Health consequences of exposure to environmental living conditions

Pathways and spatial patterns in Europe

Benjamin Aretz

https://doi.org/10.18453/rosdok_id00004763

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This PhD dissertation is written as part of a collaboration project between the University of Rostock and the University of Groningen focusing on exposure to living environment and its effect on different health outcomes in European countries with a special focus on Germany and the Netherlands. We are grateful to the German Institute for Economic Research for providing the German SOEP data used for Chapter 2, to the Lifelines Biobank, an initiative that was made possible by a subsidy from the Dutch Ministry of Health, Welfare and Sport, the Dutch Ministry of Economic Affairs, the University Medical Center Groningen (UMCG the Netherlands), University Groningen and the Northern Provinces of the Netherlands and especially Laura Nauta for providing and managing the Dutch Lifelines data used for Chapter 3, the Cogstate Research Team for their support in handling the data coming from the Cogstate Brief Battery for Chapter 3, Vanessa Didelez for statistical support in Chapter 3, the SHARE-ERIC for providing the SHARE data and their support for Chapter 4, and Statistics Netherlands as well as Jan van de Kassteele, Laurens Zwakhals, Oscar Breugelmans, Caroline Ameling & Carolien van den Brink for providing the Dutch regional data at the neighborhood level used for Chapter 5.

Colophon

Benjamin Aretz
Health consequences of exposure to environmental living conditions: Pathways and spatial patterns in Europe

PhD Dissertation, University of Rostock, Germany & University of Groningen, The Netherlands

Language editing: The University of Groningen Language Centre

Dutch translation of the summary: The University of Groningen Language Centre

Layout design: Benjamin Aretz

Print: IT- und Medienzentrum Rostock

university of groningen

Universität Rostock Traditio et Innovatio

Health consequences of exposure to environmental living conditions

Pathways and spatial patterns in Europe

PhD thesis

to obtain the degree of PhD at the
University of Groningen
on the authority of the
Rector Magnificus Prof. J.M.A. Scherpen
and in accordance with
the decision by the College of Deans

and

to obtain the degree of Dr. rer. pol. at the
University of Rostock
on the authority of the
Rector Magnificus Prof. E. Prommer
and in accordance with
the decision by the Faculty of Economic and Social Sciences.

Double PhD degree

This thesis will be defended in public on

Thursday 7 December 2023 at 14.30 hours

by

Hans Benjamin Aretz
born on 16 December 1989
in Bonn, Germany

Supervisors
Prof. F. Janssen
Prof. G. Doblhammer
Prof. L.J.G. van Wissen

Assessment Committee
Prof. S.A. Reijneveld
Prof. R. Rau
Prof. E. Zagheni
Prof. R. Hoffmann

This page is for you beloved grandpa Hans.
Family is where life begins and love never ends.
You will be always in our hearts and we never forget.
Rest in peace.

This page is for you, Milan, my beloved nephew.
Unfortunately, we never had the time to get to know each other.
I am sure that you will protect us from up there,
and one day the time will come to make up for everything.
Rest in peace, our little baby boy.

This page is for you H. Marike Boezen.
We think of you.
Rest in peace.

List of original publications

Aretz, Benjamin; Costa, Rafael; Doblhammer, Gabriele; Janssen, Fanny (2023): The association of unhealthy and healthy food store accessibility with obesity prevalence among adults in the Netherlands: A spatial analysis. *SSM – Population Health*, volume 21. Open Access. DOI: https://doi.org/10.1016/j.ssmph.2022.101332.

Aretz, Benjamin (2022): The short- and long-term effects of the Great Recession on late-life depression in Europe: The role of area deprivation. *Social Science & Medicine*, volume 294. Open Access. DOI: https://doi.org/10.1016/j.socscimed.2021.114697.

Aretz, Benjamin; Janssen, Fanny; Vonk, Judith M.; Heneka, Michael T.; Boezen, H. Marike; Doblhammer, Gabriele (2021): Long-term exposure to fine particulate matter, lung function and cognitive performance: A prospective Dutch cohort study on the underlying routes. *Environmental Research*, volume 201. Open Access. DOI: https://doi.org/0.1016/j.envres.2021.111533.

Aretz, Benjamin; Doblhammer, Gabriele; Janssen, Fanny (2019): Effects of changes in living environment on physical health: a prospective German cohort study of non-movers. *European Journal of Public Health*, volume 29, issue 6, pp. 1147-1153. Open Access. DOI: https://doi.org/10.1093/eurpub/ckz044.

Contents

1

Introduction

"Of all the forms of inequality,
injustice in health is the most
shocking and inhumane."
(Martin Luther King Jr., 1966)

1.1 Background and research question: Environmental living conditions and health in modern societies

Environmental living conditions have become a public health concern in the twentieth and twenty-first centuries, and the interactions between environmental living conditions, human populations, and their public health are of particular interest.

The world's population has increased enormously from 2.5 billion in 1950 to almost 7.9 billion in 2021 (UN 2021). This was accompanied by socioeconomic transformation processes in many societies, including urbanization and economic growth (Khoshnevis et al. 2019). These global demographic developments are connected to a number of challenges in terms of living environments and population health (O'Neill et al. 2010). First, the demand for natural resources (Krausmann et al. 2009) and energy (Rodrigue 2020, Smil 2000) has increased. As a result, higher greenhouse gas emissions have contributed to the toxicology of air pollution, which has become one of the most important environment-related public health concerns (Fuller et al. 2022). Second, climate change has destructive effects on the health of present and future generations (Romanello et al. 2021), and climate change is in turn accelerated by anthropogenic greenhouse gas emissions. Third, increasing population density and advancing urbanization have affected people's land-use, living environments, and health-related behaviors (Hunter 2000, Muttarak 2021). Fourth, an increased proportion of people lives in unhealthy living environments as a consequence (Gaub 2019, Wiedmann et al. 2020).

European societies are faced with additional health-relevant developments in recent years: multimorbidity has increased (Souza et al. 2021), as well as the prevalence of many physical and mental health-related diseases, such as obesity (Vidra et al. 2018), depression (Walrave et al. 2022), and dementia (GBD 2022). In addition, most European societies are affected by population aging as a result of the demographic transition caused by decreased birth rates and mortality (England & Azzopardi-Muscat 2017).

The Global Burden of Disease study found that one of the main drivers of these health developments, in addition to detrimental personal lifestyle determinants, are unhealthy

living environments: healthier environments could prevent one quarter of the global burden of disease (WHO 2020). Prior research suggests that interventions aimed at improving environmental living conditions may be an effective way to promote health and prevent disease (Henschel et al. 2012, Moreira et al. 2022).

The WHO has formulated considerations for a vision for cities oriented towards addressing environmental and health challenges in Europe in the twenty-first century, due to their importance:

> *"In particular, there is a need for more robust knowledge about urban systems, and how local economic and social drivers and pressures on the local infrastructure and environment impact on human and planetary health."* (Carmichael et al. 2017)

But although the health relevance of unhealthy living environments is formally on the agenda of policymakers in European countries, a detailed understanding of the health impacts of different environmental living conditions is lacking (Romanello et al. 2021). This is unfortunate because this fundamental research is needed to bridge the science–policy interface effectively and help develop effective policy interventions to tackle unhealthy living environments (Haines et al. 2017). To this end, two aspects seem to be of particular interest: first, understanding the relevant temporal pathways is essential to develop targeted intervention and prevention measures that address the problems at their roots. Second, understanding spatial patterns is useful for advising policymakers on which interventions are most promising (Devine 2004).

With this thesis, I aim to address this lack of research by conducting a set of quantitative studies on the "health consequences of exposure to environmental living conditions". The overarching research question is:

> *How are different environmental living conditions linked to physical and mental health among European adults in the twenty-first century?*

To offer a response, I will apply an innovative and extensive approach to environmental health by:

(1) considering a more holistic multilevel approach to environmental health involving physical and mental health, and five different dimensions of environmental living conditions, including the built environment, the natural environment, the local and macro-level economic environment, and the social community environment;

(2) applying an interdisciplinary approach at the intersection between demography, public health, epidemiology, economy, and geography under a single umbrella;

(3) analyzing general spatial patterns and regional differences in the association between environmental living conditions and health; and

(4) analyzing different temporal, moderating, or mediating pathways.

I will conduct my research under a common theoretical umbrella, applying several newer environment and health datasets and their linkages, and combined statistical methods from the different disciplines considered. This thesis focuses on both pathways and spatial patterns as the theory and empirical evidence suggests that they are both relevant.

1.2 Thesis outline

This thesis consists of six chapters and is based on four quantitative studies.

The current **Chapter 1** explains the societal relevance, important definitions, theories, and empirical background to the health consequences of exposure to environmental living conditions. My aim is to summarize existing environmental health theories under a single general theoretical framework for this thesis. I also describe the datasets, locations, approaches, and statistical methods used.

Chapter 2 portrays a cross-sectional ecological study of the overall associations between healthy and unhealthy food accessibility and obesity prevalence in the Netherlands. Special attention will be paid to regional differences between urban, suburban, and rural areas:

I. Study: The association of unhealthy and healthy food store accessibility with obesity prevalence among adults in the Netherlands: A spatial analysis

Chapter 3 introduces a longitudinal individual-level study on the effects of perceived environmental living conditions on health in Germany. This prospective cohort study is interested in how stable (beneficial or poor), improved, or worsened living environments are related to physical health:

II. Study: Effects of changes in living environment on physical health: a prospective German cohort study of non-movers

Chapter 4 presents a prospective cohort study on the interrelationships between long-term exposure to air pollution, lung function as a physical health measure, and cognitive performance as a mental health measure in the Netherlands:

III. *Study: Long-term exposure to fine particulate matter, lung function and cognitive performance: A prospective Dutch cohort study on the underlying routes*

Chapter 5 presents a longitudinal study applying a cross-level interaction approach and considers the moderating role of meso-level area deprivation on the effects of a macro-level financial crisis on the risk of depression in European countries using a longitudinal design:

IV. *Study: The short- and long-term effects of the Great Recession on late-life depression in Europe: The role of area deprivation*

Chapter 6 provides a summary of the main results, a discussion of the main results, a discussion of the strengths and weaknesses, a summary of the policy and societal implications of the results, and possible future directions for research in this field.

1.3 Health and environmental living conditions: definitions and theories used in this thesis

In this section, I aim to integrate the existing environmental and other health theories into an overall framework for this thesis. **Table 1** provides an overview of the theoretical background used for this thesis.

Table 1. Overview of the theoretical themes used for this thesis

Theory	Key concept	Subsection
A health map for the local human habitat	Multilevel approach to environmental health	1.3.2
The Health Development Model	Synthesis of Pathogenesis and Salutogenesis	1.3.3
Theory of Environmental Press	Adaptation	1.3.4
The theoretical approach of this thesis: health consequences of environmental living conditions in Europe	Combination of the concepts from 1.3.2, 1.3.3, 1.3.4	1.3.5

The theoretical approach applied to this thesis combines macro and meso-level perspectives on environmental health with pathway theories from the micro perspective.

Before introducing the individual theories, I will present the definitions of health and environmental living conditions used in this thesis.

1.3.1 Definitions of the key concepts: health and environmental living conditions

HEALTH

There are three different kinds of definition of health currently in common use, which refer either to a *pathogenic* or to a *salutogenic* understanding of health. The pathogenetic understanding of health focuses on the development of disease and disabilities and their risk factors. In contrast, the salutogenic understanding defines health as a continuum, and health or illness is not defined solely by objectively measured diagnoses, but also by the subjective assessment of the personal health situation (Bhattacharya et al. 2020).

The first definition comprehends health as the absence of any disease or impairment (= *pathogenic health concept*). The second definition defines health as a state of enabling people to cope with all the demands of daily life and thus also implies the absence of any disease or impairment (= *pathogenic health concept*). The third definition understands health as a state of balance in the form of an equilibrium between a person and its social and physical environment (= *salutogenic health concept*) (Sartorius 2006).

The World Health Organization defines health in line with the first and second definitions as “a state of complete physical, mental and social well-being and not merely the absence of disease or infirmity” (WHO 1995).

This thesis does not focus on a specific disease or health condition, but tries to integrate a more sophisticated approach to environmental health, including pathogenic and salutogenic elements. Newer literature has already proposed such an integrative understanding of health and defines health as an equilibrium between individual and environmental conditions: “[h]ealth is the dynamic balance of physical, mental, social, and existential well-being in adapting to conditions of life and the environment” (Krahn et al. 2021). Based on this recent health concept, this thesis includes diseases and more subjective health outcomes from both the mental and physical health dimensions. Mental health refers to an individual’s ability to cope with the normal stresses of life and involves the ability to feel, think, and act in a way that enhances a person's ability to enjoy life and deal with challenges (Prince et al. 2007). Physical health refers to overall wellbeing in terms of an individual's body, including the proper functioning of the various systems and organs

(Koipysheva et al. 2018). I did not include social wellbeing in this thesis due to the clear focus on health outcomes.

The underlying health definition considers life circumstances in addition to environmental characteristics, which is why this thesis also includes individual characteristics, such as socio-economic and lifestyle determinants, as control variables in all the studies conducted. However, environmental living conditions are at the heart of my research. **Table 2** provides an overview of the health concepts and definitions used for each study in this thesis.

Table 2. Health concepts and definitions used in this thesis

Study	Outcome	Health definition	Health concept
Study I The association of unhealthy and healthy food store accessibility with obesity prevalence among adults in the Netherlands: A spatial analysis	Small-area obesity prevalence	Obesity = BMI > 30	Physical health, pathogenic health concept
Study II Effects of changes in living environment on physical health: a prospective German cohort study of non-movers	Physical health covering physical functioning, general health, bodily pain and the role of functioning	(Changes in) composite score for subjectively assessed physical health (12-item Short-Form survey)	Physical health, salutogenic health concept
Study III Long-term exposure to fine particulate matter, lung function and cognitive performance: A prospective Dutch cohort study on the underlying routes	Cognitive performance (computerized test) = outcome Lung function (spirometry) = mediator	Two metric lung function outcomes (FEV_1, FVC) and one composite score for cognitive performance (Cogstate Brief Battery)	Physical and mental health, pathogenic health concept
Study IV The short- and long-term effects of the Great Recession on late-life depression in Europe: The role of area deprivation	Late-life depression	Depression = 4(+) depression symptoms (EURO-D depression scale)	Mental health, pathogenetic health concept

The pathogenic outcomes used for three of the studies conducted in this thesis were selected carefully for their public health relevance, namely the high burden attributable to these diseases. "Obesity" as used for *Study I* was shown to have a prevalence between 19.5% and 29.3% in Europe in 2016 (Janssen et al. 2020). "Cognitive performance" as used for *Study III* can indicate the extent of potential cognitive impairments in a prodromal phase of dementia and in younger ages, and dementia has a prevalence of 1.73% in the general population and between 21.9% and 40.8% in the population aging 85 or older (Georges et al. 2020). This is especially important in light of the aging societies found in

most European countries. "Late-life depression" (*Study IV*) has a prevalence of 29% among adult Europeans in the age of 50 or older in 2015 (Horackova et al. 2019).
The salutogenic outcome used for *Study II* was physical health and not mental health, the reason being that mental health outcomes were shown to produce same-source bias in the associations between perceived environmental living conditions and perceived health (Chum et al. 2019). Furthermore, mental health was shown to be a more relevant mediator for physical health than the reverse, which is why physical health outcomes should also reflect aspects of mental health (Ohrnberger et al. 2017).

ENVIRONMENTAL LIVING CONDITIONS

Because there is no general definition of environmental living conditions, I have aligned this thesis to the definition provided by the WHO and contoured this even more precisely by applying additional threads of theory. The WHO understands environmental health as follows:

> *"Environmental health comprises those aspects of human health and disease that are determined by factors in the environment. It also refers to the theory and practice of assessing and controlling factors in the environment that can potentially affect health."* (WHO 1990)

Environmental living conditions can thereby include the direct pathological effects of chemicals, radiation and some biological agents, and the direct or indirect effects on health of the physical, psychological, social and aesthetic environment (European Environment Agency 1995). According to newer theoretical considerations on an ecological approach to health, environmental living conditions can be roughly sub-divided into proximal and distal factors (Tomlinson et al. 2021).
Proximal environmental living conditions cover the physical and social factors in the immediate surrounding that can directly or indirectly affect the health and wellbeing of individuals and communities in a specific geographic area. These conditions are basically structured into four sub-dimensions, namely 1) the natural environment (e.g. air quality, water quality, noise pollution, and green spaces); 2) the built environment (e.g. the accessibility of local infrastructure, urbanity, the availability of public transportation, and indoor housing conditions); 3) the economic environment (e.g. regional income inequality, employment, and healthcare availability); and 4) the local social community (e.g. social

cohesion, crime and safety, and discrimination) (Barton & Grant 2006, Krieger 2008, Tomlin et al. 2021).

Distal environmental conditions cover such factors in the even wider surroundings that can indirectly affect health and wellbeing. Such distal factors can be subdivided into a) policy conditions, b) ecological conditions, and c) cultural conditions (Barton & Grant 2006, Krieger 2008, Tomlin et al. 2021).

This thesis focuses closely on the proximal natural and built environment and their associations with health (*Studies I*, *II*, *and III*), but also looks in part at economic and social conditions, as well as distal environmental characteristics and their interactions with proximal conditions (see *Study IV*). **Table 3** presents an overview and classification of the specific environmental living conditions used for each study conducted for this thesis.

Table 3. Overview of the environmental living conditions considered in this thesis

Study	Proximal vs. distal	Environmental dimension	Environmental conditions
Study I The association of unhealthy and healthy food store accessibility with obesity prevalence among adults in the Netherlands: A spatial analysis	proximal	- built environment	- local food infrastructure
Study II Effects of changes in living environment on physical health: a prospective German cohort study of non-movers	proximal	- built environment - natural environment	- general local infrastructure - environmental pollution
Study III Long-term exposure to fine particulate matter, lung function and cognitive performance: A prospective Dutch cohort study on the underlying routes	proximal	- natural environment	- air pollution
Study IV The short- and long-term effects of the Great Recession on late-life depression in Europe: The role of area deprivation	proximal and distal	- (distal) economic environment - built environment - local community	- financial crisis or recession - local infrastructure - safety and cleanness

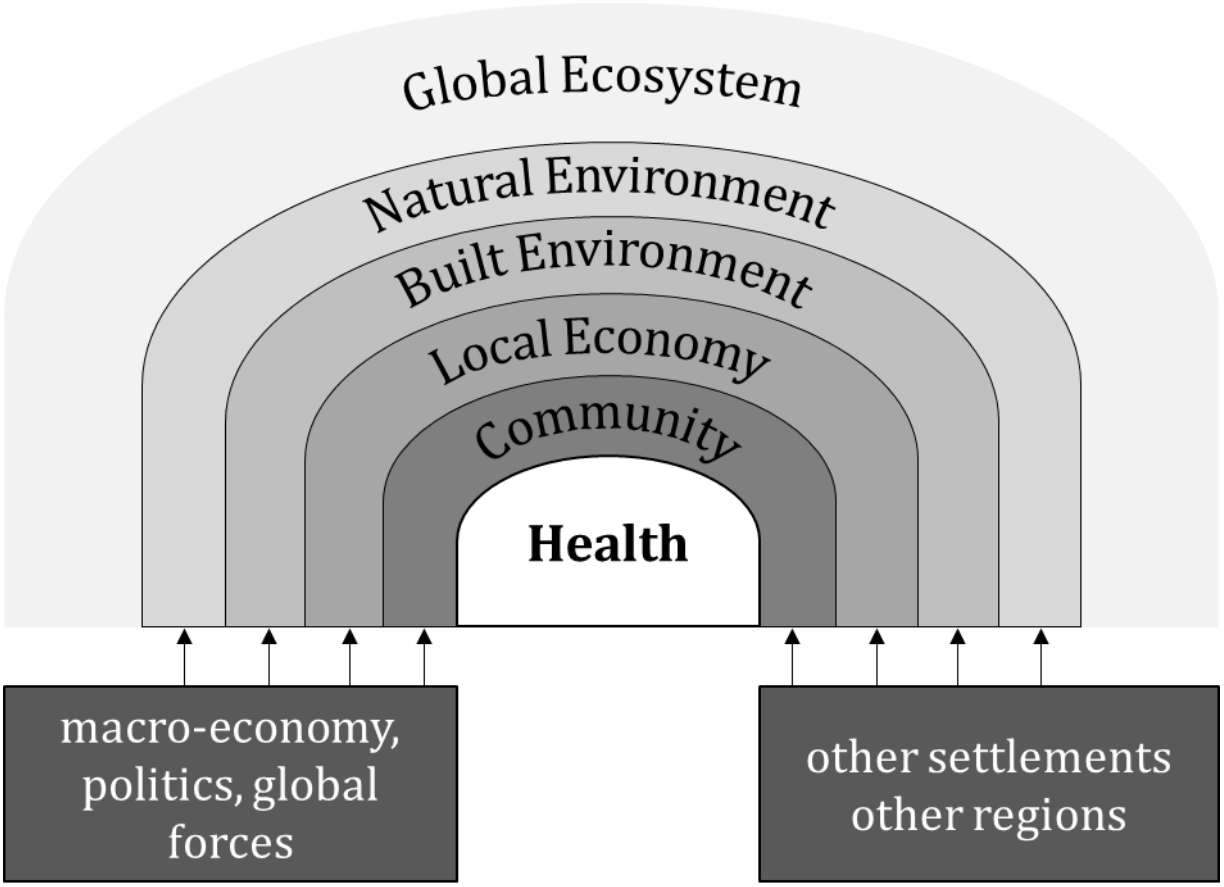
The following explains the specific underlying health theories I applied as a basis for the overall theoretical health approach to environmental living conditions, by relating the theories to the studies carried out for this thesis. The overarching topic of this thesis reflects a synthesis of environmental living conditions and health, sometimes referred to here as 'environmental health'.

1.3.2 The role of environmental living conditions: a multi-level approach to health

One challenge stands out when exploring the health effects of environmental living conditions: environmental living conditions can be located at different levels – such as the macro level or the meso level – and these conditions can be interrelated along direct or indirect pathways, and can additionally vary between regional areas (Tomlinson et al. 2021, WHO 1990).

An important framework for understanding the complexity of environmental living conditions from an overarching macro perspective is 'A health map for the local human habitat' (**Figure 3**) developed by Barton & Grant (2006). This framework has a strong focus on the human living environment and structures it into multiple spheres or levels. The theory is mainly inspired by the Dahlgren & Whitehead (1991) approach and ecosystem theories and the principle of sustainable development (Barton et al. 1995). In addition to environmental living conditions, the framework includes personal, lifestyle, and behavioral factors from the Dahlgren & Whitehead (1991) model.

Figure 1. The environmental determinants of health ('A health map for the local human habitat', simplified from the original by Barton & Grant (2006))



The approach divides between four main spheres of environmental living conditions, which are integrated into the global ecosystem. The first sphere of the living environment is the social 'Community', which is characterized by social capital and networks. The second sphere is 'Local Economy', which concerns wealth creation and markets. The third sphere, 'Built Environment', is characterized by the human-made environment and covers buildings, places, streets, and routes, while the fourth sphere – "Natural Environment" – is on the contrary, defined by environmental characteristics that are not intentionally affected by humans, such as air, water, and land.

All spheres are interrelated by macro-economics, politics, and other global forces: the macro sphere can affect other spheres from the lower levels and vice-versa. As a last important aspect, the approach integrates spatial patterns and assumes that the associations between the environment and health can differ between regional areas.
Barton & Grant (2006) introduced two additional spheres, namely Lifestyle and Activities, which are omitted in **Figure 2** because they are not central to my research for this thesis. Both spheres are assumed to act as moderators linking environmental living conditions to health. Lifestyle and activity determinants are treated here as control variables in addition to further individual-level characteristics, due to their importance for health.

Empirical evidence from population-based studies underlines the relevance of the different living environment dimensions for health proposed by Barton & Grant (2006). Lower social capital was shown to be a risk factor for developing symptoms of depression (Backhaus et al. 2020) and small social networks are associated with worse self-rated health among older adults (Youm et al. 2014). Worse local economy measured by a decrease in the unemployment rate at the regional level was shown to be associated with a higher risk of cardiovascular disease in Italy (Belotti et al. 2022). The perceived and objectively measured built environment were shown to be associated with worse health (Cerletti et al. 2021, Spring 2018). A better quality natural environment, operationalized by the accessibility of green (for example parks) or blue (for example water) spaces, or air quality, was associated with better physical or mental health (White et al. 2021, Wolf et al. 2021).

Cornerstones for this thesis

i. There are different possible regional differences in the associations between exposure to environmental living conditions and health. Furthermore, the living environment is linked across direct, indirect, and moderating pathways to health. That

is the reason why the special focus of the analytic approach of this thesis is on spatial patterns and pathways.

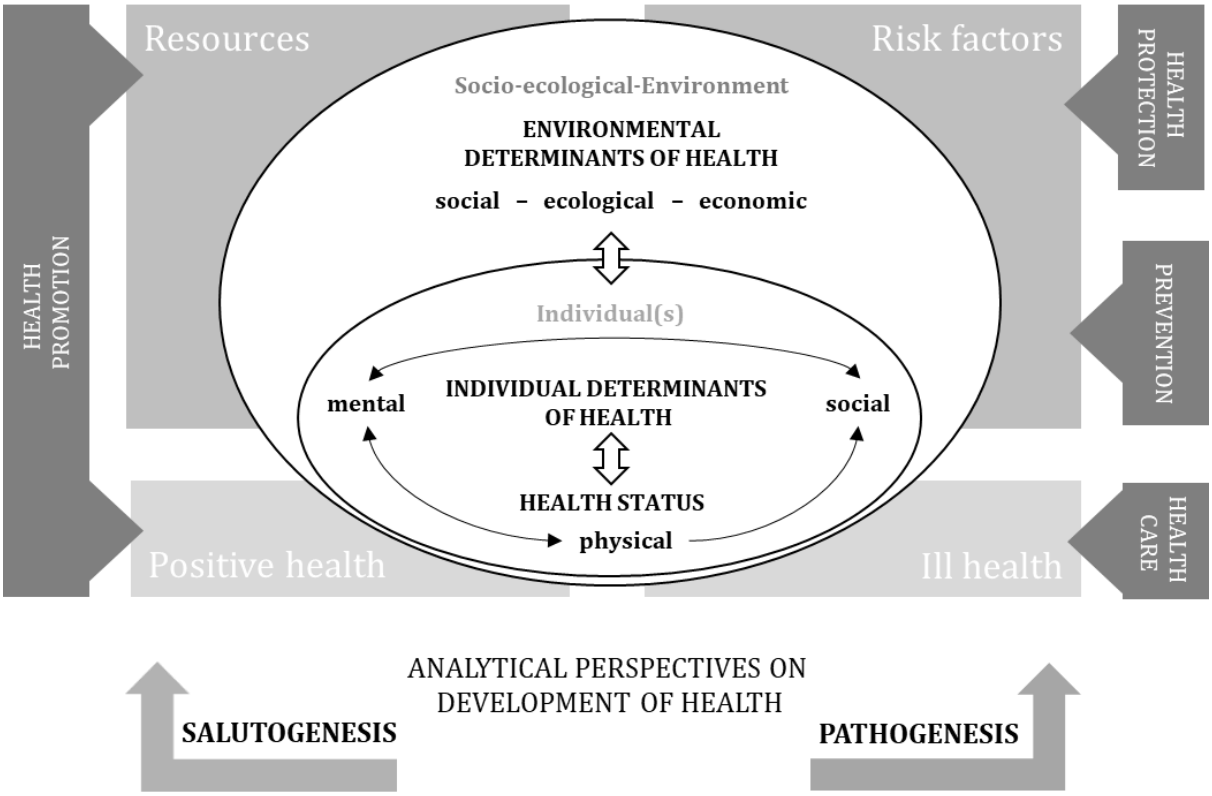
ii. Health-relevant environmental living conditions are located at different levels. This thesis applies a multi-level understanding of environmental health.

iii. The environment is structured into five different dimensions, which are relevant for health. This thesis incorporates five different dimensions of the living environment, namely the built environment, the natural environment, the local economic environment, the social (community) environment, and the macro level economy.

1.3.3 Environmental health as a continuum: the Health Development Model

For the purpose of thesis, I understand environmental health as a synthesis of pathogenesis and salutogenesis.

Figure 2. The Health Development Model (author's own figure based on Bauer et al. (2006))



The Health Development Model (**Figure 2**) suggested by the European Community Health Promotion Indicator Development (EUHPID) is a theoretical model that combines the

pathogenic and saultogenic perspectives under one umbrella (Bauer et al. 2006). The Health Development Model structures health into three dimensions, namely physical and mental health, and social wellbeing. Health is determined by environmental and individual determinants of health: there are positive resources that promote health and there are negative risk factors that can lead to ill health. Prevention can deal with specific risk factors at the individual level (e.g. smoking), and health protection concentrates on safeguards from the socio-ecological environment (e.g. air pollution or food deserts). While pure pathogenic health models only focus on the development of diseases and their risk factors (Vihinen 2017), the Health Development Model adds a salutogenic understanding of health to the approach. Antonovsky (1979) previously introduced the concept of Salutogenesis and defined health as an equilibrium or continuum. Salutogenesis focuses on factors that can support health and not only address its risk factors. Health was seen as a subjective individual condition, which needs an individual evaluation process. Health should therefore not be understood as the mere occurrence of disease, but as a person's perception of their own health condition (Antonovsky 1979). Two key concepts are of particular relevance here: a) the sense of coherence (SOC); and b) the general resistance resources (GRRs). When people have a high SOC they are able to manage everyday tensions, and to select and apply GRRs, which are defined as identity, knowledge, intelligence, social cultural capital, and preventive health orientations. The SOC is thereby a feeling of orientation, self-management, and confidence leading to the belief that challenges can be overcome (Antonovsky 1993).

In short, this health concept is based on the interrelationships between health, stress, and subjective coping strategies to deal with health challenges, diseases, or functional limitations. By applying the Salutogenesis Model to environmental health, a person can have very good health even when diagnosed with disease or where functional limitations are present, but the environmental living conditions support or compensate detrimental health aspects. The contrary can also be true, in that a person can have very poor health even without having any diagnosed disease. This could be the case, for example, when health is perceived negatively because of adverse or worsened living conditions that affect the individual's health assessment.

Cornerstones for this thesis

iv. Environmental determinants of health can be divided into risk factors that can lead to ill health and health resources that lead to positive health. This thesis integrates environmental risk factors for health (*Study I: Unhealthy food, Study II: Stable worse or worsened conditions, Study III: Exposure to air pollution, Study IV: Living in deprived areas*), but also potential environmental resources for positive health (*Study I: Healthy food, Study II: Stable beneficial or improved conditions*).

v. Health is a multidimensional concept, consisting of physical and mental health as well as social wellbeing, and there is an interplay between the different health dimensions. This thesis explores the physical (*Studies I, II, and III*) and mental dimensions of health (*Studies III and IV*) as well as their interrelationship (*Study III*), but does not consider social wellbeing due to its clear focus on health.

vi. Environmental living conditions affect health along pathogenic and salutogenic pathways. This thesis incorporates disease-outcomes (pathogenic approach) in *Studies I, III,* and *IV*, as well as health (perception) outcomes (salutogenic approach) in *Study II*.

1.3.4 Environmental health as an adaptation process: the Environmental Press Theory

During the course of their lives people experience stable or changing living environments, because they relocate or because of other secular changes. The Environmental Press Theory understands health as the degree of fit between a person's competencies – for instance physical and functional health, and cognitive and affective functioning – and the demands of their environment (Lawton et al. 1978). The assumption is that a misfit between environmental variables and personal competencies can cause press: environmental press can develop if environmental characteristics deteriorated and competencies remained stable; but the reverse is also possible, if an individual's competencies change under stable environmental characteristics. However, that does not mean that every change in personal competencies or environmental characteristics results automatically in environmental press and worsened health. If people are able to adapt to the changed conditions, either because they adjust their personal competencies – for instance through technical or social and family resources, or through the living environmental conditions in their

surroundings – they will be able to deal with new situations without experiencing a loss of health-related quality of life. (Lawton 1985)

We also know from anthropological evolution theories and empirical studies that humans are able to "occupy" environments characterized by stressful conditions by using behavioral social and physiological adaptations (Frisancho 1993). Because physiological adaptations, such as genetic and bodily changes, usually takes longer to become effective, behavioral social adaptations seem to be the more likely mechanism in this case. Humans are able to respond rapidly to changes in living environmental characteristics, such as housing conditions (Mathew & Perreault 2015) through behavioral plasticity, which is the ability of organisms to change their behavior resulting from exposure to stimuli (Komers 1997). Social behavioral adaptation might be a possible human strategy for dealing with detrimental built environments, such as housing conditions, and might prevent long-term detrimental effects on health, while this coping strategy might fail in the case of environmental pollution such as air pollution, which in contrast to housing conditions is an invisible health hazard.

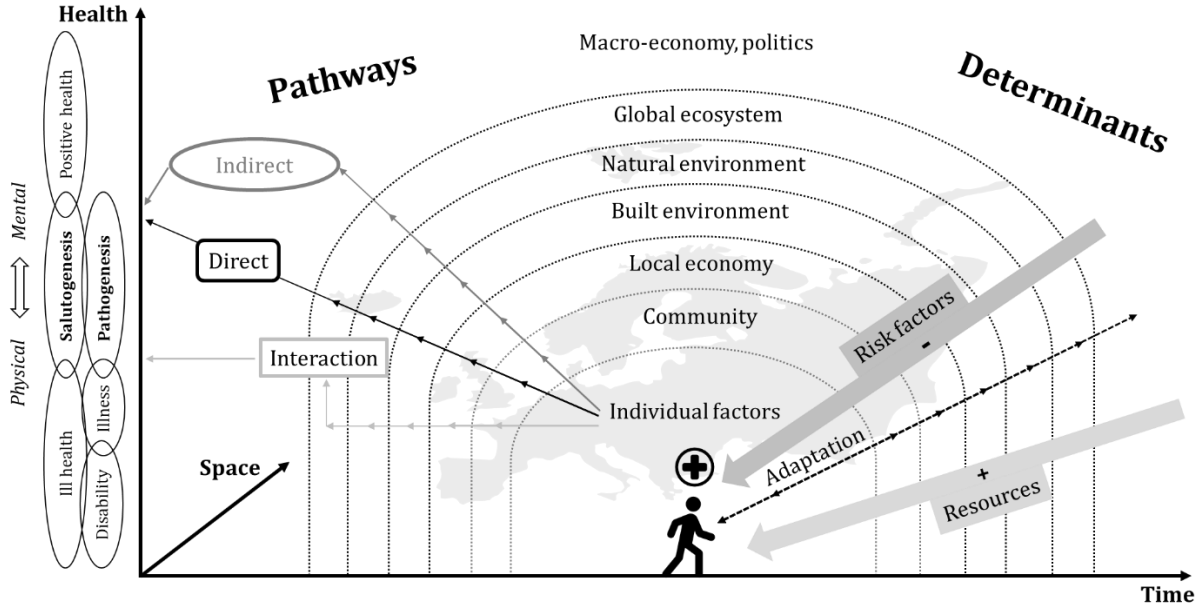
Cornerstone for this thesis

vii. Changes in environmental living conditions can produce more (worsened conditions) or less (improved conditions) stress on people, leading to subsequent deteriorations or improvements in health. Stable or chronic environmental living conditions can also affect health in the longer or shorter term if personal competencies change. This thesis includes consideration of both changes in environmental living conditions (*Study II*) and stable or chronic conditions (*Studies I, III, and IV*).

1.3.5 Summary of this section: the theoretical approach of this thesis

In the following section, I combine the three individual theories on environmental health presented above into an overall theoretical framework for this thesis. **Figure 4** shows how this framework is applied to analyze the "Health consequences of environmental living conditions". This proposed framework for environmental health incorporated the seven cornerstones from the environmental health theory derived in the previous sections.

Figure 3. The theoretical approach of this thesis: health consequences of environmental living conditions.



In contrast to the health map for local human habitat by Barton & Grant (2006), the theoretical approach compiled here incorporates a more sophisticated understanding of health by distinguishing between physical and mental health, which can be interrelated, and salutogenic and pathogenic mechanisms. Moreover, the approach includes the "Determinants" and "Pathways" hemispheres. The "Determinants" cover (negative) risk factors for health and (positive) health resources. Changes in these determinants or in the personal competencies, which are reflected by the individual factors and imply personal needs, can lead to successful or unsuccessful adaptation: if an individual's adaptation process is successful, health does not change; if it is unsuccessful, health deteriorates. The "Pathways" cover the direct, indirect, or interaction mechanisms linking individual factors, environmental conditions, and the macro level with health. These possible mechanisms include interlinks between factors from the various levels (= cross-level pathways). The two poles determining health (= y-axis) are *Time* (= x-axis) and *Space* (= z-axis). Timing is not only important to establishing the correct order between exposure and outcome, but also for assessing the magnitude of the effect of environmental exposures on health (time-dependent and dose-response) (Hill 1965). Space is important because environmental living conditions are characteristics which are inherent to the places people live, and they do not appear equally across a region (Andrew & Philips 2005).

