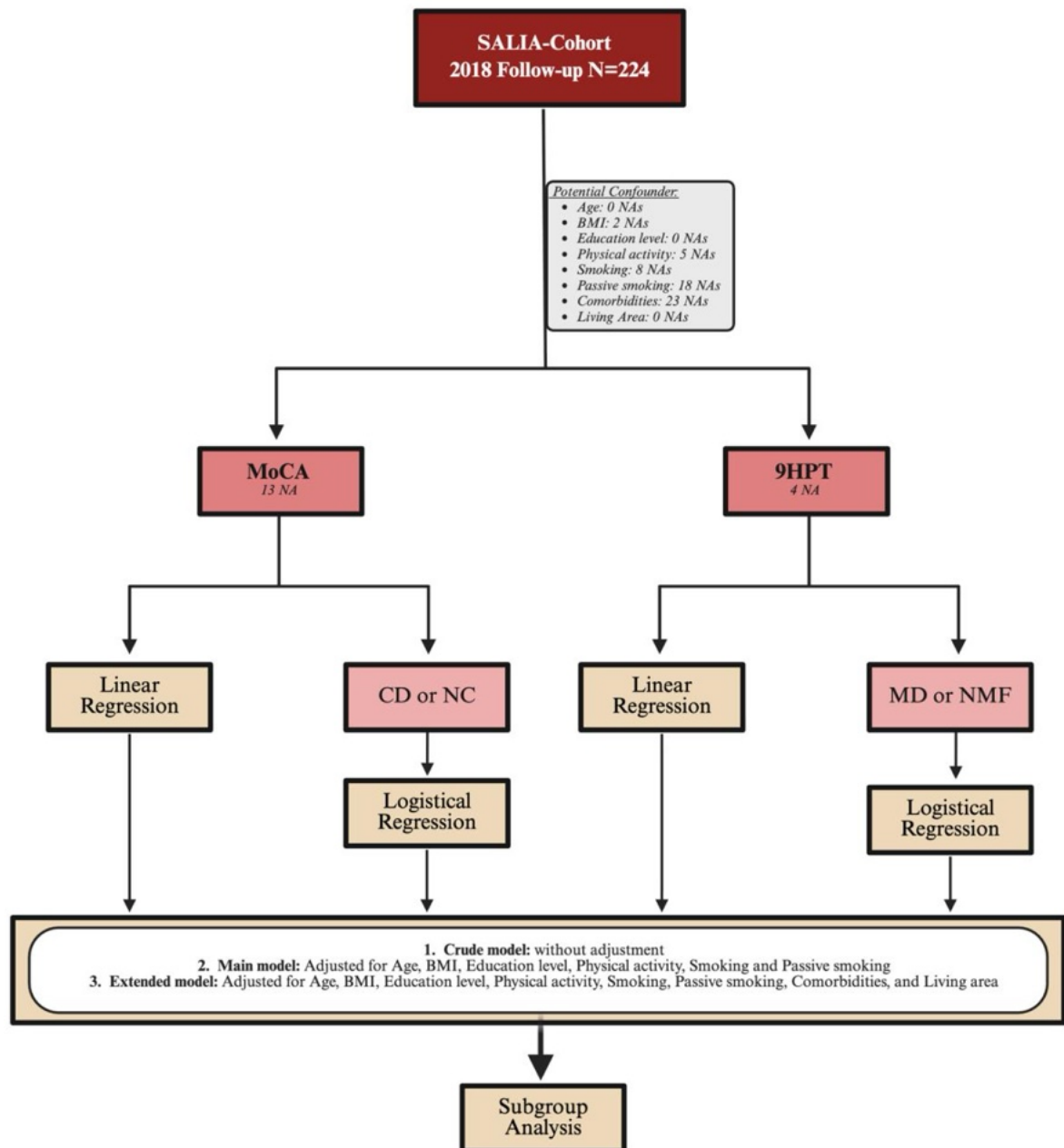


Figure 6: Workflow of study methodology [81].

CD: Cognitive decline; NC: Normal cognition; MD: Motor dysfunction; NMF: Normal motor function; NA: Not available (missing data); SALIA: Study on the influence of Air pollution on Lung function, Inflammation and Ageing.

3 Results

3.1 Descriptive Results

3.1.1 Study Group Descriptions

The study population, detailed in **Table 3**, consisted of 224 participants with a mean age of 82.8 (Standard Deviation (SD) = 3.2) years. A substantial proportion had a history of smoking (18.30%) or exposure to passive smoking (35.7%). The mean BMI was 26.3 (SD = 4.1), indicating that, on average, participants were overweight according to the WHO definition of overweight, which is a BMI of 25 or greater [82]. Over half of the participants or their life partners had more than 10 years of education (57.1%), while the remainder had 10 years or less (42.9%). The sample was fairly evenly split between rural (53.6%) and urban (46.4%) living. Just over half reported being frequently physically active (51.8%), and nearly half had at least one relevant comorbidity (44.2%).

Table 3: Characteristics of the Study Population

Characteristic (N=224)	n (%); mean (SD)
mean age	82.79 (3.17)
Active Smoking⁽¹⁾	
Ever	41 (18.30%)
Never	175 (78.13%)
Passive Smoking⁽²⁾	
Ever	80 (35.71%)
Never	126 (56.25%)
Metabolic metrics	

Characteristic (N=224)	n (%); mean (SD)
Weight	68.44 (11.27)
BMI	26.28 (4.09)
Physical activity⁽³⁾	
Frequent	116 (51.79%)
Infrequent	103 (45.98%)
Education status	
>10 years	128 (57.14%)
10 years or less	96 (42.86%)
Living area	
Rural living	120 (53.57%)
Urban living	104 (46.43%)
Comorbidities⁽⁴⁾	
Present	99 (44.20%)
Absent	102 (45.55%)

Note: Percentages may not sum to 100% for dichotomous variables due to missing data (NA). (1) = 8 NA; (2) = 18 NA; (3) = 5 NA; (4) = 23 NA.

SD: Standard Deviation.

3.1.2 Description of outcomes

Table 4 presents the cognitive and motor function outcomes of the study population. The mean MoCA score was 22.2 (SD = 3.6), with a maximum possible score of 30. A majority of participants (76.8%, n = 172) had MoCA scores < 26, indicating possible cognitive impairment, while 17.4% (n = 39) scored above this threshold. Motor function was assessed using the 9HPT, with a geometric mean completion time of 23.0 seconds (SD =

1.2). A substantial proportion of participants (60.7%, $n = 136$) had 9HPT times exceeding 21.5 seconds, whereas 37.5% ($n = 84$) completed the test within this time frame.

Table 4: Description of assessments

Outcomes	n (%); mean (SD)
MoCA⁽¹⁾	
mean MoCA Score [max. 30]	22.21 (3.56)
MoCA Score <26	172 (76.79%)
MoCA Score ≥ 26	39 (17.41%)
9HPT⁽²⁾	
geometric mean 9HPT Score	22.96 (1.20)
9HPT time > 21.5s	136 (60.71%)
9HPT time ≤ 21.5 s	84 (37.50%)

Note: Percentages may not total 100% due to missing values (NA). (1) = 13 NA; (2) = 4 NA.

MoCA: Montreal cognitive assessment; 9HPT: 9-Hole-Peg-Test; 9HPT time: Time needed to finish 9HPT. NA: Missing data, SD: Standard Deviation

3.1.3 Description of Air Pollution

Table 5 presents the distribution of PM_{2.5} exposure levels over various time lags, expressed as median values with interquartile ranges (IQR) in $\mu\text{g}/\text{m}^3$. The median PM_{2.5} concentration on the day of exposure (Lag 0) was $11.0 \mu\text{g}/\text{m}^3$ (IQR: 7.7). Over the short-term cumulative exposure period of 0–1 days, the median level was $10.9 \mu\text{g}/\text{m}^3$ (IQR: 7.1). Longer cumulative exposures showed slight variations, with median concentrations of $12.1 \mu\text{g}/\text{m}^3$ (IQR: 6.1) over 0–7 days, $12.1 \mu\text{g}/\text{m}^3$ (IQR: 3.5) over 0–14 days, and $12.8 \mu\text{g}/\text{m}^3$ (IQR: 2.8) over 0–21 days. The median PM_{2.5} concentration over the longest assessed exposure period (Lag 0–28 days) was $12.1 \mu\text{g}/\text{m}^3$ (IQR: 2.7), which remained below the WHO 24-

hour air quality guideline of 15 $\mu\text{g}/\text{m}^3$ but was more than twice the WHO annual air quality guideline of 5 $\mu\text{g}/\text{m}^3$ [83].

Table 5: Description of exposure windows

PM _{2.5} Exposure Window	Median (IQR) [$\mu\text{g}/\text{m}^3$]
lag 0	11.03 (7.66)
lag 0-1	10.88 (7.12)
lag 0-7	12.08 (6.13)
lag 0-14	12.10 (3.53)
lag 0-21	12.75 (2.76)
lag 0-28	12.07 (2.66)

PM_{2.5}: particulate matter with aerodynamic diameter of maximal 2.5 μm . IQR: Interquartile Range.

3.2 Results from Linear Regressions

3.2.1 Association Between PM_{2.5} and MoCA Score

To assess the association between PM_{2.5} exposure and MoCA scores, we conducted a linear regression analysis. In the unadjusted model (**Table 6**), the most negative effect estimate was observed for the lag 0–1 exposure window (β -estimate = -0.30, 95% CI: -1.06 to 0.46, $p = 0.43$). However, this association was not statistically significant.

Table 6: Association between PM_{2.5} and MoCA Score, no adjustments

PM _{2.5} Exposure Window	β -Estimate (95% CI)	p-value
lag 0	-0.30 (-1.07;0.47)	0.45
lag 0-1	-0.30 (-1.06;0.46)	0.43
lag 0-7	0.43 (-0.40;1.26)	0.31
lag 0-14	0.43 (-0.18;1.03)	0.17
lag 0-21	0.22 (-0.39;0.84)	0.48
lag 0-28	-0.22 (-1.03;0.59)	0.60

β -Estimate and 95% confidence interval from linear regression for unadjusted association between total MoCA Score and PM_{2.5} per 1- IQR increase. N=211.

(IQR for lag 0: 7.66 $\mu\text{g}/\text{m}^3$, lag 0-1: 7.12 $\mu\text{g}/\text{m}^3$, lag 0-7: 6.13 $\mu\text{g}/\text{m}^3$, lag 0-14: 3.53 $\mu\text{g}/\text{m}^3$, lag 0-21: 2.76 $\mu\text{g}/\text{m}^3$, lag 0-28: 2.66 $\mu\text{g}/\text{m}^3$)

PM_{2.5}: particulate matter with aerodynamic diameter of maximal 2.5 μm . IQR: Interquartile Range

The adjusted model, as illustrated in **Figure 7**, further expressed similar findings, showing no clear trend or statistically significant association after accounting for covariates. Negative effect estimates were observed in lag 0, lag 0-1 and lag 0-28.

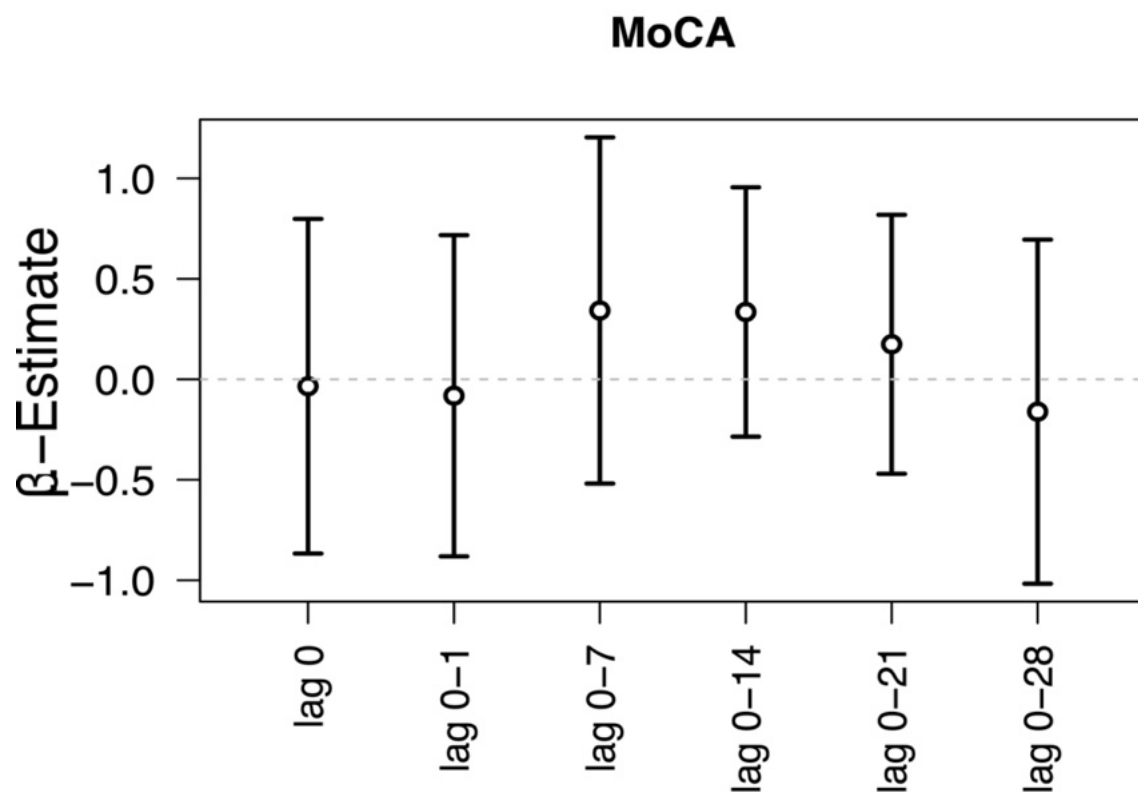


Figure 7: Association between PM_{2.5} and MoCA Score (Main model)

β-Estimate and 95% confidence interval from linear regression for the association between MoCA Score and PM_{2.5} per 1-IQR increase adjusted for age, body mass index (BMI), ever smoking, passive smoking, education level, and physical activity. N=191.