1.4 Previous research and contributions to the literature

This section focuses on the previous research on the health consequences of exposure to environmental living conditions. It presents the literature separately for each important environmental domain. Due to their higher relevance for this thesis, the built, natural, and economic environmental conditions were treated in more detail than the local community determinants. A last subsection describes the spatial patterns observed in the associations.

1.4.1 The built environment and health

The built environment was shown to be linked to mental and physical health outcomes (Schulz et al. 2018). The local infrastructure is an important subdimension of the built environment and is a central subdimension of this thesis (Grazuleviciene et al. 2021, Mason et al. 2020, Wu et al. 2022). Most studies measured the potential access to the local infrastructure using the accessibility to or availability of different facilities and social services in people's surroundings as exposure of interest (see Caspi et al. 2012 for a review). Availability is defined as the number of infrastructure locations within a specific area, while accessibility is the average distance (or proximity) to the locations (Shearer et al. 2015).

One hypothesis for why the local infrastructure is related to health is that it can provide important resources to support people in managing their everyday lives, overcome health and other issues, or at least mitigate the effects of experienced disabilities on perceived health (Glazener et al. 2021, Northridge et al. 2003). Accordingly, empirical evidence suggests that the local infrastructure is linked to health through behavioral characteristics (Gelormino et al. 2015).

In modern European societies, the local food infrastructure has particular relevance. The food infrastructure is assumed to be an obesogenic environment: systemic drivers such as regulations and economic growth, promote food consumption and overconsumption. Obesogenic determinants in the environment are the "sum of influences that the surroundings, opportunities, or conditions of life have on promoting obesity in individuals or populations" (Swinburn & Egger 2002).

Affected by environmental moderators such as sociocultural, socioeconomic, and transportation determinants, these environmental drivers affect people in their behavior patterns. The result is an individual and corporate overconsumption mainly characterized by unhealthy food intake with high total calorific value contributing to energy imbalance and obesity (Swinburn et al. 2011). Obesity is also familiarized with a set of comorbidities, e.g. cardiometabolic, digestive, respiratory, neurological, musculoskeletal, and infectious diseases, which is why obesity can be regarded as both a health outcome and a health risk factor – it thus represents an important target for preventing multimorbidity (Kivimäki et al. 2022).

Housing conditions are another significant subdimension of the built environment and are thus also a focus of this thesis. Housing conditions have been shown to be related to health (Rolfe et al. 2020). "Healthy homes" can promote physical and mental health in different ways: substandard housing can contribute to the emergence of allergies, and indoor air quality and temperature are associated with the incidence of cardiovascular diseases and dementia (Krieger 2010, Sims et al. 2020, Tsao et al. 2021). If a home is poorly equipped – for instance in terms of heating, air conditioning, and plumbing – this could then directly affect the development of diseases. Living in smaller apartments or in multiple dwelling units can contribute to the development of infectious diseases (Mao & Gao 2015, Wang et al. 2021) and has been shown to be associated with worse mental health (Foye 2017, Sarkar et al. 2021). In the sense of ontological security, the home can be understood as a secure base, which is fundamental for people to develop self-confidence and a social identity (Dupuis et al. 1998). The home is thus a place where people can exercise control, autonomy, and socialization (Tomas & Dittmar 1995).

1.4.2 The natural environment and health

The natural environment is associated with health, for instance environmental pollution (Ventriglio et al. 2020), weather (Forzieri et al. 2017), or green spaces (Annerstedt et al. 2012) A major focus of this thesis is on environmental pollution because it is well established that environmental pollution affects human health and contributes to the onset of various chronic diseases, such as cardiovascular and respiratory diseases (Briggs 2003, Fuller et al. 2022). Important characteristics that have been shown to affect physical and mental health are noise pollution (Basner et al. 2014) and air pollution (Xu et al. 2022).

Air pollution contributes the most to disease burden, which is why it deserves special attention in public health and epidemiology (Holgate 2022). Among the air pollutants, small particulate matter ($PM_{2.5}$) is assumed to pose the greatest threat to health (European Environment Agency 2022). Prominent mechanisms linking air pollution to cardiovascular health and lung functioning are oxidative stress, systemic or respiratory tract inflammation, endothelial dysfunction, autonomic imbalance, thrombogenicity, and the development of allergic sensitization (Lederer et al. 2021, Pfeffer et al. 2021).
However, how air pollutants affect brain health is rather poorly understood, despite there being increasing evidence that exposure to ambient $PM_{2.5}$ is associated with the onset of ischemic or hemorrhagic stroke and dementia (Shi et al. 2020, Verhoeven et al. 2021). The main mechanisms hypothesized to be involved in neurodegeneration caused by $PM_{2.5}$ are neuro-inflammation and other inflammation, the activation of microglia, oxidative stress, and changes in the blood-brain barrier (Block & Calderón-Garcidueñas 2009). However, empirical evidence on the specific pathways is scarce.

There is also growing evidence to suggest that green spaces can mitigate the negative health effects of air pollution, which is why they are considered an important dimension affecting environmental pollution (Ji et al. 2020). Moreover, research has shown that green environments can encourage people to perform physical activity (Zhong et al. 2022), which could be one pathway for explaining why the presence of green spaces in surroundings is positively associated with physical (Browning et al. 2022) and mental health (Alcock et al. 2014) in European countries.

1.4.3 The local and macro-level economy and health

A higher proportion of poverty in an area has been shown to be associated with worse mental and physical health (Gary-Webb et al. 2011, Margerison-Zilko et al. 2016). A similar pattern has been uncovered for contextual unemployment by applying a life course approach. A longitudinal study from Sweden found that higher unemployment in the surroundings was associated with a higher number of functional somatic symptoms (Brydsten et al. 2017). The macro-economy could directly and indirectly affect health through the local economy: it is well established that shocks located at the macro-level are associated with worse health. Recessions – prolonged economic downturns – are an important kind of macro-level shocks which have been shown to have important health impacts (see

Backhaus et al. 2022 for a review). One explanation is that economic downturns elevate an individual's symptoms of stress. Dooley & Catalano (1980) proposed a model relating economic change to behavior disorders, in which individually experienced life changes and stress are the main mediators between economic downturns and health. There is also empirical evidence that social groups experience different losses during economic downturns, which could emerge as social and health inequalities (Bartoll et al. 2014, Berghammer 2022, Lopez-Valcarcel et al. 2017, Wang et al. 2018). Existing studies suggest that a) less educated people (Kirsch & Ryff 2016), b) deprived or minority social groups (Pfeffer et al. 2013), and c) older workers (Saez et al. 2019) have been most affected by the Great Recession, the most severe global financial crisis since the 1930s. Higher socioeconomic status could make people more resilient and less sensitive to economic downturns – by having more assets, they do not fall so quickly below the subsistence level (Moser 1998). In general, it is well known that economic losses are associated with deteriorated health (Catalano et al. 2011).

1.4.4 The local community and health

The social environment, representing the community determinants in the surroundings, have been shown to be important determinants for both mental and physical health. One prospective cohort study using data from different Central and Eastern European countries found that lower social cohesion was associated with heightened symptoms of depression (CES-D) (Bertossi et al. 2019). Another study using a cross-sectional design found for four European cities that a higher number of social contacts is related to better mental health (Ruijsbroek et al. 2017). Baranyi et al. (2020) showed in a natural experiment in Scotland that higher crime rates in the area are associated with a higher risk of mental illness and a higher number of antidepressant prescriptions.

A German longitudinal study showed that social cohesion mediates the effect of the built environment on physical health (Kress et al. 2020). Cross-sectional studies found that higher neighborhood crime rates are associated with worse physical health outcomes (Lovasi et al. 2014, Sprung et al. 2019).

1.4.6 Summary of the previous research and existing research gaps

Previous studies suggest that the different dimensions of environmental living conditions proposed in the theory are indeed related to health:

1. Limited accessibility to local infrastructure is related to worse health.
2. Worse housing conditions are associated with worse health.
3. Higher exposure to environmental pollution is associated with worse health.
4. Weak local economy, which can be affected by downturns in the macro-economy, is associated with worse health.
5. A poorer local social community is related to worse health.

However, most previous studies are affected by four shortcomings, two concerning their conceptual approach, and two concerning the methods and thus the analytical approach used:

(1) First, previous studies have mainly been conducted as individual studies which simply picked out a subfield or subdimension of the topic, such as the health effects of air pollution (see outcomes of the ELAPSE-project, for example Strak et al. 2021), without any overall umbrella link to environmental health. This is unfortunate because such an approach neglects the multidimensionality of environmental health including both physical and mental health, which is why deriving sophisticated conclusions and policy recommendations from different angles to the one examined is difficult (Chukwuma 1998, Dutta et al. 2022). Different angles are important because the associations of environmental living conditions and health can appear differently between environmental domains, social groups, health outcomes, space, or time.

(2) Second, because most previous studies were conducted by public health researchers or epidemiologists, an interdisciplinary approach incorporating the holism of existing theories is missing (Marsili 2016). The field would profit from the inclusion of the social sciences owing to their knowledge of social and other inequalities and their understanding of social and other health mechanisms from an individual or group life course perspective. Although practical interdisciplinary approaches to environmental health are rare, there is an increasing interest in involving geographers and social scientists in environmental health research (Andrews et al. 2012, Brown 2013, Pebley 1998).

(3) Third, they did not apply a multi-level approach and neglected spatial patterns in the associations, despite space being an important cornerstone of environmental health. However, exploring spatial patterns carries with it two challenges, which have barely been addressed by previous spatial research in the field (de Vogli et al. 2011, Mazidi & Speakman 2017. See Cobb et al. 2015 for a systematic literature review):

a) Spatial units and their characteristics are spatially correlated, which is a key concept in geography and based on Tobler's first law that "everything is related to everything else, but near things are more related than distant things" (Tobler 1970).
b) Associations can appear spatially unequal, which is why local differences in the estimates should also be considered by research (Elliott & Wartenberg 2004).

(4) Fourth, they did not explore the temporal pathways linking environmental living conditions to health. A temporal perspective to environmental living conditions and health is essential to disentangle pathways for three reasons:

c) The cross-sectional study designs do not allow the introduction of a potential "causal" time order between exposure (environmental living conditions) and outcome (health) (see Schüle & Bolte 2015 for a review). This could lead to positive health selection of the specific living environment, for instance that people with better health would move to healthier living environments and people with worse health would move to unhealthier living environments (Diez-Roux 2004, Jokela 2014).
d) Changes in environmental living conditions over time and their effects on health cannot be observed, which makes it difficult to derive suitable policy recommendations – it remains unclear how improved or deteriorated environments affect population health (Craig et al. 2012).
e) Changes in health over time cannot be observed, which is why it is not possible to distinguish between shorter and longer-term effects to better derive time-dependent dose-response relationships and to derive interventions (Altshuler 1981, Hill 1965).

The shortcomings in the previous literature on the health consequences of environmental living conditions listed above are unfortunate because existing theories and their societal relevance already suggest that avoiding these shortcomings is relevant. A detailed under-

standing of this is essential to develop appropriate policy interventions to combat the increased disease burden caused by unhealthy living environments. That is the starting point for this thesis.

1.5 Characteristics of this thesis

This section summarizes the key characteristics of the approach, data, and methods used for this thesis. This thesis used four different health data sources for a set of different European countries, and the data are either located at the spatial or individual level. Various statistical techniques from demography, public health, epidemiology, economy, and geography were applied, including panel regression techniques (e.g. fixed effects panel regressions and generalized estimating equations), causal pathways analysis (e.g. structural equation modeling), and spatial analysis techniques (e.g. spatial lag of X modeling and geographically weighted regressions). This is explained in more detail in the following.

1.5.1 General approach and sub-objectives

The overall objective of this thesis is to empirically assess how environmental living conditions are linked to physical and mental health among European adults in the twenty-first century. The conceptual approach of this thesis has two novelties.

(1) The first novel aspect of this thesis is that it is based on a more holistic approach to environmental health. For that purpose, this thesis brigaded different existing theories suitable for analyzing environmental health into one overall theoretical framework (see 1.3). Accordingly, it integrates the multidimensionality of environmental living conditions by considering the built environment, the natural environment, the economic environment, and the local community environment, and considers physical and mental health outcomes.

(2) The second novel aspect of this thesis is that it applies an interdisciplinary approach at the intersection between demography, public health, epidemiology, economy, and geography under a single umbrella. This approach is interdisciplinary because it unites theory, data, and methods from different disciplines, specifically:

a) demography because it analyzes populations by using statistical methods, thereby concentrating on the distribution of health and morbidity over space and time (= population dynamics). Environmental living conditions can accordingly be understood as determinants as such that influence population dynamics by affecting population health and aging over a life course or across space (Rees 2020).
b) public health because it analyzes the risks, prevention, and promotion potential of different environmental living conditions, and tries to derive population-based policy recommendations for better public health (Cabaj et al. 2019).
c) epidemiology because it involves analyzing the patterns of how environmental living conditions relate to health outcomes (Chiolero 2019).
d) economy because it incorporates health consequences arising from macro-economic downturns (Kernick 2003). This was done by combining health and living environment data with economic data.
e) geography because it considers spatial patterns and regional differences by distinguishing between regional subtypes or using small-area data and applying spatial econometric modeling (Dummer 2008).

The analytical approach of this thesis integrates two further novel aspects. The analyses can be subsumed under an overall confirmatory approach dividing between two sub-approaches: **(3)** the spatial approach and **(4)** the pathway approach.

(3) The spatial approach refers to the use of geographic information and spatial analysis techniques to understand and address health issues. This is important because the theoretical and empirical background showed that environmental health can only be adequately understood from a spatial perspective. This approach includes mapping the distribution of disease, identifying spatial patterns and associations in health outcomes, and evaluating the impact of the wider and immediate environments. The spatial approach is valuable to informing policymakers and guiding the development of targeted interventions in specific regions (Elliott et al. 2006).

(4) The pathway approach refers to the understanding and addressing of complex health issues by identifying and analyzing the various factors and mechanisms that contribute to better or worse health, or the development and progression of disease. It focuses on environmental living conditions, but also considers determinants located at the individual level. That is essential because the pathway approach claims to model environment–

health associations from a causal perspective by considering important time-invariant and time-dependent characteristics from the individual level (*controlling for third variables)* and introducing a meaningful time order between exposure and the endogenous variables throughout (*timing*). The pathway approach thereby also includes moderating and mediating pathways and a temporal perspective on the topic including shorter and longer-term health effects. The pathway approach is useful for developing interventions that target specific mechanisms to prevent or mitigate the harmful effects of environmental conditions or to promote their beneficial effects on health (Bind 2019, Rothman & Greenland 2005).

In accordance with the two analytical approaches, this thesis has two sub-objectives:

1. To assess spatial patterns in the association between environmental living conditions and health (*Study I, and* partially *Study IV*);
2. To assess temporal and other pathways between environmental living conditions and health (*Studies II, III, and IV*).

1.5.2 Data and settings

This study is based on recent data from European adults aged 18 or older taken between 1999 and 2017.

The data is located either at an individual or a regional level with a focus on public health, epidemiology, geography, economy, or demography. Data from different sources were usually combined to yield comprehensive databases to obtain more powerful and meaningful findings. Depending on the underlying aims, the specific data for the individual studies were carefully selected concerning their suitability, which is why the countries, time periods, age ranges, and the levels covered differ between the studies.

Different designs, data sources, and statistical methods were used and combined to answer this thesis's research question. However, all the studies presented in this thesis can be classified as observational studies. The following briefly summarizes the data, locations, and statistical methods used in each study. **Table 4** presents an overview of the main characteristics of the data and methods used. *Study I* used health data at a small spatial level and used a cross-sectional ecological design, while *Studies II, III,* and *IV* are based on individual-level data and used prospective cohort designs. *Studies I, III,* and *IV*

linked the health data with additional data sources on external data on exposure to environmental living conditions. That is the case for *Study I*, which considered healthy and unhealthy food accessibility data from Statistics Netherlands; for *Study III*, which considered estimated long-term data on ambient air pollution from the European ELAPSE-project; and for *Study IV*, that linked economic data on the yearly unemployment rates and quarterly GDPs from the OECD to calculate country-specific durations for the Great Recession. Two studies observed the Netherlands (*Studies I* and *III*), one Germany (*Study II*), and one a set of different European countries, namely Austria, Belgium, Denmark, France, Germany, Italy, Spain, Sweden, and Switzerland (*Study IV*).

Table 4. Overview of the data and methods used for this thesis

No. study (Chapter)	Title	Approach	Data	Setting	Design	Methods
I (Chapter 2)	*The association of unhealthy and healthy food store accessibility with obesity prevalence among adults in the Netherlands: A spatial analysis*	• Spatial approach	• Statistics Netherlands (CBS) • National Institute for Public Health and the Environment (RIVM)	• Netherlands • 2,836 neighborhoods (aggregated data for 457,153 individuals) • Age 19+	• Spatial analysis • Cross-sectional (2016)	• Mapping • Moran's' I • Spatial lag of X models • Geographically-weighted regression
II (Chapter 3)	*Effects of changes in living environment on physical health: a prospective German cohort study of non-movers*	• Pathway approach	• Socioeconomic Panel (SOEP)	• Germany • 4,601 individual non-movers • Age 18+	• Individual-level • Household-level • Longitudinal, prospective (1999–2014)	• Linear regression (OLS) • Generalized estimating equations (GEE)
III (Chapter 4)	*Long-term exposure to fine particulate matter, lung function and cognitive performance: A prospective Dutch cohort study on the underlying routes*	• Pathway approach	• ELAPSE ($PM_{2.5,}$ black carbon) • LifeLines Cohort Study & Biobank	• Northern Netherlands • 49,705 individuals • Age 18+	• Individual-level • Longitudinal, prospective (2006–2015)	• Structural equation modeling (one outcome model + one mediator model)
IV (Chapter 5)	*The short- and long-term effects of the Great Recession on late-life depression in Europe: The role of area deprivation*	• Pathway approach • Partially spatial approach	• Country-specific quarterly nominal gross domestic product from OECD and yearly unemployment rates • SHARE – Survey of Health, Ageing and Retirement in Europe	• Austria, Belgium, Denmark, France, Germany, Italy, Spain, Sweden, Switzerland • 6,866 individuals • Age 50+	• Individual-level • Longitudinal, prospective (2004–2017)	• Age-standardization of prevalent or incident cases over time • Fixed effects panel regressions • Multi-level regressions

1.5.2.1 The spatial approach

The spatial approach was applied for *Study I*, which is based on health data from the Dutch National Institute for Public Health and the Environment (RIVM). Although *Study IV* partially integrated a spatial approach in distinguishing between urban and rural regional subtypes, its main approach was subsumed by the pathway approach.

Study I

This sub-study used a spatial approach. Cross-sectional data at the neighborhood level (six-digit zip code) for the Netherlands in 2016 were used: 2,836 of 2,960 neighborhoods were included, 785 of which were neighborhoods defined as urban (≥ 1500 addresses per km^2), 756 as suburban (500 ≤ 1500 addresses per km^2), and 1,295 as rural (< 500 addresses per km^2).

Average obesity prevalence (%) was the outcome of interest. The obesity data were obtained from small-area estimations from the Dutch National Institute for Public Health and the Environment (RIVM) and are based on 457,153 individuals aged 19 or older from the Dutch Health Monitor 2016. The obesity data were combined with sociodemographic and proximity data from Statistics Netherlands. Accessibility to unhealthy and healthy food was the exposure of interest and measured by the average distance to food retail locations in a neighborhood.

1.5.2.2 The pathway approach

The pathway approach was applied for three different studies: *Study II* based on the German Socio-Economic Panel (SOEP), *Study III* based on the Dutch Lifelines Cohort and Biobank (Lifelines), and *Study IV* based on the Survey of Health, Ageing and Retirement in Europe (SHARE).

Study II

Longitudinal data at the individual and household level from 1999 to 2014 were obtained from the publicly available German Socio-Economic Panel (SOEP). This provides a representative sample of the resident German adult population with the exception of people living in institutions and nursing homes. The final analysis population covered 4601 non-

movers residing in Germany and aged 18 and older at baseline (in 2004, 2006, 2008, and 2010) with a total of 16,076 health observations and 11,475 health changes.
Changing physical health was the outcome of interest and was measured using a composite score at the individual level at both at baseline and over time after baseline. Stable or changing living environmental characteristics (environmental pollution, local infrastructure, and housing conditions) were the exposure of interest and stem from perceptions reported by the heads of households (= household level). Changes in physical health are the difference between a following health score and the baseline health score.

Study III
Longitudinal data at the individual level from 2006 to 2015 were obtained from the Dutch Lifelines Biobank and Cohort Study and combined with data on fine particulate matter from the ELAPSE project. The analysis population included 49,705 participants aged 18 or older with a total of 33,788 observations. Study participants resided in the three Northern Dutch provinces of Drenthe, Groningen, and Friesland – a low-air pollution area. Lifelines combines blood sample data with data from surveys, anthropometry, spirometry, and cognitive screenings.
Cognitive performance measured using the Cogstate Brief Battery (a standardized computerized screening tool) was the outcome of interest. Long-term exposure to fine particulate matter ($PM_{2.5}$, black carbon) was the exposure of interest. Lung function (FEV_1 = forced expiratory volume in 1 second, FVC = forced vital capacity) was the potential mediator of interest.

Study IV
Longitudinal data at the individual and household level from 2004 to 2017 were obtained from the publicly available Survey of Health, Ageing and Retirement in Europe (SHARE). The analysis population included 6,866 participants aged 50 or older from Austria, Belgium, Denmark, France, Germany, Italy, Spain, Sweden, and Switzerland, with a total of 33,788 observations. The SHARE data were combined with country-level data on quarterly nominal gross domestic product from the OECD.
Late-life depression measured by the EURO-D depression scale (a 12-symptom scale) was the outcome of interest. The country-specific duration of the Great Recession was the exposure of interest, while area deprivation (yes – deprived infrastructure; no – non-deprived infrastructure) was the moderator of interest.

1.5.3 Operationalization: subjective versus objective measures

This dissertation used both subjective and objective exposure and outcome measures: two studies applied subjectively measured environmental living conditions and health outcomes (*Studies II and IV*), while the other two used objective measures (*Studies I and III*).

Subjective measures are based on self-reported and perceived conditions, and are partly considered less valid than objective measures, which comprise clinical tests or medical diagnoses (Johnston et al. 2009, Munguía-Izquierdo et al. 2021). Previous studies, however, observed higher validity for subjective environmental living conditions and health measures than for objective measures. Starting with environmental living conditions, we know from previous research that objective and subjective measures both independently predict subjective health with higher importance for health being found for the subjective measures (Duntava et al. 2021, Godhwani et al. 2019, Weden et al. 2008). However, that does not necessarily mean that one kind of measure is a better proxy for the quality of the living environment than the other. One study found that the effect of objective environmental living conditions on subjective health were strongly mediated by the subjective perceptions of the surroundings (Weden et al. 2008). This shows that, in accordance with the salutogenesis health model (Antonovsky 1993), environmental living conditions can only affect subjective health positively or negatively if they are actually considered or perceived positively or negatively. This means that subjectively-measured environmental living conditions are more strongly related to subjective health measures, because individuals are aware of the potential detrimental or beneficial effect of their environments. That is why this thesis combines subjective environmental living conditions with subjective health measures. Conversely, objective conditions were associated with objective measures of health, assuming that objective environmental living conditions can have an unconscious effect on objective health measures. **Table 5** provides an overview of the operationalizations used in the individual studies in this thesis.

Table 5. Overview of the exposure and outcome measures used.

Study	Exposure or moderator	Outcome or mediator	Kind of measure
I	Average distance to health and unhealthy food retail locations (Euclidean distance)	Obesity prevalence (%)	Objective
II	Perceived changed or stable: • local infrastructure • environmental pollution • housing conditions	Physical health – physical component summary (PCS) taken from the 12-item Short-Form Survey	Subjective
III	• Long-term exposure to ambient fine particulate matter at home address	*Outcome* = Cognitive performance: processing speed (Cogstate Brief Battery) *Mediator* = lung function (spirometry)	Objective
IV	*Exposure* = short and long-term effects of the Great Recession (OECD GDP data, country-specific) *Moderator* = perceived environmental living conditions summarized in an area deprivation index (yes/ no)	Late-life depression (Euro-D depression scale), individual feeling of depressive symptoms	Subjective

In sum, previous studies have underlined the theory presented in this thesis that objective and subjective health measures refer to different health dimensions (Kananen et al. 2021, Wuorela et al. 2020). However, they have also shown their interdependency: people with chronic diseases, which would be defined as poorer health according to a pathogenic understanding, can have better subjective quality of life than people without disease (Araújo et al. 2018).

1.5.4 Statistical analysis

This section explains the statistical methods used for both analytical approaches used in this thesis, the spatial approach and the pathway approach.

1.5.4.1 Methods used in the spatial approach

The spatial approach used for this PhD research applies a set of spatial analysis techniques that quantify and consider spatial dependency and autocorrelation. These methods were used for *Study I*.

1) Spatial distributions of access to healthy and unhealthy food and obesity prevalence were mapped across Dutch neighborhoods.
2) A univariate Global Moran's I was calculated for each of the variables used to test for spatial dependency. For this purpose, a spatial weights matrix based on a queen contiguity pattern was calculated including neighborhoods which share a common edge or a common vertex. This weighting matrix was applied to calculate Global Moran's I ranging from -1 (perfect dispersion) to 1 (perfect clustering).
3) To identify regional clusters of high obesity prevalence, a local Moran's I (LISA) was calculated and mapped.
4) Global associations between healthy and unhealthy food accessibility and obesity prevalence were assessed by applying multivariable (linear) Spatial Lag of X models (SLX), controlling for sociodemographic, SES, and lifestyle confounders. The total effects yielded from the SLX approach (TE, contribution of both the immediate and wider food surrounding) were decomposed into a direct effect (DE) and an indirect effect (IE). The direct effect shows the contribution of the immediate local food access conditions (food environment) on the local obesity prevalence, while the indirect effect shows the contribution of the wider food environment from the bordering neighborhoods on the local obesity prevalence (= spatial spillover effect).
5) To estimate local variations in the associations, geographically-weighted regressions (GWR) were estimated. A GWR estimates local parameter values. y_i is the value of the outcome variable (here, obesity prevalence) at each location i with the coordinates (u_i, v_i). The estimates of the parameters were realized using a kernel density estimation, which is a non-parametric way of estimating probability density functions (Brunsdon et al. 1996). The GWR model showing the best fit to the data based on highest R^2 and lowest AIC were chosen (= adaptive kernel with a bisquare kernel function). The results were mapped to show regional hotspots for stronger or weaker associations.

1.5.4.2 Methods used in the pathway approach

The pathway approach used for this thesis applies a set of regression techniques suitable for analyzing health data at the individual level. These methods were used for *Studies II, III, and IV* of this thesis.

Study II

1) Associations between changes in the living environment and in individual characteristics before or up to baseline and health at baseline were estimated using linear regressions (OLS). Robust standard errors by Huber/White were applied owing to heteroscedastic residuals.
2) To model the associations between changes in the living environment and subsequent changes in health over time, generalized estimating equations (GEE) using the identity link function and a normally distributed outcome variable (= changes in physical health score) were performed. By doing so, the model controlled for multiple observations per person taking the autocorrelation of repeated measurements of the same persons into account. The within-person residual covariance matrix was specified by an independent correlation structure based on the quasi-likelihood information criterion (Pan 2001). The GEE model with the best goodness-of-fit was also identified using the quasi-likelihood information criterion. All three living environment variables (local infrastructure, environmental pollution, and housing conditions) were included simultaneously in the models.

Study III

3) Mediation analysis was used to explore mediation pathways between air pollution, lung function, and cognition. For that purpose, linear structural equation models (LSEM) without feedback loops and with robust standard errors by Huber/White were estimated. Exposure and confounders were treated as exogenous variables, and lung function and cognition were regarded as endogenous variables. Two equations were introduced: an outcome equation and a mediator equation. The two equations were simultaneously estimated in the SEM.
4) The total effect was then decomposed into a direct effect and an indirect effect (Gunzler et al. 2013). To determine the statistical significance of the indirect effect we used the delta method/Sobel Test (Sobel 1982).

5) Finally, direct effect proportions and indirect effect proportions were calculated to quantify the relevance of the significant direct effect and indirect effect compared to the total effect.

Study IV

6) The Great Recession was measured as a time-dependent variable. The country-specific durations of the recession were calculated using quarterly GDP and annual unemployment data.
7) Area deprivation was measured as a country-specific z-standardized area deprivation index to consider the different deprivation levels between the countries. A time-constant dummy variable defined whether a person was living in a deprived (values greater than zero) or non-deprived area (values below or equal zero).
8) Crude and age-standardized prevalent and incident cases of late-life depression over time were calculated and visualized.
9) Binary logistic individual fixed-effect models using within-estimators (Woolridge 2010) were estimated to estimate the short and long-term effects of the Great Recession on the risk of late-life depression, and the moderating role of area deprivation in this. The models controlled for time-invariant unobserved characteristics. Hausman tests were performed and confirmed that random-effect models would not deliver consistent estimates.

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2

The association of unhealthy and healthy food accessibility with obesity prevalence among adults in the Netherlands: A spatial analysis

This chapter was published as

Benjamin Aretz, Rafael Costa, Gabriele Doblhammer, Fanny Janssen (2022). The association of unhealthy and healthy food accessibility with obesity prevalence among adults in the Netherlands: A spatial analysis. *SSM – Population Health*. Volume 21.
DOI: https://doi.org/10.1016/j.ssmph.2022.101332.

I. ABSTRACT

Introduction*:* Obesity prevalence has almost tripled in Europe since 1980, and the obesogenic (food) environment is hypothesised to be one of the main drivers. Still, empirical evidence is rare for Europe.

Objective: This ecological study explores spatial patterns of obesity prevalence of adults (aged 19+) in the Netherlands in 2016. It studies, in particular, its global associations with (un)healthy food store accessibility while assessing local differences and evaluating the importance of the immediate versus the wider food surroundings.

Methods: In our ecological study, we used small-area estimated obesity prevalence (adults, aged 19+) from 2,836 neighbourhoods (six-digit postal codes, wijken) and combined this with measures from Statistics Netherlands on accessibility to (unhealthy) fast food and (healthy) fresh food. Spatial lag of X (SLX) models were estimated for the entire Netherlands to explore global associations. Separate models for urban, suburban, and rural neighbourhoods and a geographically weighted regression (GWR) were estimated to explore and visualise local variations in the associations. Total associations from the SLX models were then decomposed to yield contributions of the immediate and wider food surroundings.

Results*:* Regional clusters of high obesity were observed in selected areas in the north-east, the south-west, and south-east. Limited accessibility to unhealthy food was globally associated with lower obesity prevalence, whereas better accessibility to fresh food stores and supermarkets was not. The association regarding worse accessibility to unhealthy food was strongest for urban neighbourhoods, especially for the Randstad region. In urban settings, also better accessibility to fresh food stores proved relevant. The wider food surrounding proved more important than the immediate food surrounding, throughout.

Discussion*:* Public policies addressing obesity might be more effective when reducing the presence of unhealthy food rather than expanding healthy food supply. Moreover, they should focus on urban regions and high obesity clusters, thereby considering wider food surroundings.

Key words

Local food environment, obesity, spatial analysis, spatial lag of X model, geographically weighted regression

II. FULL PAPER

1. INTRODUCTION

Obesity prevalence globally has more than doubled since 1980 (NCD Risk Factor Collaboration 2019) and is a growing public health concern. Within Europe, obesity prevalence has almost tripled since 1980 (World Health Organization 2022). The emergence of obesogenic (food) environments is thought to be one of the main drivers of the rapid increase in obesity prevalence, as postulated by the obesogenic environment theory (Egger & Swinburn 1997, WHO 2022). The World Health Organisation therefore recommends creating a health-promoting environment (WHO 2022). However, empirical evidence on the association between unhealthy and healthy food accessibility and obesity is rare for Europe, and previous research, primarily conducted for the US, has revealed mixed results (Brown et al. 2019, Morales & Berkowith 2016). Knowing about the importance of food accessibility for obesity is essential for developing policy interventions to fight against obesity and its burden.

It is assumed that the obesogenic food environment can affect obesity in two ways, either at the macro level through the food laws and food technology in the country, or at the micro-level through the physical presence of or access to food that can influence people's diets (Egger & Swinburn, 1997). The micro-level food environment in particular is seen as one of the most important risk factors for obesity (Giskes et al. 2011, Lim et al. 2020). That is, easy access to unhealthy food combined with limited access to healthy food may lead to supernutrition, e.g. intake of food with a high proportion of fat and a high energy-density (Swinburn et al. 1999, Swinburn et al.2011).

Previous studies on the association between food environments and obesity — either using individual-level or spatial-level data — have focused on the USA and reveal inconsistent results (see Cobb et al. 2015 for a systematic literature reviews). One cross-sectional study from the US using census tracts data on local food stores and individual-level data on obesity found that the presence of healthy food stores (supermarkets) is related to lower obesity prevalence, and the presence of convenience stores to higher obesity prevalence (Morland et al. 2006). Another cross-sectional study from the US using individual-level data on BMI and GIS-derived data on food proximity found that proximity of fast food and non-fast food restaurants to home or work were not associated with BMI (Jeffery et al. 2006).

However, the previous studies in the US that found these associations did not show that healthy or unhealthy food environments are globally associated with lower or higher obesity/ being overweight (Michimi & Wimberly 2010, Morland et al. 2006, see Cobb et al. 2015 for a review). In fact, important differences were observed between regional subtypes (see Lam et al. 2021 for a systematic literature review). A spatial analysis based on county-level data for the US found a positive association between access to supermarkets and obesity in metropolitan districts and a negative association in non-metropolitan districts (Michimi & Wimberly 2010). People living in disadvantaged neighbourhoods, so called "healthy food deserts", are forced to travel longer distances to reach food environments that offer healthy and fresh foods, compared to people in wealthier neighbourhoods, where grocery stores are easier to reach (Larson et al. 2009). These differences in outcomes by regional subtype could, in fact, also be (part of) the reason why previous studies have revealed mixed results. Most of these studies have focused on global associations in the entire study region instead of (additionally) differing between regional subtypes.

Very little research for European countries has been conducted (Fraser et al. 2012, Mackenbach et al. 2019, Walker et al. 2020); there are hardly any spatial analyses on the relationship between food accessibility and obesity. This is unfortunate, as such analyses may help to support (regional) decision makers in addressing public health concerns and indicating where interventions are most needed. Furthermore, it is not possible to translate the findings for the US directly to the European context due to the significant differences in their spatial structures and population composition (Eurostat 2021, Burleyson 2020) as well as in food laws and regulations. For instance, EU regulations regarding additives in food products are stricter than in the US (Lehto et al. 2017).

This ecological study explores spatial patterns of obesity prevalence of adults (aged 19+) in the Netherlands in 2016, focusing on global associations with (un)healthy food store accessibility while assessing local differences and evaluating the importance of the immediate versus the wider food surroundings.

We formulated three research questions:

1) How is unhealthy and healthy food accessibility associated with obesity prevalence in the Netherlands?

2) How does the association between food accessibility and obesity prevalence vary locally in the Netherlands?
3) How relevant for predicting obesity prevalence is unhealthy and healthy food supply in either the immediate or the wider surrounding of people?

The first two research questions build on the existing research, thereby extending it to a European setting. The third research question represents an additional step compared to most of the previous studies concerning local differences in the association between food accessibility and obesity. This is likely to provide additional evidence on where to focus public policies.

Based on the discussed theoretical and empirical background we formulated these three hypotheses;

Our first hypothesis is that better accessibility to unhealthy food is globally associated with higher obesity prevalence and better accessibility to healthy food with lower obesity prevalence, in line with the obesogenic environment theory.

Our second hypothesis is that food accessibility is more relevant for obesity prevalence in regions characterised by higher degrees of urbanisation in line with the previous studies from the US.

Our third hypothesis is that the direct food surrounding is more important than the wider food surrounding, due to the proximity to people's homes.