(IQR for lag 0: 7.66 µg/m³, lag 0-1: 7.12 µg/m³, lag 0-7: 6.13 µg/m³, lag 0-14: 3.53 µg/m³, lag 0-21: 2.76 µg/m³, lag 0-28: 2.66 µg/m³).

PM_{2.5}: particulate matter with an aerodynamic diameter of a maximum of 2.5 µm. 9HPT: 9-Hole-Peg-Test. IQR: Interquartile Range.

Similarly, in the model with extended adjustments (**Table 7**), the strongest negative effect estimate was found for the lag 0–28 exposure window (β -estimate = -0.17, 95% CI: -1.06 to 0.71, $p = 0.70$). However, the confidence interval included zero and therefore did not reach the significance level of $p < 0.05$.

Table 7: Association between PM_{2.5} and MoCA Score with extended adjustments

PM _{2.5} Exposure Window,	β -Estimate (95% CI)	p-value
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lag 0	0.17 (-0.69;1.04)	0.70
lag 0-1	0.09 (-0.76;0.94)	0.84
lag 0-7	0.27 (-0.64;1.19)	0.56
lag 0-14	0.31 (-0.36;0.98)	0.36
lag 0-21	0.23 (-0.45;0.92)	0.51
lag 0-28	-0.17 (-1.06;0.71)	0.70

β -Estimate and 95% confidence interval from linear regression for the association between total MoCA Score and PM_{2.5} per 1- IQR increase adjusted for age, body mass index (BMI), ever smoking, passive smoking, education level, physical activity, living area, and comorbidities. N=175.

(IQR for lag 0: 7.66 $\mu\text{g}/\text{m}^3$, lag 0-1: 7.12 $\mu\text{g}/\text{m}^3$, lag 0-7: 6.13 $\mu\text{g}/\text{m}^3$, lag 0-14: 3.53 $\mu\text{g}/\text{m}^3$, lag 0-21: 2.76 $\mu\text{g}/\text{m}^3$, lag 0-28: 2.66 $\mu\text{g}/\text{m}^3$)

PM_{2.5}: particulate matter with aerodynamic diameter of maximal 2.5 μm . IQR: Interquartile Range

3.2.2 Association Between PM_{2.5} and 9HPT Time

We performed a linear regression analysis to evaluate the influence of short-term exposure to PM_{2.5} and 9HPT time. **Table 8** shows the results from the crude linear regression analysis to assess the association between PM_{2.5} exposure and logarithmic 9HPT time across various exposure windows. The largest negative effect was observed in lag 0-7. However, P-values for all exposure windows were greater than 0.05, indicating no statistically significant associations.

Table 8: Association between PM_{2.5} and 9HPT time, no adjustments

PM _{2.5} Exposure Window	%-Change (95% CI)	p-value
lag 0	-1.25 (-4.95;2.60)	0.52
lag 0-1	0.69 (-3.01;4.54)	0.72
lag 0-7	2.67 (-1.48;7.00)	0.21
lag 0-14	0.66 (-2.36;3.76)	0.67
lag 0-21	-0.46 (-3.48;2.64)	0.77

lag 0-28	-0.86 (-4.80;3.25)	0.68
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Percentage change and 95% confidence interval from linear regression for unadjusted association between logarithmic 9HPT time and PM_{2.5} per 1- IQR increase. N=220.

(IQR for lag 0: 7.66 µg/m³, lag 0-1: 7.12 µg/m³, lag 0-7: 6.13 µg/m³, lag 0-14: 3.53 µg/m³, lag 0-21: 2.76 µg/m³, lag 0-28: 2.66 µg/m³)

PM_{2.5}: particulate matter with aerodynamic diameter of maximal 2.5 µm. CI: Confidence Interval. 9HPT: 9-Hole-Peg-Test. IQR: Interquartile Range.

We then adjusted the regression model for potential confounders. The adjusted models showed that higher PM_{2.5} exposure at the lag 0–7 exposure window was associated with slower motor performance (4.42% increase in 9HPT time per 6.13 µg/m³ increase in PM_{2.5} (95% CI: 0.20 to 8.82; $p = 0.04$)). Results for the other exposure windows were not statistically significant but showed a similar trend. Detailed results are illustrated in **Figure 8**.

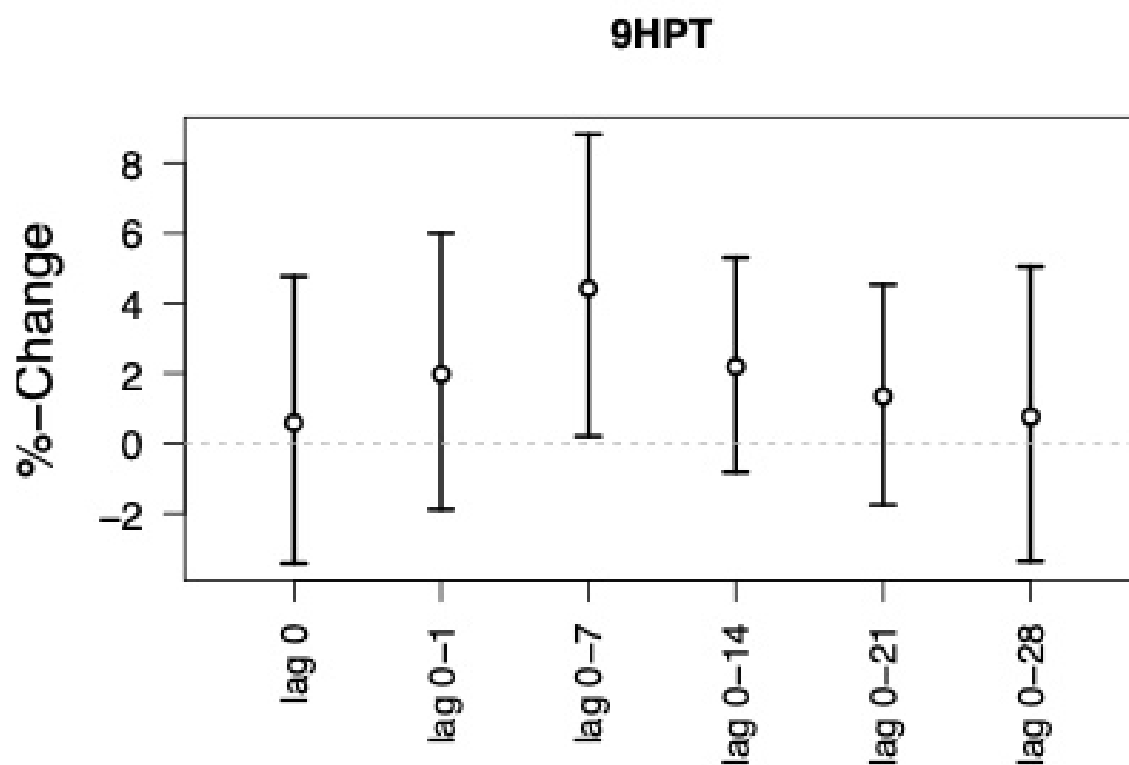


Figure 8: Association between PM_{2.5} and 9HPT Time (Main model)

Results

Percentage change and 95% confidence interval from linear regression for the association between logarithmic 9HPT time and PM_{2.5} per 1-IQR increase adjusted for age, body mass index (BMI), ever smoking, passive smoking, education level, and physical activity. N=197.

(IQR for lag 0: 7.66 µg/m³, lag 0-1: 7.12 µg/m³, lag 0-7: 6.13 µg/m³, lag 0-14: 3.53 µg/m³, lag 0-21: 2.76 µg/m³, lag 0-28: 2.66 µg/m³).

PM_{2.5}: particulate matter with an aerodynamic diameter of a maximum of 2.5 µm. 9HPT: 9-Hole-Peg-Test. IQR: Interquartile Range.

In a further step, the regression model was extended to include additional covariates. After this extended adjustment, the strongest positive association between PM_{2.5} exposure and 9HPT time was again observed at the lag 0–7 exposure window, indicating a 3.41% increase in 9HPT time for every 6.13 µg/m³ increase in PM_{2.5} (95% CI: –1.04 to 8.06; p = 0.13). Although not statistically significant, similar positive trends were observed across other exposure windows. A detailed overview of the extended model results is provided in **Table 9**.

Table 9: Association between PM_{2.5} and 9HPT time with extended adjustments

PM _{2.5} Exposure Window	%-Change (95% CI)	p-value
lag 0	0.68 (-3.48;5.02)	0.75
lag 0-1	1.66 (-2.43;5.92)	0.43
lag 0-7	3.41 (-1.04;8.06)	0.13
lag 0-14	2.39 (-0.86;5.74)	0.15
lag 0-21	2.04 (-1.25;5.45)	0.23
lag 0-28	0.97 (-3.29;5.41)	0.66

Percentage change and 95% confidence interval from linear regression for association between logarithmic 9HPT time and PM_{2.5} per 1- IQR increase adjusted for age, body mass index (BMI), ever smoking, passive smoking, education level, physical activity, living area, and comorbidities. N=181.

(IQR for lag 0: 7.66 µg/m³, lag 0-1: 7.12 µg/m³, lag 0-7: 6.13 µg/m³, lag 0-14: 3.53 µg/m³, lag 0-21: 2.76 µg/m³, lag 0-28: 2.66 µg/m³)

PM_{2.5}: particulate matter with aerodynamic diameter of maximal 2.5 µm. CI: Confidence Interval.

9HPT: 9-Hole-Peg-Test. IQR: Interquartile Range.

3.3 Results from Logistic Regressions

3.3.1 Association Between PM_{2.5} and Cognitive Decline

In the logistic regression analysis assessing the association between PM_{2.5} exposure and cognitive decline, the crude model (**Table 10**) showed the highest effect estimates for lag 0 (OR = 1.68, 95% CI: 0.95–3.10, $p = 0.09$) and lag 0-28 (OR = 1.72, 95% CI: 0.94–3.28, $p = 0.09$) exposure windows. However, these associations were not statistically significant. Other exposure windows, such as lag 0-7 and lag 0-14, had ORs below 1, but their confidence intervals included 1, indicating no definitive link between PM_{2.5} exposure and cognitive decline.

Table 10: Association between PM_{2.5} and Cognitive Decline, no adjustments

PM _{2.5} Exposure Window	Odds ratio (95% CI)	p-value
lag 0	1.68 (0.95;3.10)	0.09
lag 0-1	1.31 (0.76;2.32)	0.35
lag 0-7	0.70 (0.37;1.27)	0.25
lag 0-14	0.91 (0.59;1.42)	0.68
lag 0-21	1.31 (0.84;2.05)	0.24
lag 0-28	1.72 (0.94;3.28)	0.09

Odds ratio and 95% confidence interval from logistic regression for unadjusted association between cognitive decline and PM_{2.5} per 1- IQR increase. N=211.

(IQR for lag 0: 7.66 µg/m³, lag 0-1: 7.12 µg/m³, lag 0-7: 6.13 µg/m³, lag 0-14: 3.53 µg/m³, lag 0-21: 2.76 µg/m³, lag 0-28: 2.66 µg/m³)

PM_{2.5}: particulate matter with aerodynamic diameter of maximal 2.5 µm. CI: Confidence Interval.

IQR: Interquartile Range.

The adjusted model, as illustrated in **Figure 9**, showed further similar findings, showing no statistically significant associations after accounting for covariates in the main model.

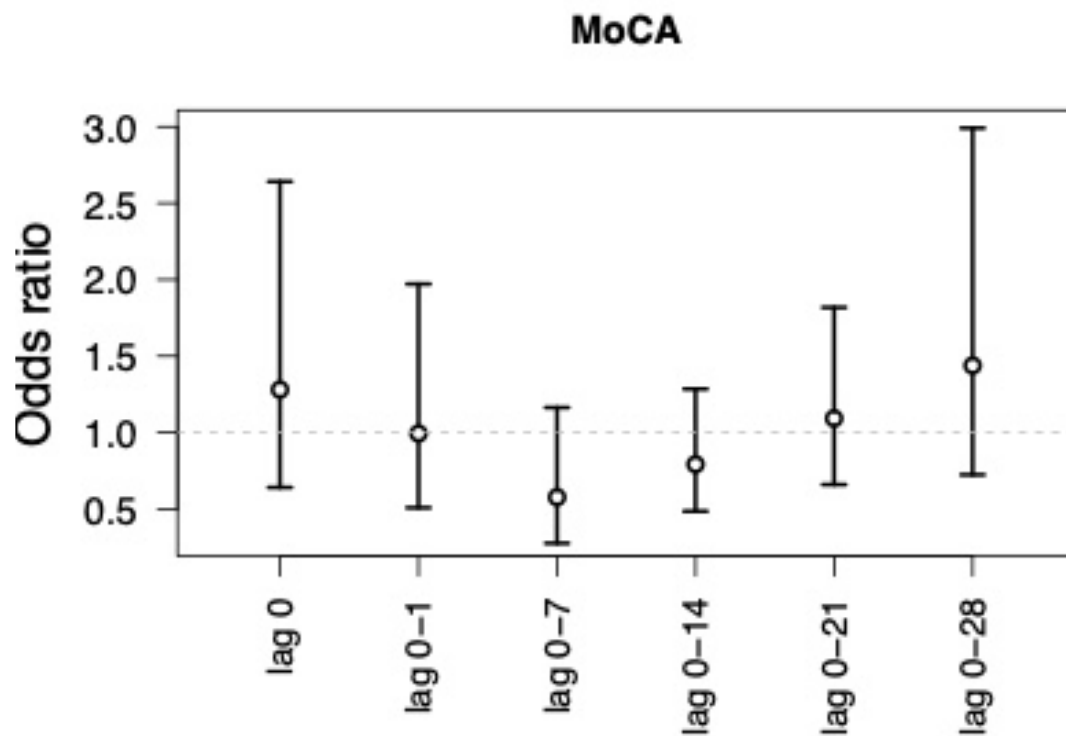


Figure 9: Association between PM_{2.5} and Cognitive Decline with adjustments

Odds ratio and 95% confidence interval from logistic regression for the association between cognitive decline tested by the MoCA test, and PM_{2.5} per 1-IQR increase, adjusted for age, body mass index (BMI), ever smoking, passive smoking, education level, and physical activity. N=191.

(IQR for lag 0: 7.66 $\mu\text{g}/\text{m}^3$, lag 0-1: 7.12 $\mu\text{g}/\text{m}^3$, lag 0-7: 6.13 $\mu\text{g}/\text{m}^3$, lag 0-14: 3.53 $\mu\text{g}/\text{m}^3$, lag 0-21: 2.76 $\mu\text{g}/\text{m}^3$, lag 0-28: 2.66 $\mu\text{g}/\text{m}^3$).

PM_{2.5}: particulate matter with an aerodynamic diameter of a maximum of 2.5 μm . 9HPT: 9-Hole-Peg-Test. IQR: Interquartile Range.

The extended model (**Table 11**) yielded similar results, with the highest OR observed for the lag 0-28 window (OR = 1.51, 95% CI: 0.75–3.20, $p = 0.26$), although the wide confidence interval, including 1, indicates uncertainty. The lowest OR was observed for the lag 0-7 window (OR = 0.55, 95% CI: 0.25–1.18, $p = 0.13$); however, this association did not reach statistical significance.

Table 11: Association between PM_{2.5} and Cognitive Decline with extended adjustments

PM _{2.5} Exposure Window	Odds ratio (95% CI)	p-value
lag 0	1.19 (0.57;2.55)	0.64
lag 0-1	0.91 (0.44;1.90)	0.80
lag 0-7	0.55 (0.25;1.18)	0.13
lag 0-14	0.79 (0.46;1.34)	0.38
lag 0-21	1.09 (0.64;1.87)	0.76
lag 0-28	1.51 (0.75;3.20)	0.26

Odds ratio and 95% confidence interval from logistic regression for association between cognitive decline and PM_{2.5} per 1- IQR increase adjusted for age, body mass index (BMI), ever smoking, passive smoking, education level, physical activity, living area, and comorbidities. N=175.

(IQR for lag 0: 7.66 µg/m³, lag 0-1: 7.12 µg/m³, lag 0-7: 6.13 µg/m³, lag 0-14: 3.53 µg/m³, lag 0-21: 2.76 µg/m³, lag 0-28: 2.66 µg/m³)

PM_{2.5}: particulate matter with aerodynamic diameter of maximal 2.5 µm. CI: Confidence Interval.

IQR: Interquartile Range.

Overall, across all models, logistic regression found no statistically significant evidence of a link between PM_{2.5} exposure and cognitive decline.

3.3.2 Association Between PM_{2.5} and Motor Dysfunction

The logistic regression analysis examining the link between PM_{2.5} exposure and motor dysfunction showed no strong associations in the crude model (**Table 12**). The highest OR was observed for the lag 0-1 window (OR = 1.38, 95% CI: 0.90–2.15, p = 0.14), followed by lag 0 (OR = 1.21, 95% CI: 0.78–1.89, p = 0.39). However, none of the exposure windows demonstrated statistical significance, as all confidence intervals included 1. The 0-21 lag window had an OR below 1 (OR = 0.88, 95% CI: 0.62–1.24, p = 0.46), but this was not statistically significant.

Table 12: Association between PM_{2.5} and Motor dysfunction, no adjustments

PM _{2.5} Exposure Window	Odds ratio (95% CI)	p-value
lag 0	1.21 (0.78;1.89)	0.39
lag 0-1	1.38 (0.90;2.15)	0.14
lag 0-7	1.32 (0.82;2.12)	0.25
lag 0-14	1.08 (0.77;1.53)	0.66
lag 0-21	0.88 (0.62;1.24)	0.46
lag 0-28	1.02 (0.64;1.62)	0.94

Odds ratio and 95% confidence interval from logistic regression for unadjusted association between motor dysfunction and PM_{2.5} per 1- IQR increase. N=220

(IQR for lag 0: 7.66 µg/m³, lag 0-1: 7.12 µg/m³, lag 0-7: 6.13 µg/m³, lag 0-14: 3.53 µg/m³, lag 0-21: 2.76 µg/m³, lag 0-28: 2.66 µg/m³)

PM_{2.5}: particulate matter with aerodynamic diameter of maximal 2.5 µm. CI: Confidence Interval.

IQR: Interquartile Range.

After adjusting for potential confounders, the main model for binary motor dysfunction, illustrated in **Figure 10**, showed a higher OR for motor dysfunction per IQR increase in PM_{2.5} exposure, mainly in early exposure windows (lag 0, lag 0-1 and lag 0-7). These results were, however, not significant.

Unlike the main model from the linear regression, logistic regression's main model for binary motor dysfunction did not yield a significant association for short-term PM_{2.5} exposure across any exposure window.

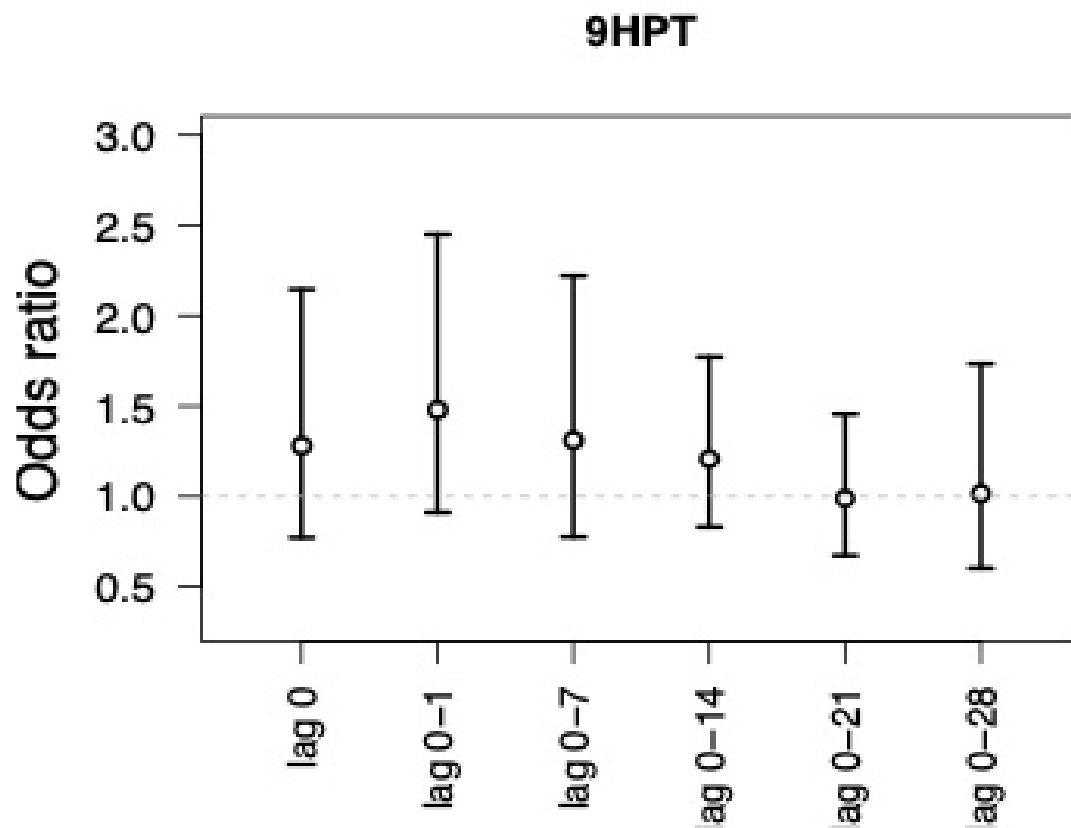


Figure 10: Association between PM_{2.5} and Motor dysfunction (Main model)

Odds ratio and 95% confidence interval from logistic regression for the association between motor dysfunction tested by the 9HPT test, and PM_{2.5} per 1-IQR increase, adjusted for age, body mass index (BMI), ever smoking, passive smoking, education level, and physical activity. N=197.

(IQR for lag 0: 7.66 µg/m³, lag 0-1: 7.12 µg/m³, lag 0-7: 6.13 µg/m³, lag 0-14: 3.53 µg/m³, lag 0-21: 2.76 µg/m³, lag 0-28: 2.66 µg/m³).

PM_{2.5}: particulate matter with an aerodynamic diameter of a maximum of 2.5 µm. 9HPT: 9-Hole-Peg-Test. IQR: Interquartile Range.

In the extended model (**Table 13**), the highest OR was again seen in the lag 0-1 window (OR = 1.39, 95% CI: 0.83–2.39, $p = 0.22$), but it did not reach significance. Similarly, the lag 0-7 window had the lowest OR (1.16, 95% CI: 0.66–2.03, $p = 0.61$), though the confidence interval suggests considerable variability. Overall, across both crude and adjusted models for binary outcomes, there was no significant evidence of an association between short-term exposure and 9HPT-defined fine motor dysfunction.

Table 13: Association between PM_{2.5} and Motor dysfunction, extended adjustments

PM _{2.5} Exposure Window	Odds ratio (95% CI)	p-value
lag 0	1.27 (0.75;2.19)	0.37
lag 0-1	1.39 (0.83;2.39)	0.22
lag 0-7	1.16 (0.66;2.03)	0.61
lag 0-14	1.19 (0.79;1.80)	0.41
lag 0-21	1.03 (0.68;1.56)	0.89
lag 0-28	1.04 (0.60;1.83)	0.89

Odds ratio and 95% confidence interval from logistic regression for association between motor dysfunction and PM_{2.5} per 1- IQR increase adjusted for age, body mass index (BMI), ever smoking, passive smoking, education level, physical activity, living area, and comorbidities. N=181.

(IQR for lag 0: 7.66 µg/m³, lag 0-1: 7.12 µg/m³, lag 0-7: 6.13 µg/m³, lag 0-14: 3.53 µg/m³, lag 0-21: 2.76 µg/m³, lag 0-28: 2.66 µg/m³)

PM_{2.5}: particulate matter with aerodynamic diameter of maximal 2.5 µm. CI: Confidence Interval.