2. MATERIAL AND METHODS

2.1 Setting

Our ecological study was based on all adults aged 19 or older living in private households in 2016 in the Netherlands. The spatial units of interest are neighbourhoods (according to a six-digit postal code, *wijken*) which are coherent regions of neighbourhoods without a formal status that are based on characteristics such as age structure, geographical barriers (e.g. busy roads), having similar urban and/or architectural features, or having similar functional, social, or political characteristics (Statistics Netherlands 2017).

All spatial units with valid data on the variables used were included in our analysis. Of the initial 2,960 neighbourhoods, 77 neighbourhoods – most of them small - could not be included in this study due either to missing information in obesity prevalence (n = 30) or to a missing value in any other variable of interest (n = 47). The final study sample covered 2,836 neighbourhoods in total.

We explored spatial patterns for the entire Netherlands and also differentiated between regional subtypes: urban (≥ 1500 addresses per km^2), suburban (500 ≤ 1500 addresses per km^2), and rural neighbourhoods (< 500 addresses per km^2) in line with the definition of Statistics Netherlands (Statistics Netherlands 2022a). This resulted in 785 neighbourhoods defined as urban, 756 as suburban, and 1,295 as rural neighbourhoods. Urban neighbourhoods were more predominant in the west (see Supplementary Figure S1 for the spatial distribution across the Netherlands).

In a sensitivity analysis, we used a different definition of urban and suburban subtypes developed by the OECD (OECD 2019) which were based on functional urban areas (FUA), thereby differing between urban cores (n = 1,007) and commuting zones (n = 1,032).

2.2 Outcome: Obesity data

The adult obesity prevalence data by neighbourhood in 2016 were obtained from the National Institute of Public Health and the Environment (RIVM) website (RIVM 2022a). The data represent estimated small-area proportions of obese (BMI ≥ 30) people and were available every four years. We decided to use the 2016 data instead of the most recent 2020 data because the 2020 data were affected by the COVID-19 pandemic. RIVM calculated small-area estimators for different health and lifestyle determinants across neighbourhoods in the Netherlands in 2016, using individual-level data from the Dutch Health Monitor 2016 collecting data from about 3.5% of the whole Dutch population (n = 457,153, age 19+, RIVM 2022b). This monitor ("De Gezondheidsmonitor") is a national survey database conducted every four years to observe the public health and lifestyle characteristics of Dutch individuals. Small-area estimations are necessary because the number of cases gathered in the Dutch Health Monitor are generally not sufficient to deliver per se valid measures for small-area characteristics. To yield small-area estimations, the RIVM uses generalized structured additive regression (STAR) modelling to carry out parameters via restrictive maximum likelihood (REML). 12 indicators at individual (age,

sex, ethnicity, marital status), household (household type, size, capital, yearly income, income source, and home ownership) and neighbourhood (urbanisation, neighbourhood code) level were used to predict the small area obesity, smoking, and alcohol intake prevalence data for 2016. For further information on the methodology used, see van de Kassteele et al. 2017.

2.3 Exposure: Food environment data

We studied unhealthy and healthy food supply in people's surroundings simultaneously by focusing on accessibility to three different food environment domains, namely 1) fast food stores (including grill/lunch rooms), which were defined as unhealthy food supply, 2) fresh food stores (e.g. vegetable shops, bakeries, health food shops), which were defined as healthy food supply, and 3) supermarkets, which were defined as healthy food supply in accordance with previous studies (Helbich et al. 2017, Michimi & Wimberly 2010). For more detailed definitions of these three food environment domains, see **Supplementary Table S1** showing English translations of the Dutch definitions, or see the original source (Statistics Netherlands 2017). Accessibility is defined here as access to food store locations operationalised by their proximity in a person's surroundings (Downs et al. 2020). Proximity was measured by the average Euclidean distance to the next food facilities in 2016 and reflects the average distance between a resident's address and the nearest food store locations in a neighbourhood.

2.4 Confounding variables: Sociodemographic, SES, and lifestyle data

We combined the obesity and food environment data at neighbourhood level additionally with socioeconomic and lifestyle data. As socioeconomic determinants, obtained from Statistics Netherlands (Statistics Netherlands 2022b), we included sex (male inhabitants as a percentage), age (people aged 19 to 44 as a percentage, people aged 45 to 64 as a percentage, people aged 65 or older as a percentage), population density (number of people per km^2), migration status (non-western immigrants as a percentage), unemployment (social welfare recipients as a percentage), and income (yearly income per inhabitant * 1,000 Euros).

Lifestyle factors covered low alcohol consumption (percentage of those drinking not more than one glass of alcohol per day) and smoking (percentage of current smokers). Like the obesity prevalence data, these lifestyle data stem from the small-area estimations from

the National Institute of Public Health and the Environment (RIVM 2022c, van de Kassteele et al. 2017).

2.5 Methods

We linked the neighbourhood-level data obtained from the different sources by their unique six-digit postal codes.

As an explorative pre-analysis, univariate Global Moran's I was calculated for each of the variables used to test for spatial dependency. The spatial weights matrix used assumed a queen contiguity pattern, that is neighbourhoods share a common edge or a common vertex Wij.

Subsequently, this weighting matrix was used to calculate Global Moran's I ranging from -1 (perfect dispersion) to 1 (perfect clustering):

$$I_x = \left(\frac{n}{\sum_i \sum_j W_{ij}}\right) * \left(\frac{\sum_i \sum_j W_{ij}(x_i-\bar{x})(x_j-\bar{x})}{\sum_i (x_i-\bar{x})^2}\right) \quad \text{(i)}$$

where i and j index the neighborhoods, $\bar{x}$ is the mean value x of the variable of interest, and W_{ij} is the weight matrix.

We then mapped the spatial distribution of obesity prevalence across Dutch neighbourhoods in 2016 and visualised regional clusters of high obesity prevalence based on a local indicator of spatial association (LISA), which was done using local Moran's I:

$$I_i = \frac{x_i-\bar{x}}{S_i^2} * \sum_{j=1, j\neq i}^{n} w_{i,j}(x_j - \bar{x}) \quad \text{(ii)}$$

with $S_i^2 = \frac{\sum_{j=1, j\neq i}^{n}(x_j-\bar{x})^2}{n-1}$.

In regard to our first research question on the global associations between (un)healthy food accessibility and obesity prevalence, we estimated multivariable (linear) Spatial Lag of X models (SLX) controlling for sociodemographic, SES, and lifestyle confounders:

$$y = X\beta + WX\theta + \varepsilon \quad \text{(iii)}$$

where Y represents an $N \times 1$ vector consisting of one observation on the dependent variable for every unit in the sample (i $=$ 1, … , N), X denotes an $N \times K$ matrix of explanatory variables associated with the $K \times 1$ parameter vector β, and $\varepsilon = (\varepsilon_1, \dots, \varepsilon_N)^T$ is a vector of independently and identically distributed disturbance terms with zero mean and variance

σ^2. The WX matrix of exogenous spatial lags is a $N \times K$ vector. Consequently, the vector of response parameters θ is just like β of order $K \times 1$. We checked whether the residuals of obesity, the outcome of interest, was distributed normally among the neighbourhoods studied (**Supplementary Figure S2**).

Robust Lagrange Multiplier diagnostics for spatial dependence in linear models showed coherently that spatial econometric models outperform OLS regressions (error dependence $p < 0.001$, spatially lagged dependent variable $p < 0.001$). We further decided that SLX outperformed SEM because spatial Hausman tests ($p < 0.001$) revealed that SEM would deliver biased estimators. We controlled all models for age, e.g. the proportions of people in the age of 45 to 64 and in the age of 65 or older, but not additionally for the proportion of people in the age of 19 to 44 due to multicollinearity and a VIF > 10 when including this variable. Multicollinearity diagnostics revealed then acceptable correlations between the exogenous variables (VIF < 2 for the entire Netherlands, VIF < 5 for urban neighbourhoods, VIF < 3 for suburban neighbourhoods, VIF < 2 for rural neighbourhoods).

In regard to our second research question on the local variations in the associations between food accessibility and obesity, we first estimated an interaction model by regional subtype and food accessibility and for the entire Netherlands, and then stratified for regional subtypes (i.e. urban, suburban, and rural settings). Second, we estimated a geographically weighted regression (GWR). The GWR approach opens up the possibility of showing specific regional effect variations in the entire study region that do not necessarily relate only to global urban-rural differences.

A GWR estimates local parameters values. y_i is the value if the outcome variable (here obesity prevalence) at each location i with the coordinates (u_i, v_i). β_0 represents the local estimated intercept and β_j is the local estimated effect parameter of a variable j.

$$y_i = \beta_0(u_i, v_i) + \sum_{j=1}^{k} \beta_j (u_i, v_i) x_{ij} + \varepsilon_i. \qquad \text{(iv)}$$

The estimations of the parameters were realised by using a kernel density estimation, which is a non-parametric way of estimating probability density functions (Brunsdon et al. 1996). For that purpose, the optimal kernel function and the bandwidth to be used have to be chosen. The bandwidth was then used as a smoothing parameter for the shape of the kernel function. The optimisation of the bandwidth was evaluated based on both

Akaike's Information Criterion (AIC) and Cross Validation (CV). We decided to use the GWR model showing the best fit to the data based on highest R^2 and lowest AIC. This was true for an adaptive kernel with a bisquare kernel function, which showed the best model fit when the AIC method was used. To find out exactly where in the Netherlands a reduction of unhealthy food accessibility would be beneficial to fight obesity, we performed the GWR for unhealthy fast food accessibility solely (but still controlled for all confounding variables). This was necessary because we found a (partially) high local correlation between unhealthy and healthy food accessibility which would bias the GWR estimations.

In regard to our third research question, we further decomposed each of the total effects yielded (TE, contribution of both the immediate and wider food surrounding) from the SLX approach into a direct effect (DE) and an indirect effect (IE). The direct effect shows the contribution of the local food environment on the local obesity prevalence, the indirect effect shows the contribution of the food environment in bordering locations (i.e. neighbourhood) on the local obesity prevalence. This indirect effect is also called spatial spillover effect. The indirect effects in the SLX models (equation iii) are reflected by the parameter estimates θ of the WX variables, and the direct effects by the parameter estimates β of the X variables.

All calculations were conducted on R 4.1.1 (R Core Team 2021) using packages sp, spdep, spatialreg, spgwr.

3. RESULTS

3.1 Descriptive results and mapping: The explorative pre-analyses

The average prevalence of obesity was 14.26% in the entire Netherlands in 2016. Obesity prevalence was slightly higher in urban neighbourhoods (14.61%) compared to suburban (14.19%) and rural (14.09%) settings (**Table 1**).

The average distance to the nearest fresh food store was 1.29 km, which was slightly lower compared to a fast-food store (average 1.39 km) or a supermarket (average 1.52 km). In rural settings, the same pattern was visible (fresh food: 2.0 km, fast food: 2.24 km, supermarket: 2.38 km). In urban and suburban settings, however, the next fast food store was more proximate (urban: 0.50 km, suburban: 0.84 km) than the next fresh food store (urban: 0.51 km, suburban: 0.87 km) or supermarket (urban: 0.63, suburban: 0.97 km).

All variables used were significantly spatially correlated (Moran's I with $p < 0.001$) showing that proximal neighbourhoods were more similar in the characteristics observed than more distal neighbourhoods. This was true for the entire Netherlands, but also when we stratified into urban, suburban, and rural regional subtypes (**Table 1**).

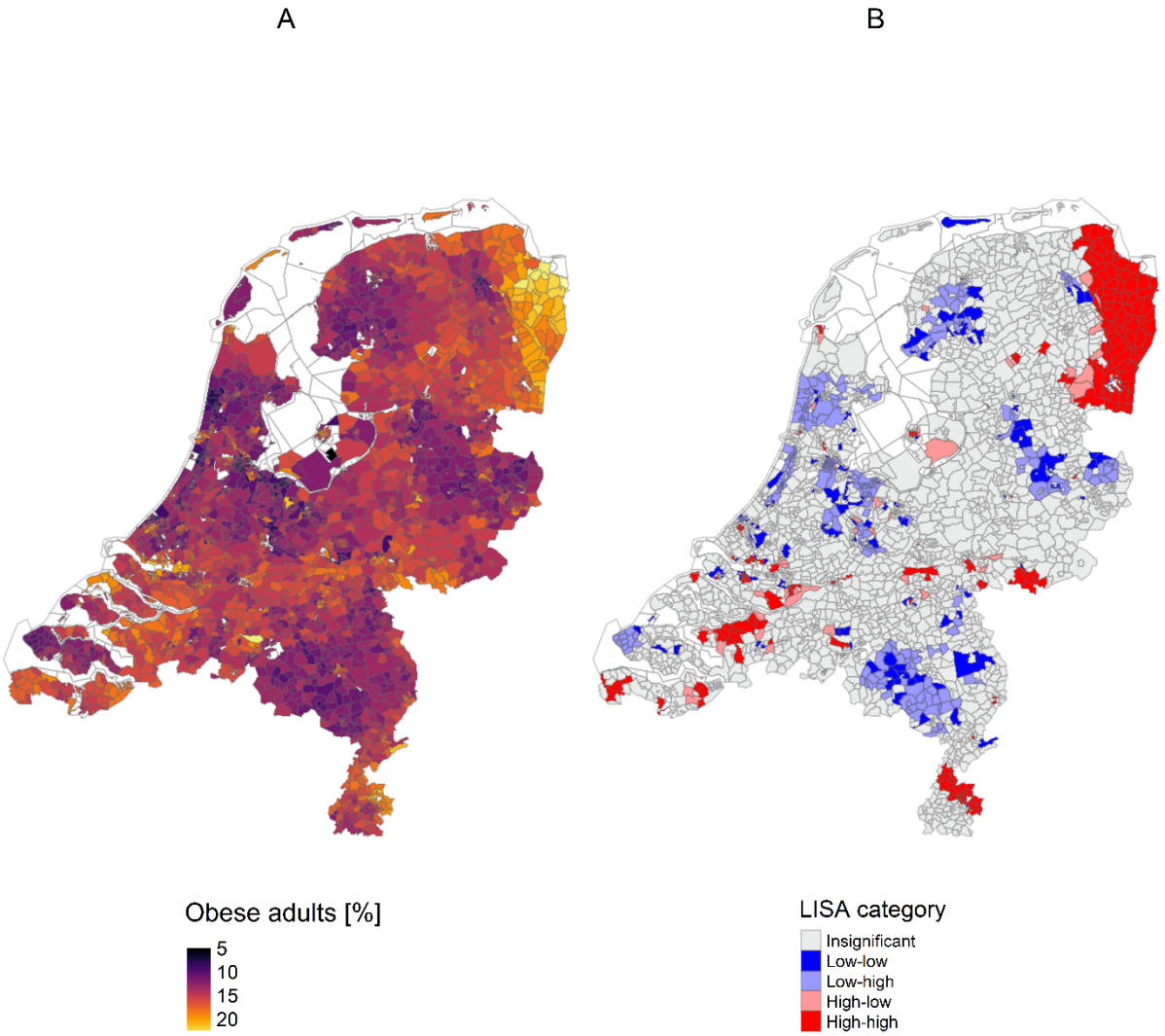
Table 1. Descriptive statistics and spatial correlations of the variables used for the neighbourhoods: study participants ages 19 and older in the Netherlands in 2016

Variable	**Descriptive statistics**				**Univariate Moran's I**			
Regional (sub-) type	Netherlands	Urban	Suburban	Rural	Netherlands	Urban	Suburban	Rural
Number of neighbourhoods	n = 2,836	n = 785	n = 756	n = 1,295	n = 2,836	n = 785	n = 756	n = 1,295
Outcome								
Obesity prevalence, % (sd)	14.26 (2.71)	14.61 (3.23)	14.19 (2.47)	14.09 (2.48)	0.60**	0.67**	0.51**	0.68**
Food environment								
Average distance to next **fast food** store [km], % (sd)	1.39 (1.37)	0.50 (0.26)	0.84 (0.38)	2.24 (1.61)	0.35**	0.30**	0.12**	0.25**
Average distance to next **fresh food** store [km], % (sd)	1.29 (1.24)	0.51 (0.27)	0.87 (0.39)	2.00 (1.50)	0.27**	0.32**	0.08*	0.18**
Average distance to next **supermarket** [km], % (sd)	1.52 (1.36)	0.63 (0.26)	0.97 (0.41)	2.38 (1.59)	0.27**	0.31**	0.07*	0.15**
Confounders								
Males, % (sd)	50.27 (2.10)	49.22 (2.26)	49.80 (1.82)	51.17 (1.74)	0.17**	0.16**	0.06	0.09**
People ages 19 to 44, % (sd)	28.49 (6.31)	33.50 (7.99)	27.93 (4.91)	25.79 (3.44)	0.51**	0.49**	0.14**	0.26**
People ages 45 to 64, % (sd)	30.29 (4.81)	26.76 (4.40)	29.96 (4.18)	32.62 (3.97)	0.34**	0.35**	0.11**	0.24**
People ages 65 and older, % (sd)	19.09 (5.97)	18.23 (7.50)	19.60 (6.30)	19.31 (4.52)	0.27**	0.28**	0.20**	0.30**
Population density, no. of inhabitants/ km^2 (sd)	2082.53 (3388.40)	5749.22 (4371.99)	1492.02 (1635.99)	204.60 (349.85)	0.68**	0.55**	0.26**	< 0.01
Non-western immigrants, % (sd)	7.14 (9.65)	16.67 (12.69)	6.13 (5.57)	1.95 (2.38)	0.61**	0.53**	0.16**	0.10**
Social welfare recipients, % (sd)	3.33 (1.30)	3.50 (0.84)	3.39 (1.15)	3.19 (1.57)	0.21**	0.43**	0.23**	0.24**
Yearly net income [*1,000 Euros], % (sd)	25.04 (4.80)	25.31 (6.28)	25.64 (4.28)	24.52 (3.90)	0.47**	0.51**	0.40**	0.48**
Low alcohol consumption, % (sd)	39.36 (6.43)	42.40 (7.83)	39.52 (5.26)	37.41 (5.28)	0.62**	0.62**	0.54**	0.76**
Smokers, % (sd)	20.17 (4.15)	23.81 (4.64)	19.17 (3.05)	18.55 (2.83)	0.58**	0.54**	0.29**	0.62**

Notes: No, number; sd, standard deviation; km, kilometre(s). Significant results are denoted with *p < 0.05, **p < 0.01.

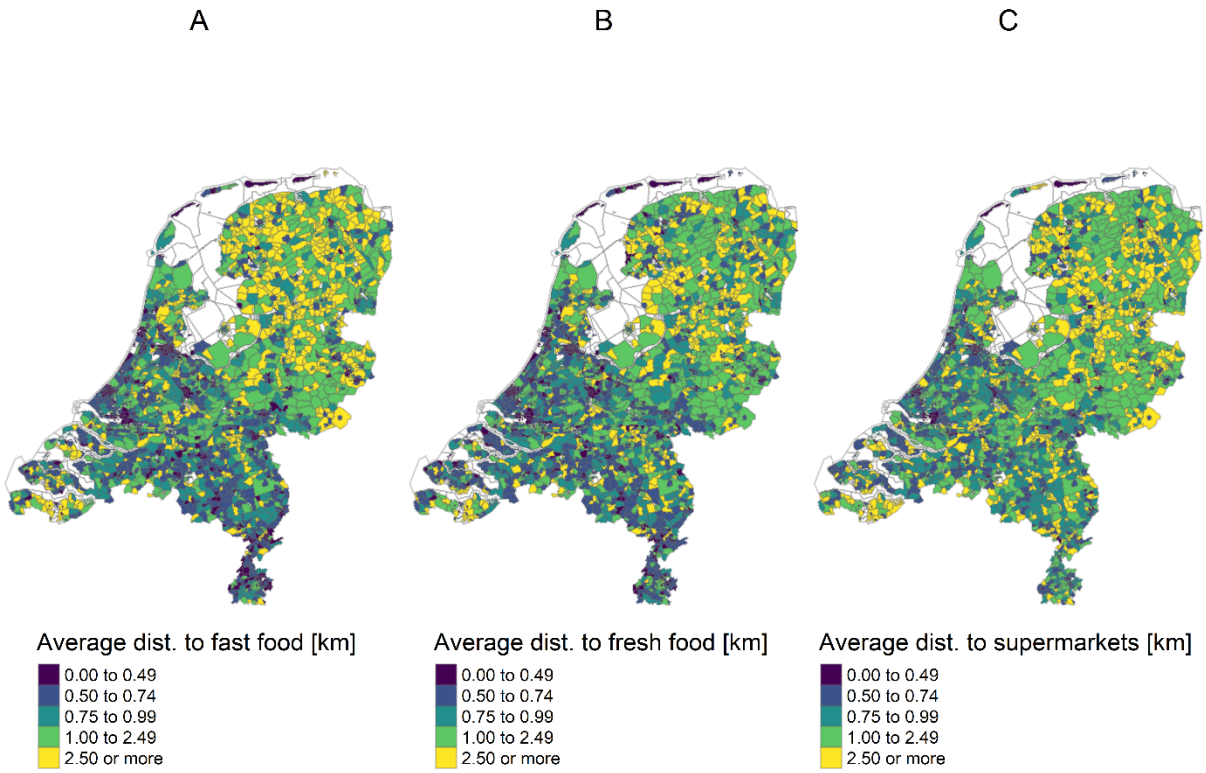
Higher obesity was observed in the north-east, south-west, and south-east of the country (**Figure 1, A**), which were shown to be statistically significant clusters of high obesity (evaluated by local Moran's I/ LISA map) (**Figure 1, B**).

Figure 1. The spatial distribution of obesity prevalence and significant obesity clusters in the Netherlands in 2016



Accessibility to both unhealthy and healthy food was generally better in the south of the Netherlands than in the north (**Figure 2, A, B, C**).

Figure 2. The spatial distribution of unhealthy and healthy food accessibility in the Netherlands in 2016



Notes: No, number; km, kilometre(s); %, percentage. Accessibility to fast food stores defined as unhealthy food (A); accessibility to fresh food stores defined as healthy food (B); accessibility to supermarkets defined as healthy food (C). Neighbourhoods that are not part of the analysis sample are coloured white.

3.2 The global associations between unhealthy and healthy food accessibility and obesity prevalence in the Netherlands in 2016

In regard to our first research question, our spatial lag X model for the entire Netherlands showed that worse fast food accessibility (i.e. increase in the average distance to the next fast food store) was associated with lower obesity prevalence (TE: -0.15, p = 0.02) (**Table 2, Entire Netherlands**). For the average distance to the next fresh food store and supermarkets we found no significant global associations for the entire Netherlands. We further found in the multivariate model that obesity prevalence was higher in suburban (TE: +1.03, p < 0.01), but not in rural neighbourhoods, compared to urban neighbourhoods.

3.3 Regional variations in the association between food accessibility and obesity: Regional subtype analyses

In regard to our second research question focusing on differences in the association between food accessibility and obesity between regional subtypes, we first introduced interaction terms among all of the three food accessibility variables (fast food, fresh food, supermarkets) and the regional subtype variable in the model for the entire Netherlands (we will only refer to the total effects (TE)). This interaction model revealed significant interactions for fast food accessibility and rural neighbourhoods (TE: +2.73, $p < 0.01$, ref. urban), and fresh food accessibility and suburban (TE: -4.65, $p < 0.01$, ref. urban) as well as rural neighbourhoods (-5.03, $p < 0.01$, ref. urban) (**Supplementary Table S2**).

We then estimated Spatial Lag X models stratified by the regional subtype, meaning separately for urban, suburban, and rural neighbourhoods. The stratified models showed that worse accessibility to fast food (i.e. an increase in the average distance to the next fast food store) was related to lower obesity prevalence in urban (TE: -2.94, $p < 0.01$), suburban (TE: -0.65, $p = 0.03$), and rural neighbourhoods (TE: -0.12, $p = 0.04$) with the highest effect size for urban settings (**Table 2, Urban & Suburban & Rural**).

For fresh food accessibility, we found statistically significant associations only for urban neighbourhoods. That is to say, worse accessibility to the next fresh food store (i.e. increase in the average distance to the store) was associated with higher obesity prevalence (TE: +3.71, $p < 0.01$).

For supermarket accessibility, no statistically significant associations were observed in the SLX models.

We estimated a sensitivity analysis using a different definition of urban and suburban subtypes developed by the OECD (OECD 2019), which were based on functional urban areas (FUA). This model confirmed the results from our main models (**Supplementary Table S3**), but showed worse model performances (R^2 FUA urban cores = 0.7803 < R^2 Main urban = 0.8182; R^2 FUA commuting zone = 0.6351 < R^2 Main suburban = 0.6964).

Table 2. The associations between unhealthy and healthy food accessibility and obesity prevalence at the ecological level among study participants ages 19 and older in the Netherlands in 2016: results from Spatial Lag of X models

	Netherlands			**Urban**			**Suburban**			**Rural**		
Variable	DE[b]	IE[c]	TE[d]	DE[b]	IE[c]	TE[d]	DE[b]	IE[c]	TE[d]	DE[b]	IE[c]	TE[d]
Food environment												
Average distance to next **fast food** store, km	-0.02	-0.13*	-0.15*	-0.98**	-1.94**	-2.94**	-0.09	-0.56*	-0.65*	-0.04	-0.08	-0.12*
Average distance to next **fresh food** store, km	-0.07	0.10	0.03	1.17**	2.54**	3.71**	-0.36	0.23	-0.13	-0.08	0.07	-0.01
Average distance to next **supermarket**, km	-0.02	0.13	0.11	-0.21	0.17	-0.05	-0.27	0.36	0.09	0.02	0.03	0.04
Confounders												
Males, %	-0.10**	-0.04	-0.14**	-0.08**	<0.01	-0.08*	-0.05	-0.04	-0.09*	-0.03	-0.08**	-0.12**
People ages 19 to 44, % (ref.)	-	-	-	-	-	-	-	-	-	-	-	-
People ages 45 to 64, %	0.12**	0.14**	0.26**	0.15**	0.07**	0.22**	0.12**	0.05*	0.16**	0.07**	0.13**	0.21**
People ages 65 and older, %	0.06**	0.02	0.07**	0.05**	0.04*	0.09**	0.03**	0.01	0.04**	0.08**	0.01	0.09**
Population density[a], no. of inhabitants/ km^2	-	-	-	-1.14	-4.82	-5.97**	4.04	-1.08	2.97	43.81**	-27.65	16.17
Non-western immigrants, %	< 0.01	-0.03*	-0.03**	-0.02	0.02	<0.01	0.01	-0.03	-0.02	-0.04	-0.09	-0.12**

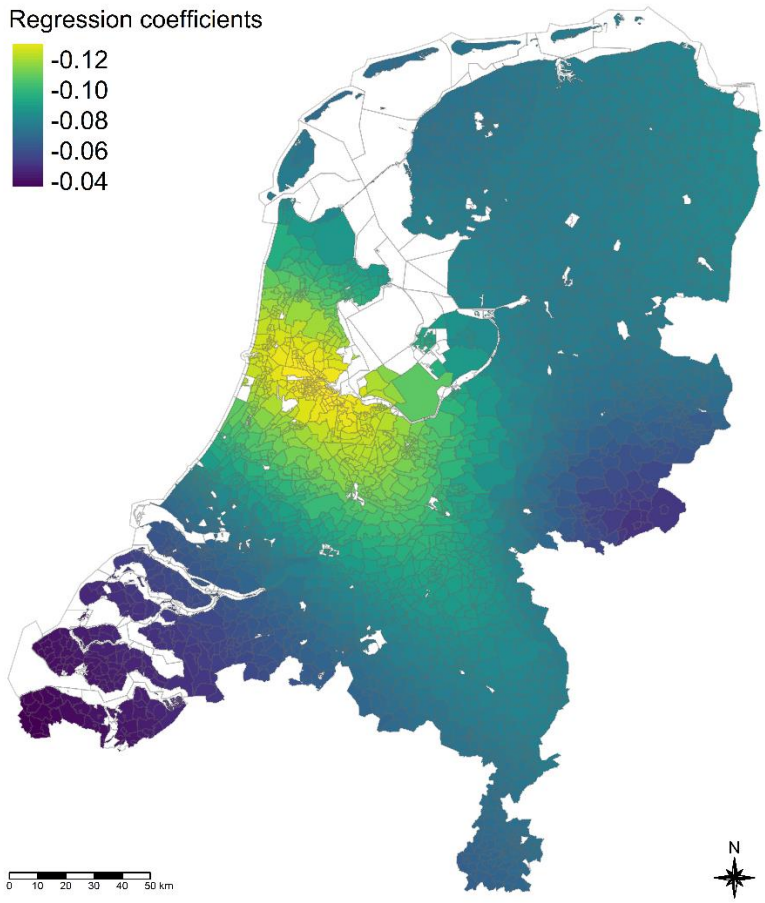
Social welfare recipients, %	0.22**	0.10*	0.32**	0.43**	0.30**	0.73**	0.24**	-0.08	0.17*	0.14**	0.13*	0.26**
Yearly net income [*1,000 Euros]	-0.10**	-0.11**	-0.21**	-0.10**	-0.05**	-0.15**	-0.19**	-0.06**	-0.25**	-0.09**	-0.06*	-0.15**
Low alcohol consumption, %	0.18**	0.02	0.20**	0.24**	-0.05**	0.19**	0.14**	0.02	0.16**	0.12**	0.06**	0.18**
Smokers, %	0.28**	-0.02	0.26**	0.20**	-0.02	0.18**	0.22**	0.09**	0.31**	0.45**	-0.06	0.39**
Regional subtype, ref. Urban												
Suburban	0.26*	0.77**	1.03**									
Rural	0.36*	-0.10	0.25									
R^2	*0.6796*			*0.8182*			*0.6964*			*0.5983*		

Notes: No, number; sd, standard deviation; km, kilometre(s). Significant results are denoted with *p < 0.05, **p < 0.01. The models were controlled for sex, age, population density or regional subtype, migration status, unemployment, income, alcohol consumption, and smoking. [a] Point estimators ×10-5. [b] DE = direct effect, which is the contribution of the local food environment on the local obesity prevalence (immediate food surrounding). [c] IE = indirect effect, which is the contribution of the food environment in bordering locations on the local obesity prevalence (wider food surrounding). [d] TE = total effect, which is the sum of the direct and indirect effect and the total contribution of the food environment.

3.4 Visualisation of local differences in the association between unhealthy food accessibility and obesity prevalence across the Netherlands in 2016

In regard to our second research question and our interest in visualising local differences in food accessibility-obesity associations, we also performed a geographically weighted regression revealing local variations across the entire Netherlands. The GWR was performed for fast food accessibility and not for the other food accessibility variables due to the importance of fast food accessibility found in the global associations (Spatial Lag of X models).

Figure 3. The spatial variations in the associations between fast food accessibility and obesity prevalence in the Netherlands in 2016 (geographically weighted regression)



Notes: The map shows the regression coefficients for fast food accessibility (measured in average distance to the next fast food store) on obesity prevalence (in %) across the Netherlands. Coefficients were estimated by a geographically weighted regression (GWR) model using a bisquare weighting function and an adaptive bandwidth evaluated by using Akaike's Information Criterion (AIC). Neighbourhoods that are not part of the analysis sample are coloured white. The model was controlled for sex, age, regional subtype, migration status, unemployment, income, alcohol consumption, and smoking.

Also, our GWR analysis did indeed show important local effect variations of unhealthy food accessibility on obesity prevalence in 2016 (**Figure 3**). That is, stronger relationships (coloured yellow and bright green, β: -0.12 to -0.10) were observed in the Randstad — a conurbation in the central-western Netherlands consisting mainly of the four largest Dutch cities (Amsterdam, Rotterdam, The Hague, and Utrecht) and one of the largest metropolitan regions in Europe. The strongest relationships were seen around the metropolitan region of Amsterdam (yellow). The weakest relationships were observed for the south-west around the region of Zeeland (β: -0.06 to -0.04), that is mainly characterized by rural neighbourhoods. Model performance was good (Global R^2 = 0.6760), but slightly worse than the Spatial Lag of X model for the entire Netherlands and unhealthy food (R^2 = 0.6817, **Supplementary Table S4, Entire Netherlands**).

3.5 The decomposition of global and local associations between food accessibility and obesity

In regard to our third research question and our interest in the contributions of the immediate versus the wider food environment in the food accessibility-obesity associations, we decomposed each of the total associations into a direct effect (DE, immediate food surrounding) and an indirect effect (IE, wider food surrounding).

The decomposition showed that for the entire Netherlands and unhealthy fast food, the contribution of the wider food surrounding was more important (IE: -0.13, $p < 0.01$, 87% of the TE) than the contribution of the non-significant immediate food surrounding (-0.02, $p = 0.671$, 13% of the TE). (**Table 2, Entire Netherlands**)

For the regional subtypes, we found that the wider food surrounding was more important than the immediate food surrounding throughout. Significant contributions were found for fast food accessibility in urban (IE: - 1.94, $p < 0.01$, 66% of the TE) and suburban (IE: -0.59, $p = 0.032$, 83% of the TE) but not in rural settings. For fresh food accessibility, we found a significant contribution of the wider food surrounding in urban settings only (IE: + 2.54, $p < 0.01$, 69% of the TE). (**Table 2, Urban & Suburban**)

4. DISCUSSION

4.1 Key findings

Regarding the geographic distribution of obesity prevalence in the Netherlands in 2016, our results show that obesity prevalence was slightly higher in urban neighbourhoods (14.61%) compared to suburban (14.19%) and rural (14.09%) settings. In the univariate analysis, regional clusters of high obesity were observed in selected areas in the north-east, south-west, and south-east of the country, which are characterised by lower population density and mainly suburban and rural neighbourhoods. When we controlled for food accessibility, socio-demographic and socio-economic determinants, obesity prevalence proved significantly higher in suburban than in urban or rural neighbourhoods. This illustrates that the clusters of obesity prevalence we observed are also the regions that perform less regarding socio-economic development, and exhibit a higher extent of ageing.

Regarding the nationwide association of obesity prevalence with (un)healthy food store accessibility, we observed that worse accessibility to unhealthy food was globally associated with lower obesity prevalence in the entire Netherlands, but there were no associations for healthy food and supermarket accessibility.

Regarding the local differences in the food accessibility-obesity associations, we found that worse accessibility to unhealthy food was associated with lower obesity prevalence in urban, suburban, and rural neighbourhoods taken separately, but this seems to be more important for urban and suburban than for rural neighbourhoods. Better accessibility to fresh food stores was only relevant for obesity in urban settings. Again, no associations were found for supermarket accessibility. Interesting variations across the entire Netherlands were visualised, and the associations were strongest in the Randstad, one of the largest metropolitan regions in Europe.

Regarding the contribution of the immediate versus wider food surrounding, we found for the entire Netherlands and the regional subtypes that the contributions of the wider food surrounding (= food environment in bordering neighbourhoods) on obesity were more important than the contributions of the immediate food surrounding (= food environment in the same neighbourhood).

In line with previous research, this study found for the confounding variables that higher prevalence of obesity is associated with a higher share of males, middle age, unemployment, lower income, higher alcohol consumption, and smoking.

4.2 Discussion of our findings

Our finding that food accessibility is relevant for obesity (*research question 1*) has already been shown in previous studies conducted for the US, which used either BMI (Chen et al.2019) or obesity (Huang 2021, Mazidi et al. 2017, Michimi & Wimberly) as outcomes. Our results indicate that this association – and the underlying theory of an obesogenic environment - might be important for European countries as well, as illustrated by the case of the Netherlands.

In line with the obesogenic environment theory, we found that unhealthy fast food was more relevant than healthy fresh food. One explanation for this finding could be that if people have to decide to buy convenience food, they use the option with the lowest (relative) time costs (Probst et al. 2006, Pucher & Renne 2005). Unhealthy fast food is often ready-to-eat so that the effort required to prepare meals is eliminated. If (convenient) healthy fresh food is not easy to reach, people could switch to other, potentially unhealthier food sources in the closer surroundings. This explanation is supported by our finding that better accessibility to unhealthy food was associated with higher obesity (but not better healthy food accessibility to lower obesity prevalence) also in rural neighbourhoods, although healthy fresh food is, on average, more proximate there.

Another interesting finding of our study was that accessibility to supermarkets, which were defined as locations offering healthy food in accordance with previous research (Michimi & Wimberly, Helbich et al. 2017), was not spatially related to obesity prevalence. This could be explained by the fact that supermarkets do not offer a clear assortment of unhealthy or healthy foods, but rather a mixture of both. For the Netherlands, however, a previous study on the proportion of healthy and unhealthy foods promoted in the country came to the result that the majority, about 70%, of promotions were categorised as unhealthy food in Dutch supermarkets (Ravensbergen et al. 2015). On the other hand, the intention to go to a supermarket is likely to be more deliberate with a view for healthy food consumption, compared to fast food restaurants. Second, we know for fast food restaurants that the main motivation to go there is to have a quick, spontaneous meal nearby (Rydell et al. 2008). Because we did not measure which products people really bought and

eat, but only measured their accessibility, we were not able to disentangle the factual mechanisms explaining this finding. More research is needed here to explore and combine shopping motivations and the real nutrition behaviours of people shopping in supermarkets.