IQR: Interquartile Range.

3.4 Results from Subgroup Analysis

To test the robustness of the results and further examine the association between MoCA Scores, 9HPT time, cognitive decline, motor dysfunction and short-term PM_{2.5} exposure, we conducted sensitivity analyses among different subgroups (Covariates) using linear and logistic regression.

3.4.1 Association Between MoCA Score, 9HPT time and short-term PM_{2.5} exposure stratified by Covariates

First, we conducted a stratified linear regression analysis on the association between MoCA score and PM_{2.5} exposure windows for each covariate, including education level, physical

activity, smoking, and passive smoking from the main model, and comorbidities and living area.

Among participants living in rural areas, each IQR increase in PM_{2.5} exposure across the Lag 0–7 exposure window was significantly associated with a 1.16-point increase in MoCA score (β -estimate = 1.16; 95% CI: 0.04 to 2.28), indicating an unexpected positive effect, while the MoCA score association in women living in urban areas was not significant. In other groups, no statistically significant association between MoCA scores across the PM_{2.5} exposure windows were observed (see **Table 14**).

Table 14: Association between MoCA Score and PM_{2.5} stratified by covariates

Covariate	β -Estimate (95% Confidence Interval)					
	Lag 0	Lag 0-1	Lag 0-7	Lag 0-14	Lag 0-21	Lag 0-28
Education level						
Low (N=107)	-0.21 (-1.44;1.02)	-0.37 (-1.54;0.81)	0.09 (-1.16;1.34)	0.36 (-0.56;1.28)	0.43 (-0.50;1.36)	-0.06 (-1.26;1.15)
High (N=84)	0.21 (-0.90;1.32)	0.24 (-0.81;1.30)	0.70 (-0.48;1.88)	0.42 (-0.43;1.27)	-0.06 (-0.95;0.84)	-0.26 (-1.47;0.96)
Physical activity						
Infrequent (N=97)	0.38 (-0.69;1.44)	0.39 (-0.63;1.41)	0.62 (-0.51;1.76)	0.33 (-0.54;1.21)	0.24 (-0.74;1.21)	-0.16 (-1.41;1.09)
Frequent (N=94)	-0.42 (-1.77;0.94)	-0.58 (-1.88;0.73)	0.11 (-1.24;1.45)	0.48 (-0.44;1.39)	0.22 (-0.68;1.13)	-0.11 (-1.33;1.12)
Smoking						
Ever Smoker (N=37)	-0.66 (-2.54;1.22)	-0.48 (-2.5;1.49)	1.29 (-0.56;3.14)	0.70 (-0.72;2.11)	0.95 (-0.66;2.56)	0.65 (-1.34;2.65)
No Smoker (N=154)	0.1 (-0.68;1.18)	-0.04 (-0.82;0.93)	0.21 (-0.86;1.09)	0.44 (-0.28;1.12)	0.23 (-0.36;1.05)	-0.21 (-1.10;0.76)
Passive Smoking						
Ever (N=74)	-0.18 (-1.37;1.00)	-0.06 (-1.20;1.09)	0.65 (-0.69;1.99)	0.29 (-0.71;1.28)	0.49 (-0.52;1.49)	0.64 (-0.62;1.91)
Never (N=117)	0.14 (-0.99;1.28)	-0.04 (-1.13;1.04)	-0.05 (-1.17;1.07)	0.25 (-0.55;1.05)	-0.01 (-0.83;0.82)	-0.80 (-1.93;0.32)
Comorbidities						
With (N=88)	-0.12 (-1.37;1.41)	-0.14 (-1.36;1.24)	-0.45 (-1.92;1.17)	0.25 (-0.89;1.57)	0.35 (-0.48;1.75)	-0.35 (-1.67;1.01)
Without (N=81)	0.04 (-1.24;1.32)	0.111 (-1.18;1.40)	0.872 (-0.33;2.07)	0.472 (-0.36;1.30)	0.143 (-0.79;1.07)	0.215 (-1.08;1.51)
Living Area						
Urban Living (N=87)	-0.20 (-1.47;1.07)	-0.67 (-1.90;0.56)	-0.80 (-2.15;0.55)	-0.41 (-1.56;0.73)	0.40 (-0.69;1.49)	-0.01 (-1.30;1.28)

Covariate	β-Estimate (95% Confidence Interval)					
	Lag 0	Lag 0-1	Lag 0-7	Lag 0-14	Lag 0-21	Lag 0-28
Rural Living (N=104)	0.16 (-0.96;1.28)	0.39 (-0.68;1.45)	1.16* (0.04;2.28)	0.67 (-0.04;1.40)	0.29 (-0.50;1.08)	0.20 (-0.10;1.40)

β -Estimate and 95% confidence interval from linear regression for association between MoCA Score and and PM_{2.5} per 1- IQR increase at different exposure windows stratified by Covariates.

(IQR for lag 0: 7.66 $\mu\text{g}/\text{m}^3$, lag 0-1: 7.12 $\mu\text{g}/\text{m}^3$, lag 0-7: 6.13 $\mu\text{g}/\text{m}^3$, lag 0-14: 3.53 $\mu\text{g}/\text{m}^3$, lag 0-21: 2.76 $\mu\text{g}/\text{m}^3$, lag 0-28: 2.66 $\mu\text{g}/\text{m}^3$)

PM_{2.5}: particulate matter with aerodynamic diameter of maximal 2.5 μm . IQR: Interquartile Range.

*p-value<0.05

Several subgroup analyses showed statistically significant associations between 9HPT time and short-term PM_{2.5} exposure. Among women with a high education level, a 7.99% increase in 9HPT time per IQR increase in PM_{2.5} at lag 0-7 (95% CI: 0.69 to 15.81) was observed, indicating slower motor performance, whereas the estimated increase in 9HPT time among women with a low education level was not significant. Among women who were less frequently physically active, slower fine motor function was also observed with a 7.59% increase in 9HPT time per IQR increase in PM_{2.5} at lag 0-7 (95% CI: 1.20 to 14.38). Women who had a previous history of passive smoking showed a 6.79% increase in 9HPT time per IQR increase in PM_{2.5} at lag 0-7 (95% CI: 0.11 to 13.91). Despite that, the non-smoking history showed a 6.19% increase in 9HPT time per IQR increase in PM_{2.5} at lags 0-7 (95% CI: 1.30 to 11.31). Women who lived in urban areas also had slower motor performance with an 8.17% increase in 9HPT time per IQR increase in PM_{2.5} at lag 0-7 (95% CI: 0.69 to 16.20).

No other statistically significant associations were observed across the remaining PM_{2.5} exposure windows (see **Table 15**).

Table 15: Association between 9HPT time and PM_{2.5} stratified by Covariates

Covariates	%-Change (95% Confidence Interval)					
	Lag 0	Lag 0-1	Lag 0-7	Lag 0-14	Lag 0-21	Lag 0-28
Education level						
Low (N=112)	-3.07 (-7.88;1.20)	-1.28 (-6.00;3.68)	2.39 (-2.78;7.84)	1.54 (-2.31;5.55)	2.21 (-1.69;6.26)	1.04 (-3.97;6.32)
High (N=85)	5.28 (-1.60;12.63)	6.29 (-0.22;13.21)	7.99* (0.69;15.81)	3.73 (-1.37;9.09)	0.79 (-4.46;6.32)	0.54 (-6.56;8.18)
Physical activity						

Covariates	% -Change (95% Confidence Interval)					
	Lag 0	Lag 0-1	Lag 0-7	Lag 0-14	Lag 0-21	Lag 0-28
Infrequent (N=102)	2.96 (-2.96;9.23)	4.42 (-1.24;10.40)	7.59* (1.20;14.38)	3.63 (-1.17;8.67)	2.09 (-3.20;7.65)	1.06 (-5.72;8.33)
Frequent (N=95)	-1.76 (-7.28;4.09)	-0.69 (-6.09;5.03)	1.62 (-4.04;7.62)	1.07 (-2.86;5.15)	1.06 (-2.80;5.08)	1.11 (-4.07;6.56)
Smoking						
Ever (N=38)	-5.62 (-15.27;5.13)	-3.77 (-13.59;7.18)	-0.13 (-9.58;10.31)	2.49 (-5.06;10.64)	2.49 (-6.03;11.78)	2.57 (-8.25;14.66)
Never (N=159)	1.78 (-2.71;6.46)	3.10 (-1.23;7.62)	6.19* (1.30;11.31)	2.63 (-0.88;6.26)	1.39 (-2.07;4.98)	0.57 (-3.98;5.33)
Passive Smoking						
Ever (N=77)	-0.20 (-5.87;5.81)	1.82 (-3.75;7.72)	6.79* (0.11;13.91)	3.03 (-1.84;8.14)	1.30 (-3.52;6.35)	-0.67 (-6.69;5.74)
Never (N=120)	1.48 (-4.27;7.57)	2.11 (-3.33;7.85)	3.75 (-1.91;9.74)	2.01 (-2.01;6.19)	1.41 (-2.72;5.71)	2.11 (-3.59;8.16)
Comorbidities						
With (N=91)	3.37 (-2.37;9.45)	3.35 (-1.99;8.97)	4.15 (-2.31;11.03)	0.81 (-4.25;6.14)	-0.19 (-4.74;4.58)	0.87 (-4.81;6.89)
Without (N=87)	-3.79 (-10.21;3.10)	-1.40 (-8.14;5.83)	4.00 (-2.64;11.10)	3.91 (-0.65;8.67)	3.45 (-1.60;8.76)	0.515 (-6.33;7.86)
Living Area						
Urban Living (N=89)	5.24 (-1.89;12.88)	5.55 (-1.24;12.82)	8.17* (0.69;16.20)	4.79 (-1.46;11.43)	3.32 (-2.51;9.50)	2.07 (-4.81;9.45)
Rural Living (N=108)	-2.35 (-6.93;2.45)	0.37 (-4.17;5.14)	2.28 (-2.68;7.50)	1.69 (-1.49;4.98)	1.44 (-2.00;5.01)	0.31 (-4.79;5.68)

Percentage change and 95% confidence interval from linear regression for association between 9HPT time and PM_{2.5} per 1- IQR increase at different exposure windows stratified by Covariates.

(IQR for lag 0: 7.66 µg/m³, lag 0-1: 7.12 µg/m³, lag 0-7: 6.13 µg/m³, lag 0-14: 3.53 µg/m³, lag 0-21: 2.76 µg/m³, lag 0-28: 2.66 µg/m³)

PM_{2.5}: particulate matter with aerodynamic diameter of maximal 2.5 µm. IQR: Interquartile Range.

*p-value<0.05

3.4.2 Association Between Cognitive Decline, Motor Dysfunction, and short-term PM_{2.5} Exposure Stratified by covariates

We conducted a logistic regression analysis to examine the association between cognitive decline and motor dysfunction stratified by various covariates.

Table 16 presents the odds ratios and 95% confidence intervals for the association between cognitive decline and PM_{2.5} stratified by covariates. Among women who lived in urban areas, the odds of cognitive decline were 3.52 times higher per IQR increase in PM_{2.5} at

the longest exposure window “lag 0–28” (OR = 3.52; 95% CI: 1.04 to 11.92). Other associations did not reach statistical significance.