Our finding that unhealthy fast food accessibility and healthy fresh food accessibility play a more important role in regions with a higher degree of urbanity (*research question 2*) — which was also found for the USA (Michimi & Wimberly 2010) — might be explained by the existence of a certain threshold distance, beyond which the distance to healthy food locations no longer impacts obesity, as postulated by Michimi & Wimberly, 2010. Rural residents have to travel longer distances when they do their daily activities (Probst et al. 2006, Pucher & Renne 2005), which means that their relative (time) costs weigh less heavy when they want to reach an appropriate food location, especially when cars have to be used for transportation (Zijlstra et al. 2022). Our findings are in line with previous results for the US which — by using census data from 2006 at the county level — found relationships between healthy food accessibility and adult obesity prevalence for metropolitan (urban) regions, but not for non-metropolitan (rural) regions (Michimi & Wimberly 2010). Compared to the previous research for the US, our study yielded further evidence of the importance of a distinction between regional subtypes when studying the associations between food accessibility and obesity. This was underlined by both approaches used in this paper, namely the multivariate global regression approach (Spatial Lag of X model) and by the local regression approach (geographically weighted regression). Taking the findings from both approaches together, we can conclude that for the Netherlands especially the risk of obesity for inhabitants living in the Randstad could be most affected by easy access to unhealthy food. There is an expected increase in the next decades in urban population in Europe (Pineda et al. 2018) and the Netherlands (Statistics Netherlands 2019), which calls for special attention to food environment risks in such high-urbanicity regions.

Another interesting finding of our study was that the indirect effects (i.e. wider food environment) contributed more to the total effects compared to the direct effects (i.e. immediate food environment), and this was true for the healthy as well as the unhealthy food environments and independent of the regional subtype (*research question 3*). The food environment (both healthy and unhealthy) in bordering neighbourhoods may therefore be more important for developing obesity than the food environment in people's direct,

immediate surroundings. This is in line with a study for the US, which showed that the average distance between the food establishments and homes was 2.6 miles and only 34% of the food establishments people went to were in participants neighbourhood census tract (Liu et al. 2015). One pathway explaining this finding could be that residential areas are normally further away from commercial areas, where food locations are more present. This would indicate that people usually travel across administrative borders to buy most of their daily food. Furthermore, most people do not work in the same neighbourhood in which they live in. More than 20% of Europeans commute at least 90 minutes daily (SD Worx 2018). The Netherlands Environmental Assessment Agency found that Dutch commute on average 19 kilometres per day (Netherlands Environmental Assessment Agency 2020). This would explain why people have to necessarily travel between neighbourhoods in their daily lives, and may then purchase food on their way home.

Another explanation for the relevance of the indirect effects could lie in the existence and usage of delivery services and outlets in the wider surroundings of people, so people could buy food easily from a larger radius. A previous Dutch study found that between 2004 and 2018 a remarkable increase in delivery outlets was observed (Pinho et al. 2020). Of note, delivered (fast) food is primarily classified as unhealthy food (Partridge et al. 2020).

Finally, a possible explanation for the importance of the wider food surrounding could simply lie in the small area units we used (neighbourhood level).

In sum, we argue that our findings based on data for 2016 are suitable to derive appropriate policy implications for the post-Covid era in the Netherlands. General patterns and differences in the food landscapes between urban, suburban, and rural settings were already existent in the Netherlands in 2016 (Pinho et al. 2020) and additional descriptive results showed that, from 2016 to 2019, there were just slight changes in the accessibility to the different food locations for the entire Netherlands, but also for urban, suburban, and rural settings (results not shown). Pinho et al. (2020) observed for example a small increase in the availability of fast food restaurants from 2004 to 2018. If this trend has continued until today, the associations between unhealthy food and obesity observed in our study could be even stronger, which is why our results are still of public and policy relevance.

4.3 Evaluation of data and methods

The added value of our study lies in the following three aspects:

First, we have distinguished different regional subtypes in order to consider structural urban-suburban-rural differences contributing to varying associations between food accessibility and obesity (see Lam et al. 2021). Second, we have use spatial econometric modelling, which was possible due to the ecological design of our study. This has rarely been used in previous research (see the studies using non-spatial econometric regression models: de Vogli et al. 2011, Mazidi & Speakman 2017), so that it has been difficult to derive policy interventions where they are most needed. Third, our study integrates both unhealthy and healthy food accessibility, considering that different kinds of food locations may stand in a competitive relationship when people buy food (Mason et al. 2013, Walker et al. 2020).

However, our study is not without limitations.

First, obesity and the lifestyle confounders used all stem from small-area estimations conducted by the RIVM (RIVM 2022, van de Kassteele et al. 2017). This was done because the small sample size of the health survey requires the use of small-area estimations in order to reach a valid outcome. Even when the data are based on estimations, they come from an extensive individual-level data source covering 457,153 Dutch adults. Validity analyses showed good model performance for the small-area estimation models (van de Kassteele et al. 2017).

Second, we used obesity prevalence as an outcome instead of a more continuous measure such as (metric) weight or BMI. Exploring the effects of food environment on weight or BMI may draw a more differentiated picture of both the regional differences in excessive weight and the dose-response-relationship. However, at small area levels, these data are generally not available, and would result in additional difficulties in obtaining robust values at the small area level.

Third, we decided to take the definitions for unhealthy and healthy food from Statistics Netherlands because no other data were available to measure food environments more adequately. Although this makes the definitions specific for the Dutch context, it is difficult to compare the results to other countries, which may use different definitions of unhealthy fast food and healthy fresh food.

Fourth, our study used the average distance to nearest food locations as an indicator to measure the extent to which people have access to unhealthy or healthy food. This, however, does not imply that people indeed purchase (and eat) food from these food locations. Additionally, we do not know how long people are exposed to the food environmental characteristics measured in 2016 due to the cross-sectional design and missing information on the duration of residence. A previous longitudinal study in the Netherlands found that, over 18 months, an increase of the number of grocery stores was associated with a decrease in BMI, while an increase in the number of fast-food restaurants was associated with an increase in BMI (Acciai et al. 2022). This suggests that already shorter exposure durations can change the factual nutrition behaviour and subsequently people's BMI or risk of obesity. We tried to integrate this by introducing a time lag between the independent variables (most from 2015) and the dependent variable (from 2016). This lagged model confirmed our main results (Supplementary Table S5).

Future studies could try to regard the exposure time, differ between accessibility and actual access, exploring whether better accessibility to unhealthy food does indeed lead to an increase in unhealthy food consumption. Currently such data, when available, tend to be used purely for individual level studies. We recommend using these data for ecological studies as well, because they can answer different questions. Individual-level studies could investigate the lagged association between food environmental characteristics and obesity by using longitudinal data to gain insights into how long it takes until (changes) in the food environment lead to changes in BMI and the risk of obesity.

4.4 Conclusion

The findings of our ecological study for the Netherlands suggest that Dutch public health policies and urban planners should focus more on reducing unhealthy food supply than on expanding healthy food supply when they aim to reduce obesity prevalence.

Attention is especially demanded in urban areas of the Netherlands and specifically in the Randstad region, which have the strongest associations between unhealthy fast food accessibility and obesity prevalence, but also in the suburban and rural areas in the northeast, southwest, and southeast that showed high obesity clusters, which are linked to their socio-demographic and socio-economic situation.

The larger importance of the wider food surroundings compared to the immediate food surroundings thus calls for a superordinate policy strategy across municipal administrative borders in fighting obesogenic food environments.

Acknowledgements

We thank Statistics Netherlands for providing the data, the GIS centre in Groningen for the support in processing the geodata, and Renée Lüskow for language editing. Special thanks go to Anna-Victoria Holtz, who contributed to the literature review. No conflict of interest to declare.

Highlights

- Evidence on the spatial association of food supply with obesity is rare for Europe.
- Unhealthy & healthy food accessibility are globally related to obesity prevalence.
- There are local differences in the associations between regional subtypes.
- Unhealthy food accessibility proved most important for obesity in urban regions.
- The wider food surrounding is more important than the immediate food surrounding.

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III. SUPPLEMENTARY MATERIAL

Supplementary Table S1. Definitions of the three food environment domains used in accordance with Statistics Netherlands (source: Statistics Netherlands 2017, authors' translation into English)

Food environment domain	Definition
Fast food	Fast food restaurant, grill room/shawarma shop, lunch room, pancake house and ice cream parlour.
Fresh food	Greengrocer, baker, pie shop, coffee/tea shop, delicatessen shop, cheese shop, mini supermarket, nut shop, poulterer, health food shop, butcher's shop, off-licence, fish shop, wine shop, confectionery shop, night shop, frozen food shop.
Supermarkets	Large supermarkets: Shop with several types of daily goods and a minimum area of 150 m^2.

Supplementary Table S2. The associations between unhealthy and healthy food accessibility and obesity prevalence at the ecological level among study participants ages 19 and older in the Netherlands in 2016: results from Spatial Lag of X models including interaction terms for the food accessibility variables and the regional subtype variable

	Netherlands		
Variable	DE[b]	IE[c]	TE[d]
Food environment			
Average distance to next **fast food** store, km (urban)	-0.18	-2.33**	-2.52**
Average distance to next **fresh food** store, km (urban)	1.06**	3.70**	4.76**
Average distance to next **supermarket**, km (urban)	-0.01	0.24	0.23
Confounders			
Males, %	-0.10**	-0.05*	-0.14**
People ages 45 to 64, %	0.12**	0.12**	0.24**
People ages 65 and older, %	0.06**	0.02	0.08**
Population density[a], no. of inhabitants/ km^2	-	-	-
Non-western immigrants, %	<-0.01	-0.02	-0.02**
Social welfare recipients, %	0.21**	0.09*	0.30**
Yearly net income [*1,000 Euros]	-0.10**	-0.09**	-0.20**
Low alcohol consumption, %	0.18**	0.02	0.19**
Smokers, %	0.30**	<0.01	0.30**
Regional subtype, ref. urban			
Suburban	1.29**	1.96**	3.24**
Rural	1.02**	0.84	1.86**
Food environment × regional subtype			
Average distance to next **fast food** store, suburban (ref. urban)	0.16	1.06	1.22
Average distance to next **fast food** store, rural (ref. urban)	0.16	2.25**	2.41**
Average distance to next **fresh food** store, suburban (ref. urban)	-1.18*	-4.00**	-5.18**
Average distance to next **fresh food** store, rural (ref. urban)	-1.14**	-3.62**	-4.76**
Average distance to next **supermarket**, suburban (ref. urban)	-0.39	0.82	0.43
Average distance to next **supermarket**, rural (ref. urban)	<0.01	-0.15	-0.15
R^2		*0.6903*	

Notes: No, number; sd, standard deviation; km, kilometre(s). Significant results are denoted with *p < 0.05, **p < 0.01. [a] Point estimators × 10-5. [b] DE = direct effect, which is the contribution of the local food environment on the local obesity prevalence (immediate food surrounding). [c] IE = indirect effect, which is the contribution of the food environment in bordering locations on the local obesity prevalence (wider food surrounding). [d] TE = total effect, which is the sum of the direct and indirect effect and the total contribution of the food environment.

Supplementary Table S3. Sensitivity analysis based on Spatial Lag of X models (SLX): The associations between unhealthy and healthy food accessibility and obesity prevalence at the ecological level among study participants ages 19 and older in Dutch cities and commuting zones (FUA approach) in 2016

	FUA urban cores			**FUA commuting zones**		
Variable	DE[a]	IE[b]	TE[c]	DE[a]	IE[b]	TE[c]
Food environment						
Distance to next fast food store, km	-0.21	**-0.47***	**-0.07****	-0.04	**-0.22****	**-0.26****
Distance to next fresh food store, km	-0.03	**0.58***	**0.60***	<-0.01	0.07	0.07
Distance to next supermarket, km	-0.04	-0.25	-0.29	-0.06	0.02	-0.05
R^2	*0.7803*			*0.6351*		

Notes: No, number; km, kilometre(s). Significant results are denoted with *p < 0.05, **p < 0.01. The models were controlled for sex, age, population density, migration status, unemployment, income, alcohol consumption, and smoking. [a] DE = direct effect, which is the effect of the local food environment on the local obesity prevalence (immediate food surrounding effect). [b] IE = indirect effect, which is the effect of the food environment in bordering locations on the local obesity prevalence (wider food surrounding). [c] TE = total effect, which is the sum of the direct and indirect effect.

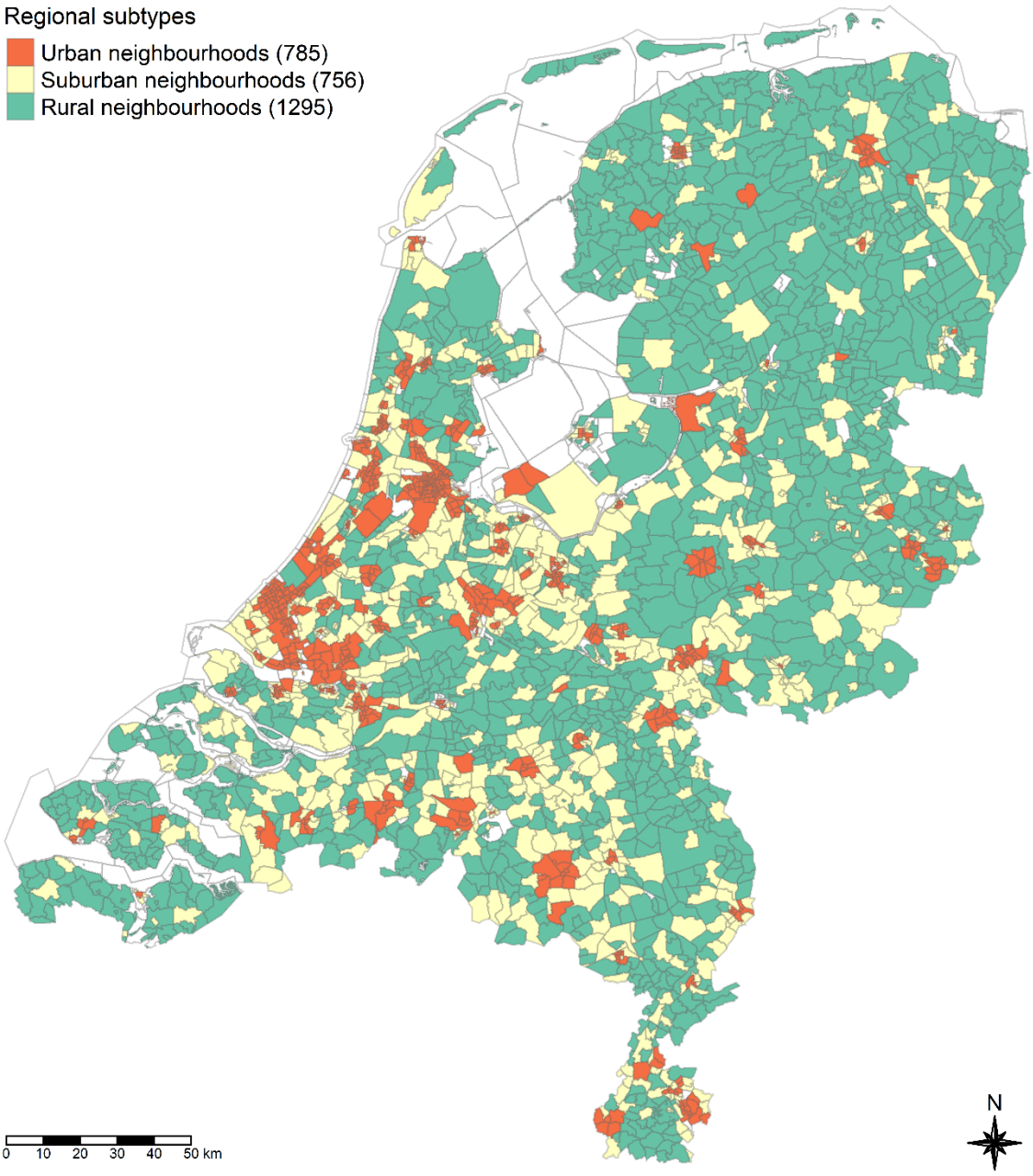
Supplementary Table S5. Lagged Model: The associations between unhealthy and healthy food accessibility in 2015 and obesity prevalence in 2016 at the ecological level among study participants ages 19 and older in the Netherlands: results from Spatial Lag of X models

	Netherlands			**Urban**			**Suburban**			**Rural**		
Variable	DE[b]	IE[c]	TE[d]	DE[b]	IE[c]	TE[d]	DE[b]	IE[c]	TE[d]	DE[b]	IE[c]	TE[d]
Food environment												
Average distance to next **fast food** store, km	-0.05	-0.17**	-0.22**	-0.63	-1.87**	-2.50**	-0.18	-0.68*	-0.86**	-0.08*	-0.15*	-0.23**
Average distance to next **fresh food** store, km	-0.05	0.17*	0.12	0.89*	2.36**	3.25**	-0.31	0.32	0.01	-0.05	0.13	0.08
Average distance to next **supermarket**, km	-0.02	0.10	0.09	-0.47	-0.50	-0.98	-0.11	0.47	0.36	0.02	0.06	0.08
Confounders												
Males, %	-0.08**	-0.09**	-0.17**	-0.06	-0.06	-0.12*	-0.08*	-0.05	-0.13**	-0.02	-0.09**	-0.11**
People ages 19 to 44, %	-	-	-	-	-	-	-	-	-	-	-	-
People ages 45 to 64, %	0.12**	0.15**	0.26**	0.14**	0.06*	0.21**	0.09**	0.04*	0.13**	0.08**	0.11**	0.19**
People ages 65 and older, %	0.05**	<-0.01	0.05**	0.05**	0.01	0.06**	0.02*	<0.01	0.03	0.08**	0.01	0.09**
Population density[a], no. of inhabitants/ km^2	-	-	-	-1.62	-10.54*	-12.17**	4.32	-7.22	-2,90	31.39*	-40,56	-9.16

Non-western immigrants, %	<0.01	-0.04**	-0.04**	<-0.01	<-0.01	-0.01	<0.01	-0.02	-0.02	-0.05*	-0.02	-0.07
Social welfare recipients, %	0.22**	0.13**	0.34**	0.32**	0.31**	0.63**	0.21**	0.08	0.29**	0.13**	0.17**	0.30**
Yearly net income [*1,000 Euros]	-0.10**	-0.08**	-0.18**	-0.13**	<-0.01	-0.13**	-0.16**	-0.04	-0.20**	-0.08**	-0.05*	-0.13**
Low alcohol consumption, %	0.17**	0.04*	0.21**	0.21**	0.02	0.23**	0.14**	0.02	0.16**	0.13**	0.05**	0.18**
Smokers, %	0.28**	0.01	0.29**	0.15**	<0.01	0.16**	0.27**	0.07*	0.34**	0.46**	-0.02	0.44**
Regional subtype, ref. Urban												
Suburban	0.26*	0.82**	1.08**									
Rural	0.35*	0.09	0.44*									
R^2	*0.6591*			*0.7618*			*0.6989*			*0.6111*		

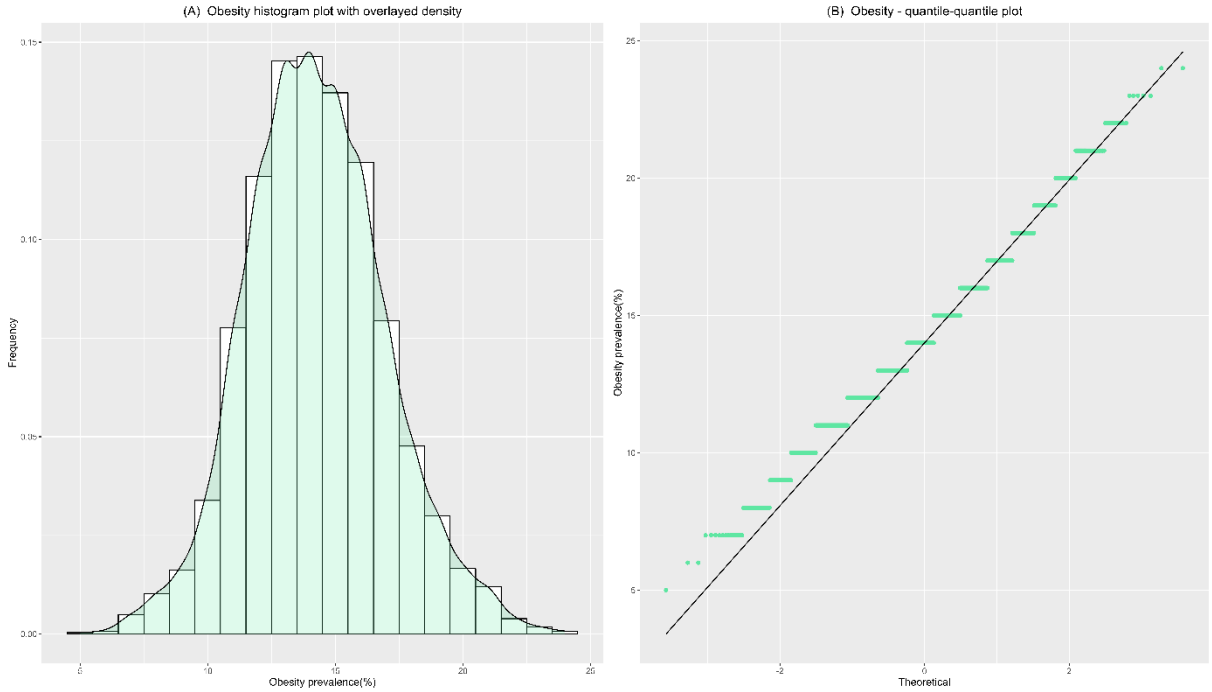
Notes: No, number; sd, standard deviation; km, kilometre(s). Accessibility variables (exposure of interest), sex, age, population density, migration status, unemployment, and income stem from 2015, while obesity (outcome of interest) and the lifestyle determinants (no availability of previous data) stem from 2016. Significant results are denoted with *p < 0.05, **p < 0.01. [a] Point estimators ×10-5. [b] DE = direct effect, which is the contribution of the local food environment on the local obesity prevalence (immediate food surrounding). [c] IE = indirect effect, which is the contribution of the food environment in bordering locations on the local obesity prevalence (wider food surrounding). [d] TE = total effect, which is the sum of the direct and indirect effect and the total contribution of the food environment.

Supplementary Figure S1. The spatial distribution of regional subtypes in the Netherlands in 2016



Notes: Neighbourhoods that are not part of the analysis sample are coloured white.

Supplementary Figure S2. The distribution of obesity prevalence and its residuals



Notes: Histogram of obesity prevalence and its overlaid density (A), quantile-quantile plot for visual testing of normal distributed residuals of obesity prevalence (B).

3

Effects of changes in living environment on physical health: A prospective German cohort study of non-movers

This chapter was published as

Benjamin Aretz, Gabriele Doblhammer, Fanny Janssen (2019). Effects of changes in living environment on physical health: a prospective German cohort study of non-movers. *European Journal of Public Health*. Volume 29. Issue 6.
DOI: https://doi.org/10.1093/eurpub/ckz044.

I. ABSTRACT

Background: Longitudinal studies on associations between changes in living environment and health are few and focus on movers. Next to causal effects, differences in health can, however, result due to residential mobility. The present study explored changes in living environment related to (changes in) physical health among non-movers. Causality was reinforced by a novel study design.

Methods: We obtained longitudinal data on both living environment and physical health covering 4,601 non-movers aged 18+ with 16,076 health observations from the German Socio-Economic Panel (GSOEP) between 1999 and 2014. Changing and stable perceived living environment from three domains (infrastructure, environmental pollution, housing conditions) were included at household level. We performed linear regressions with robust standard errors and generalised estimating equations to predict the Physical Component Summary (PCS) at baseline and changes in PCS over time.

Results: Stable moderate and worst as well as worsened environmental pollution and infrastructure were associated with worse PCS at baseline, as were stable poor and worsened housing conditions. Stable worst infrastructure was associated with negative changes in PCS for both sexes. Men's changes in PCS were more affected by worsened environmental pollution than women's.

Conclusion: A suboptimal living environment has short and long-term negative effects on physical health. Because even short-term changes in the living environment have an immediate influence on an individual's health status and health trajectories, public attention to living environment is essential to fight existing health inequalities.

Key words: changes in living environment, Physical Component Summary, changes in physical health, non-movers, causal inference

II. FULL PAPER

1. INTRODUCTION

Numerous epidemiological studies have found that an advantaged living environment was associated with good health and a disadvantaged living environment with worse health.[1-6]Accordingly, the living environment is an important dimension of public health; it strengthens social and health inequalities.

However, most previous studies on the topic have pursued cross-sectional designs[7] (see Schüle & Bolte for a review) or just used the baseline measurement of living environment characteristics in a longitudinal design[8] and cannot control for social selection[9, 10]. Other studies concentrated only on the movers[3, 4] but those approaches may lead to biased results due to specific individual characteristics that may affect the decision to move (e.g. health, socioeconomic determinants)[11] and they neglect secular changes in living environments of the non-movers.

The few previous longitudinal studies[3, 4, 6] found less evidence supporting the hypothesis of causal environmental effects on people's health, or found only weak evidence for the beneficial effects of advantaged living environments. One study identified lower mortality risks for people living in greener areas[12], but another study detected hardly any positive health effect of moving to a neighbourhood with more green qualities[6].

The unique contribution of our study is that we explored longitudinal associations of changing or stable living environments characteristics related to physical health and most importantly, subsequent health changes among non-movers in Germany. We impose a strict time-order between cause and outcome and control for time-varying individual characteristics. We hypothesised that disadvantaged or worsening living environments are associated with a negative health and health development over time; whereby beneficial or improving living environments may lead to good health and positive changes in physical health.

2. METHODS

2.1 Data and sample

Longitudinal data from 1999 to 2014 were obtained from the publicly available German Socio-Economic Panel (GSOEP), a representative prospective cohort study of German adults[13]. The yearly waves contain, among other information, data on socioeconomic and sociodemographic characteristics at the individual level. Information on the living environment at the household level is available on a five-year basis: 1999, 2004, 2009. Physical health in the form of the Physical Component Summary (PCS) (see outcomes) is available on a two-year basis from 2002 onwards.

The present study used all participants aged 18 and older at baseline. The baseline is defined as the first health measurement of people in the age 18 or older from wave 2004 onwards and took place in the waves 2004, 2006, 2008, 2010 due to the two-year basis of the health data. A minimum of two health measurements and two observations of the living environmental characteristics were required to become part of the analysis population (see Supplementary Figure 3).

The final analysis population covered 4,601 non-movers residing in Germany and aged 18 and older at baseline (in 2004, 2006, 2008, 2010) with a total of 16,076 health observations and 11,475 health changes (from 2004 to 2014). The total number of changes in PCS covers all changes in PCS within a person summed up over all participants. This study was conducted in accordance with all principles embodied in the Declaration of Helsinki.

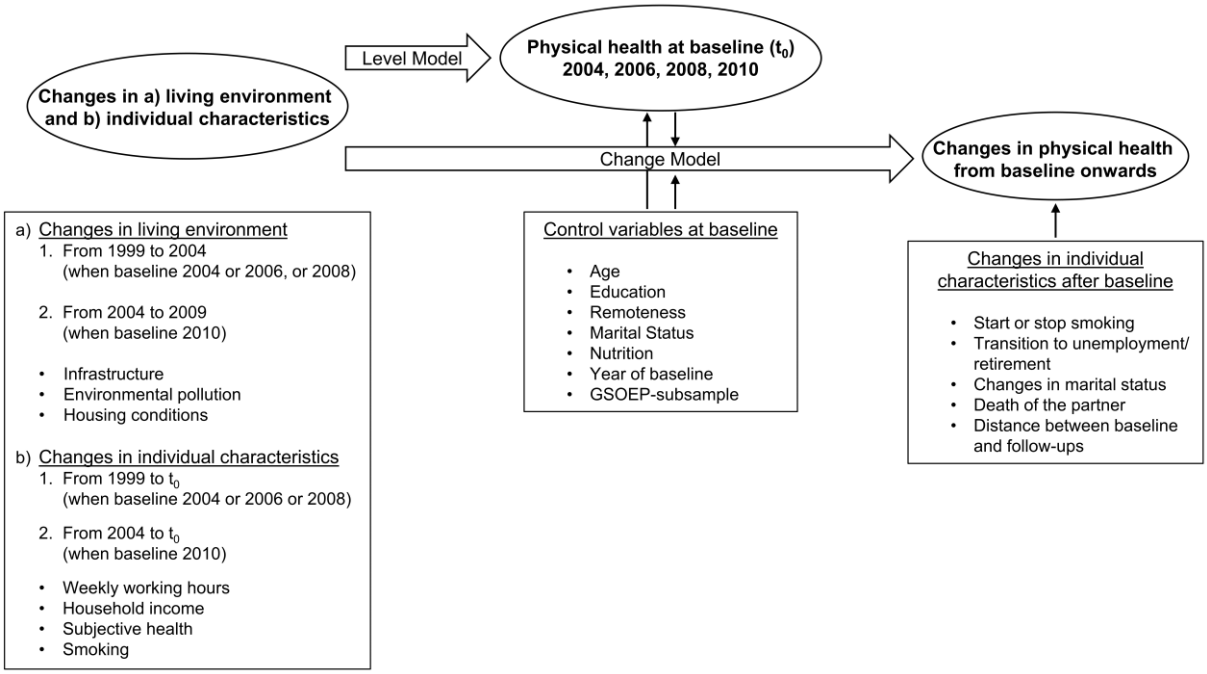
2.2 Study design

We strengthened the causal explanatory power of our findings by using a novel approach including four methodological strategies that reduce the confounding effects by selected migration/health selection into living environments:

a) imposing a strict time order between living environment and physical health to exclude the possibility of reverse causation, b) predicting changes in health over time and not only in regard different health levels, c) including only non-movers, among whom health selection into living environments does not play a role, d) and controlling for important time-invariant and time-varying individual characteristics. We defined two models: the Level Model and the Change Model. In the Level Model, we related the health status at baseline to changes in the environment and in individual characteristics before baseline. In the

Change Model, we explored changes in health from baseline onwards, dependent on changes in the environment before baseline, as well as changes in individual characteristics before and after baseline, and health at baseline (**Figure 1**).

Figure 1. Study design for the analysis of changes in the living environment on physical health among German non-movers aged 18 and above



To ensure that the Change Model does not indicate participants' migration trajectories through relocations in new living environments after baseline, we excluded after baseline movers to avoid potential confounding.

2.3 Measures

2.3.1 Outcomes

Physical health was measured by the Physical Component Summary (PCS), which is one of the two main dimensions of the 12-Item Short Form Survey version 2, invented by the RAND Corporation[14]. PCS is a psychometric tool and consists of six self-reported variables (5-point Likert scale): two on physical functioning, one on general health, one on bodily pain, and two on the role of functioning, which altogether loaded on one principal component, called PCS[15]. The GSOEP reports the PCS as a metric variable (min = 0; max = 100) with higher scores indicating better health. The score was mean-centred to a value of 50, which means that scores lower or higher than 50 indicate worse or better health than the

average in the whole GSOEP sample. For the baseline outcome (n = 4,601), we estimated the reliability of PCS indicating a high internal consistency with a Cronbach's alpha of 0.88.

In the Level Model PCS is the main outcome measure. In the Change Model a change in physical health (Δy_i) from baseline onwards is the main outcome measure. We used the baseline PCS score as a basis to calculate the change scores. A change $\Delta y_i = y_{it} - y_{it_0}$ is the difference between the PCS score from a following valid wave (t) of a subject (i) minus the PCS score of the baseline (t_0). Thus negative scores of Δy indicate individual health deterioration compared to baseline PCS score, a score of zero denotes unchanged health, and positive scores individual health improvements. We used a maximum of three changes in PCS for one individual from baseline onwards to ensure reasonable proximity between measures of living environment and health.

2.3.2 Predictors

We included predictors from two main domains, namely the living environment which is our domain of interest, and individual characteristics which may confound our results. We captured three external dimensions of the living environment, namely infrastructure, environmental pollution and housing conditions, and, distinguished between stable, improved and worsened living environments. Additionally, we added relocation to identify whether changed or stable living environment to identify only participants who did not move. Remoteness, which measured the distance of the people's residence to the next city centre at baseline, served as a control variable. As for the individual characteristics, we identified relevant demographic, socio-economic and lifestyle determinants from the literature covering age, sex, education, weekly working hours, household income, smoking, marital status, death of the partner and subjective health. **Table 1** provides the list of all abovementioned predictors, their full descriptions, the reclassifications, and the final categories. In addition, we accounted for design variables: the year of baseline (at baseline), the GSOEP-subsample (at baseline) which indicates the random sample the participant belongs to[13], and the distance between the PCS follow-up to the baseline.

Table 1. Measures of time-invariant and time-varying living environment and individual characteristics, German Socio-Economic Panel 1999–2014

Time period[a]	Time dimension[b]	Domain	Measure	Description	Reclassification/ Calculation	Final categories
Up to baseline	Time-varying	Living environment	Infrastructure	Accessibility to retail, (social) services and public transport (11 items, 5-point Likert scale, Cronbach's alpha = 0.98, all items loaded on one factor with eigenvalue > 1 estimated by principal component analysis)	Aggregation into an average Likert scale per wave with a minimum of 5 valid items to be included [range, 1-3.96]. Changes greater than one standard deviation between the two measurements were coded as improved or worsened infrastructure. All others were allocated to stable infrastructure by forming the average score of the two measurements and dividing this into tertiles.	Stable best, stable moderate, stable worst, improved, worsened
			Environmental pollution	Disturbances on air pollution, noise pollution and lack of green spaces (5-point Likert scale, Cronbach's alpha = 0.74, all items loaded on one factor with eigenvalue > 1 estimated by principal component analysis)	Aggregation into one summary scale [range, 3- 15]. Changes greater than one standard deviation between the two measurements were coded as improved or worsened pollution. All others were allocated to stable pollution by forming the average score of the two measurements and dividing this into tertiles.	Stable best, stable moderate, stable worst, improved, worsened
			Housing conditions	An item asking for inside conditions of the residential building	Aggregation of the two highest and the two lowest categories Moves of one category were coded as improved or worsened housing conditions.	Stable good, stable in need of renovation, improved, worsened
			Relocation	A question since which year people live in actual residential building	Changes in the year of living in actual residential building	Yes (movers), no (non-movers)

		Individual characteristics	Weekly working hours	An item asking for weekly working hours	Aggregation of persons that were not employed, in vocational training, in military service, community service or worked in a sheltered workshop	Stable full-time employment, stable part-time employment, stable marginal employment, stable not employed/ retired, increased working hours, decreased working hours
			Household income	An item asking for the yearly post-government household income	Dividing into income quintiles	Stable 1. quintile, stable 2. quintile, stable 3. quintile, stable 4. quintile, stable 5. quintile, more income, less income
			Subjective health	A question on how the person rated the own health in general	No reclassification applied	Stable very good, stable good, stable satisfactory, stable poor, stable bad, improved, worsened
			Smoking	A question about whether persons smoke	Aggregation of non-smokers and former smokers	Yes, no, started smoking, stopped smoking
At baseline	Time-invariant	Living environment	Remoteness	An item asking for the distance in kilometres to the next city centre	No reclassification applied	< 10, 10-24, 25-39, 40-59, > 59
		Individual characteristics	Age	A question on when the person was born	Difference between wave year and birth year	Metric variable ranged between 18 and 96
			Sex	An item asking for the sex	No reclassification applied	Male, female
			Education	An item asking for highest school degree	Aggregation of the ISCED-97 scale into three educational groups	Low, middle, high
			Marital status	An item asking for the person's marital status	No reclassification applied	Married, single, widowed, divorced, separated
			Nutrition	A question about to what extent do persons follow a health-conscious diet	No reclassification applied	Very much, much, not so much, not at all
After baseline	Time-varying	Individual characteristics	Unemployment/ retirement	Event/ transition variable (dummy) that measures when persons became unemployed/ retired	Comparison of the previous state at baseline and the state at waves afterwards	Unemployment/ retirement (yes)

Marital status	Event/ transition variables (dummies) that measures when persons experienced changes in marital status	Comparison of the previous state at baseline and the state at waves afterwards	Married, single, widowed, divorced, separated (yes)
Death of the partner	Event/ transition variable (dummy) that measures when persons experienced a death of the partner	Comparison of the previous state at baseline and the state at waves afterwards	Death of the partner (yes)
Start/ stop Smoking	Event/ transition variables (dummies) that measures when persons started or stopped smoking	Comparison of the previous state at baseline and the state at waves afterwards	Start smoking (yes) Stop smoking (yes)

Notes: ISCED-1997, International Standard Classification of Education 1997. [a]: Three different time periods were distinguished, namely the period up to baseline, the period at baseline and the period after baseline. [b]: Time dimension indicates whether the measures have time-invariant or time-varying values.

From both domains, living environment and individual characteristics, the predictors were included either as time-invariant variables (at baseline) or as time-varying ones (up to baseline/ from baseline onwards).

All time-varying living environmental characteristics were calculated by forming the difference of the two available assessments. They were assessed by the key-person of the household (household head) and were then linked to all individuals in the same household.

All time-varying individual characteristics up to baseline were calculated by forming the difference between the measurement of each covariate at the time of first wave of living environment examination (1999 or 2004) and the assessment at baseline of this variable. For both individual and living environmental characteristics, we defined a change (for metric variables equal or greater than one standard deviation) across all waves as improved or worsened living environment and distinguished between stable, improved and worsened characteristics.

In the Change Model, we added some event variables controlling for changes in individual characteristics after baseline. They were represented through several dichotomous variables, with the value one if an event occurred and zero otherwise.

2.4 Statistical analysis

In the Level Model, we examined associations between changes in the living environment and in individual characteristics before or up to baseline and PCS at baseline using linear regressions. We selected the Level Model with the highest adjusted R squared and applied robust standard errors by Huber/White[16, 17] due to heteroscedastic residuals (Breusch-Pagan test: $P < 0.001$). In the Change Model, we performed generalised estimating equations[18, 19] using the identity link function and a normally distributed outcome variable (= changes in PCS score). By doing this, we controlled for multiple observations per person taking the autocorrelation of repeated measurements of the same persons into account. The within-person residual covariance matrix was specified by an independent correlation structure based on the quasi-likelihood information criterion.[20] The Change Model with the best goodness of fit was identified by using the quasi-likelihood information criterion as well. All three living environment variables were included simultaneously in the

Level and the Change Model. All calculations were performed using Stata/IC 12.1, and procedures *reg* and *xtgee*.

3. RESULTS

The analysis sample consisted of 4,601 participants, of whom 2,171 (47.19%) were men and 2,430 (52.81%) women. In this sample, 720 (15.6%) experienced changing infrastructure, 686 (14.91%) differences in environmental pollution, and 873 (19.0%) changes in housing conditions (Supplementary Table 3).

From baseline onwards, we included 16,076 PCS observations which resulted in 11,475 changes in PCS, of which 4,980 were positive health changes and 6,495 negative changes. PCS changes ranged between -46.24 and 40.46, with an average decline of -1.49 over all PCS changes and stronger average declines for women (-1.56) than men (-1.41) over time.

3.1 Level Model

Changes in living environmental characteristics influenced health at baseline (**Table 2**) compared to those experiencing stable best characteristics. People living in environments with worsened infrastructure experienced worse health at baseline (-0.77; 95% CI: -1.53, -0.01). Respondents who experienced worsened environmental pollution had the worst PCS (-1.21; 95% CI: -2.11, -0.31), but stable moderate (-1.04; 95% CI: -1.56, -0.51) and worst pollution (-0.72; 95% CI: -1.29, -0.14) were also related to worse PCS. Living under stable worst (-0.97; 95% CI: -1.54, -0.39) and worsened (-1.00; 95% CI: -1.75, -0.24) housing conditions was connected to lower PCS score at baseline as well.

For all characteristics we found that PCS of people who experienced improved conditions did not differ significantly from those with stable best conditions.

Table 2. Associations between changes in living environment before baseline and Physical Component Summary (PCS) at baseline (Level Model[a]) as well as changes in PCS from baseline onwards (Change Model[b]), German Socio-Economic Panel 1999-2014

Variable	Level Model[c]		Change Model[d]		Change Model with interaction[d]	
	Coeff.	**95% CI**	**Coeff.**	**95% CI**	**Coeff.**	**95% CI**
Infrastructure						
Stable best	Ref.		Ref.			
Stable moderate	-0.44	-1.00, 0.12	-0.14	-0.61, 0.32		
Stable worst	-0.56	-1.13, 0.01	-0.84	-1.33, -0.35		
Improved	-0.03	-0.99, 0.93	-0.49	-1.35, 0.36		
Worsened	-0.77	-1.53, -0.01	-0.37	-1.00, 0.25		
Environmental pollution						
Stable best	Ref.		Ref.		Ref.	
Stable moderate	-1.04	-1.56, -0.51	-0.75	-1.18, -0.31	-0.85	-1.46, -0.25
Stable worst	-0.72	-1.29, -0.14	-0.66	-1.15, -0.17	-0.97	-1.64, -0.31
Improved	0.15	-0.66, 0.96	-0.53	-1.23, 0.17	-0.25	-1.21, 0.71
Worsened	-1.21	-2.11, -0.31	-0.86	-1.64, -0.08	-1.73	-2.86, -0.60
Housing conditions						
Stable good	Ref.		Ref.			
Stable in need of renovation	-0.97	-1.54, -0.39	-0.28	-0.76, 0.20		
Improved	-0.17	-0.86, 0.51	-0.08	-0.64, 0.49		
Worsened	-1.00	-1.75, -0,24	-0.55	-1.17, 0.09		
Environmental pollution x sex						
Stable moderate, women					0.20	-0.65, 1.05

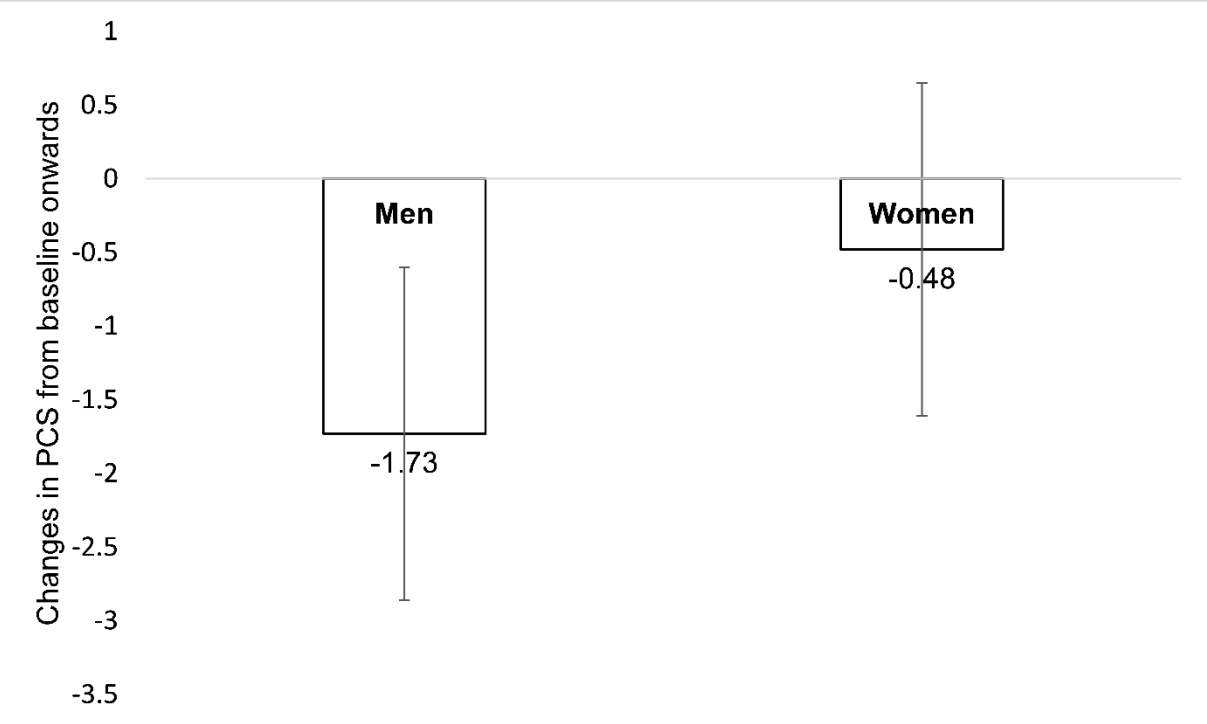
Stable worst, women	0.57	-0.34, 1.48
Improved, women	-0.56	-1.93, 0.81
Worsened, women	1.67	0.15, 3.19
Sex		
Men	Ref.	
Women	-0.42	-1.01, 0.18

Notes: Coeff., coefficient; CI, confidence interval; Ref., reference. [a] Estimated from a linear regression with robust standard errors by Huber/White. [b] Estimated from generalised estimating equations using the identity link function and a normally distributed outcome variable. [c] Model was controlled for time-invariant characteristics at baseline (age, remoteness, education, marital status, nutrition behaviour, year of baseline, GSOEP-subsample) and time-varying characteristics up to baseline (weekly working hours, household income, subjective health, smoking). [d] Model was controlled for all variables from the Level Model (see [c]) and additionally for PCS at baseline as well as time-varying characteristics from baseline onwards (start or stop smoking, transition to unemployment or retirement, changing marital status, death of the partner, distance between follow-ups and baseline in years).

3.2 Change Model

For infrastructure, stable worst (-0.84; 95% CI: -1.33, -0.35) conditions were associated with negative changes in PCS. For environmental pollution, living under stable moderate (-0.75; 95% CI: -1.18, -0.31), worst (-0.66; 95% CI: -1.15, -0.17) and worsened (-0.86; 95% CI: -1.64, -0.08) conditions was connected with negative health changes. Again, changes in the PCS of respondents with improved conditions did not differ significantly from those with stable best conditions. In addition, we found an interaction between environmental pollution and sex in the Change Model, which indicates that men were more prone to worsened pollution (-1.73; 95% CI: -2.86, -0.60) than women (-0.48; 95% CI: -1.54, 0.58) (**Figure 2**, **Table 2**).

Figure 2. Interaction between sex and worsened environmental pollution by using the Change Model (ref. men, stable best environmental pollution)



To strengthen the causality of the Change Model, we only explored non-householders, who did not report perceived living environment by themselves and used the reports of another member of the household. These models were estimated sex-specific (**Supplementary Table 4**). Results did not change and underlined the sex differences concerning environmental pollution.

4. DISCUSSION

4.1 Summary of principal findings

Stable moderate and worst as well as worsened environmental pollution and infrastructure were associated with worse PCS at baseline, which was also true for stable poor and worsened housing conditions. Stable worst infrastructure was associated with negative changes in PCS for both sexes. Men's changes in PCS were more affected by worsened environmental pollution than women's.

4.2 Evaluation of data and methods

Our study has two strengths compared to previous studies in the field. First, we considered both repeated health and living environment assessments, which had only been done by a few previous studies in the field.[7] To the best of our knowledge, this is the first study in the field that has explored changes in health over time among non-movers, and not only health levels, while additionally controlling for time-varying individual characteristics. We controlled for baseline health to make sure that the results were not confounded by poor or good health at baseline.

Second, our results stem from a study design which imposes a strict time dimension between exposure and outcome to avoid reverse causation, and we concentrated on all-time non-movers (before and after baseline) to exclude positive health selection into living environments due to relocation. Investigating movers is problematic because of either unobserved individual characteristics of the movers or the health status as a reason for an individual's decision to move.[3, 4, 12]

Nevertheless, our study does have some limitations. First, the design covers short-term changes in living environment, i.e. changes within five years. Contextual effects may, however, show effects over the entire life course in the form of cumulated exposures or in critical periods.[21] However, for air pollution it has been shown that even short-term deprivations influence people's health.[22, 23] Due to their proximity to physical health it is especially the changes in physical environment, represented in our study by environmental pollution and infrastructure, which might become health-relevant rather rapidly.

Second, perceived living environment in the GSOEP was assessed at the household level. Even if there is a certain degree of autocorrelation between the household members within a household, perceptions can differ among the individual household members.

However, it is unlikely that our gender-specific findings are the result of a gender bias in asking household heads only, as the distribution is 57.16% male and 42.84% female.

Third, the living environment measures used stem from householders' subjective assessments. Using both subjective outcome measures and subjective predictors can lead to potential same source bias.[24, 25]

However, the causal explanation of our findings is strengthened by a series of (sensitivity) analyses, which takes care of some of the limitations and leads to unchanged results. First, we restricted the sample to non-householders who do not suffer from same-source bias (**Supplementary Table 4**). Second, we estimated a Change Model with at least two health changes for each individual assuming that one health change might be potentially unreliable. (**Supplementary Table 5**). Third, we estimated a Level Model including all participants with at least one health measurement at baseline (**Supplementary Figure 3**) to tackle a possible selection bias (**Supplementary Table 6**).

4.3 Interpretation of findings

Our study shows that, in line with our hypotheses, stable suboptimal and declining levels of environmental pollution and infrastructure influence the current level of health as well as changes in health.

On the one hand, this result suggests that suboptimal conditions have short and long-term negative effects; on the other hand, observing a relationship for changes in health strengthens the causal interpretation of our findings. For housing conditions, we did not find relations in the Change Model, suggesting that these conditions have a predominantly short-term effect on physical health only. Furthermore, including the Change Model makes it possible to compare the results of the strategy commonly used in the field (using health levels) and our novel strategy used in this study (using changes in health over time). The commonalities and differences between the findings in the Level Model and the Change Model point to the importance of both approaches. There was also strong evidence for sex-specific relationships because men's changes in physical health were more affected by worsened environmental pollution than women's.

One major mechanism behind the observed short- and long-term relationships might be that beneficial or deprived physical characteristics of living environments influence peo-

ple's bodily conditions and may delay or accelerate ageing processes in addition to individual age-related factors.[26] A previous longitudinal study[27] which focused on changes in the built environment and changes in amount of walking, found that an increasing density of infrastructure promotes more walking. Walking provides better health[28] due to positive effects on physical and cognitive functioning[29]. There is also empirical evidence that higher levels of environmental pollution, e.g. air and noise pollution, are associated with worse physical and mental health. Exposures to fine particles impair the lung function and cause further physical and cognitive decline thereafter.[30] It has also been shown that relocating from high to low polluted areas (or vice versa) is associated with subsequent changes in lung function growth.[31]A high level of noise pollution, especially nocturnal noise exposure, influences people's sleeping behaviour and can thus affect health negatively.[32]

We only found associations for housing conditions in the Level Model. This could be explained by two possible mechanisms: First, housing conditions only have a short-term (and not a long-term) effect on physical health. Second, changes in housing conditions reflect migration trajectories of the past and have no causal effect on physical health. However, another previous study on changes in housing conditions on health gives some support to the hypothesis that changes in housing conditions do indeed have a short-term effect on physical health outcomes.[33]

Our sex specific finding, that worsened environmental pollution and changes in physical health were more negative for men's health developments, is supported by a previous cross-sectional study which found associations between perceived physical problems (air quality, waste disposal) and self-rated health only for men.[34] Three possible explanations for gender differences in the association between changes in the living environment and health are discussed in the literature.[35]

First, men and women perceive or experience their living environments in different ways.[36] In our study, this hypothesis is less applicable, because the questions on the living environment were answered by the key-person of the households only.

Second, the dose of exposure to the different living environmental characteristics differ between men and women, which may also be influenced by different social roles[37]. Results from the German Time Use Survey in 2012/13[38] seem to support this explanation. That is, men spend more time with outside physical activities.

Third, sex differences in the vulnerability for specific (changes in) environmental characteristics, in terms of sensibility of bodies and biological systems,[39] can lead to different health consequences for men than for women.

To summarise, our study reinforces existing theoretical frameworks and shows that not only lifestyle but also the external characteristics of living environment affects people's health.[40]

4.4 Conclusion

The present findings provide strong evidence that people's perceived physical health depends, among other things, on their housing conditions, as well as the quality of the infrastructure and the environmental pollution they experience in their immediate surroundings. A suboptimal living environment has short and long-term negative effects on physical health. Because even short-term changes in the living environment have an immediate influence on an individual's health status and health trajectories, public attention to living environment is essential in fighting existing health inequalities.

Acknowledgments

The authors are grateful to the German Institute for Economic Research for providing the data. Special thanks go to Renée Lüskow, who was responsible for the language editing.

Highlights

- A suboptimal living environment has short and long-term negative effects on physical health among people aged 18+ in Germany.
- Worsening of environmental pollution seems to be more relevant for men's health.
- Due to the methodological approach used, the findings provide strong evidence for causality.
- Even short-term changes in living environment can influence people's physical health.
- Living environment is essential to fighting existing health inequalities.

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III. SUPPLEMENTARY MATERIAL

Supplementary Table 3. Descriptive Statistics of the Analysis Sample (n = 4,373) for All Variables Used, German Socio-Economic Panel 1999-2014

Variable	Men			Women		
	%	No. of obs.	Mean[a] (SD)	%	No. of obs.	Mean[a] (SD)
PCS at baseline	47.04	2,063	45.04 (9.90)	52.96	2,310	44.03 (10.04)
PCS from baseline onwards	47.09	5,840	44.27 (9.96)	52.91	6,563	43.17 (10.11)
Relocation before baseline						
Yes (movers)	13.09	270		13.25	306	
No (non-movers)	86.91	1,793		86.75	2,004	
Age						
50-54	30.05	620		28.10	649	
55-59	13.72	283		13.46	311	
60-64	14.54	300		14.03	324	
65-69	14.20	293		13.68	316	
70-74	14.30	295		12.77	295	
75+	13.18	272		17.97	415	
Infrastructure						
Stable best	30.54	630		28.40	656	
Stable moderate	25.21	520		26.88	621	
Stable worst	28.02	578		27.23	629	
Improved	7.17	148		7.32	169	
Worsened	9.06	187		10.17	235	
Environmental pollution						
Stable best	38.15	787		38.53	890	
Stable moderate	25.74	531		23.98	554	
Stable worst	19.97	412		21.21	490	
Improved	9.11	188		9.78	226	
Worsened	7.03	145		6.49	150	
Housing conditions						
Stable good	62.72	1,294		62.55	1,445	
Stable in need of renovation	16.24	335		15.71	363	
Improved	11.97	247		12.03	278	
Worsened	9.06	187		9.70	224	
Contacts to neighbours						
Stable best	11.63	240		12.25	283	
Stable moderate	33.69	695		33.85	782	
Stable worst	7.95	164		7.01	162	
Improved	23.12	477		23.59	545	
Worsened	23.61	487		23.29	538	
Remoteness						
Residence in the city center	8.00	165		9.48	219	

Distance < 10 kilometers	23.75	490	24.50	566
Distance 10-24 kilometers	26.81	553	26.10	603
Distance 25-39 kilometers	15.80	326	14.50	335
Distance 40-59 kilometers	13.67	282	14.55	336
Distance > 59 kilometers	11.97	247	10.87	251
Education				
Low	11.97	247	24.63	569
Middle	52.21	1,077	51.52	1,190
High	35.82	739	23.85	551
Weekly working hours				
Stable full-time employment	39.55	816	14.20	328
Stable part-time employment	0.78	16	11.04	255
Stable not employed/retired	40.14	828	51.69	1,194
Increased working hours	2.96	61	7.71	178
Decreased working hours	16.58	342	15.37	355
Household income				
Stable 1. quintile	9.36	193	17.88	413
Stable 2. quintile	10.28	212	10.48	242
Stable 3. quintile	9.26	191	8.01	185
Stable 4. quintile	9.21	190	7.45	172
Stable 5. quintile	14.30	295	11.08	256
Increased income	26.81	553	22.68	524
Decreased income	20.79	429	22.42	518
Subjective health				
Stable very good	0.82	17	1.13	26
Stable good	18.27	377	16.10	372
Stable satisfactory	24.24	500	24.72	571
Stable poor	6.88	142	9.00	208
Stable bad	1.65	34	1.99	46
Improved	17.11	353	17.66	408
Worsened	31.02	640	29.39	679
Smoking status				
Yes	21.86	451	16.67	385
No	68.01	1,403	76.84	1,775
Started	7.71	159	4.37	101
Stopped	2.42	50	2.12	49
Marital status				
Married	78.53	1,620	65.24	1,507
Single	5.19	107	4.07	94
Widowed	6.54	135	19.48	450
Divorced	8.00	165	9.61	222
Separated	1.75	36	1.60	37
Nutrition behaviour				
Very much	6.35	131	12.64	292

Much	41.01	846	51.30	1,185
Not so much	46.73	964	33.64	777
Not at all	5.91	122	2.42	56
Events after baseline				
Start smoking	2.96	61	2.86	66
Stop smoking	6.11	126	4.85	112
Unemployment/retirement	12.02	248	11.34	262
Separated	0.82	17	1.00	23
Divorced	0.97	20	1.34	31
Married	3.15	65	2.25	52
Death of the partner	1.79	37	3.85	89

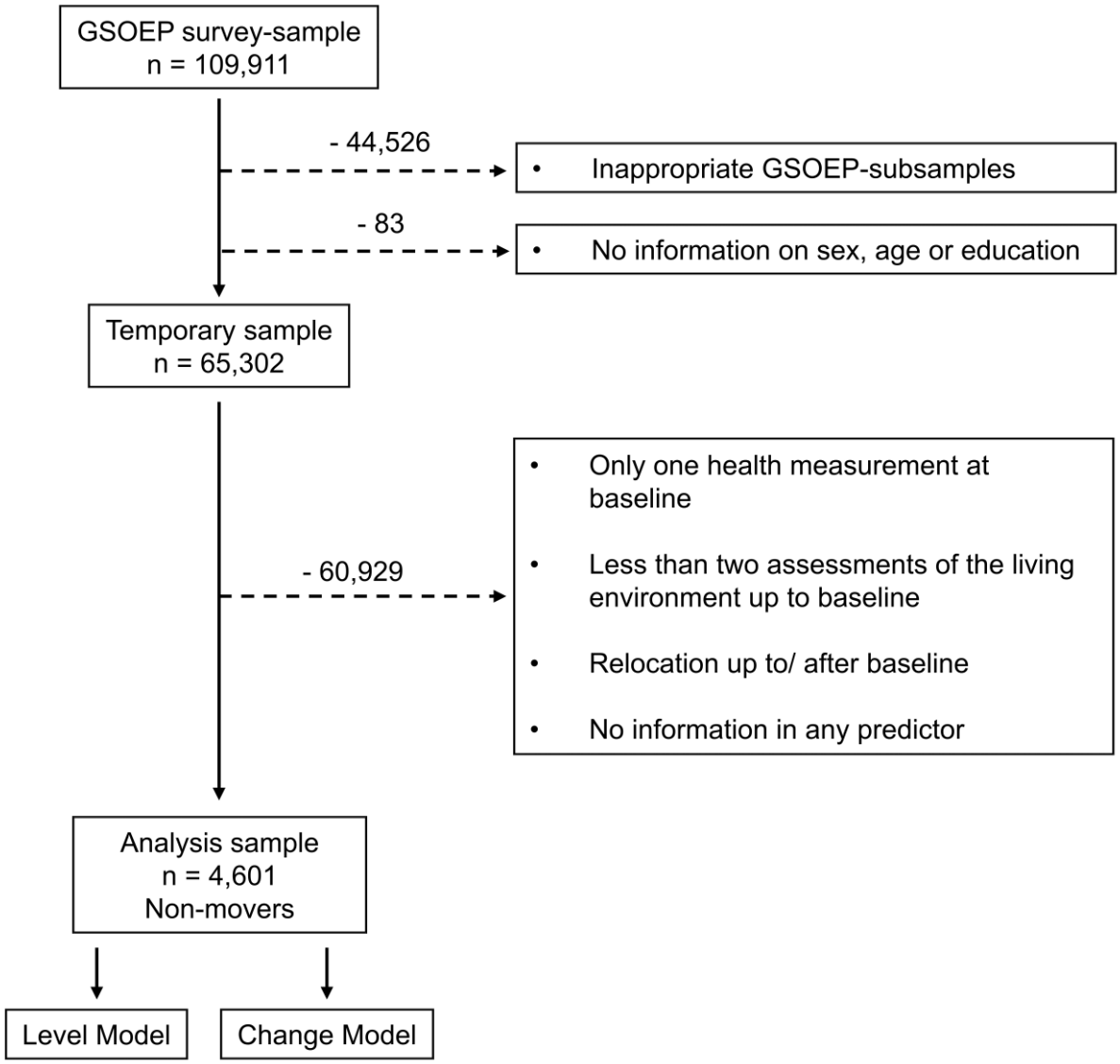
Notes: No., number; Obs., observations; SD, standard deviation; PCS, Physical Component Summary. [a] Mean PCS at baseline was calculated by using the measurement of PCS at baseline and mean PCS from baseline onwards was calculated by using the multiple PCS measurements from baseline onwards.

Supplementary Table 4. Change Model[a] - Associations between infrastructure, environmental pollution, and changes in Physical Component Summary (PCS) for householders and non-householders, German Socio-Economic Panel 1999-2014

Variable	Non-householders[b]			
	Men (n = 555)		Women (n = 1,357)	
	Coeff.	95% CI	Coeff.	95% CI
Infrastructure				
Stable best	Ref.		Ref.	
Stable moderate	0.60	-1.19, 1.30	-0.43	-1.30, 0.44
Stable worst	-1.68	-3.02, -0.35	-0.98	-1.83, -0.13
Improved	-0.50	-2.32, 1.33	0.16	-1.51, 1.83
Worsened	-1.50	-3.22, 0.23	0.06	-1.13, 1.25
Environmental pollution				
Stable best	Ref.			
Stable moderate	-1.57	-2.72, -0.43	-0.77	-1.59, 0.04
Stable worst	-1.27	-2.49, -0.04	-0.59	-1.55, 0.37
Improved	-1.45	-3.44, 0.54	-0.44	-1.72, 0.84
Worsened	-2.84	-4.80, -0,88	0.62	-0.70, 1.94
Housing conditions				
Stable best	Ref.		Ref.	
Stable worst	0.71	-0.62, 2.03	-0.15	-1.04, 0.74
Improved	0.74	-0.85, 2.33	-0.35	-1.48, 0.78
Worsened	1.05	-0.44, 2.53	-0.11	-1.30, 1.08

Notes: Coeff., coefficient; CI, confidence interval; Ref., reference. [a] Estimated from generalised estimating equations using the identity link function and a normally distributed outcome variable.

Supplementary Figure 3. Study flow chart based on the GSOEP data from 1999 to 2014 illustrating the construction of the analysis sample covering 4,601 non-movers aged 18+ in Germany



4

Long-term exposure to fine particulate matter, lung function and cognitive performance: A prospective Dutch cohort study on the underlying routes

This chapter was published as

Benjamin Aretz, Fanny Janssen, Judith M. Vonk, Michael T. Heneka, H. Marike Boezen, Gabriele Doblhammer (2021). Long-term exposure to fine particulate matter, lung function and cognitive performance: A prospective Dutch cohort study on the underlying routes. Environmental Research. Volume 201.
DOI: https://doi.org/10.1016/j.envres.2021.111533

I. ABSTRACT

Background: Exposure to fine particulate matter and black carbon is related to cognitive impairment and poor lung function, but less is known about the routes taken by different types of air pollutants to affect cognition.

Objectives: We tested two possible routes of fine particulate matter ($PM_{2.5}$) and black carbon (BC) in impairing cognition, and evaluated their importance: a direct route over the olfactory nerve or the blood stream, and an indirect route over the lung.

Methods: We used longitudinal observational data for 49,705 people aged 18+ from 2006 to 2015 from the Dutch Lifelines cohort study. By linking current home addresses to air pollution exposure data from ELAPSE in 2010, long-term average exposure to $PM_{2.5}$ and BC was assessed. Lung function was measured by spirometry and Global Initiative (GLI) z-scores of forced expiratory volume in 1s (FEV_1) and forced vital capacity (FVC) were calculated. Cognitive performance was measured by cognitive processing time (CPT) assessed by the Cogstate Brief Battery. Linear structural equation modeling was performed to test direct/indirect associations.

Results: Higher exposure to $PM_{2.5}$ but not BC was related to higher CPT and slower cognitive processing speed [Total Effect $PM_{2.5}$: FEV_1 model = 8.31×10^{-3} (95% CI: 5.71×10^{-3}, 10.91×10^{-3}), FVC model = 8.30×10^{-3} (95% CI: 5.69×10^{-3}, 10.90×10^{-3})]. The direct association of $PM_{2.5}$ constituted more than 97% of the total effect. Mediation by lung function was low for $PM_{2.5}$ with a mediated proportion of 1.32% (FEV_1) and 2.05% (FVC), but higher for BC (7.01% and 13.82% respectively).

Discussion: Our results emphasise the importance of the lung acting as a mediator in the relationship between both exposure to $PM_{2.5}$ and BC, and cognitive performance. However, higher exposure to $PM_{2.5}$ was mainly directly associated with worse cognitive performance, which emphasises the health-relevance of fine particles due to their ability to reach vital organs directly.

Key words: Fine particulate matter; black carbon, cognitive performance; lung function; pathways; mediation analysis

II. FULL PAPER

1. INTRODUCTION

Air pollution contributes substantially to the global burden of disease; it is responsible for 4.2 million deaths, about 8000 deaths per year in Europe (Lelieveld et al. 2019), and for 103.1 million lost years of healthy life globally in 2015 (Cohen et al. 2017).

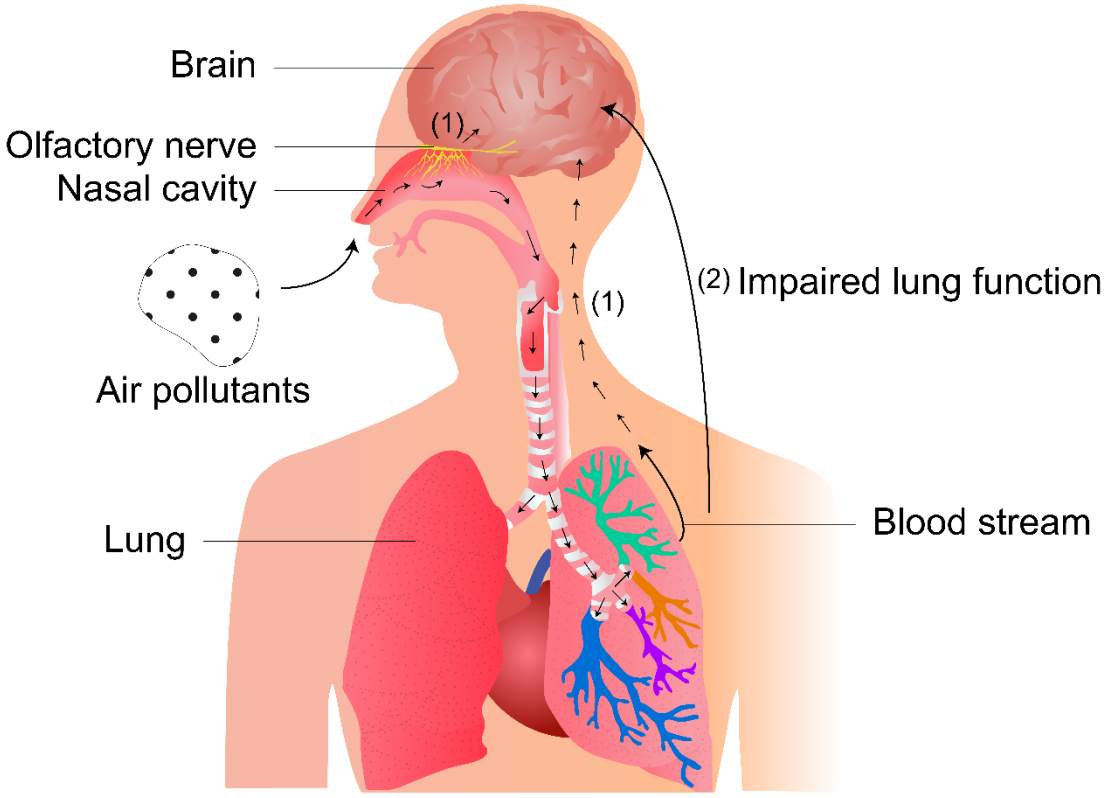
There is also recent evidence that exposure to air pollution is associated with lower cognitive performance (Zhang et al. 2018) and a higher incidence of dementia (Carey et al. 2018). A cohort study from Germany investigated the relationship between air pollution and cognitive functioning as well as local brain atrophy measured by magnetic resonance imaging (Nußbaum et al. 2020). In this study, higher exposure to $PM_{2.5}$ and $PM_{2.5\ absorbance}$ was related to lower cognitive functioning, and higher $PM_{2.5}$ was additionally associated with local brain atrophy. A double-cross over experiment suggested that short-term exposure to $PM_{2.5}$ had adverse effects on cognitive functioning measured by the Mini-Mental State Examination (MMSE) (Shehab and Pope 2019). A prospective cohort study among older Chinese adults, which also measured cognitive performance by using the MMSE, found that each 10-$\mu g/m^3$ increase in $PM_{2.5}$ was associated with a 5.1% increase in the risk of poor cognitive functioning (Wang et al. 2020). In the US, a doubling in BC level was related to 1.57 times higher odds of low MMSE scores (Colicino et al. 2017). A study, which explored the relationship between exposure to different constituent of $PM_{2.5}$ and cognitive functioning among older Puerto Rican in the US, found that long-term exposure to BC, nickel, sulfur, silicon, and $PM_{2.5}$ in general were related to slower mental speed or decreased recognition (Wurth et al. 2018).

Although, we know more about the negative effects of particulate matter on cognitive performance, the exact routes by which air pollutants may unfold their neurotoxic effects have barely been tested empirically, and there are substantial gaps in the knowledge of the underlying causal mechanisms (Griffiths and Mudway 2018). Commonly, two hypotheses are discussed (Block and Calderón-Garcidueñas 2009).

First, air pollutants may damage the brain directly by entering through the olfactory nerve or the lung, with subsequent entry into the blood stream providing access to the brain (**Figure 1**, path 1). It is mainly very fine particles which are assumed to follow this route (Block and Calderón-Garcidueñas 2009; González-Maciel et al. 2017).

Second, air pollutants may enter the lung by inhalation, thus impairing lung function or causing pulmonary inflammation (**Figure 1**, path 2).

Figure 1. Routes taken by inhaled fine particles to cause subsequent cognitive impairment



Description: Mainly smaller air pollutants (fine particles) may damage the brain directly by entering through the olfactory nerve or the lung, with subsequent entry into the blood stream providing access to the brain (path1). Air pollutants may also enter the lung by inhalation, thus impairing lung function or causing pulmonary inflammation (path 2). Impaired lung function may cause lower (abnormal) blood oxygen levels (hypoxemia) leading to systemic inflammation, oxidative stress, cerebral arterial stiffness and small-vessel damage. Air pollutants also cause inflammatory responses of immune cells residing in the lung, e.g. pulmonary macrophages, thereby adding to or causing a substantial systemic presence of inflammatory mediators.

After inhalation, especially fine particles can penetrate the deepest parts of the lung, e.g. the alveoli, due to their small size (Xing et al. 2016). Impaired lung function may cause lower (abnormal) blood oxygen levels (hypoxemia) leading to systemic inflammation, oxidative stress, cerebral arterial stiffness and small-vessel damage (Lutsey et al. 2018). Air pollutants also cause inflammatory responses of immune cells residing in the lung, e.g. pulmonary macrophages, thereby adding to or causing a substantial systemic presence of inflammatory mediators (Guarnieri and Balmes 2014).

In accordance with this second hypothesis, previous research showed that ambient air pollution is a major health risk contributing substantially to respiratory mortality (Lelieveld et al. 2019), and air pollution is related to lower pulmonary function (Adam et al. 2015), higher COPD prevalence (Bloemsma et al. 2016), higher asthma prevalence (Zheng et al. 2015), higher lung cancer mortality (Dimakopoulou et al. 2014), and a higher burden of COPD (Cohen et al. 2015). But, the negative effect of small particulate matter on lung function, however, is still contested. A meta-analysis of five cohorts in the European Study of Cohorts for Air Pollution Effects (ESCAPE) observed that higher levels of NO_2, but not of PM_{10} and $PM_{2.5}$, were associated with lower levels of forced expiratory flow in one second (FEV_1) and forced expiratory flow (FVC) among adults (Adam et al. 2015). On the contrary, the Framingham Heart Study found that also relatively low levels of $PM_{2.5}$ were related to lower FEV1 and FVC, and an accelerated decline in lung function (Rice et al. 2015). For Black Carbon (BC), there is evidence from a women's cohort from Boston, Massachusetts, that higher levels of BC were associated with decreased lung function in terms of FEV_1 and FVC (Suglia et al. 2008).