Table 16: Association between cognitive decline and PM_{2.5} stratified by Covariates

Covariates	Odds ratio (95% Confidence Interval)					
	Lag 0	Lag 0-1	Lag 0-7	Lag 0-14	Lag 0-21	Lag 0-28
Education level						
Low (N=107)	1.11 (0.45;2.77)	0.96 (0.41;2.27)	0.49 (0.19;1.25)	0.66 (0.34;1.29)	0.89 (0.45;1.76)	1.36 (0.56;3.32)
High (N=84)	1.52 (0.47;4.90)	1.14 (0.36;3.62)	0.77 (0.22;2.63)	0.93 (0.42;2.08)	1.53 (0.64;3.70)	1.68 (0.48;5.86)
Physical activity						
Infrequent (N=97)	1.13 (0.38;3.36)	0.84 (0.30;2.35)	0.76 (0.24;2.35)	0.92 (0.38;2.22)	1.36 (0.48;3.84)	3.12 (0.72;13.57)
Frequent (N=94)	1.42 (0.54;3.77)	1.18 (0.45;3.03)	0.47 (0.17;1.27)	0.65 (0.34;1.23)	0.94 (0.50;1.77)	1.06 (0.45;2.52)
Smoking						
Ever Smoker (N=37)	3.17 (0.58;17.35)	1.50 (0.28;7.98)	0.84 (0.13;5.46)	0.10 (0.22;4.33)	0.96 (0.19;5.00)	1.58 (0.24;10.60)
No Smoker (N=154)	1.35 (0.58;3.15)	1.22 (0.28;7.98)	0.59 (0.13;5.46)	0.69 (0.22;4.33)	1.08 (0.19;5.00)	1.53 (0.66;3.56)
Passive Smoking						
Ever (N=74)	1.26 (0.39;4.09)	0.72 (0.24;2.13)	0.52 (0.13;1.99)	0.76 (0.32;1.81)	0.96 (0.40;2.31)	1.52 (0.45;5.09)
Never (N=117)	1.28 (0.52;3.15)	1.17 (0.48;2.82)	0.61 (0.25;1.46)	0.81 (0.44;1.48)	1.14 (0.61;2.14)	1.43 (0.60;3.43)
Comorbidities						
With (N=88)	2.15 (0.72;6.44)	1.61 (0.60;4.30)	0.93 (0.34;2.58)	0.92 (0.40;2.15)	1.15 (0.54;2.44)	1.69 (0.63;4.53)
Without (N=81)	0.77 (0.24;2.45)	0.43 (0.12;1.49)	0.29 (0.09;1.02)	0.64 (0.32;1.30)	0.99 (0.46;2.16)	1.17 (0.38;3.61)
Living Area						
Urban Living (N=87)	2.15 (0.59;7.80)	2.50 (0.70;8.95)	0.88 (0.27;2.86)	1.56 (0.67;3.62)	1.79 (0.80;4.02)	3.52* (1.04;11.92)
Rural Living (N=104)	0.83 (0.27;2.55)	0.49 (0.17;1.41)	0.34 (0.10;1.14)	0.61 (0.30;1.24)	0.94 (0.46;1.97)	0.88 (0.29;2.70)

Odds ratio and 95% confidence interval from logistic regression for association between cognitive decline and PM_{2.5} per 1- IQR increase at different exposure windows stratified by Covariates.

(IQR for lag 0: 7.66 µg/m³, lag 0-1: 7.12 µg/m³, lag 0-7: 6.13 µg/m³, lag 0-14: 3.53 µg/m³, lag 0-21: 2.76 µg/m³, lag 0-28: 2.66 µg/m³)

PM_{2.5}: particulate matter with aerodynamic diameter of maximal 2.5 µm. IQR: Interquartile Range.

*p-value<0.05

The association between short-term exposure to PM_{2.5} and motor dysfunction among different subgroups, detailed in **Table 17** indicates that among women with lower physical activity, a higher OR for motor dysfunction at lag 0-1 was observed (OR = 1.91; 95% CI: 1.00–3.65). This suggests an increased risk of motor dysfunction shortly after higher PM_{2.5} exposure among less active women.

Among stratified groups for education level, smoking status, passive smoking, comorbidities, and living area, no significant association between motor dysfunction and PM_{2.5} was observed.

Table 17: Association between motor dysfunction and PM_{2.5} stratified by Covariates

Covariates	Odds ratio (95% Confidence Interval)					
	Lag 0	Lag 0-1	Lag 0-7	Lag 0-14	Lag 0-21	Lag 0-28
Education level						
Low (N=112)	1.00 (0.51;1.96)	1.19 (0.62;2.29)	1.40 (0.70;2.79)	1.29 (0.77;2.15)	1.32 (0.79;2.23)	1.34 (0.67;2.69)
High (N=85)	1.71 (0.77;3.80)	1.91 (0.89;4.10)	1.13 (0.49;2.58)	1.09 (0.60;1.97)	0.65 (0.35;1.22)	0.66 (0.28;1.53)
Physical activity						
Infrequent (N=102)	1.74 (0.88;3.43)	1.91* (1.00;3.65)	2.01 (0.98;4.13)	1.51 (0.87;2.61)	1.04 (0.58;1.88)	0.87 (0.40;1.85)
Frequent (N=95)	0.82 (0.34;1.95)	0.91 (0.39;2.13)	0.67 (0.28;1.60)	0.93 (0.53;1.65)	0.92 (0.52;1.62)	1.28 (0.57;2.84)
Smoking						
Ever Smoker (N=38)	0.77 (0.20;2.93)	0.82 (0.28;7.98)	1.31 (0.13;5.46)	3.13 (0.22;4.33)	1.90 (0.19;5.00)	1.37 (0.34;5.45)
No Smoker (N=159)	1.47 (0.83;2.60)	1.79 (0.28;7.98)	1.39 (0.13;5.46)	1.03 (0.22;4.33)	0.86 (0.19;5.00)	0.92 (0.51;1.65)
Passive Smoking						
Ever (N=77)	1.67 (0.75;3.70)	1.77 (0.81;3.88)	2.26 (0.93;5.54)	1.30 (0.69;2.45)	0.86 (0.45;1.63)	0.92 (0.41;2.09)
Never (N=120)	1.13 (0.56;2.26)	1.34 (0.69;2.60)	1.05 (0.53;2.08)	1.19 (0.73;1.93)	1.08 (0.66;1.77)	1.18 (0.58;2.40)
Comorbidities						
With (N=91)	1.51 (0.70;3.24)	1.79 (0.86;3.72)	1.73 (0.75;3.98)	0.97 (0.51;1.86)	0.61 (0.33;1.13)	0.80 (0.38;1.67)
Without (N=87)	0.874 (0.39;1.98)	0.878 (0.38;2.06)	1.044 (0.47;2.32)	1.346 (0.78;2.31)	1.316 (0.73;2.39)	1.100 (0.47;2.59)
Living Area						
Urban Living (N=89)	1.90 (0.79;4.58)	2.04 (0.86;4.84)	1.79 (0.57;2.32)	1.63 (0.75;3.57)	1.22 (0.61;2.47)	1.41 (0.59;3.40)

Results

Rural Living (N=108)	1.11 (0.56;2.19)	1.41 (0.73;2.72)	1.15 (0.57;2.32)	1.13 (0.73;1.78)	0.96 (0.59;1.56)	0.85 (0.41;1.77)
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Odds ratio and 95% confidence interval from logistic regression for association between motor dysfunction and PM_{2.5} per 1- IQR increase at different exposure windows stratified by Covariates.

(IQR for lag 0: 7.66 µg/m³, lag 0-1: 7.12 µg/m³, lag 0-7: 6.13 µg/m³, lag 0-14: 3.53 µg/m³, lag 0-21: 2.76 µg/m³, lag 0-28: 2.66 µg/m³) PM_{2.5}: particulate matter with aerodynamic diameter of maximal 2.5 µm. IQR: Interquartile Range.

*p-value<0.05

4 Discussion

4.1 Study and results Overview

This study investigated the effects of short-term exposure to fine particulate matter (PM_{2.5}) on cognitive and motor performance and dysfunctions in elderly women participating in the SALIA Cohort. Cognitive function was assessed using the MoCA, and motor function was evaluated with the 9HPT. Initially, we applied linear regression models to examine the association between PM_{2.5} exposure windows varying from lag 0 to lag 0-28 and performance scores. Subsequently, we used evidence-based cut-offs to classify participants as having cognitive decline or motor dysfunction. All models were adjusted stepwise for potential confounding factors identified through baseline assessments and follow-up interviews. Furthermore, we conducted subgroup analyses to test the robustness of the findings. This study aimed to test the hypothesis that higher short-term PM_{2.5} exposure is associated with worse cognitive and motor performance. Our findings provide partial support for this hypothesis for motor function, but not for cognitive outcomes.

Linear and logistic regression models were employed to assess the relationship between short-term PM_{2.5} exposure and cognitive and motor function across various exposure windows using the MoCA or 9HPT. For the MoCA score, no statistically significant associations were observed in either unadjusted or adjusted linear regression models. In terms of motor performance assessed by 9HPT, after adjusting for potential confounders, a significant 4.42% increase in 9HPT time per IQR increase in PM_{2.5} was observed in the lag 0–7 window ($p = 0.040$), indicating slower motor performance when exposed to higher air pollution in last week. This effect was attenuated and became non-significant in other models, although it tended to point in the same direction across other exposure windows. Logistic regression models assessing the likelihood of cognitive decline and motor dysfunction showed no statistically significant associations with PM_{2.5} exposure across the exposure windows, though some crude models indicated elevated odds ratios, particularly for lag 0 and lag 0–28. Overall, our results do not provide evidence for a consistent

relationship between short-term PM_{2.5} exposure and cognitive outcomes. However, we found a significant association between higher short-term PM_{2.5} exposure and motor slowing.

To further assess the robustness of our findings and explore the associations between short-term air pollution and cognitive and motor performance, we conducted a subgroup analysis using covariates and detailed linear and logistic regression.

Linear regression testing for cognitive performance revealed that higher PM_{2.5} exposure at the lag 0–7 window was significantly associated with higher MoCA scores among women living in rural areas. In contrast, no significant association was observed among women living in urban areas and other covariates across the examined exposure windows. When testing for motor performance, the stratified analyses suggest that the association between higher PM_{2.5} exposure may vary across different subgroups of women, particularly within the lag 0–7 exposure window. Significant associations of slower motor performance were observed among women with higher educational level, those who were less physically active, and those with a history of passive smoking. The same patterns were also observed among women without a smoking history and those living in urban areas.

For cognitive decline and motor dysfunction outcomes assessed through logistic regression, a statistically significant association with increased odds of cognitive decline at lag 0–28 was observed only among women living in urban areas (OR = 3.52; 95% CI: 1.04–11.92). No significant associations between PM_{2.5} exposure and cognitive decline were observed in the other covariate groups. These findings suggest that the residential environment may play an important role in cognitive deterioration, potentially interacting with air pollution exposure. Overall, the subgroup analysis highlights selective but meaningful associations, emphasising the complex interplay between environmental exposures, sociodemographic characteristics, and outcomes.

4.2 Methods Discussion

This study employed a Cross-Sectional design to investigate the short-term effects of ambient PM_{2.5} exposure on cognitive and motor function in elderly women from the SALIA cohort. While the cross-sectional approach enabled the assessment of exposure-outcome associations at a specific point in time, it does not allow conclusions regarding causality. However, the observational design was appropriate for exploring potential short-term effects of air pollution and health impact by measuring the outcome and exposure at the same time and is commonly used in environmental research [84, 85].

The study design employed daily PM_{2.5} concentrations, matched to participants' residential addresses, and averaged these over multiple lag windows: lag 0–1, 0–7, 0–14, 0–21, and 0–28 days before each assessment, similar to the approach conducted by Lee et al. with more extended periods [70]. These lag windows were chosen to capture both immediate lag 0 and delayed effects up to four weeks of PM_{2.5} exposure, matched with the study conducted by Gao et. al. [68]. This extended approach acknowledges that cumulative effects may occur immediately or develop over several days or weeks. However, cumulative average PM_{2.5} concentrations across different lag windows could be correlated with one another and may mask short peaks in PM_{2.5} that could be biologically relevant. Future studies could combine cumulative and non-cumulative exposure approaches, for example by applying averaged lag models alongside analyses of daily PM_{2.5} concentrations, to better identify critical exposure windows and the effects of pollution peaks from those of cumulative exposure.

The use of both linear and logistic regression models provided complementary perspectives on the relationship between PM_{2.5} exposure and neurological outcomes. Linear models preserved the full variability of the cognitive and motor performance measures, allowing the detection of subtle changes across the outcome spectrum, whereas logistic regression enabled the assessment of clinically relevant impairment based on previously established cut-off values. Despite this innovative, analytical approach, defining impairment solely

through test scores and clinical cut-off values may not necessarily reflect the full range and complexity of cognitive and motor function in this ageing population.

The assessment of cognitive function using the MoCA represents another important methodological consideration. The MoCA is considered a highly reliable tool for detecting the early stages of dementia, particularly MCI (Compare Chapter 2.2). Previous studies investigating the association between short-term PM_{2.5} exposure and cognitive performance have commonly used the Mini-Mental State Examination (MMSE) [67, 68]. The MMSE is, similar to MoCA, a 30-point questionnaire that assesses cognitive domains such as orientation, attention, memory, language, and visuospatial skills, and has been widely used for detecting moderate to severe dementia mostly in clinical settings [86]. However, as the majority of SALIA cohort population had not been diagnosed with dementia according to self-reported questionnaires, the use of the MoCA was appropriate for identifying subtle cognitive changes that may precede clinically apparent MCI or dementia, since MoCA is considered superior for detecting early-stage dementia and MCI [87].

Motor performance was evaluated using the 9HPT, an objective measure of upper limb dexterity and fine motor function. The use of this test allowed the investigation of motor changes potentially relevant to neurodegenerative processes without relying on self-reported symptoms. A cut-off value of 21.5 seconds, based on normative data for women aged 75 years and older [76], was used to stratify the study population into two groups: those with and without motor impairment. A related previous study investigated the impact of short-term air pollution on hospital admissions for PD and reported that such exposure may exacerbate PD symptoms [70]. To our knowledge, this is the first study to apply this specific approach to examine the relationship between fine motor performance, dysfunction and short-term exposure to air pollution.