Although the hypothesised direct and indirect pathways taken by inhaled air pollutants, there are hardly any cohort studies which explored the interrelations between air pollution, lung function and cognition. To our knowledge, only one cohort study exists that explored the mediating role of FEV_1 and FVC in cognitive impairment caused by long-term exposure to NO_2, PM_{10}, and $PM_{2.5}$ (Hüls et al. 2018). However, this study observed just a small, female cohort in Germany and did not find any significant mediation by lung function. But it showed that there was a total effect/ a general relationship in the way that higher exposure to fine particulate matter was related to poor cognitive performance.

Due to the existing lack of research in exploring the interrelation between air pollution, lung function and cognition, this new cohort study has thus two objectives. First, it empirically tests the hypothesised routes taken by fine particulate matter in general ($PM_{2.5}$) and Black Carbon (BC), which is, next to the ultrafine particles (UFP), a major component of $PM_{2.5}$., to impair people's cognitive performance. Second, it evaluates the importance of the found routes in impairing cognition.

2. METHODS

2.1 Study population and design

We explored data from the Netherlands, a low pollution setting, and used longitudinal observational data for people aged 18+ from 2006 to 2015 from the Dutch Lifelines cohort study. Lifelines is a multi-generational prospective cohort study on multifactor risks for diseases, which recruited about 10% of the population in the three provinces of the Northern Netherlands, from whom 110,908 adults had a baseline and a follow-up assessment (Scholtens et al. 2015). Current (and for a sensitivity analysis past) residential addresses of each participant were obtained from municipal administration data. The Lifelines Cohort Study is conducted according to the principles of the Declaration of Helsinki and is approved by the medical ethical committee of the University Medical Center Groningen, The Netherlands.

In our study design, we tackled the issue of correct causal time order between the mediator (lung function) and outcome (cognitive performance) of interest. For this purpose, we distinguished between two time periods. The first time period is the baseline (2006-2012), at which the participants were recruited for the Lifelines cohort study and the exposure to fine particulate matter at participants' residential address as well as the lung function was assessed. And the second time period is the follow-up (2014-2015), at which the participants' cognitive performance was assessed.

All participants aged 18+ with data available on residential addresses at baseline, with valid air pollution exposure data, a valid lung function measurement at baseline (2006-2012), and a valid measurement of cognitive performance at follow-up (2014-2015) were included (**Supplementary Figure S1)**. Our final sample size was 49,705 people (see **Supplementary Table S3** for a comparison of the descriptive statistics among participants with complete and incomplete data).

2.2 Outcome assessment: cognitive performance measured by cognitive processing time (CPT)

To measure the participants' cognitive performance in our follow-up period (2014-2015), we used the Cogstate Brief Battery (CBB), which is an age-specific validated standardised computerised tool to measure four domains of cognitive performance: psychomotor

speed (reaction time = primary outcome), visual attention (reaction time = primary outcome), visual learning (reaction time and accuracy = primary outcomes), and working memory (accuracy = primary outcome) (Lim et al. 2013).

The CBB has been used in several studies to detect (mild) cognitive impairment (Maruff et al. 2009) and Alzheimer's disease (Maruff et al. 2013; Lim et al. 2012), and has shown to have good test-retest reliability (Darby et al. 2002) and validity (Hammers et al. 2012). The CBB measures were either used as single speed measures from four domains of cognitive performance, or they were used as composite scores, which are constructed by aggregating the single primary outcome measures for reaction time or accuracy (Lim et al. 2012). Composite scores seem to have a greater sensitivity to cognitive impairment than the single CBB measures (Lim et al. 2012; Maruff et al. 2013).

The CBB comprises four card tasks in the space of 11 minutes, reflecting the four cognitive domains: detection (2 min), identification (2 min), visual learning and memory (5 min), and working memory (2 min). Each task displays a textual instruction screen with a description of the task requirements. Each consists of several exercises (e.g. related to speed or accuracy) to be solved by selecting the "Yes" or "No" buttons on the screen (Lim et al. 2013). The CBB can be conducted un-supervised, which was also shown by evidence from clinical practice (Cromer at al. 2015). The participants should be able to use a computer keyboard or mouse with one hand and should be able to see the computer screen. In Lifelines, the CBB was provided in a systematic fashion. Participants completed the CBB during a visit to the Lifelines location under supervision.

Clinical practice has shown that the cognitive processing speed, defined as the ability to process information rapidly, is closely associated with the ability to solve (complex) cognitive tasks (Lichtenberger et al. 2013) and is thus one of the most important domains of cognitive performance (Salthouse and Ferrer-Caja 2003). Accordingly, we obtained a speed composite score using the speed measures from detection, identification and working memory task as primary outcomes in consultation with the Cogstate research team.

Each speed measure reflects the mean time for correct responses in each domain and was log (10)-transformed for better normality. A composite score measuring the overall cognitive processing time (CPT) was computed by summing up the speed scores of the three tasks. Positive scores mean that people had higher CPT (= higher reaction time and thus lower speed) and worse cognitive performance, and negative scores that they had lower

CPT (= lower reaction time and thus faster speed) and thus better cognitive performance. To control our cognitive speed outcome (CPT) for the accuracy of responses given, we accounted for the composite score of accuracy of given responses and the total number of trials per participant in the three CBB domains we used.

2.3 Exposure assessment: fine particulate matter and black carbon

We used exposure data (spatial resolution = 100 × 100 meters) on two ambient air pollutants available in the Lifelines dataset: particulate matter (PM) of particulates with diameters of 2.5 μm and smaller ($PM_{2.5}$) and the black carbon (BC) proportion in the $PM_{2.5}$. By using land-use regression models for the year 2010, which were developed in the project "Effects of Low-Level Air Pollution: A Study in Europe" (ELAPSE) (see de Hoogh et al. 2018 for a detailed description), the 2010 annual mean $PM_{2.5}$ and BC concentrations were estimated. These estimated concentrations were allocated to the participants home addresses in Lifelines at baseline (2006-2012).

In brief, satellite-derived and chemical transport model estimates were used to develop fine spatial scale land use regression (LUR) models for Western Europe for 2010. $PM_{2.5}$ concentrations were derived from the European Air Quality Database (AirBase v8) and BC annual means from the monitoring campaign conducted in the "European Study of Cohorts for Air Pollution Effects" (ESCAPE) (Eeftens et al. 2012). The developed LUR models in ELAPSE for all included sites explained 62% of the variance $PM_{2.5}$, whereas for BC 54% was explained. Spatiotemporal stability was relatively high. Stability tests at country level showed that the agreement between $PM_{2.5}$ levels estimated with the model developed for 2010 and that developed for 2013 was 70.1% for the Netherlands. The relationship between measured average concentrations for the AirBase stations showed an agreement of 68.3% over time (2010 to 2013) for the Netherlands (de Hoogh et al. 2018).

For a second type of exposure assessment used as a sensitivity analysis, Lifelines linked the current and past home addresses of the individuals to the average annual concentrations for $PM_{2.5}$ and BC, which were estimated for 2010 and came from the LUR developed in ELAPSE. The purpose of this time-weighted average (TWA) exposure model was to investigate if the results change when we take exposure history into account. For this purpose, Lifelines used the Municipal Personal Record Database (Zijlema et al. 2016) that contains the home addresses and thus the geolocations of all individuals who live or have lived in the Netherlands so that residential mobility and length of exposure can be traced.

For each air pollutant and individual, we calculated time-weighted average concentrations by using the residential locations of the participants' address history and the allocated average exposure concentrations in 2010, and weighting them by the duration of residence at a specific location (exposure time of the data) (Cohen et al. 1996). This was done for every location of the participants' address history up to baseline. For example, a person had lived in Groningen from 1998 to 2003 (residence duration of five years), moved from Groningen to Drenthe and lived in Drenthe for five years. The baseline of this person was in the year 2008 (and the person was still living at the same address in Drenthe) so that the residence duration in Drenthe up to baseline was again five years. Then, the 2010 exposure values from the ELAPSE project for the Groningen and Drenthe home addresses of this participant were multiplied each with the duration of five years, summed up, and then divided by the total duration (10 years). In this TWA-model, we included participants with available address history of at least ten years only (exposure time ≥ 10 years).

2.4 Mediator assessment: lung function

The indirect route assumed that higher exposure to fine particulate matter was related to lower lung function and less oxygen saturation causing worse cognition subsequently. Previous studies found that both FEV_1 and FVC were associated with the oxygen saturation in blood in people with lung diseases (Ardestani & Abbaszadeh 2014), e.g. COPD, but also in the general adult population (Vold et al. 2012). Both lung function measures FEV_1 and FVC thus reflect the proposed indirect route properly why we treated them as potential mediators in our study.

Lung function at baseline (2006-2012) was assessed by Lifelines through spirometry, performed by trained medical staff according to American Thoracic Society guidelines using a Welch Allyn Version 1.6.0.489 PC-based SpiroPerfect with CardioPerfect workstation software. We used two volume measures, the forced expiratory volume in one second (FEV_1) and the forced vital capacity (FVC), as outcome variables. To come up with interpretable scores, we used age-, sex-and height-specific reference values for FEV_1 and FVC as provided by the Global Lung Initiative (GLI) (Quanjer et al. 2012). Subsequently, the predicted proportion of the empirical lung function scores compared to the predicted reference scores were calculated for all both lung function measures. Scores beyond 100%

mean that people had better lung parameters compared to the reference values, whereas scores lower than 100% mean that they had worse.

2.5 Assessment of potential confounders

We controlled for age, sex, socio-demographic and lifestyle confounders, and respiratory and cognition-related diseases either at baseline (2006-2012) only, or as time-dependent variables for both baseline and follow-up (2014-2015). In detail, age, province of residence (Drenthe, Groningen, Friesland, other), education, BMI, hypertension, and age were included as time-dependent confounders by controlling lung function for the baseline information and CPT for the follow-up information.

Education level was defined as the highest education level completed (none, primary, lower secondary vocational, secondary vocational, senior general secondary, higher vocational, university, other). Income was measured by an individual's net income per month (less than 1,500 Euro, between 1,500 and 2,500 Euro, higher than 2,500 Euro, unknown/ unexpressed). Body mass index (BMI) was calculated as the individual's measured weight divided by measured height square and categorised in one of three groups: less than 25, between 25 and less than 30, and equal to or higher than 30. Hypertension was operationalised by a systolic pressure higher than 139 mmHg or a diastolic pressure higher than 89 mmHg. Systolic and diastolic blood pressure was measured by medical staff. Prevalence of respiratory diseases, namely asthma and COPD, as well as cognition-related diseases, namely multiple sclerosis, depression, diabetes (type I or II), and stroke, was derived by a question whether a doctor has ever diagnosed that specific disease in participants before (yes/ no). Pack-years of cigarettes smoked (1 pack-year = 20 cigarettes per day/ 1 year) were calculated from the baseline questionnaire collecting data on a person's smoking history.

In the sensitivity models using the time-weighted average exposure assessment (TWA-model), we controlled additionally for the total time period in days (continuous variable) to which the long-term exposure to air pollution applied.

2.6 Statistical analysis

We used mediation analysis to explore whether the association between air pollution (X) and CPT (Y) followed a direct route to the brain or was mediated by lung function (*M*). We

performed linear structural equation models (SEM) without feedback loops and with robust standard errors by Huber/ White (Breusch-Pagan-Test, $p < 0.001$). Exposure and confounders were treated as exogenous variables, and lung function as well as CPT were seen as endogenous variables. We introduced an outcome equation (equation 1) and a mediator equation (equation 2), whereby C_n denote the specific confounding variables, and θ_0 to θ_n, and β_0 to β_n are the unobserved parameters (see also **Supplementary Figure S2** for the model approach):

$$Y = \theta_0 + \theta_1 X + \theta_2 M + \theta_3 C_1 + \theta_4 C_2 \ldots + \theta_n C_n + \varepsilon_2 \quad \text{(i)}$$

$$M = \beta_0 + \beta_1 X + \beta_2 C_1 + \beta_3 C_2 + \cdots + \beta_n C_n + \varepsilon_1 \quad \text{(ii)}$$

We estimated the two equations simultaneously and performed subsequently a decomposition of the total effect (the following usage of the words total, indirect or total effect does not imply causality; terms represent standard technical terms) $TE = \theta_1 + \beta_1 \times \theta_2$ into a direct effect $DE = \theta_1$ and the two separate indirect paths (β_1, θ_2). The both indirect path coefficients can be combined into one indirect effect $IE = \beta_1 \times \theta_2$ (Gunzler et al. 2013). To test the significance of the indirect effect (IE) we used the delta method/ Sobel Test (Sobel 1982). We calculated direct effect proportions ($DEP = \frac{(\theta_1)}{(\theta_1 + \beta_1 \times \theta_2)} \times 100$) and indirect effect proportions ($IEP = \frac{(\beta_1 \times \theta_2)}{(\theta_1 + \beta_1 \times \theta_2)} \times 100$) to quantify the importance of the significant direct effect and indirect effect compared to the total effect. The significance threshold was .05 and all tests were 2-sided. The calculations were performed using Stata MP 13.1.

We performed three kinds of sensitivity analyses. First, we checked the robustness of our SEM approach to ensure that our results were valid. We applied causal mediation analysis using a potential outcome approach with bootstrapping (1,000 iterations) for inference evaluation. Causal mediation analysis was performed by using the "mediation" package in Stata, which is based on the "mediation" package for causal mediation analysis in R (Tingley et al. 2014).

Second, we estimated SEMs for study participants aged 45 because the air pollution effects on cognitive performance are assumed especially evident for those ages when cognitive decline has generally started (Singh-Manoux et al. 2012).

Third, we calculated time-weighted average concentrations over a minimum of ten years up to baseline based on participants' residential history (TWA-model) to investigate if the results change when we take exposure history into account.

3. RESULTS

3.1 Characteristics of the study participants

Of the 49,705 participants 25,915 (52.14%) had faster Cognitive Processing Time (CPT) and 23,790 (47.86%) slower CPT than the mean at follow-up (2014-2015) (**Table 1**).

The average exposure to $PM_{2.5}$ was 14.92 [min = 9.35, max = 20.12] $\mu g/m^3$, and 1.22 [min = 0.68, max = 2.79] $\mu g/m^3$ to BC (**Figure 2**). For lung function, the average FEV_1 was 3.50 liters (96.54% predicted) and FVC 4.56 liters (100.78% predicted) (**Table 1**).

There were 23,773 (47.83%) people who had zero pack-years of cigarettes smoked, suggesting that they were never-smokers, and the smokers had an average of 11.25 pack-years. The body mass index of 19,892 (40.02%) participants indicated they were overweight (30>BMI ≥ 25), and 7,063 (14.21%) were obese (BMI ≥ 30) at baseline. The proportion of obese people increased to 15.32% at follow-up. 7.65% of the participants had prevalent asthma at baseline diagnosed by a doctor, 4.69% COPD, 7.10% diabetes, 9.79% depression, and 0.53% had ever a stroke before baseline. Age at baseline ranged from 18 to 88 and the average age was 44.77 years, whereas the average age was 48.94 years (min = 20, max = 92) at follow-up.

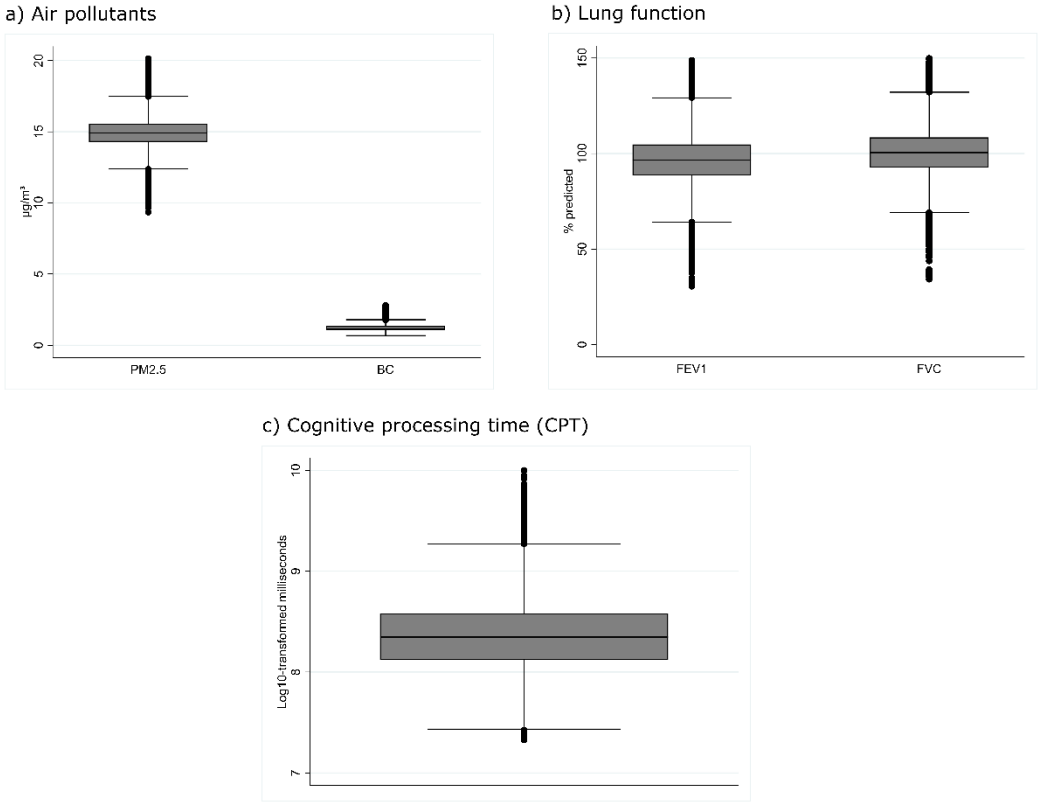
Table 1. Descriptive statistics of the study participants (n = 49,705) at baseline (2006-2012) and at follow-up (2014-2015) in the study population based on the Dutch Lifelines Cohort Study

Characteristic	Baseline (2006-2012)	Follow-up (2014-2015)
Sex, No. (%)		
Women	29422 (59.19)	
Men	20283 (40.81)	
Age, mean (SD)	44.77 (11.41)	48.94 (11.35)
Province of residence, No. (%)		
Drenthe	10065 (20.25)	10117 (20.35)
Friesland	22279 (44.82)	22087 (44.44)
Groningen	16721 (33.64)	16402 (33.00)
Other	640 (1.29)	1099 (2.21)
Educational level, No. (%)		
No education	124 (0.25)	130 (0.26)
Primary education	565 (1.14)	426 (0.86)
Lower or preparatory vocation	5549 (11.16)	5302 (10.67)
Junior general secondary education	6728 (13.54)	6805 (13.69)
Secondary vocational education	15386 (30.95)	15006 (30.19)
Senior general secondary education	4538 (9.13)	4101 (8.25)
Higher vocational education	12803 (25.76)	13635 (27.43)
University education	3175 (6.39)	3517 (7.08)
Other	837 (1.68)	783 (1.58)
Net income per month, No. (%)		
Lower than 1500 Euro	6497 (13.07)	
1500 to 2500 Euro	13413 (26.99)	
Higher than 2500 Euro	23302 (46.88)	
Do not know/ do not want to tell	6493 (13.06)	
Pack-years of cigarettes smoked, No. (%)[a]		
Never smokers	23773 (47.83)	
Lower/ equal than the 50th percentile of ever smokers	13184 (26.52)	
Higher than the 50th percentile of ever smokers	12748 (25.65)	
BMI, No. (%)		
Lower than 25	22750 (45.77)	22211 (44.69)
25 to lower than 30	19892 (40.02)	19877 (39.99)
Higher/ equal than 30	7063 (14.21)	7617 (15.32)
Hypertension, No. (%)[b]		
Yes	8597 (17.30)	11074 (22.28)
No	41108 (82.70)	38631 (77.72)
Asthma, No. (%)[c]		
Yes	3803 (7.65)	

No	45902 (92.35)	
COPD, No. (%)[c]		
Yes	2332 (4.69)	
No	47373 (95.31)	
Diabetes, No. (%)[c]		
Yes	3528 (7.10)	
No	46177 (92.90)	
Depression, No. (%)[c]		
Yes	4865 (9.79)	
No	44840 (90.21)	
Stroke, No. (%)[c]		
Yes	262 (0.53)	
No	49443 (99.47)	
Multiple Sclerosis, No. (%)[c]		
Yes	114 (0.23)	
No	49591 (99.77)	
Long-term air pollution (one-year annual mean concentrations), mean (SD)[d]		
PM2.5 (in μg/ m^3) from ELAPSE, year 2010	14.92 (1.01)	
BC (in μg/ m^3) from ELAPSE, year 2010	1.22 (0.22)	
Lung function, mean (SD)[e]		
FEV_1 (L), % predicted	3.50 (0.82), 96.54 (12.72)	
FVC (L), % predicted	4.56 (1.03), 100.78 (12.14)	
Number of total CBB trials, mean (SD)[f]		140.26 (24.65)
Accuracy of given CBB responses, mean (SD)[g]		3.76 (0.47)
Less accurate (lower values) than the mean, No. (%)		21958 (44.18)
More accurate (higher values) than the mean, No. (%)		27747 (55.82)
Cognitive processing time (CPT), log10-transformed milliseconds, mean (SD)[h]		8.37 (0.34)
Faster CPT (lower values) than the mean, No. (%)		25915 (52.14)
Slower CPT (higher values) than the mean, No. (%)		23790 (47.86)

Abbreviations: BMI, body mass index (calculated as weight in kilograms divided by height in meters squared); NO_2, nitrogen dioxide; PM_{10}, coarse particulate matter; $PM_{2.5}$, (fine) particulates with diameters of 2.5 μm and smaller; BC, black carbon proportion in the fine particulate matter. [a] Pack-years of cigarettes smoked were calculated from the baseline questionnaire (1 pack-year = 20 cigarettes per day in 1 year). [b] Hypertension was defined when systolic pressure was higher than 139 mmHg or diastolic pressure higher than 89 mmHg (blood pressure was measured by medical staff). [c] Prevalence of diseases at baseline was assessed by questions, whether a specific disease was diagnosed by a doctor or not. [d] Long-term air pollution concentrations were assessed as one-year annual mean concentrations at participants' baseline address and were estimated for the year 2010 by the ELAPSE models/ project. [e] Lung function was measured by spirometry by trained medical staff. [f] Number of CBB trials represents the total number of responses given by the participants during the three subtests (detection, identification, working-memory) of the Cogstate Brief Battery. [g] Accuracy was measured by the proportion of correct responses. For each domain (detection, identification, working-memory), the accuracy of each response to each trial was recorded. The three already arcsine-transformed measures from the Cogstate Brief Battery were summed to measure the total accuracy. [h] Cognitive Processing Time was measured by using three single (detection, identification, working-memory) log10-transformed speed measures from the Cogstate Brief Battery. The three measures were summed up to measure the total average reaction time.

Figure 2. Distribution of long-term exposure to PM2.5 and BC at baseline (2006–2012), lung function at baseline and cognitive processing time at follow-up (2014–2015)



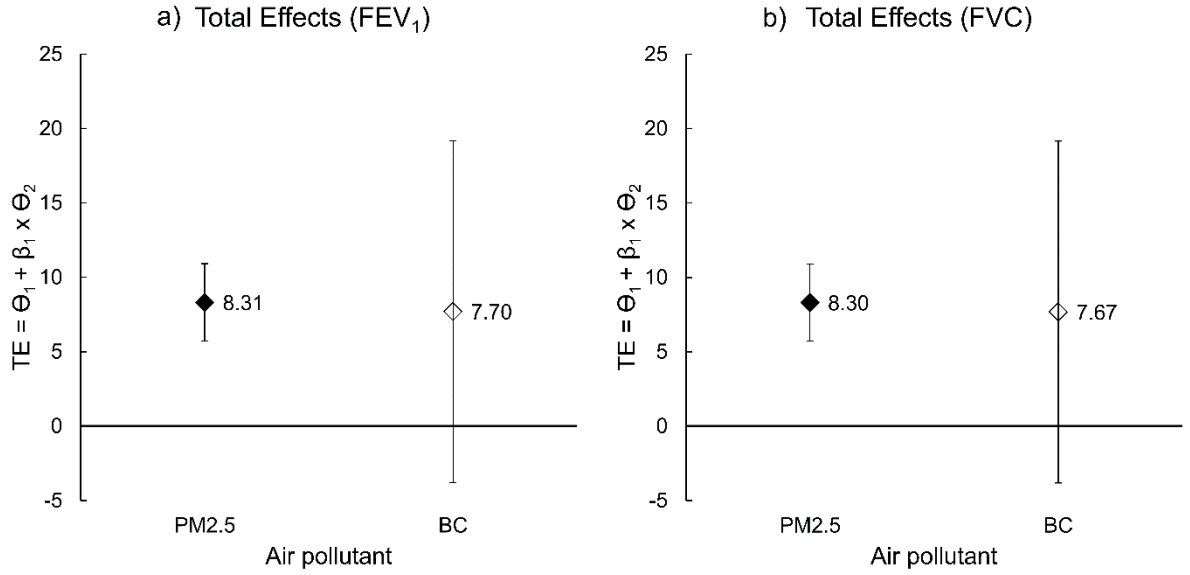
Notes: PM2.5, (fine) particulates with diameters of 2.5 µm and smaller; BC, black carbon proportion in the fine particulate matter; FEV1, Forced Expiratory Volume in 1 s; FVC, Forced Volume Capacity. Description: Boxplots included a) long-term exposure to fine particulate matter at the study participants' baseline address, b) lung function measures at baseline (2006–2012), and c) cognitive processing time (CPT), the outcome of interest, at follow-up (2014–2015). The boxes indicate the interquartile range (IQR) and the line in the center indicates the median concentration. Outlier observations are shown as circles.

3.2 Associations between Air Pollution Exposure and Cognitive Processing Time (CPT)

First, we estimated the total effect showing the overall associations between long-term air pollution exposure at baseline and CPT at follow-up (2014-2015). We found that higher exposure to $PM_{2.5}$ was significantly related to slower CPT and so worse cognitive performance even when we controlled for both lung function mediators, namely FEV_1 [$PM_{2.5}$: 8.31×10^{-3} (95% CI: 5.71×10^{-3}, 10.91×10^{-3})] and FVC [$PM_{2.5}$: 8.30×10^{-3} (95% CI: 5.69×10^{-3}, 10.90×10^{-3})] (**Figure 3**, **Supplementary Table S1**). An increase in $PM_{2.5}$ exposure of one $\mu g/m^3$ is accordingly related to an increase in cognitive processing time of 2% (re-calculation, e.g. for FEV_1, as follows: $(10^{0.00831} - 1) \times 100 = 1.93$).

We additionally estimated adjusted CPT predictions for the values of $PM_{2.5}$ from the minimum integer value (9) to the maximum (20) value under our model assumptions (**Supplementary Figure S3**).

Figure 3. Total Effects: Associations between long-term exposure to PM2.5 and BC, and cognitive processing time (CPT)



Notes: PM2.5, (fine) particulates with diameters of 2.5 µm and smaller; BC, black carbon proportion in the fine particulate matter; FEV1, Forced Expiratory Volume in 1 s; FVC, Forced Volume Capacity. Interval plots show the Total Effects (a, b) of the associations between long-term exposure to fine particulate matter (in µg/m3) and Cognitive Processing Time (CPT), which is the log10-transformed total reaction time, measured by the Cogstate Brief Battery. The models related to each unit increase of long-term exposure to PM2.5 or BC. Shown values for point estimators, lower and upper confidence intervals were multiplied by 10^3.

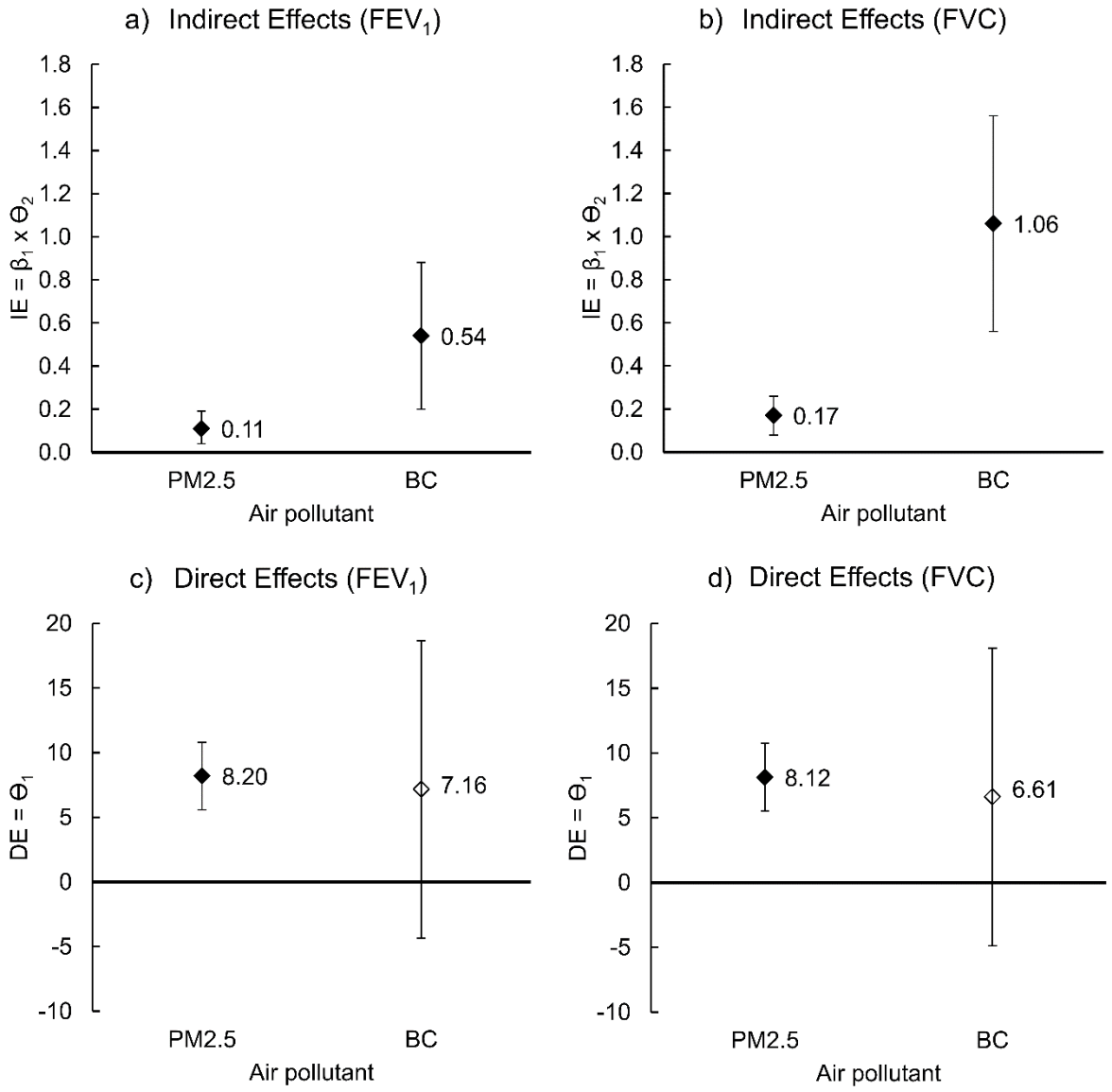
This showed that in our linear model people exposed to an average value of $16\mu/m^3$ or higher had worse cognitive performance than the mean in our study population (CPT = 8.37 log10-transformed milliseconds, red line in **Figure S3**) had. For BC, however, no significant total associations existed.

3.3 Mediation analysis and decomposition of the total effect into the direct and indirect effect

Second, we conducted a decomposition of the total effects into a direct and an indirect effect. The direct effect represents the direct route of air pollutants through the olfactory nerve or the lung, with subsequent entry into the blood stream, providing access to the brain. The direct effects for $PM_{2.5}$ on CPT were seen even when we controlled for lung function measures at baseline (2006-2012), so the indirect routes, namely for FEV_1 [$PM_{2.5}$:

8.20×10^{-3} (95% CI: 5.59×10^{-3}, 10.80×10^{-3})] and FVC [$PM_{2.5}$: 8.12×10^{-3} (95% CI: 5.52, 10.73)]. No significant direct effects were found for BC (**Figure 4**).

Figure 4. Decomposition of the associations between long-term exposure to $PM_{2.5}$ and BC, and cognitive processing time (CPT)

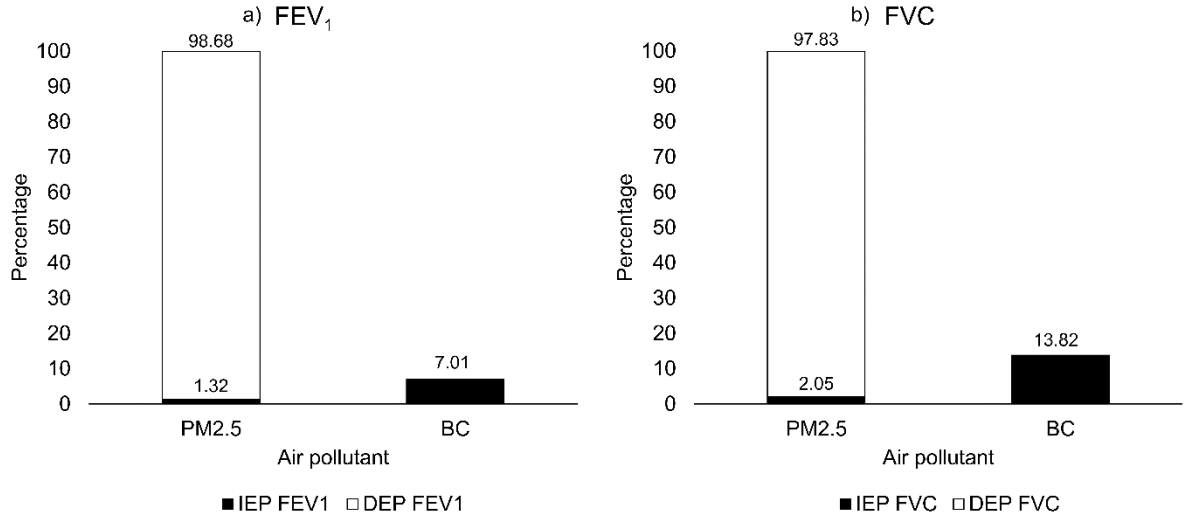


Notes: PM2.5, (fine) particulates with diameters of 2.5 µm and smaller; BC, black carbon proportion in the fine particulate matter; FEV1, Forced Expiratory Volume in one second; FVC, Forced Volume Capacity. Interval plots show the decompositions of the Total Effects into direct and indirect effects. The models related long-term exposure to fine particulate matter (in µg/m³) to Cognitive Processing Time (CPT), which is the log10-transformed total reaction time, measured by the Cogstate Brief Battery. The Indirect Effects a), b) represent the indirect routes over the lung function measures FEV1 and FVC (potential mediators) and the Direct Effects c), d) the direct routes over the olfactory nerve/ blood stream. The models related to each unit increase of long-term exposure to $PM_{2.5}$ or BC. Shown values for point estimators, lower and upper confidence intervals were multiplied by 10^3.

The indirect effect represents the indirect route of air pollutants, which first impair the lung, which in turn leads to worse cognitive performance. For $PM_{2.5}$, we observed mediation by both lung function measures, namely for FEV_1 [$PM_{2.5}$: 0.11×10^{-3} (95% CI: 0.04×10^{-3}, 0.19×10^{-3})] and FVC [$PM_{2.5}$: 0.17×10^{-3} (95% CI: 0.08×10^{-3}, 0.26×10^{-3})] (**Figure 4** and see **Supplementary Table S1** for the estimation parameters of β_1, θ_1 and θ_2). We also found indirect effects for BC, namely for both lung function measures (BC, FEV_1: [0.54×10^{-3} (95% CI: 0.20×10^{-3}, 0.88×10^{-3}); BC, FVC: [1.06×10^{-3} (95% CI: 0.56×10^{-3}, 1.56×10^{-3})].

Our first sensitivity analysis using g-formula supported our results and showed that our model approach came to nearly the same estimations (**Supplementary Table S2**). The second sensitivity analysis including participants aged 45 and older only (see **Supplementary Table S4** for descriptive statistics) showed also same results than the all-participant model in line with our hypothesis (**Table 2**). Our third sensitivity analysis (TWA-model) used the estimated time-weighted average concentrations of $PM_{2.5}$ and BC based on the participants' address history of the last ten years at least, excluding all those with less than ten years of address history (see **Supplementary Table S4** for descriptive statistics).