Potential confounder selection was guided by established risk factors for cognitive and motor decline and was restricted by the relatively small sample size. The use of both a main and an extended adjustment model represented an attempt to balance adequate control of

confounding with the risk of model overfitting. Meteorological factors, such as temperature and humidity, and other air pollutants were not included in the adjustment models. Some previous studies have considered climatic variables and other pollutants as potential confounders when examining the short-term health effects of air pollution [65, 66, 69, 70]. However, given the relatively small sample size and the need to avoid model overfitting, the analysis was primarily restricted to individual-level confounders. Therefore, residual confounding by unmeasured climatic or environmental factors cannot be ruled out and needs to be considered in future studies with larger populations.

The stratified analyses enabled the exploration of potential effect modification by individual participant characteristics, representing a strength of the study by providing insight into potentially vulnerable subgroups. Nevertheless, the relatively small sample size within some subgroups may limit the precision of the estimates and may result in wider confidence intervals. Therefore, it must be interpreted with caution, while still offering valuable data for future research on the short-term effects of air pollution, with the aim of studying those subgroups.

4.3 Results discussion

Findings from the main model indicated a significant 4.42% increase in 9HPT time per IQR increase in PM_{2.5} levels over the lag 0–7 day window ($p = 0.040$), suggesting slower motor performance associated with short-term exposure to air pollution in elderly women. Slower motor performance and rigidity are characteristic symptoms of PD [29]. These findings are consistent with a previous study by Lee et al., which reported that an increase in the 8-day (lag 0–7) moving average of PM_{2.5} was significantly associated with PD symptoms aggravation among women and men (odds ratio [95% CI]: 1.61 [1.14–2.29] per 10 $\mu\text{g}/\text{m}^3$) [70]. Motor dysfunction predicted by logistic regression was not significant for short-term air pollution exposure in Lag 07, in contrast with the observation from linear regression. This may be attributable to the dichotomisation of the 9HPT score, which may have resulted in a loss of information compared with the continuous outcome measure or

to the 9HPT score cut-off used, which primarily reflected the mean score of the 75+ age group and therefore did not accurately reflect fine motor dysfunction [76]. To our knowledge, no well-established 9HPT score cut-off representing fine motor dysfunction has been identified yet. Further research is needed to identify and validate such a threshold.

On the other hand, we found no significant association between short-term exposure to PM_{2.5} and cognitive performance or cognitive decline, as measured by the MoCA test, in the main model. In contrast, the main findings of previous studies indicated that higher short-term exposure to PM_{2.5} significantly impacts cognitive performance when measured using the MMSE [67, 68]. This discrepancy may be primarily due to our relatively small study population ($n = 224$), of whom approximately 77% scored below 26 points and were therefore classified as having cognitive decline. Another possible explanation may relate to differences in methodology. While the two similar studies investigating short-term exposure to air pollution and cognitive performance used the MMSE and were conducted in different populations (younger and older men) [67, 68], our study employed the MoCA in a sample of elderly women. Nevertheless, this contrast highlights the need for further research into the short-term effects of air pollution on cognitive performance.

Previously published studies from the SALIA cohort reported that long-term exposure to air pollution was associated with an increased risk of mild cognitive impairment (MCI) [56, 57]. These findings should be considered when interpreting the results of the present study, since all analyses were employed on the same study population. However, the current study addressed a different research question by focusing on short-term exposure to air pollutants rather than long-term exposure. In addition, previous studies examined traffic-related air pollution, such as distance to busy roads and focused mainly on other air pollutants or pollutant metrics such as PM₁₀ and NO₂. Cognitive impairment was assessed in both previous analyses using CERAD-Plus battery tests, which include different subtests that may address specific domains of the human brain [88], whereas this study employed MoCA for cognitive assessment. Therefore, the absence of a significant association between short-term air pollution exposure and cognitive decline observed in the main

analysis of this study does not necessarily contradict the previous SALIA findings, since different research questions, time-frame and methods were employed.

Among women living in rural areas, slightly higher MoCA scores were observed with an increase in short-term PM_{2.5} exposure at lag 0–7 exposure window. Elderly living in urban areas may have a higher risk of developing oxidative stress and cognitive impairment than the elderly in rural areas [89]. This is mostly due to the fact that people living in urban areas are more exposed to PM_{2.5} and therefore have higher PM_{2.5} levels compared to those living in rural areas [90]. A possible explanation for this controversial observation is that elderly populations living in rural areas may have relatively preserved baseline cognitive functioning, potentially reflecting higher cognitive reserve, which may buffer against the effects of small daily variations in ambient PM_{2.5} exposure. According to the cognitive reserve concept, individuals with greater reserve can maintain cognitive performance despite age-related or environmental brain insults [91]. This may suggest that subtle changes in PM_{2.5} are insufficient to produce measurable cognitive decline in a certain population with high reserves unless exposure exceeds a certain threshold. However, the observed association was in the opposite direction, with higher short-term PM_{2.5} exposure being associated with slightly higher MoCA scores. This finding may reflect residual confounding, random variation due to the limited sample size, or other unmeasured factors rather than a true beneficial effect of PM_{2.5} on cognitive function. Therefore, it should be interpreted with caution and requires confirmation in larger studies.

Among urban-living women, a statistically significant association with increased odds of cognitive decline per PM_{2.5} increase at lag 0–28 was observed. This finding is consistent with previous research suggesting that adverse effects of air pollution on cognitive decline may be more pronounced in urban environments, indicating a potential interaction between PM_{2.5} exposure and urban residence [89]. Populations in urban areas are generally more affected by air pollution due to industrial activity and increased traffic. The lag 0–28 exposure window represents a rather mid-term period that may capture delayed responses to air pollution exposure. Overall, these findings are consistent with prior evidence

indicating that sustained or repeated exposure to air pollution has been associated with adverse cognitive outcomes [92].

In terms of motor function, slower motor performance per PM_{2.5} increase was observed among elderly women with a high household level of education (12 years or more), demonstrated by a 7.99% increase in 9HPT time in the lag 0–7 window. Among elderly women with low household education, no significant changes were observed. This result should be interpreted with caution, as a higher intelligence quotient (IQ) is genetically associated with PD and, therefore, bad motor functioning [93]. However, higher educational attainment itself is not significantly associated with PD and is therefore not considered a significant risk factor [94]. A possible explanation may be due to individuals with higher IQs being more likely to pursue extended education, or their brain chemistry may be more sensitive to subtle changes in air pollution. However, these results may also be attributable to chance. Further research is required to clarify these findings and explore the underlying mechanisms.

Slower motor performance with PM_{2.5} increase was also observed among the elderly with lower levels of physical activity, reflected by a 7.59% increase in 9HPT time when at lag 0–7 exposure window. Physically inactive elderly individuals are at a higher risk of developing PD symptoms such as bradykinesia (slowness of movement) [95]. This observation suggests that very small changes in short-term air pollution may have no effect on physically active elderly women.

In both non-smoking status and passive smoking groups, slower motor performance was associated with PM_{2.5} increase; among passive smokers, a 6.79% increase, and non-smokers, a 6.19% increase in 9HPT time at lag 0–7 exposure window. Active smoking is widely considered a protective factor against PD in the elderly [96]. Therefore, elderly women who have never actively smoked may be at increased risk for slower motor function from changes in air pollution. Although passive smoking has been suggested as a protective factor, its effects may be limited due to typically lower levels and shorter durations of exposure compared to active smoking.

Among women living in urban areas with higher levels of air pollution, slower motor performance was observed with increasing PM_{2.5} exposure, reflected by an 8.17% increase in 9HPT completion time during the lag 0–7 exposure window. These findings are consistent with the main study results, which also indicated slower motor performance associated with air pollution exposure. This observation, together with the previously cautiously interpreted findings of better cognitive performance among women residing in rural areas and cognitive decline among those living in urban environments, may suggest that urban populations may represent a particularly vulnerable group for short-term exposure to air pollution, underscoring the need for further investigation to confirm these findings in a larger population and to clarify underlying potential mechanisms.

4.4 Strengths and Limitations

One limitation of this study is the relatively small sample size, which is primarily due to the ageing population of the remaining SALIA cohort participants (see Section 4.2). This may have reduced the statistical power to detect weaker associations, particularly in subgroup analyses and logistic regression. Furthermore, selective participation of healthier individuals at follow-up may have introduced healthy survivor bias, as participants who remained in the cohort are likely to be healthier than those who were lost to follow-up or had died.

Due to data availability, participants from households with 12 or fewer years of education received an additional point to their total MoCA score. This approach slightly differs from the recommendation in the MoCA manual, which is based solely on the participant's own educational attainment. Another consideration is the use of residential addresses to estimate air pollution exposure. While this method allows for individualised exposure assessment, it assumes that participants spend most of their time at home. Given the advanced age of the participants, this assumption is likely reasonable; however, it may not fully capture personal exposure variability.

A fourth limitation may include uncaptured confounding factors. While most relevant individual confounders were identified and included in the analysis, other potential confounders were not included due to the sample size and to avoid overadjustment bias (see Section 4.2). Furthermore, subgroup analyses were performed without adjustment for multiple testing. Consequently, some of the statistically significant results may represent chance findings and should therefore be considered when interpreting those results.

While this study was designed to focus on a specific population group, namely elderly women, who are underrepresented in similar studies, other population groups were not included. Therefore, the observed effects cannot be generalised and should remain specific to the population group of elderly women. Another limitation is that the assessment of potential confounding factors relied on self-reported questionnaires. Although these tools

are widely used in epidemiological research, they are subject to recall bias and may not accurately reflect participants' true lifestyle or health status.

This study makes a valuable, innovative contribution to air pollution and neurodegenerative research by focusing exclusively on elderly women in Europe. This population is, to our knowledge, underrepresented in studies examining the neurological effects of short-term air pollution.

A significant strength of the study lies in its use of high-quality, validated, and sensitive clinical tools, along with two regression models in three adjustment levels. Cognitive function was assessed using the MoCA, which is considered superior to the MMSE used in previous studies for detecting early cognitive impairment and mild cognitive decline. Motor performance was evaluated with the 9-Hole Peg Test, a reliable and objective measure of fine motor skills and dexterity, often affected in early stages of neurodegenerative conditions like PD. Additionally, the study employed the use of multiple lag windows, up to 1 month, further enabling the analysis of immediate and delayed effects of short-term air pollution exposure.

The unique nature of the SALIA cohort study, which enrolled participants who are healthy living in their homes and allowed conducting the tests in their own home addresses, ensured high-quality real data acquisition, away from work or hospital routines. Another strength is the high-resolution exposure assessment, with a small spatial assessment individualised according to each participant's home address.

4.5 Future implications and clinical impact

These findings, together with previous evidence, highlight the clinical potential of considering air pollution and lifestyle as modifiable environmental determinants in the prevention and management of neurodegenerative diseases [97]. According to the German Environment Agency (UBA), by 2025, PM_{2.5} air pollution levels in many regions met European limit values but still exceeded the WHO guideline limits of 5 µg/m³ (annual

mean) and 15 $\mu\text{g}/\text{m}^3$ (24-hour mean) [83, 98]. Reducing air pollution may therefore represent a promising preventive strategy for neurodegenerative diseases.

However, exposure to air pollution and lifestyle factors not only contribute to neurodegenerative disease but also raise serious concerns, such as increased mortality due to cardiovascular diseases and emergency hospitalisations for cardiac and cerebrovascular events [99, 100]. Future research should aim to replicate these findings in larger and more diverse populations and further investigate the underlying mechanisms by which air pollution affects motor and cognitive function in the short term. Still, it may be interesting to examine these effects on the cardiovascular system. This is particularly relevant given that cardiovascular disease remains one of the leading causes of death worldwide [101].

Clinicians could proactively investigate the complex interplay between environmental factors and human health. To achieve that, more high-quality data regarding human health should be routinely collected and analysed to better understand this complex interplay. This may be done using standardised, easy-to-operate, high-quality assessments such as 9HPT and MoCA, along with the integration of lifestyle, environmental exposure history and cardiovascular evaluation. Healthcare teams may then optimise monitoring and early intervention with a more personalised and preventive approach for high-risk populations.

In clinical settings, physicians, nurses and health care professionals may also help reinforce preventive strategies by promoting physical activity, reducing indoor pollution exposure, and educating patients about the health risks of air pollution and preventive measures.

4.6 Conclusion

This study explored the short-term effects of $\text{PM}_{2.5}$ exposure on cognitive and motor performance in elderly women from the SALIA cohort. While no statistically significant association was found between short-term $\text{PM}_{2.5}$ exposure and cognitive performance as measured by the MoCA, a significant association was observed between short-term exposure and slower motor performance, particularly in the lag 0–7 day window. These

findings suggest that motor function may be a sensitive early marker of neurotoxic effects from air pollution in elderly women.

The study further highlighted the relevance of individual lifestyle and environment, particularly in education level, physical activity, smoking status, and urban versus rural living, in shaping vulnerability to air pollution. The use of sensitive tools such as MoCA and 9HPT, high-resolution exposure data, and stratified analyses allowed for insights into the complexity of lifestyle, environmental exposures, and neurological outcomes. Still, more needs to be done to further understand this complex interplay.

These findings underscore the importance of considering short-term air pollution exposure as a potential risk factor for motor decline and human health in elderly populations. Given the global trends of population ageing and increasing urbanisation, protecting vulnerable groups should be a key public health priority.

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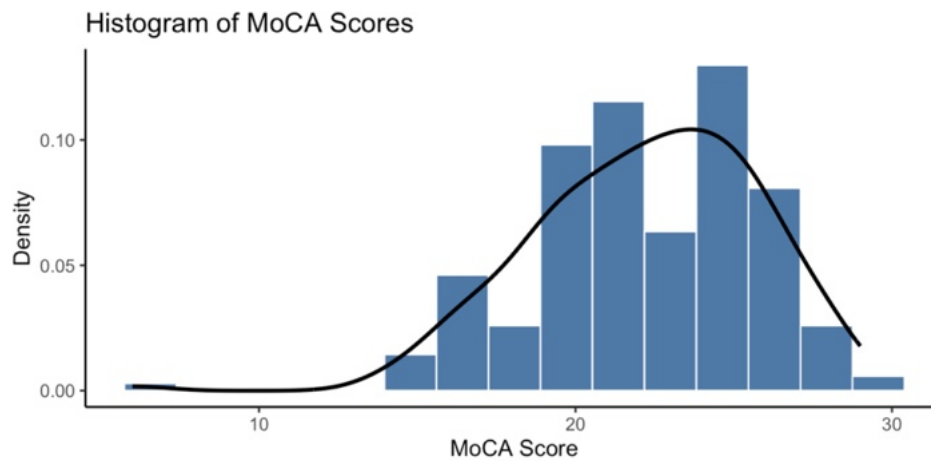
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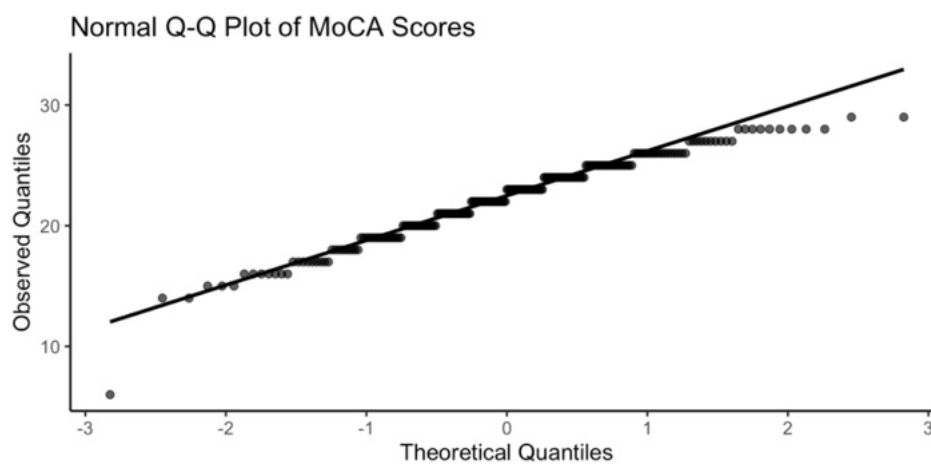
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6 Appendix

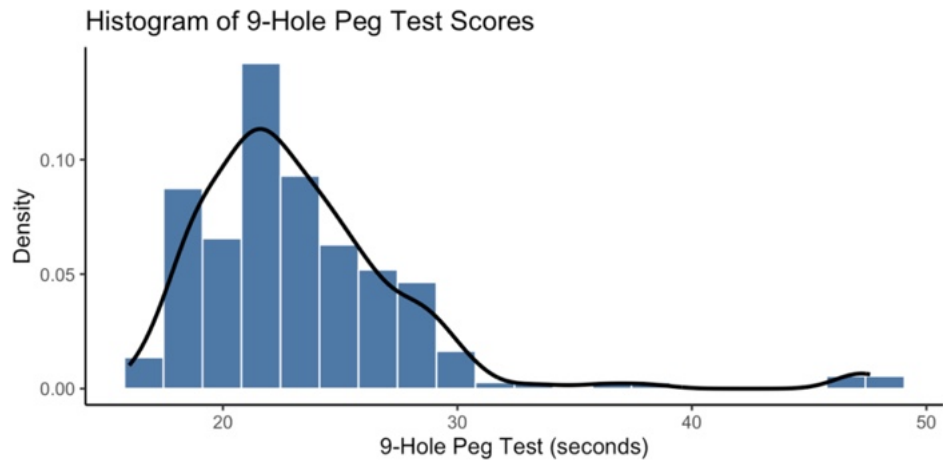
6.1 Distribution Plots



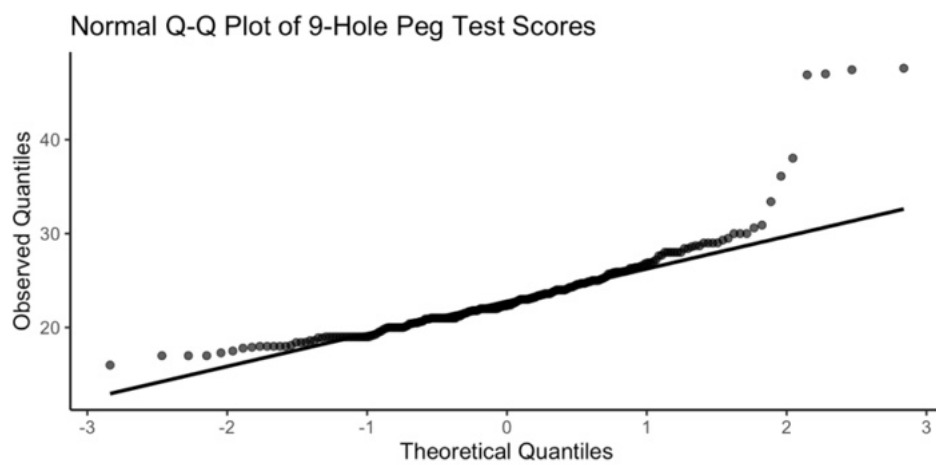
Supplementary Figure 1



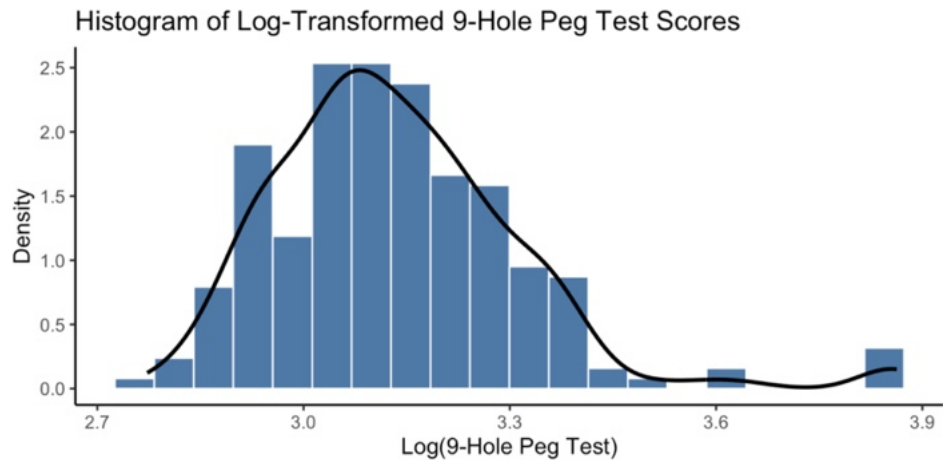
Supplementary Figure 2



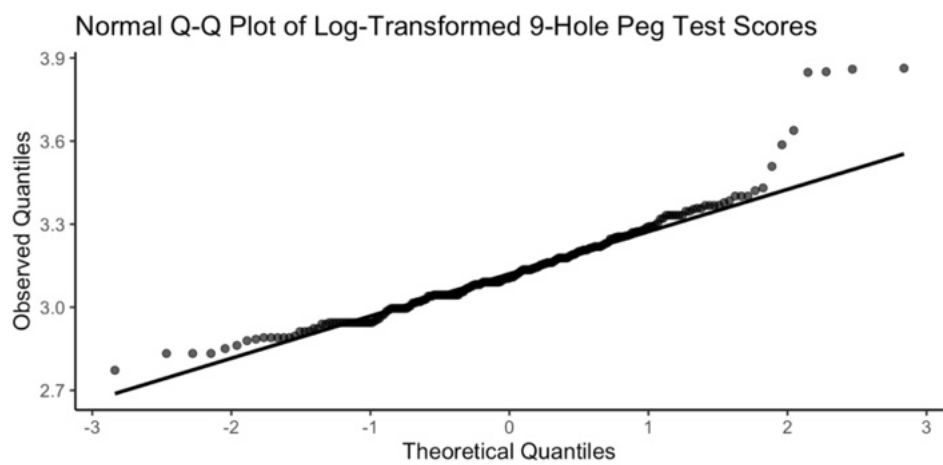
Supplementary Figure 3



Supplementary Figure 4



Supplementary Figure 5



Supplementary Figure 6

6.2 SALIA 2017 Questionnaire (German)



SALIA 2017

Studie über den Einfluss von Luftverschmutzung auf
Lunge und entzündliche Erkrankungen im Alter

ID: _____

Allgemeine Fragen

1 Wie groß sind Sie? _____ cm

2 Wie viel wiegen Sie? _____ kg

3 Haben Sie jemals geraucht? ☐ nie
☐ ja, bis heute noch
☐ ja, aber ich habe endgültig aufgehört im Jahr _____

Wenn Sie geraucht haben:

3.1 In welchem Alter haben Sie angefangen zu rauchen? Im Alter von _____ Jahren

3.2 Wie viele Zigaretten rauchen/rauchten Sie durchschnittlich am Tag? _____ Zigaretten

4 Raucht oder rauchte jemand anderes in Ihrem Haushalt oder Ihrer Umgebung?..... ☐ nein
☐ ja, heute noch
☐ ja, bis vor _____ Jahren

Fragen zu Ihrer Gesundheit

5 Welche der folgenden **Krankheiten** bestehen bei Ihnen nach **ärztlichem Urteil**?

5.1	Bronchialasthma	☐ ja	☐ nein
5.2	Chronische Bronchitis	☐ ja	☐ nein
5.3	Chronisch obstruktive Atemwegserkrankung (COPD)	☐ ja	☐ nein
5.4	Lungenemphysem	☐ ja	☐ nein
5.5	Heuschnupfen	☐ ja	☐ nein
5.6	Atopisches Ekzem/Neurodermitis	☐ ja	☐ nein
5.7	Rheumatische Erkrankungen	☐ ja	☐ nein
5.8	Bluthochdruck	☐ ja	☐ nein
5.9	Erhöhte Blutfette (Cholesterine)	☐ ja	☐ nein
5.10	Depression	☐ ja	☐ nein
5.11	Parkinson	☐ ja	☐ nein
5.12		☐ ja	☐ nein

5.13	Demenzerkrankung (z. B. Alzheimer).....	☐ ja	☐ nein	
	Osteoporose			
6	Hatten Sie schon einmal folgende Erkrankungen:			zum ersten Mal im Alter von
6.1	einen Herzinfarkt?	☐ ja	☐ nein	____ Jahren
6.2	einen Schlaganfall?	☐ ja	☐ nein	____ Jahren

7	Wurde bei Ihnen Diabetes (Zuckerkrankheit) festgestellt?	☐ ja	☐ nein	____ Jahren
	<u>Wenn JA:</u>			
7.1	Wie werden Sie derzeit behandelt?	☐ nur mit Tabletten		
	(Denken Sie bitte auch an gespritztes Insulin und Insulinpumpen)	☐ nur mit Insulin		
		☐ mit Insulin und Tabletten		
		☐ nur Diät/Ernährung		
		☐ keine Behandlung		
8	Wurde bei Ihnen jemals Krebs festgestellt?	☐ ja	☐ nein	
	<u>Wenn JA</u> , um welche Krebsart handelt es sich?			im Alter von
8.1	Brustkrebs	☐ ja	☐ nein	____ Jahren
8.2	Darmkrebs	☐ ja	☐ nein	____ Jahren
8.3	Lungenkrebs	☐ ja	☐ nein	____ Jahren
8.4	Unterleibskrebs	☐ ja	☐ nein	____ Jahren
8.5	Magenkrebs.....	☐ ja	☐ nein	____ Jahren
8.6	Hautkrebs.....	☐ ja	☐ nein	____ Jahren
8.7	anderer Krebs: 1)	☐ ja	☐ nein	____ Jahren
	2)			____ Jahren
	3)			____ Jahren
8.8	Wenn Sie Hautkrebs hatten, um welche Krebsart handelte es sich?.....	☐ Melanom (schwarzer Hautkrebs)		