Figure 5. The importance of the found Indirect (IEP) and Direct Effects (DEP) of long-term exposure to PM2.5 and BC on cognitive processing time (CPT) calculated as proportions in percentage of the Total Effects



Notes: PM2.5, (fine) particulates with diameters of 2.5 µm and smaller; BC, black carbon proportion in the fine particulate matter; FEV1, Forced Expiratory Volume in 1 s; FVC, Forced Volume Capacity; IEP, indirect effect proportion; DEP, direct effect proportion. Bars show the found significant indirect effects (IEP) and the direct effect proportions (DEP) found in the decomposition of the total effects for both lung function measures FEV1 a) and FVC b) acting as potential mediators. Indirect effect proportions were calculated by dividing the size of the indirect effects by their total effects. The direct effect proportions were calculated by dividing the size of the direct effects by their total effects.

Results did not change as compared to our main model (**Table 2**), which indicates that the exposure concentrations at baseline address used in our study may be considered as a valid proxy for chronic long-term exposure. By calculating the importance of direct and indirect effects, we found that 98.68% (FEV_1) or 97.83% (FVC) of the total effect of $PM_{2.5}$ was directly associated with cognitive performance. The highest indirect effect proportions were seen for BC (FVC, 13.82%) and the lowest indirect effect proportion was seen for $PM_{2.5}$ by FEV_1 (1.32%) (**Figure 5**).

3.4 The influence of confounders on the associations between fine particulate matter and cognitive performance

As expected, higher age at follow-up was correlated with worse cognitive performance [9.16×10^{-3} (95% CI: 8.89×10^{-3}, 9.43×10^{-3})], and higher educated people had better cognitive performance [-104.61×10^{-3} (95% CI: -161.23, -48.00)] than participants without any educational level. Prevalent diabetes [38.41×10^{-3} (95% CI: 27.36×10^{-3}, 49.46×10^{-3})] as well as a stroke in the past [57.33×10^{-3} (95% CI: 13.29×10^{-3}, 101.36×10^{-3})] were related to poor cognition, all other morbidities did not show significant effects on cognitive performance. Men [men: -26.75×10^{-3} (95% CI: -32.08×10^{-3}, -21.41×10^{-3})] fared better than women.

Participants with prevalent COPD [FEV_1: -6.35% predicted (95% CI: -7.00, -5.69); FVC: -2.78% predicted (95% CI: -3.32, -2.25)] and asthma [FEV_1: -4.19% predicted (95% CI: -4.64, -3.73); FVC: -1.09% predicted (95% CI: -1.49, -0.69)] had worse lung function. But also diseases, which were not directly related to respiratory health, were associated with worse lung function, namely stroke [FEV_1: -3.49% predicted (95% CI: -5.19, -1.80); FVC: -2.62% predicted (95% CI: -4.15, -1.09)], diabetes [FEV_1: -0.79% predicted (95% CI: -1.24, -0.35); FVC: -1.08% predicted (95% CI: -1.50, -0.65)], and hypertension [FEV_1: -1.18% predicted (95% CI: -1.50, -0.87); FVC: -1.19% predicted (95% CI: -1.49, -0.89)].

Lower income, a higher number of packyears and obesity, but not a lower educational level, were associated with lower FEV_1 and FVC. Higher age at baseline was related to both higher FEV_1 and FVC indicating that the age-standardisation by the GLI reference values was not fully successful for our cohort and an additional inclusion of age in our models was important to avoid confounding by age. For sex, we found an association with FVC only confirming that the sex-standardisation was successful for FEV_1, but not for FVC.

4. DISCUSSION

4.1 Summary of the findings

To the best of our knowledge, our cohort study is one of the first to demonstrate the importance of the direct and the indirect route over the lung taken by inhaled fine particulate matter in general and Black Carbon in particular in cognitive impairments for both genders.

In the low pollution setting of the Netherlands, higher exposure to $PM_{2.5}$ was associated with slower cognitive processing time at follow-up (2014-2015) among participants aged 18+, and associations were also evident in a sensitivity model including participants aged 45 and older. Further analyses showed that, based on our model assumptions, an average $PM_{2.5}$ exposure level of 16 to 20 $\mu g/m^3$ was related to worse cognitive performance compared to the mean in our study population, whereas people experiencing only 9 to 14 $\mu g/m^3$ on average had better cognitive performance. By decomposing the total effects into a direct and an indirect effect respectively, we showed that $PM_{2.5}$ was directly related to slower cognitive processing time and, thus to worse cognitive performance. This direct effect constituted more than 97% of the total effect of $PM_{2.5}$ on cognitive performance when we included mediation by lung function at baseline (2006-2012) in our model. In addition to the direct effect, there was also small significant indirect effects for both lung function measures FEV_1 and FVC contributing just about 1% to 2% to the total effect.

For BC, the associations were solely mediated via lung function. We found significant indirect effects, which contributed about 7.01% (FEV_1) to 13.82% (FVC) to the total effects. Both mediations however, were too small to translate significance to the total effect since there were insignificant direct effects which contribute (partially) to the total effect as well.

As most important covariates/ confounders, we identified age, educational level and diabetes prevalence for cognitive performance, and prevalence of COPD, asthma, stroke, diabetes, and hypertension as well as income and packyears for lung function.

The main aim of this study was to test the two hypothesised routes taken by fine particulate matter in general ($PM_{2.5}$) and Black Carbon (BC) as one of the main components of the fine particulate matter. Our results indicate that the direct route may be more important for $PM_{2.5}$ and the indirect route for BC.

4.2 Interpretation and comparison of the findings

Our finding that BC may not be able to cross the direct route to reach the brain is contrary to earlier findings for people 60 and older (Colicino et al. 2017; Wurth et al. 2018). Explanations for this could be that we applied a low pollution setting or that we explored participants in the age of 18 or older, who are less fragile than older people. Previous research accordingly found that older people (≥ 65 years old) are more prone to the negative effects of air pollution (Shumake et al. 2013; Simoni et al. 2015) than younger people. If PM2.5 can reach the human's brain through the direct route according to the results of our study, then BC may follow this route as well since BC is a part of PM2.5 and is of very small size.

We found that $PM_{2.5}$, however, may affect cognition directly. It is known that fine particles, e.g. $PM_{2.5}$ and especially ultrafine particles (diameter < 0.01µm), a component of $PM_{2.5}$ as well, are potentially able to penetrate the central nervous system, resulting in subsequent neuroinflammation (Maher et al. 2016). We further know that microglia may be activated by the direct route, but also upon occurrence of systemic neuroinflammation (Widmann and Heneka 2014). In vivo and in vitro studies also provide insights into the neurotoxic effect of PM exposure; i.e., higher levels of PM are linked to significantly higher levels of pro-inflammatory cytokines such as interleukin, as well as tumor necrosis factor and glial responses indicating the presence of inflammation (Kilian and Kitazawa 2018). In turn, neuroinflammation is an important risk factor for neurodegenerative diseases, e.g. Alzheimer's and Parkinson's disease (Glass et al. 2010; Heneka et al. 2015; Sarlus and Heneka 2017). Another possibility is that the pollutants inhaled reach the brain via the lung, which provides the initial entry to the body, and then pass from the alveoli into the bloodstream, using circulation to reach the central nervous system (CNS) (Lee and Shah 2018). We further know that exposure to $PM_{2.5}$ is associated with DNA methylation, which may in turn affect lung function or/ and brain health negatively (Shi et al. 2019).

Additionally, we found evidence for the relevance of the indirect route over the lung in cognitive impairments by fine particulate matter. That is, $PM_{2.5}$ to a small extent and BC to a greater extent affect cognitive performance by first impairing the lung function and subsequently leading to cognitive impairment. For BC, this seemed to be the main route in our study to unfold adverse cognition effects, since we found that the effect of BC on cognitive performance was solely mediated by FEV_1 and FVC with a mediated proportion

of about 7% to 14% and we found no evidence that BC is able follow the direct route. Previous studies have also found that higher exposure to BC and $PM_{2.5}$ are associated with lower FEV_1 and FVC (Guo et al. 2018; Lepeule et al. 2014), and inflammatory processes in the lung, oxidative stress and activation of microglia cells resulting in subsequent neuroinflammation have been suggested as causal pathways (Guarnieri and Balmes 2014). However, the fact that the found mediated proportion is only 7.01% to 13.82% for BC suggests that there are potential additional routes missed in our study, e.g. cardiovascular health/ diseases, which could be relevant in impairing cognition by BC. We know accordingly from previous research that higher exposure to BC was related to adverse cardiovascular outcomes (Gan et al. 2011). In turn, another study has found that better cardiovascular health was related to better cognitive health (Kulshreshtha et al. 2019).

Our study was conducted in the low-pollution setting of adults aged 18+ in the Netherlands. For $PM_{2.5}$ (14.92 $\mu g/m^3$), the exposure level was clearly lower compared to the relatively restrictive EU-wide limit values (25 $\mu g/m^3$ for $PM_{2.5}$) (Guerreiro et al. 2018), and also lower compared to previous epidemiological cohort studies (ECRHS, 16 $\mu g/m^3$; EGEA, 15 $\mu g/m^3$; E3N, 15 $\mu g/m^3$; SALIA, 18 $\mu g/m^3$; SAPALDIA, 17 $\mu g/m^3$) (Jacquemin et al. 2015). This was also true for BC, which was 1.22 $\mu g/m^3$ in our study, but 1.5 $\mu g/m^3$ or higher in other cohorts (ECRHS, 2.0 $\mu g/m^3$; EGEA, 2.1 $\mu g/m^3$; E3N, 1.8 $\mu g/m^3$; SALIA, 1.5 $\mu g/m^3$; SAPALDIA, 1.9 $\mu g/m^3$) (Jacquemin et al. 2015). Higher exposure levels in other spatial units or countries may result in even stronger associations between air pollution and cognition than what is demonstrated in this study's population, under the assumption of a non-linear, e.g exponential, dose-response relationship. To the best of our knowledge, there is no previous study which evaluated the dose-response relation between fine particulate matter and cognitive performance among adults, so that more research is needed here.

4.3 Strengths and limitations

Our study has several strengths. First, we did not only explore the overall relationship (total effect) between fine particulate matter and cognitive performance as done by previous research (Power et al. 2011; Wurth et al. 2018; Zhang et al. 2018), but additionally performed a decomposition of the total effects in order to disentangle the potential routes taken by the air pollutants, which are closely related to causal mechanisms/ pathways. For this purpose, we applied a causal mediation approach by using SEM. To the best of

our knowledge, the only previous cohort study that explored the mediating role of lung function was not able to find any significant indirect effects (Hüls et al. 2018), potentially because they observed only a small female cohort in Germany. The adverse total effect of $PM_{2.5}$ they observed, however, supports our results.

Second, in a sensitivity model (TWA-model) we calculated time-weighted average concentrations over a minimum of ten years up to baseline to check if the results change when we took exposure history into account. We found same results in this TWA-model why we assumed that the used one-year average concentrations were good proxies for long-term exposure. Using one-year mean concentrations only, as done in previous studies (Colicino et al. 2017; Nußbaum et al. 2020; Wang et al. 2020; Wurth et al. 2018), may confound the results by unobserved positive health selection into living environments with low exposure levels (Oakes 2014), even when our third sensitivity model showed that this is not true in our study.

Third, we used a standardised and multidimensional (composite) outcome variable, cognitive processing time (CPT), which was computed in close contact with the Cogstate research team, to measure the participants' cognitive performance. The speed measures coming from the CBB may be summarised into a composite, also used to determine the overall cognitive performance and not only to detect clinical abnormalities (in single cognition domains). Previous studies mostly used the MMSE as an outcome to measure mild cognitive impairment, e.g. when MMSE scores were ≤ 25 (Colicino et al. 2017; Shehab and Pope 2019; Wang et al. 2020). This, however, has a relative lack of sensitivity when detecting subtle cognitive impairments (Proust-Lima et al. 2007) and detailed differences in cognitive performance within a specific population.

Fourth, a series of sensitivity analyses confirmed our results. (1) A replication analyses using a counterfactual approach and bootstrapping for testing the causal routes (**Supplementary Table S2**), yielded similar results to our SEM approach, also when we stratified by age (age<45, age≥45. (2) This was also true when we used our model strategy (SEM) for the analysis of individuals aged 45 and older only, which gives even more plausibility to our results, because previous research suggested that cognitive decline starts from the mid-40s (Singh-Manoux et al. 2012). (3) Using time-weighted average concentrations over a minimum of ten years up to baseline (historical addresses of the participants' residence linked to concentrations estimated for 2010) did not change our results.

Despite the strengths of our study, there are some limitations. First, ambient air pollution concentrations at the residential address, especially those estimated by land use regression models, do not reflect the overall air pollution people are indeed exposed to in their living environments. People are also exposed to (potentially different) air pollution levels, which are relevant for brain health, during daily road travel or when they are indoor (Saenz et al. 2018). Second, we used the air pollution exposure data from the ELAPSE project, which seems to have better quality than previous data (de Hoogh 2018). But, the data were only available for the year 2010 and these data from 2010 were linked to the participants' baseline address or address history, so that it is possible that these concentrations for 2010 are poor proxies for long-term/ chronic exposure concentrations at home. We feel however, that our sensitivity model including a time-weighted average exposure assessment of at least ten years, supports the assumption that the 2010-exposure concentrations also reflect long-term chronic exposure. Third, we analysed only the levels of health and not the changes in health over time, which suggests generally more causal explanatory power. We, however, minimised the effect of this limitation by ensuring correct causal time order between cause (in the TWA sensitivity model), mediator and outcome. Furthermore, in the TWA sensitivity model we included only those participants for whom exposure data was available for at least ten years, and verified our results by performing causal mediation analyses with a potential outcome approach (see our first sensitivity analysis). Fourth, we were not able to account for genetic factors, e.g. the apolipoprotein-ε4 allele (APOE-ε4), which are known to be the most prevalent genetic risk factors for Alzheimer's disease (Miyata and Smith 1996), and whose variants modify the association between air pollution and cognitive impairment resulting in a stronger air pollution effect for APOE risk variant carriers (Schikowski et al. 2015). Fifth, our models assumed a linear dose/-response relationship between air pollution exposure and cognitive performance. In doing so, we followed previous studies in the field, which explored e.g. the dose-response relationship between $PM_{2.5}$ and daily deaths (Schwartz et al. 2002), $PM_{2.5}$ and daily respiratory deaths (Ren et al. 2017), prenatal exposure to $PM_{2.5}$ and development of brain white matter and cognition in later childhood (Peterson et al. 2015), which all identified a linear relationship. However, there is also evidence for the existence of non-linear relations between $PM_{2.5}$ and mortality due to respiratory disease (COPD, lung cancer, lower respiratory infection), especially for lower concentrations below 25 $\mu g/m^3$ (Cohen et al. 2017).

4.4 Conclusion

Our study provides new insights in the association between ambient exposure to fine particulate matter and brain health by disentangling underlying direct and indirect pathways over lung function. Our results emphasise the importance of the lung acting as a mediator in this relationship. Especially BC seems to impair the lung or activate inflammatory responses of immune cells residing in the lung, causing subsequent cognitive impairments. Thus, brain health seems to depend on, among others, a good lung function, and lung function in turn may benefit from low air pollution exposure. Fine particles as $PM_{2.5}$ seem to mainly follow the direct route, which calls for a special attention to fine particles due to their ability to reach vital organs directly. Future research is needed that explores, beside of the indirect lung function route found in our study, further pathways taken by inhaled air pollutions to subsequently affect cognition.

Acknowledgements

We thank Lifelines for providing the data and their support. The Lifelines Biobank initiative was made possible by a subsidy from the Dutch Ministry of Health, Welfare and Sport, the Dutch Ministry of Economic Affairs, the University Medical Center Groningen (UMCG the Netherlands), University Groningen and the Northern Provinces of the Netherlands. We further thank the Cogstate Research Team for their support in handling the data coming from the Cogstate Brief Battery, and Renée Lüskow for her language editing.

Highlights

- Direct/indirect routes taken by $PM_{2.5}$/BC are proposed pathways to impair the brain.
- Higher exposure to $PM_{2.5}$ was directly and indirectly related to worse cognition.
- More than 97% of the total effect for $PM_{2.5}$ was constituted by the direct effect.
- For BC, we found indirect effects over lung function only (7–14% contribution).

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III. SUPPLEMTARY MATERIAL

Supplementary Table S1. Decomposition of the associations between long-term exposure to $PM_{2.5}$ and BC, and cognitive processing time (CPT) showing single parameters among the entire study population

Air pollutant	Lung function measure	Estimations		
		β_1	θ_2	θ_1
$PM_{2.5}$	FEV_1	**-0.2335356** (-0.3454307, -0.1216405)	**-0.0004829** (-0.0006933, -0.0002725)	**0.0081947** (0.0055922, 0.0107971)
	FVC	**-0.3222027** (-0.4284042, -0.2160013)	**-0.0005337** (-0.0007551, -0.0003123)	**0.0081234** (0.0055202, 0.0107266)
BC	FEV_1	**-1.101765** (-1.601716, -0.6018149)	**-0.0004934** (-0.000704, -0.0002828)	0.0071594 (-0.004326, 0.0186448)
	FVC	**-1.927674** (-2.402697, -1.452650)	**-0.0005495** (-0.000771, -0.000328)	0.0066109 (-0.004882, 0.0181038)

Notes: FEV_1, Forced Expiratory Volume in one second; FVC, Forced Volume Capacity, $PM_{2.5}$, (fine) particulates with diameters of 2.5 µm and smaller; BC, black carbon proportion in the fine particulate matter**.** Table shows the decompositions of the Total Effects of the associations between long-term exposure to fine particulate matter (in $\mu g/m^3$) and Cognitive Processing Time (CPT), which is the log10-transformed total reaction time, measured by the Cogstate Brief Battery into the single estimation parameters from the used equations. The direct (Direct Effect) and the indirect (Indirect Effect) routes over the lung function measures FEV_1 and FVC (potential mediators) were modelled simultaneously by performing linear structural equation models with robust standard errors by Huber/ White. Illustrated were the point estimators and confidence intervals coming from single models for each air pollutant, controlled for sex, age, province of residence, educational level, income, pack-years of cigarettes smoked, hypertension, asthma, COPD, diabetes, depression, stroke, multiple sclerosis, BMI, the CBB accuracy, and the total number of CBB trials. Shown values for point estimators, lower and upper confidence intervals were not transformed after estimation. Bold values mark significant coefficients.

Supplementary Table S2. Sensitivity analysis of the model approach: Causal mediation analyses using a counterfactual approach and bootstrapping

Air pollutant	Lung function measure	Total Effect	Indirect Effect	Direct Effect	Mediation/ Direct Effect
		$\theta_1+\beta_1\times\theta_2$	$\beta_1\times\theta_2$	θ_1	
Age < 45	**n = 23893**				
$PM_{2.5}$	FEV_1	**8.25** (4.93, 11.63)	**0.11** (0.01, 0.23)	**8.15** (4.81, 11.59)	Mediation + direct effect
	FVC	**8.24** (4.94, 11.61)	**0.19** (0.02, 0.36)	**8.06** (4.72, 11.50)	Mediation + direct effect
BC	FEV_1	-4.55 (-20.50, 11.67)	**0.31** (0.01, 0.69)	-4.86 (-20.89, 11.67)	Mediation
	FVC	-4.60 (-18.07, 9.14)	**0.75** (0.12, 1.42)	-5.35 (-18.99, 8.72)	Mediation
Age 45+	**n = 25812**				
$PM_{2.5}$	FEV_1	**7.53** (4.07, 11.06)	**0.12** (0.02, 0.23)	**7.41** (3.89, 11.05)	Mediation + direct effect
	FVC	**7.52** (4.07, 11.03)	**0.19** (0.07, 0.32)	**7.33** (3.82, 10.95)	Mediation + direct effect
BC	FEV_1	7.94 (-8.32, 24.48)	**1.03** (0.41, 1.73)	6.90 (-9.66, 23.99)	Mediation
	FVC	7.89 (-8.23, 24.32)	**1.84** (0.96, 2.75)	6.06 (-10.41, 23.05)	Mediation

Notes: $PM_{2.5}$, (fine) particulates with diameters of 2.5 μm and smaller; BC, black carbon proportion in the fine particulate matter; FEV_1, Forced Expiratory Volume in one second; FVC, Forced Volume Capacity. Table shows the decompositions of the Total Effects of the associations between long-term exposure to fine particulate matter (in $\mu g/m^3$) and Cognitive Processing Time (CPT), which is the log10-transformed average reaction time, measured by the Cogstate Brief Battery. The direct (Direct Effect) and the indirect (Indirect Effect) routes over the lung function measures FEV_1 and FVC (potential mediators) were modelled simultaneously by performing g-formula method using bootstrapped standard errors (1,000 iterations). Illustrated were the point estimators and confidence intervals coming from single models for each air pollutant, controlled for sex, age, province of residence, educational level, income, pack-years of cigarettes smoked, hypertension, asthma, COPD, diabetes, depression, stroke, multiple sclerosis, BMI, the CBB accuracy, and the total number of CBB trials. Shown values for point estimators, lower and upper confidence intervals were not transformed after estimation. Shown values for point estimators, lower and upper confidence intervals were multiplied by 10^3. Bold values mark significant paths.

Supplementary Table S4. Descriptive statistics: Sensitivity models among participants aged 45+ only and by using exposure history and time-weighted average air pollution concentrations (TWA-model)

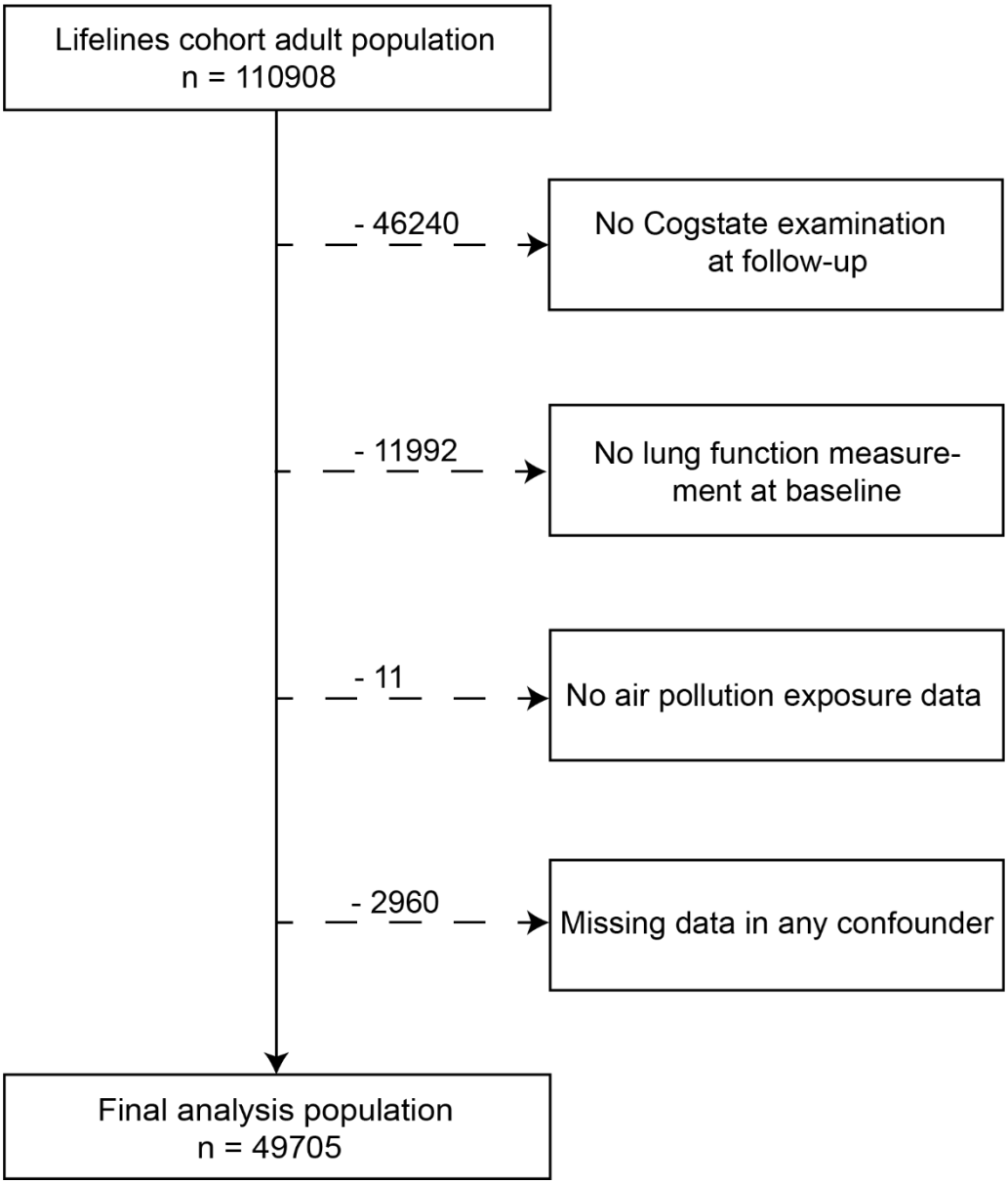
Characteristic	Baseline (2006-2012)	Follow-up (2014-2015)	Baseline (2006-2012)	Follow-up (2014-2015)
	Participants aged 45+ only		TWA-model	
No. of participants	n = 25812		n = 31232	
Sex, No. (%)				
Women	14888 (57.68)		18342 (58.73)	
Men	10924 (42.32)		12890 (41.27)	
Age, mean (SD)	53.42 (7.23)	57.47 (7.15)	43.95 (11.02)	
Province of residence, No. (%)				
Drenthe	5470 (21.19)	5478 (21.22)	5006 (16.03)	5076 (16.25)
Friesland	11458 (44.39)	11388 (44.12)	16112 (51.59)	15968 (51.13)
Groningen	8524 (33.02)	8436 (32.68)	9652 (30.90)	9386 (30.05)
Other	360 (1.40)	510 (1.98)	462 (1.48)	802 (2.57)
Educational level, No. (%)				
No education	96 (0.37)	98 (0.38)	61 (0.20)	69 (1.57)
Primary education	386 (1.50)	308 (1.19)	310 (0.99)	217 (0.70)
Lower or preparatory vocation	3900 (15.11)	3865 (14.97)	3130 (10.02)	2946 (9.43)
Junior general secondary education	4484 (17.37)	4624 (17.91)	3909 (12.52)	4005 (12.82)
Secondary vocational education	6896 (26.72)	6713 (26.01)	9352 (29.94)	9042 (28.95)
Senior general secondary education	2182 (8.45)	2179 (8.44)	3022 (9.68)	2665 (8.53)
Higher vocational education	6032 (23.37)	6163 (23.88)	8614 (27.58)	9206 (29.48)
University education	1313 (5.09)	1346 (5.21)	2321 (7.43)	2601 (8.33)
Other	523 (2.03)	516 (2.00)	513 (1.64)	481 (1.54)
Net income per month, No. (%)				
Lower than 1500 Euro	2542 (9.85)		4283 (13.71)	
1500 to 2500 Euro	7243 (28.06)		8474 (27.13)	
Higher than 2500 Euro	12280 (47.58)		14688 (47.03)	
Do not know/ do not want to tell	3747 (14.52)		3787 (12.13)	
Pack-years of cigarettes smoked, No. (%)[a]				
Never smokers	10332 (40.03)		14895 (47.69)	
Lower/ equal than the 50th percentile of ever smokers	6871 (26.62)		8482 (27.16)	
Higher than the 50th percentile of ever smokers	8609 (33.35)		7855 (25.15)	
BMI, No. (%)				
Lower than 25	10155 (39.34)	10101 (39.13)	15026 (48.11)	14630 (46.84)
25 to lower than 30	11601 (44.94)	11432 (44.29)	12254 (39.24)	12252 (39.23)
Higher/ equal than 30	4056 (15.71)	4279 (16.58)	3952 (12.65)	4350 (13.93)
Hypertension, No. (%)[b]				
Yes	6056 (23.46)	8059 (31.22)	4869 (15.59)	6526 (20.90)
No	19756 (76.54)	17753 (68.78)	26363 (84.41)	24706 (79.10)

Asthma, No. (%)[c]				
Yes	1647 (6.38)		2322 (7.43)	
No	24165 (93.62)		28910 (92.57)	
COPD, No. (%)[c]				
Yes	1430 (5.54)		1342 (4.30)	
No	24382 (94.46)		29890 (95.70)	
Diabetes, No. (%)[c]				
Yes	2303 (8.92)		2056 (6.58)	
No	23509 (91.08)		29176 (93.42)	
Depression, No. (%)[c]				
Yes	2648 (10.26)		3158 (10.11)	
No	23164 (89.74)		28074 (89.89)	
Stroke, No. (%)[c]				
Yes	209 (0.81)		139 (0.45)	
No	25603 (99.19)		31093 (99.55)	
Multiple Sclerosis, No. (%)[c]				
Yes	59 (0.23)		62 (0.20)	
No	25753 (99.77)		31170 (99.80)	
Long-term air pollution, mean (SD)[d]				
PM2.5 (in μg/ m^3) one-year annual mean concentration	14.88 (1.02)			
BC (in μg/ m^3) one-year annual mean concentration	1.20 (0.20)			
PM2.5 (in μg/ m^3), TWA based on address history data			14.95 (0.95)	
BC (in μg/ m^3), TWA based on address history data			1.25 (0.21)	
Total exposure time (in days) for TWA data			8567.56 (2448.31)	
Lung function, mean (SD)[e]				
FEV1 (L), % predicted	97.63 (13.73)		96.63 (12.58)	
FVC (L), % predicted	102.64 (12.84)		100.69 (12.07)	
Number of CBB trials, mean (SD)[f]		142.37 (25.94)		139.87 (24.35)
Accuracy of given responses, mean (SD)[g]		3.68 (0.52)		3.77 (0.46)
Less accurate (lower values) than the mean, No. (%)		11020 (42.69)		13963 (44.71)
More accurate (higher values) than the mean, No. (%)		14792 (57.31)		17269 (55.29)
Cognitive processing time (CPT), log10-transformed milliseconds, mean (SD)[h]		8.46 (0.34)		8.35 (0.33)
Faster CPT (lower values) than the mean, No. (%)		13406 (51.94)		16278 (52.12)
Slower CPT (higher values) than the mean, No. (%)		12406 (48.06)		14954 (47.88)

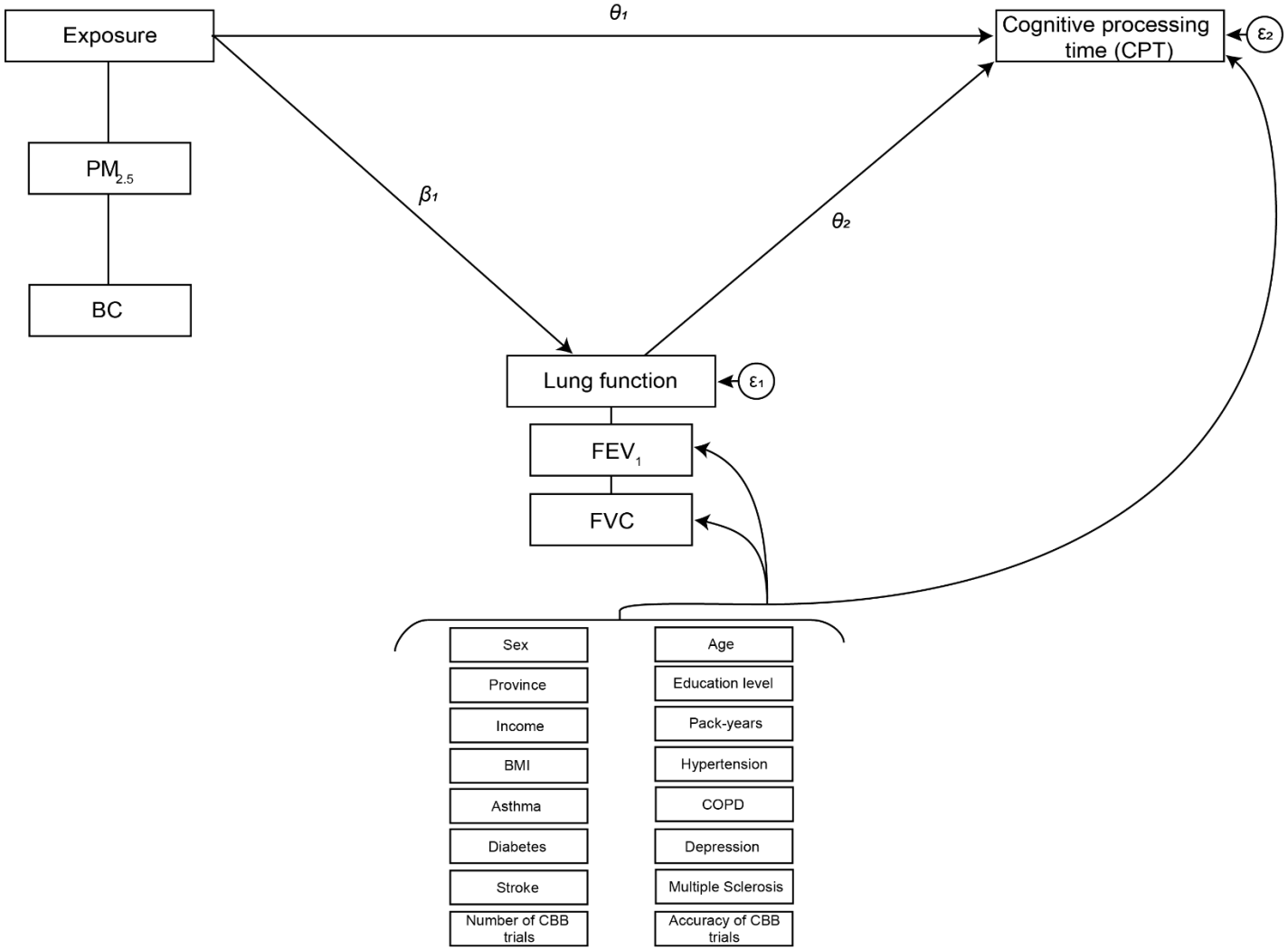
Notes: BMI, body mass index (calculated as weight in kilograms divided by height in meters squared); $PM_{2.5}$, (fine) particulates with diameters of 2.5 μm and smaller; BC, black carbon proportion in the fine particulate matter. [a] Pack-years of cigarettes smoked were calculated from the baseline questionnaire (1 pack-year = 20 cigarettes per day in 1 year). [b] Hypertension was defined when systolic pressure was higher than 139 mmHg or diastolic pressure higher than 89 mmHg (blood pressure was measured by medical staff). [c] Prevalence of diseases at baseline was assessed by questions, whether a specific disease was diagnosed by a doctor or not. [d] Long-term air pollution concentrations were assessed either as one-year annual mean concentrations at participants' baseline address and were estimated for the year 2010 by the

ELAPSE models/ project, or as time-weighted average concentrations up to the 31st December before the baseline year (TWA-model) by using the estimated concentrations for the year 2010 and the participants' residential address history (= exposure history). [e] Lung function was measured by spirometry by trained medical staff. [f] Number of CBB trials represents the total number of responses given by the participants during the three subtests (detection, identification, working-memory) of the Cogstate Brief Battery. [g] Accuracy was measured by the proportion of correct responses. For each domain (detection, identification, working-memory), the accuracy of each response to each trial was recorded. The three already arcsine-transformed measures from the Cogstate Brief Battery were summed to measure the total accuracy. [h] Cognitive Processing Time was measured by using three single (detection, identification, working-memory) log10-transformed speed measures from the Cogstate Brief Battery. The three measures were summed up to measure the total average reaction time.