- ☐ Basaliom, Plattenepithelkarzinom
(weißer, heller Hautkrebs)
- ☐ weiß nicht

Fragen zu Allergien und Hauterkrankungen			
9	Hatten Sie irgendwann einmal Heuschnupfen?	☐ ja	☐ nein
	<u>Wenn JA:</u>		
9.1	Wie alt waren Sie, als der Heuschnupfen zum ersten Mal auftrat?	_____	Jahre
9.2	Wie viele Jahre besteht/bestand der Heuschnupfen?	_____	Jahre
10	Hatten Sie irgendwann einmal Neurodermitis (atopisches/endogenes Ekzem)?	☐ ja	☐ nein
	<u>Wenn JA:</u>		
10.1	Wie alt waren Sie, als die Neurodermitis bzw. das atopische Ekzem zum ersten Mal auftrat?	_____	Jahre
10.2	Wie viele Jahre besteht/bestand die Neurodermitis bzw. das atopische Ekzem?	_____	Jahre
11	Hatten Sie irgendwann einmal Bronchialasthma?	☐ ja	☐ nein
	<u>Wenn JA:</u>		
11.1	Wie alt waren Sie, als das Bronchialasthma zum ersten Mal auftrat?	_____	Jahre
11.2	Wie viele Jahre besteht/bestand das Bronchialasthma?	_____	Jahre
12	Hatten Sie irgendwann einmal einen juckenden Hautausschlag, der stärker oder schwächer über mindestens 6 Monate auftrat?	☐ ja	☐ nein
	<u>Wenn JA:</u>		
12.1	Trat dieser juckende Hautausschlag auch in den letzten 12 Monaten bei Ihnen auf?	☐ ja	☐ nein
12.2	In welchem Alter trat dieser Hautausschlag zum ersten Mal auf?	_____	Jahren

Fragen zu Atemwegserkrankungen	
13	Wie oft waren Sie im Laufe der letzten 12 Monate erkältet? mal
14	Husten Sie gewöhnlich morgens, gleich nach dem Aufstehen, oder sonst im Laufe des Tages? ☐ ja ☐ nein
	<u>Wenn JA:</u>
14.1	Haben Sie bei diesem Husten Auswurf? ☐ ja ☐ nein
14.2	Besteht der Husten während eines Jahres insgesamt länger als 3 Monate? ☐ ja ☐ nein
14.3	Leiden Sie unter diesem Husten schon länger als 2 Jahre? ☐ ja ☐ nein
15	Hatten Sie jemals in den letzten 12 Monaten ein pfeifendes oder brummendes Geräusch in Ihrem Brustkorb? ☐ ja ☐ nein
	<u>Wenn JA:</u>
15.1	Hatten Sie dieses Pfeifen oder Brummen, wenn Sie nicht erkältet waren? ☐ ja ☐ nein
15.2	Sind Sie irgendwann in den letzten 12 Monaten wegen eines Hustenanfalls aufgewacht?... ☐ ja ☐ nein

Fragen zu Ihren Lebensumständen	
16	Welchen Familienstand haben Sie? ☐ verheiratet ☐ ledig ☐ geschieden ☐ verwitwet
17	Wie lange wohnen Sie in Ihrer jetzigen Wohnung? seit Jahren
18	Wie groß ist Ihre Wohnung etwa? m ²
19	Wie wird Ihre jetzige Wohnung überwiegend beheizt? ☐ Zentralheizung ☒ Etagenheizung ☐ Heizung in Einzelräumen
19.1	<u>Wenn Sie keine Zentralheizung haben, womit wird geheizt?</u> ☐ Gas ☐ Kohle/Holz ☐ Öl ☐ Elektrizität
20	Benutzen Sie in Ihrer Wohnung Gas zum:
20.1	Kochen? ☐ ja ☐ nein
20.2	Warmwasserbereiten? ☐ ja ☐ nein

21	Würden Sie Ihre Wohnung als feucht bezeichnen?	☐ ja	☐ nein
22	Gab oder gibt es Schimmel- oder Stockflecken in Ihrer Wohnung (außer auf Nahrungsmitteln)?	☐ ja	☐ nein
Angaben zu Ihrem Befinden Bitte beantworten Sie jede der vorgelegten Fragen, indem Sie bei den Antwortmöglichkeiten nur das Kästchen ankreuzen, das am besten auf Sie zutrifft.			
23	Wie würden Sie Ihren Gesundheitszustand im Allgemeinen beschreiben?		
	☐ ausgezeichnet ☐ sehr gut ☐ gut ☐ weniger gut ☐ schlecht		
24	Im Folgenden sind einige Tätigkeiten beschrieben, die Sie vielleicht an einem normalen Tag ausüben. Sind Sie durch Ihren derzeitigen Gesundheitszustand bei diesen Tätigkeiten eingeschränkt? Wenn ja, wie stark?		
		ja, stark eingeschränkt	ja, etwas eingeschränkt nein, überhaupt nicht eingeschränkt
24.1	Mittelschwere Tätigkeiten, z. B. einen Tisch verschieben, staubsaugen, kegeln, Golf spielen	☐	☐ ☐
24.2	Mehrere Treppenabsätze steigen	☐	☐ ☐
25	Hatten Sie in den vergangenen 4 Wochen aufgrund Ihrer körperlichen Gesundheit irgendwelche Schwierigkeiten bei der Arbeit oder anderen alltäglichen Tätigkeiten?		
25.1	Ich habe weniger geschafft als ich wollte	☐ ja	☐ nein
25.2	Ich konnte nur bestimmte Dinge tun	☐ ja	☐ nein
26	Hatten Sie in den vergangenen 4 Wochen aufgrund seelischer Probleme irgendwelche Schwierigkeiten bei der Arbeit oder anderen alltäglichen Tätigkeiten (z. B. weil Sie sich niedergeschlagen oder ängstlich fühlten)?		
26.1	Ich habe weniger geschafft als ich wollte	☐ ja	☐ nein
26.2	Ich konnte nicht so sorgfältig wie üblich arbeiten	☐ ja	☐ nein

27	Inwieweit haben Schmerzen Sie in den vergangenen 4 Wochen bei der Ausübung Ihrer Alltagstätigkeiten behindert?
	☐ überhaupt nicht ☐ ein bisschen ☐ mäßig ☐ ziemlich ☐ sehr

In diesen Fragen geht es darum, wie Sie sich fühlen und wie es Ihnen in den letzten 4 Wochen gegangen ist. Bitte kreuzen Sie in jeder Zeile das Kästchen an, das Ihrem Befinden am ehesten entspricht.

28	Wie oft waren Sie in den vergangenen 4 Wochen:	immer	meistens	ziemlich oft	manchmal	selten	nie
28.1	Ruhig und gelassen?	☐	☐	☐	☐	☐	☐
28.2	Voller Energie?	☐	☐	☐	☐	☐	☐
28.3	Entmutigt und traurig?	☐	☐	☐	☐	☐	☐
29	Wie häufig haben Ihre körperliche Gesundheit oder seelischen Probleme in den vergangenen 4 Wochen Ihre Kontakte zu anderen Menschen (Besuche bei Freunden, Verwandten usw.) beeinträchtigt?	☐ immer	☐ meistens	☐ manchmal	☐ selten	☐ nie	
30	Können Sie auf jemanden zählen, der Ihnen bei den täglichen Aufgaben hilft, z. B. beim Einkaufen, Putzen, beim Kochen bzw. wenn Sie irgendwohin gefahren werden sollen?	☐ Nein ☐ Ja, habe aber in den letzten 12 Monaten keine Hilfe dieser Art gebraucht ☐ Ja, und die Unterstützung war angemessen ☐ Ja, hätte aber mehr Hilfe bei diesen täglichen Aufgaben gebraucht als ich erhalten habe					

31	Können Sie auf jemanden zählen, der Sie gefühlsmäßig unterstützt, z. B. mit Ihnen über Probleme spricht, Ihnen bei einer Entscheidung hilft?	☐ Nein ☐ Ja, habe aber in den letzten 12 Monaten keine Hilfe dieser Art gebraucht ☐ Ja, und die Unterstützung war angemessen ☐ Ja, hätte aber mehr gefühlsmäßige Unterstützung gebraucht als ich erhalten habe					
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Im nächsten Teil werden Sie nach Tätigkeiten gefragt, die im Rahmen eines ganz normalen Tagesablaufes anfallen. Bitte geben Sie an, wie schwierig die Ausführung für Sie persönlich zurzeit wäre oder ist.

32	Wie schwierig ist/wäre es für Sie folgende Tätigkeiten allein auszuführen:	überhaupt nicht schwierig	etwas schwierig	schwierig	sehr schwierig	kann ich nicht
32.1	Zum Arzt, Apotheke, Krankengymnastik oder anderen medizinischen Einrichtungen zu gehen (evtl. mit öffentlichen Verkehrsmitteln)?	☐	☐	☐	☐	☐
32.2	Ihre Wohnung sauber zu machen?	☐	☐	☐	☐	☐
32.3	Lebensmittel, Kleidung, Haushaltsartikel usw. einzukaufen?	☐	☐	☐	☐	☐
32.4	Wäsche zu waschen, zu bügeln?	☐	☐	☐	☐	☐

32.5	Ihre finanziellen Angelegenheiten zu regeln?	☐	☐	☐	☐	☐
32.6	Briefe zu schreiben, Formulare auszufüllen?	☐	☐	☐	☐	☐
32.7	Besuch zu empfangen und zu bewirten?	☐	☐	☐	☐	☐
32.8	Zu telefonieren?	☐	☐	☐	☐	☐

33	Wie würden Sie das Verhältnis zu Ihren unmittelbaren Nachbarn beschreiben?	☐ gut	☐ überwiegend gut	☐ schlecht	☐ keine bzw. wenige Kontakte
34	Zu wie vielen Personen in der Nachbarschaft oder im Quartier haben Sie intensivere Kontakte?	☐ 1 - 2	☐ 3 - 5	☐ mehr als 5	☐ keine
35	Wie viele Personen in der Nachbarschaft oder im Quartier können Sie bei Bedarf um Hilfe bitten?	☐ 1 - 2	☐ 3 - 5	☐ mehr als 5	☐ keine
36	Wie beurteilen Sie die Erreichbarkeiten von Versorgungseinrichtungen in Ihrer Wohnumgebung:				
		gut	geht so	schlecht	
36.1	Einkäufe des täglichen Bedarfes?	☐	☐	☐	
36.2	Ärzte?	☐	☐	☐	
36.3	Freizeiteinrichtungen (z. B. Café)?	☐	☐	☐	
37	Wie zufrieden sind sie mit:				
		zufrieden	geht so	unzufrieden	
37.1	Ihrer Wohnung?	☐	☐	☐	

- | | | | | |
|------|---------------------------------|--------------------------|--------------------------|--------------------------|
| 37.2 | Ihren Nachbarn? | ☐ | ☐ | ☐ |
| 37.3 | Ihrem Quartier/Stadtteil? | ☐ | ☐ | ☐ |
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Herzlichen Dank für Ihre Teilnahme!

Acknowledgements (German)

Ich möchte mich an dieser Stelle herzlich bei Prof. Dr. Tamara Schikowski für die Aufnahme in ihre Arbeitsgruppe bedanken. Mein besonderer Dank gilt ihr für die kontinuierliche Unterstützung, die offene und erreichbare Art und die engagierte und familiäre Betreuung dieses Themas.

Ebenso danke ich Prof. Dr. Christian Herder herzlich für die geschätzte Betreuung dieses Projekts, die wertvolle Kommentare sowie die unkomplizierte und angenehme Kommunikation.

Ein besonderer Dank gilt zudem Sara Kress, die jederzeit ein offenes Ohr für Fragen, Anregungen und Ideen hatte. Claudia Wigmann danke ich herzlich für die Unterstützung bei den statistischen Methoden sowie für ihre wertvollen Erklärungen und Hilfestellungen im Bereich der Statistik. Ebenso möchte ich Bo Sun für die freundliche Unterstützung danken.

Anschließend möchte ich mich beim gesamten SALIA-Studenten-Team, dem ganzen IUF- und DDZ-Team bedanken für die nette und kollegiale Zusammenarbeit, die zeitliche Verfügbarkeit, die nette Unterstützung.