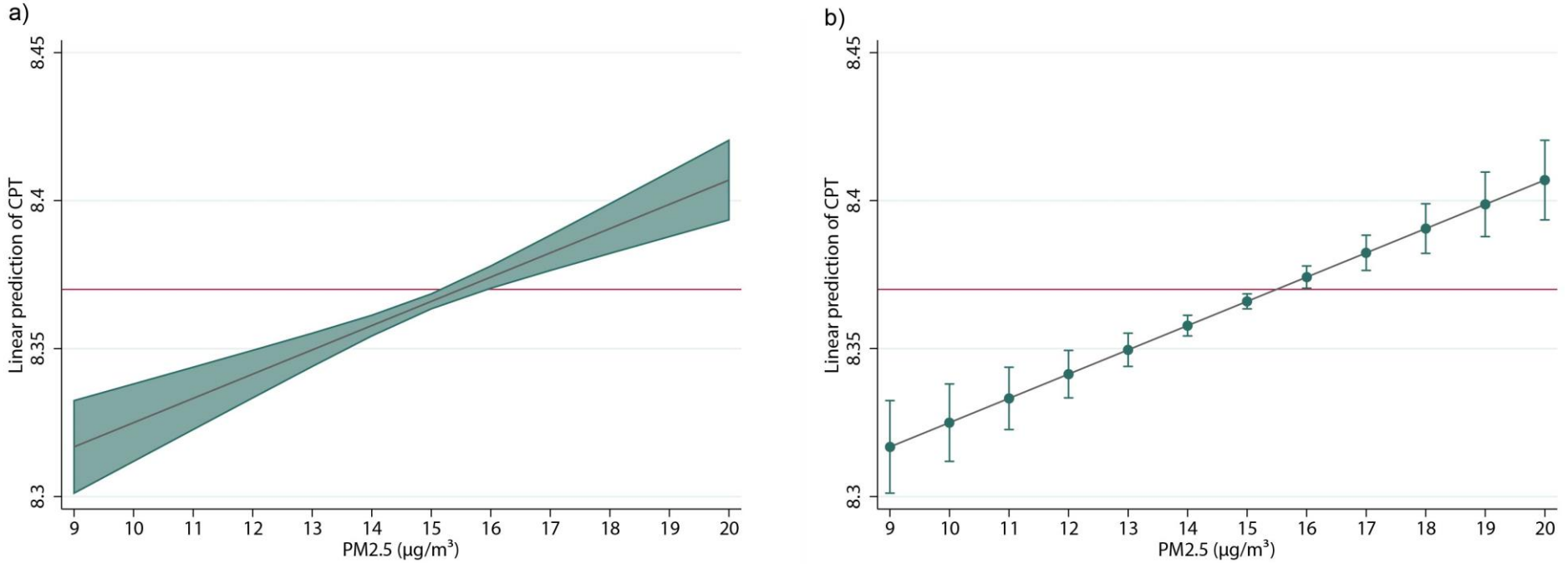
Supplementary Figure S1. Construction of the study population based on the Lifelines cohort study population aged 18+



Supplementary Figure S2. Used structural equation model (SEM) to test the direct and indirect routes of air pollutants on cognitive processing time (CPT)

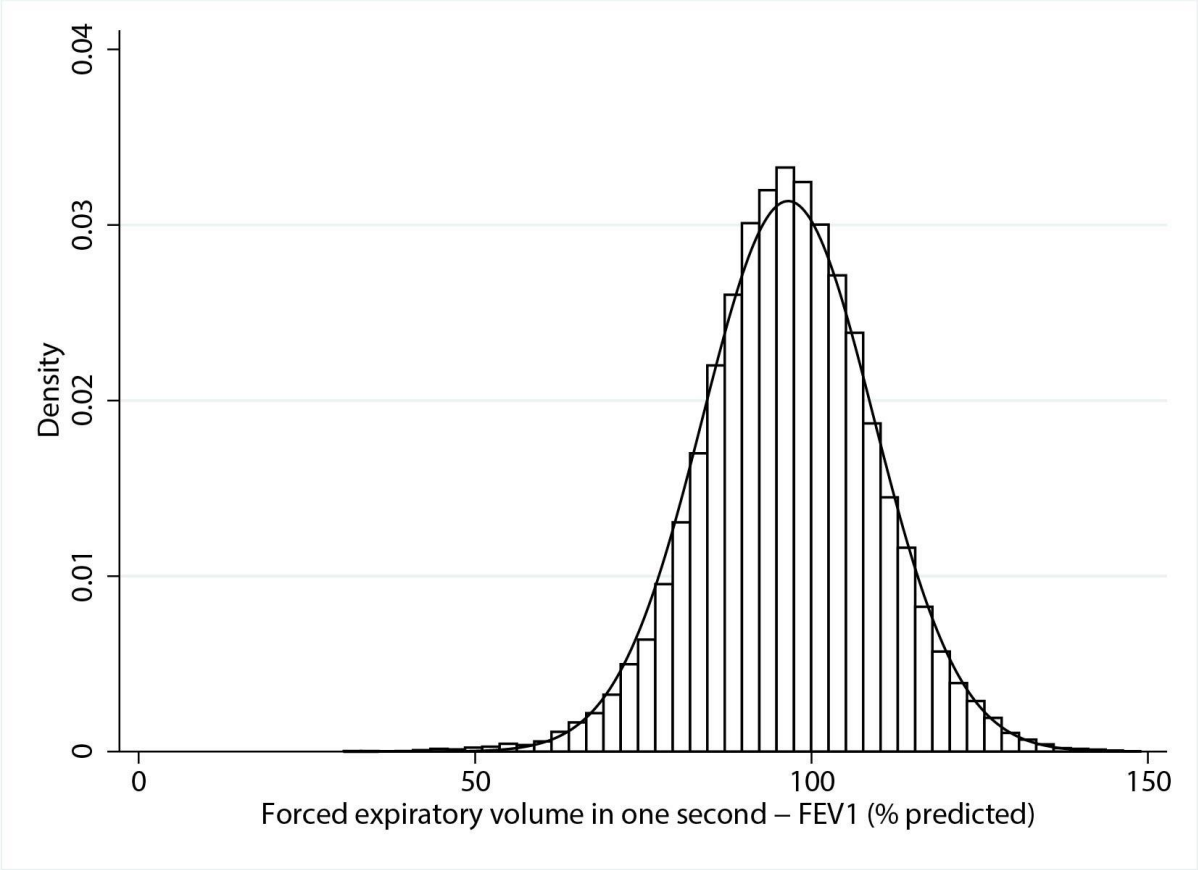


Supplementary Figure S3. Adjusted predictions of cognitive processing time (CPT) for the Total Effects of $PM_{2.5}$

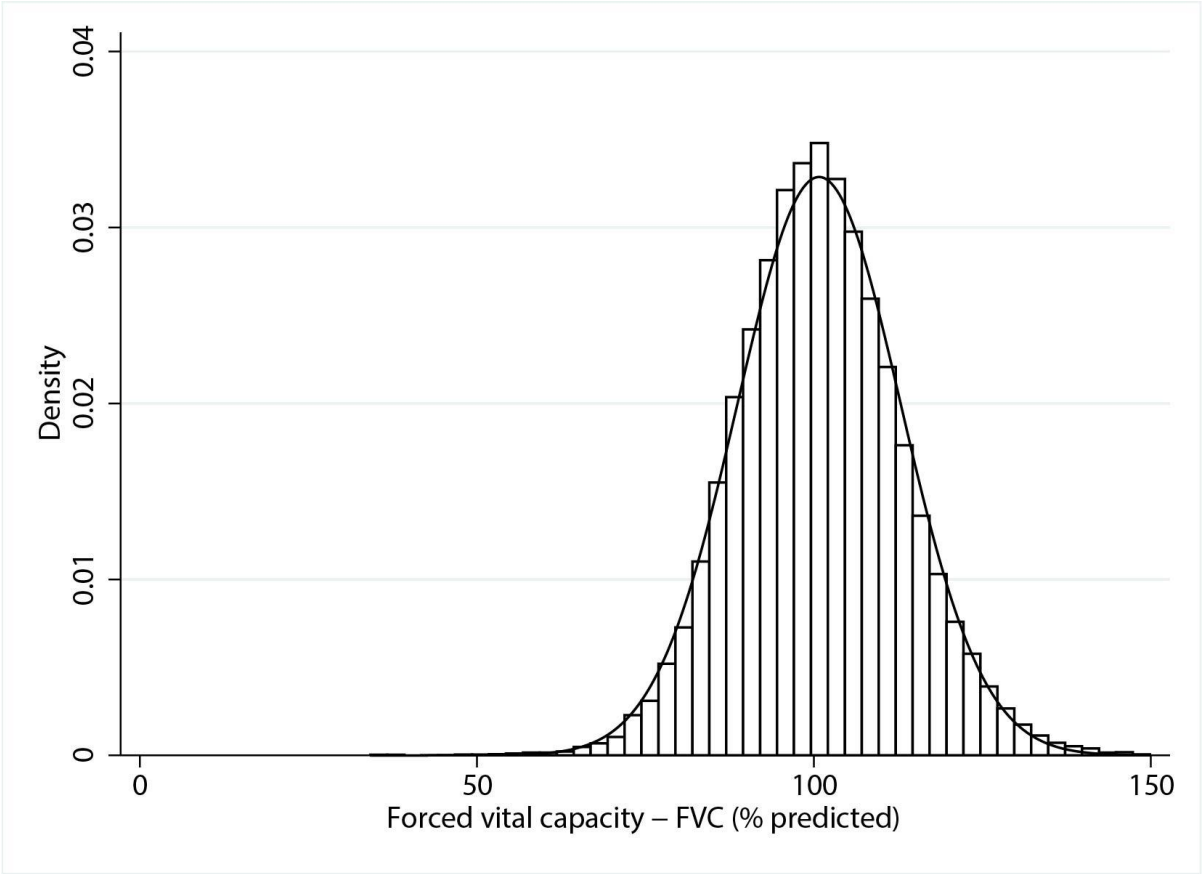


Notes: $PM_{2.5}$, (fine) particulates with diameters of 2.5 μm and smaller; BC, black carbon proportion in the fine particulate matter; CPT, cognitive processing time. Adjusted Predictions of cognitive processing time (CPT, log10-transformed milliseconds) for the Total Effects of $PM_{2.5}$ were estimated for each single integer exposure value between the minimum and the maximum by a linear model. The linear predictions (grey line) of CPT were controlled for sex, age, province of residence, educational level, income, pack-years of cigarettes smoked, hypertension, asthma, COPD, diabetes, depression, stroke, multiple sclerosis, BMI, the CBB accuracy, and the total number of CBB trials. Green lines show the 95% confidence intervals for the point estimators. The red line marked the mean value of CPT (8.37) of the entire study population.

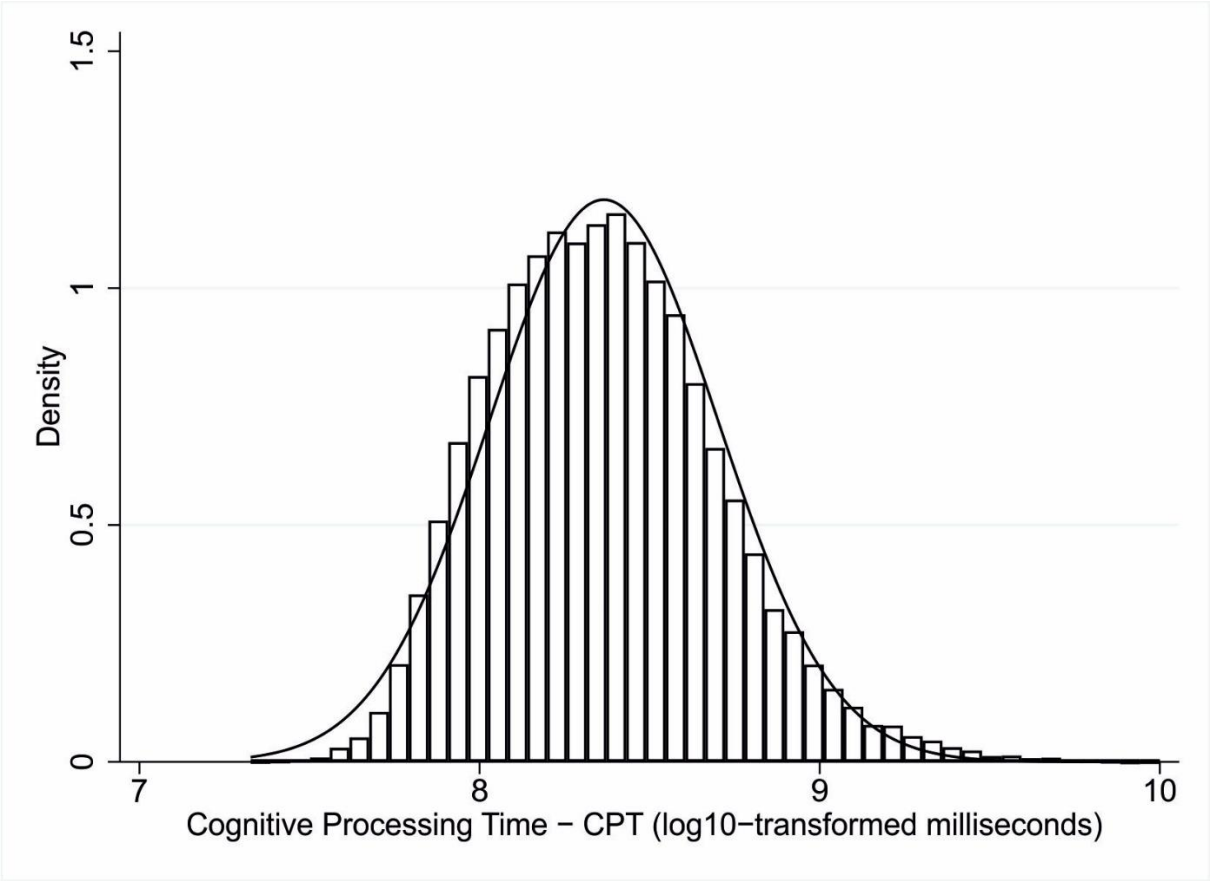
Supplementary Figure S4. Distribution of the mediator variable (FEV_1)



Supplementary Figure S5. Distribution of the mediator variable (FVC)



Supplementary Figure S6. Distribution of the outcome variable (CPT)



5

The short- and long-term effects of the Great Recession on late-life depression in Europe: The role of area deprivation

This chapter was published as

Benjamin Aretz (2022). The short- and long-term effects of the Great Recession on late-life depression in Europe: The role of area deprivation. Social Science & Medicine. Volume294.
DOI: *https://doi.org/10.1016/j.socscimed.2021.114697*.

I. ABSTRACT

Introduction: The prevalence of depression increases in times of economic crises. Less is known about whether people living in advantaged or disadvantaged areas suffer equally from negative effects of crisis.

Objective: To explore the role of area deprivation on the short- and long-term effects of the Great Recession in Europe on late-life depression.

Methods: Individual panel data from Austria, Belgium, Denmark, France, Germany, Italy, Spain, Sweden, Switzerland of the SHARE (age 50+, n = 6,866) between 2004 and 2017 were used. Late-life depression (LLD) was measured by the EURO-D scale (4+ symptoms). Area deprivation was assessed by a country-specific z-standardized scale measuring perceived access to various services and quality of the social and built environment. Quarterly country-level GDP and yearly unemployment data were explored to define country-specific durations of the Great Recession. Individual fixed effects panel regressions were estimated controlling for time-varying socioeconomic and health-related confounders.

Results: Prevalence and incidence of late-life depression was generally higher in deprived than in non-deprived areas, and these differences in prevalence and incidence increased during the Great Recession. Regressions showed that the Great Recession was related to a 23% higher long-term risk of late-life depression (OR: 1.23, CI: 1.05-1.44) for all study participants. In the short-term of the Great Recession, people from deprived areas had a 22% higher risk of late-life depression (OR: 1.22, CI: 1.02-1.46) than people from non-deprived areas.

Conclusion: The findings suggest that older adults exposed to adverse area determinants suffer more from the negative short-term effects of a severe economic crisis on depression and mental health inequalities may have increased between people living in deprived versus non-deprived areas. This potential increase in mental health inequalities warrants particular attention for those people living in deprived areas.

Key words: Economic crisis, Great Recession, late-life depression, EURO-D, area deprivation, fixed effect estimation, SHARE

II. FULL PAPER

1. INTRODUCTION

The World Health Organization estimated that the total number of people worldwide living with depression in 2015 was 322 million, which was 4.4% of the global population (WHO 2017). Depression was also the mental disorder with the highest prevalence in Europe (Alonso et al. 2004, Wittchen et al. 2011). For adults ages 50 and older in 2015, estimations from 27 European countries in the Survey on Health, Ageing and Retirement in Europe (SHARE) showed a high prevalence of late-life depression (LLD) of 29% (Horackova et al. 2019). Late-life depression is characterised by the presence of multiple minor depressive symptoms occurring in an older person (usually over 50 or 60 years of age) (Blazer 2003). Because depression is associated with a wide range of physical health comorbidities (Smith et al. 2014), avoiding mental health problems and their risk factors can substantially reduce costs, morbidity, and mortality in Europe (Wykes et al. 2015).

It is well known that individual-level risk factors, e.g. morbidities, limitations in activities of daily-living, unhealthy lifestyle, low or high BMI, and inactivity/ loneliness contribute to the onset of late-life depression (Aziz & Steffens 2013). However, there is also growing evidence that economic crises at the macro-level are related to a higher risk of depression (Economou et al. 2013; Frasquilho et al. 2015, Weinberger et al. 2018, see Parmar et al. 2016 for a literature review). Previous studies that focused on the individual-level factors involved revealed that this higher risk of depression was caused by unemployment, a decrease in well-being, and income losses, which in turn were affected by the altered macro-level economic situation (Taplin et al. 2012). An economic crisis brings on (perceived) economic insecurity, unemployment, poverty, psychological distress and anxiety, and social stress (Mucci et al. 2016), which are assumed to be some of the main drivers leading to depressive symptoms (Chang et al. 2016; Krishnan & Ranga 2002). Hence, these risk factors could directly increase the risk of depression, or they could translate into stressful life-events in the family or social peer-groups (Li et al. 2019). Research suggests further that vulnerable social groups experienced disproportionate short-term losses in wage and health during the Great Recession (Bacigalupe et al. 2016, Hoynes et al. 2012, Reibling et al. 2017, Rugh et al. 2010). These authors defined “vulnerable” as pertaining to people

at risk of poverty or social exclusion, e.g. (self-) employed people (compared to retired) or older people living alone.

Although it is well known that socioeconomic, physical, and social area-level characteristics are associated with the presence and severity of depression (Beyer et al. 2014, Cohen-Cline et al. 2015, Fone et al. 2014, Generaal et al. 2019, Strachan et al. 2017), previous research on the effects of economic crises on depression has focused mainly on the effects of individual-level risk factors (Bacigalupe et al. 2016, Hoynes et al. 2012, Reibling et al. 2017, Rugh et al. 2010). There is rare evidence that the number of foreclosures at the area-level is associated with the onset of depression (Cagney et al. 2014). Consequently, it is largely unknown whether people living in advantaged or disadvantaged areas suffer equally from negative effects of economic crises, once individual-level factors have been controlled for. Furthermore, most previous studies on the effect of a recession on mental health outcomes have focused on either the short- (Mattei et al. 2014, Modrek et al. 2015) or on the long-term (Forbes & Krueger 2019, Wang & Fattore 2020) effects; they did not regard the two of them.

This prospective cohort study explores the role of area deprivation as an important area-level dimension in the short- and long-term effects of the Great Recession on the risk of late-life depression among participants in Europe aged 50 and older. The Great Recession was treated as a case study, conducted in the design of a natural experiment, representing an example of a severe macro-level economic crisis. The Great Recession, a global economic downturn which had its climax between 2007 and 2009, was the most severe economic crisis since the Great Depression in the 1930s (Albers & Jonung 2012). It is the most demonstrative example of a macro-level economic crisis in our times.

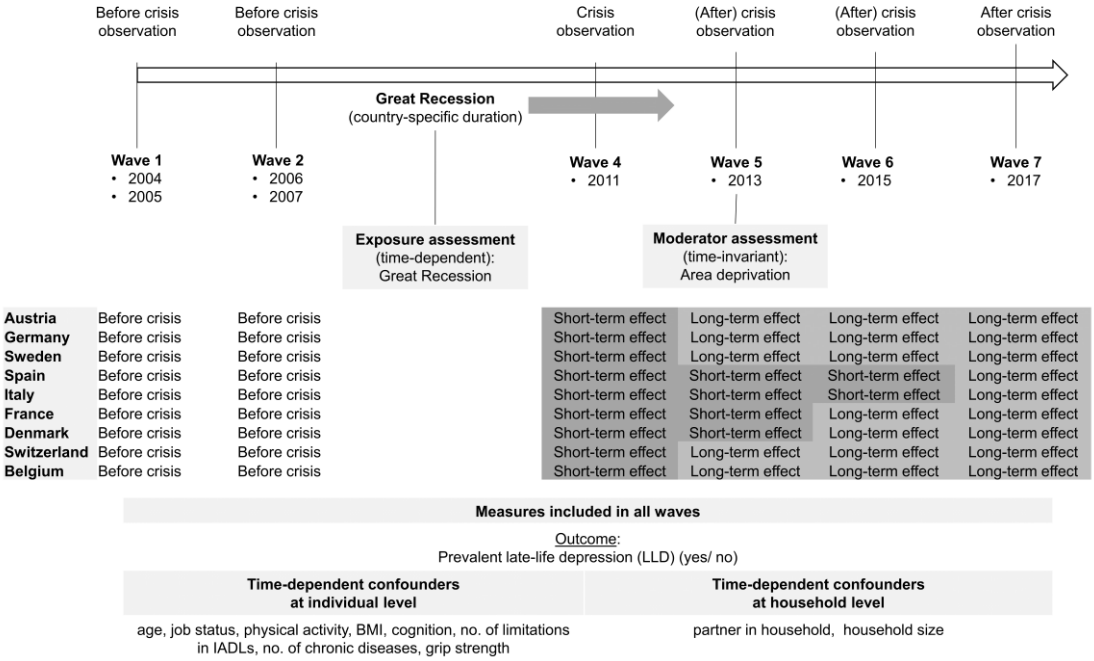
First, this study hypothesised that the Great Recession increased the risk of late-life depression in older people in Europe. Second, it was assumed that, due to previous findings on the mental health importance of area-level determinants, people living in deprived areas had a higher risk of LLD, especially in the years immediately following the Great (short-term), than did people from non-deprived areas.

2. MATERIAL AND METHODS

2.1 Study population and design

This prospective cohort study used individual and household panel data from the cross-national and harmonised panel Survey of Health, Ageing and Retirement in Europe (SHARE). SHARE focuses on the socioeconomic and health situation of adults aged 50 and older. It covers seven waves from 2004 to 2017, including information on more than 140,000 participants from 28 European countries (Börsch-Supan et al. 2013). SHARE is conducted every two years according to the principles of the Declaration of Helsinki and was reviewed and approved by the Ethics Committee of the University of Mannheim, Germany.

Figure 1. Study design to explore the role of area deprivation in the effects of the Great Recession on the risk of late-life depression



The current study uses individual and household data from SHARE countries that participated in all waves conducted up to 2017, namely wave 1 (2004-2005), wave 2 (2006-2007), wave 4 (2011-2012), wave 5 (2013), wave 6 (2015), and wave 7 (2017) (see **Figure 1** for an illustration of the design).

To define country-specific durations of the Great Recession (see further down), country-level economic data between 2004 and 2017 were used. This includes quarterly nominal gross domestic product (GDP) per head in US dollars from OECD calculated using the expenditure approach (OECD 2021), and yearly unemployment rates (UR) among people aged 15 to 74 at country-level from Eurostat based on labour force surveys (LFS) (Eurostat 2021).

2.2 Analysis sample

The initial SHARE sample covered 95,534 participants aged 50 and over from the 9 countries which participated in all waves conducted (Austria, Belgium, Denmark, France, Germany, Italy, Spain, Sweden, Switzerland). To be eligible for the current study, people had to be aged 50 or over in the first wave (reducing the sample by 3,046 participants), and needed to have valid information on LLD in both waves conducted before the Great Recession had started (wave 1 & wave 2) and at least in one wave thereafter (reducing by 82,345 participants).

Participants were also excluded if they had already been diagnosed as depressed by a doctor (n = 1,746) before baseline (wave 1, 2004/ 05) in order to include only incident LLD cases during the observation time.

People who had relocated during the observation time (n = 1,531) were removed because area deprivation could have changed in these cases. Consequently, 6,866 participants at baseline (2004-2005) with a total of 33,788 observations during the analysis time could be studied for people living in these nine countries. Because the fixed effects models solely use changes within individuals over time, 3,114 participants who had experienced changes in present/ non-present LLD with 15,677 observations were included in the main model. In the sensitivity analysis using multi-level mixed effects models, the study population contained 6,866 participants with 33,788 observations.

2.3 Exposure assessment: the short- and long-term effect of the Great Recession

A recession is defined as two consecutive quarters of negative economic growth compared to a basis quarter (Gaski 2012). To encompass differing durations of the Great Recession (from here onwards Recession) per country, country-level GDP data were used in a descriptive/ explorative fashion to identify country-specific SHARE waves defined as

short-term effect (STE) and long-term effect (LTE) assessments. For this purpose, a categorical variable with three values was computed, indicating whether the outcome measure occurred either before the Recession had started, in the short run (= short-term effect (STE)), or in any of the waves thereafter (long-term effect (LTE)). The long-term effect consequently comprises the effect for at least one year after the Recession has ended. (see **Supplementary Figures 1 to 3** and their descriptions)

2.4 Outcome assessment: late-life depression (LLD)

In SHARE, the EURO-D depression symptom scale was applied to measure late-life depression (LLD) which is characterised by the presence of multiple minor depressive symptoms occurring in an older person (usually over 50 or 60 years of age) (Blazer 2003).

EURO-D was developed in a European Union initiative by the EURODEP Concerted Action Programme consisting of 14 European geriatric centres and focused on late-life depression (Prince et al. 1999). EURO-D consists of 12 items covering the following depression symptoms: (1) depressed mood, (2) pessimism, (3) suicidality, (4) guilt, (5) sleep trouble, (6) less interest in things, (7) irritability, (8) less appetite, (9) fatigue, (10) concentration problems, (11) enjoyment of almost nothing in life, and (12) tearfulness (Castro-Costa et al. 2008).

In our study, a threshold of four was used to differentiate between LLD-free (0-3 depression symptoms) and LLD-prevalent (4-12 depression symptoms) cases, in line with the optimal cut-off point that was defined in previous validation studies (Castro-Costa et al. 2008, Guerra et al. 2015, Prince et al. 1999).

2.5 Moderator assessment: perceived area deprivation

Perceived area deprivation was computed as an own-calculated country-specific and relative measure using the items on area characteristics available in SHARE. Area deprivation in SHARE was assessed based on eight surveyed area characteristics measured at the household-level in wave 5 (2013). The items assessed the local built and social environment, as well as access to local infrastructure (see Supplementary Table 4). The items were representative for all household members based on responses by the household respondent (Myck et al. 2015). In SHARE, the household respondent is usually defined as the household member who makes the main contribution to the household income.

The following items were answered using a 4-point-Likert-scale (strongly agree, agree, disagree, strongly disagree) and referred to the first dimension, namely the social and built environment: 1) feeling part of the area, 2) vandalism is a big problem in the area, 3) area is kept clean, 4) helpful people in the area. The other four items covered the second dimension, namely the accessibility to local infrastructure, and also used a 4-point-Likert-scale (very easy, easy, difficult, very difficult): 5) easy to get to the nearest bank or cash point, 6) easy to get to the grocery shop or supermarket, 7) easy to get to the nearest general practitioner or the health centre, 8) easy to get to the pharmacy. Because perceived area deprivation levels may differ between countries, ADI was then country-specific z-standardised (mean = 0, SD= 1). This was done using information from all participants of the SHARE to avoid potential selection bias. Values below or equal to zero were defined as a non-deprived area and values greater than zero as deprived area. Area deprivation was measured only in wave 5 (2013), so the resulting ADI was treated as a time-invariant variable for the entire observation time from 2004 to 2017. This was possible because only people who did not relocate during the observation time were part of the study population (find a detailed review of the used approach in the discussion).

2.6 Assessment of potential confounders at individual- and household-level

At the individual level, time-varying confounders related to socio-demographics, social environment, lifestyle, and health/ morbidity were controlled for because these had already been designated as relevant risk factors of depression in the literature (Aziz & Steffens 2013). Starting with the socio-demographic confounders, age in years (50-64, 65-79, 80+) and job status (retired, employed or self-employed, unemployed, permanently sick or disabled, homemaker, other, missing values) were used.

The lifestyle variables included were physical activity (yes, no), whereby activity means that participants do vigorous physical activity in daily life at least sometimes, such as sports, heavy housework or a job that involves physical labour, and Body-Mass-Index (BMI) (< 18.5 underweight, 18.5-24.9 normal, 25-29.9 overweight, 30+ obesity, missing values).

Additionally, the models accounted for important health and morbidity confounders. Cognitive functioning, measured by episodic memory and recall of a 10-word list, was categorised in terciles. As a proxy for physical health/ frailty, isometric grip strength of the

stronger of both hands in kilograms was used, in addition to the number of prevalent limitations in Instrumental Activity of Daily Living (IADL) (0, 1, 2 or more). To control for comorbidities, the number of chronic diseases (0, 1, 2 or more) was applied covering all available morbidities in SHARE, namely hypertension, high blood cholesterol, stroke or cerebral vascular disease, diabetes, chronic bronchitis or emphysema, asthma, arthritis, osteoporosis, cancer, stomach or duodenal ulcer, Parkinson disease, cataract, hip fracture or femoral fracture.

At the household level, the models considered, in a time-dependent fashion, whether participants were living together with a partner in a household (yes, no) and the household size (1, 2, 3, 4+).

The SHARE interviewers assessed if the participants' residence was in a big city, the suburbs of a big city, a large town, a small town, or a rural area or village. This variable was categorised into a binary variable to divide between (time-invariant) urban (big city, suburb, large town, small town) and rural areas (rural area/ village).

2.7 Statistical analyses

To determine if area deprivation moderated the short- and long-term effects of the Great Recession on the risk of late-life depression, binary logistic individual fixed effect (FE) models using within-estimators were applied. The advantage of such models is that they can control for person-specific time-constant (unobserved) heterogeneity, e.g. sex and country of residence (Woolridge 2010) (1). Although time-invariant characteristics per se cannot be interpreted in FE models, interactions between a time-invariant and a time-dependent variable can be estimated. In this study, this was the case for the time-dependent effects of the Recession (exposure/ treatment) on the risk of LLD (outcome of interest) in dependency of area deprivation (potential moderator).

Let Y_{it} equal LLD-prevalent or LLD-free of person i at time t and let the time-dependent categorical variable for the short- or long-term effect of the Recession (STE_{it} and LTE_{it}) denote whether the observed time periods were defined as short- or long-term effects. $Area\ deprivation_i$ was a time-constant dummy variable defining whether a person i was living in a deprived or non-deprived area. α_i denotes the individual fixed effects including all time-invariant (observed or unobserved) characteristics and u_{it} is the idiosyncratic

error, specific to person i and time period t and thus including all time-dependent unobserved characteristics.

$$Y_{it} = \beta_1(STE_{it}/\ LTE_{it}) * \beta_2(Area\ deprivation_i) + \alpha_i + u_{it} \quad \text{(i)}$$

Hausman tests were performed to test for endogeneity, the correlation between predictors and the error term, with the hypothesis that no correlation is present (Hausman 1978). All tests showed highly significant results ($p < 0.001$), confirming that random-effect models would not deliver consistent estimations.

In a sensitivity analysis, a multi-level model with mixed effects (ME) using random-intercepts for countries, households, and individuals were performed due to the hierarchical nature of the data (clustering over countries, households, and time per individual). An exchangeable correlation matrix was used for showing best model fit (lowest AIC). The between-individual effect is assumed to be random and the model was fitted by using the restricted maximum likelihood estimation (REML).

The SHARE data are distributed to registered users only. However, to ensure openness, transparency, and reproducibility of our analyses, Supplementary Material including additional tables, figures, descriptions, and the script/ code was provided here (Aretz 2022).

2.8 Analysis strategy: main analyses

After description of the sample, the main analyses were presented in two steps.

First, age-standardised prevalence and incidence rates of LLD in the study population over time were calculated separately for people living in deprived and non-deprived areas for 2004 to 2017. For the age-standardised rates, the 2013 European Standard Population developed by Eurostat (European Commission 2013) using the following age groups (population weights in brackets) was used: 50-64 (0.4875), 65-79 (0.3625), 80+ (0.1500).

Second, a multivariate FE model including an interaction term between the Recession and area deprivation was applied to find out whether general STE and LTE of the Recession existed, and/or if these effects depended on living in deprived or non-deprived areas.

2.9 Analysis strategy: sensitivity analyses

A set of nine sensitivity analyses were performed. In the first, a model among non-household respondents only was estimated to check how relevant same source bias (moderator and outcome are subjectively measured) was. In sensitivity models 2 to 4, two interaction-terms, namely first for area deprivation and the GR and second for urban/ rural area and GR, were incorporated stepwise. In sensitivity model 5, the main model was calculated among participants with at least four instead of three observations per participant in the main model to ensure that the results do not reflect only panel attrition effects. A sixth sensitivity model was applied among participants aged 65 and older, the age at which most participants were retired and had a stable income over time. This was done to exclude (missed) changing income was an important confounder. In sensitivity model 7, mixed effects using random intercepts for countries, households, and participants were estimated to validate the results gathered from the main FE models by regarding the hierarchical nature of the SHARE data.

To check if the results are robust when using the degree of depression as outcome two additional models were estimated. Sensitivity model 8 used the number of depressive symptoms as outcome and was performed using linear fixed effect regression with robust standard errors. Sensitivity model 9 used the degree of depression as outcome (0 symptoms = no depression, 1 symptom = very less depression, 2-3 symptoms = less depression, 4-5 symptoms = moderate depression, 6 symptoms = severe depression, 7+ symptoms = very severe depression).

3. RESULTS

3.1 Characteristics of the study participants

Altogether, 6,866 participants were part of the study population (**Table 1**). On average, participants had 5 observations during the observation time (min = 3, max =6).

7,333 participants (21.70%) had at least in one wave prevalent LLD during the observation time from 2004 to 2017. The proportion of participants with LLD increased in each SHARE wave from initially 18.44% in 2004/05 to 24.77% in 2017.

In 2004/05 (at baseline), 34.47% of the participants had lived in deprived areas and this proportion increased slightly to 38.05% in 2017. In wave 1, 71.31% had lived in urban

and 27.83% in rural areas. The proportion of participants who were living together with a partner in the same household decreased between 2005 and 2017 from 79.58% to 68.87% (see **Supplementary Table S1** for descriptive statistics of all variables).

In 2004/05, the average age was 63.34 years and nearly half of them (49.55%) were retired. The proportion of retired increased to 81.95% in 2017. Over time, more people were physical inactive (5.94% in 2004/05 and 13.88% in 2017), fewer were free of chronic diseases (no disease in 2004/05: 27.75%, no disease in 2017: 17.92%). Fewer had limitations in ADL (none in 2004/05: 91.12%, none in 2017: 79.01%), and more people had low grip strength (22.88 kg in 2004/05 and 36.08 kg in 2017). The proportion of obese increased from 17.96% initially to 19.20% in 2017, as well as those who were underweight from 0.82% to 1.17%.

Table 1. Selected descriptive statistics of the study participants during the observation time from 2004 to 2017

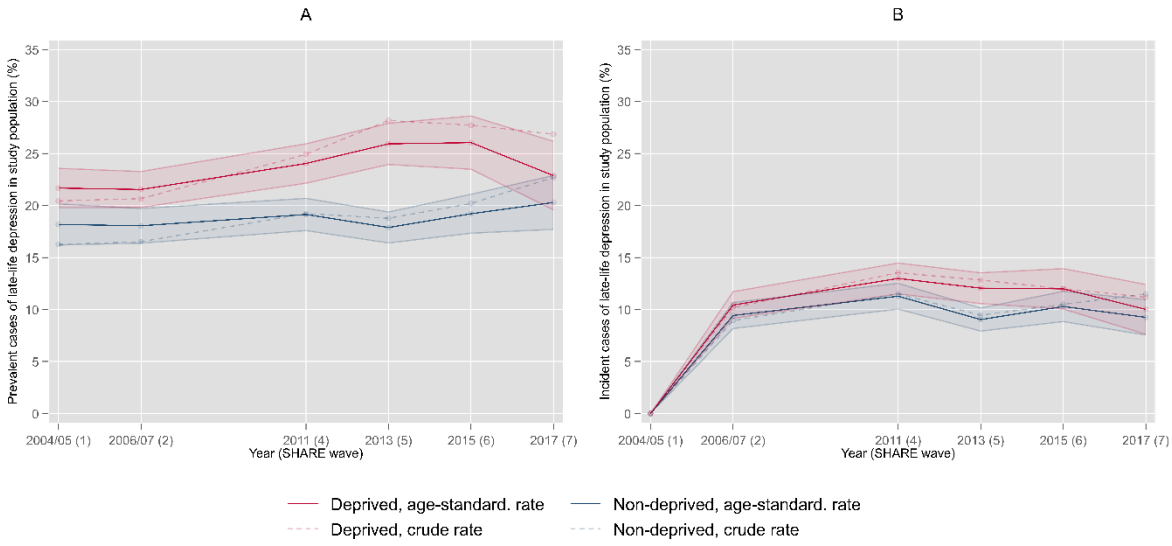
Characteristic	Wave 1[a] (2004-2005)	Wave 2[a] (2006-2007)	Wave 4 (2011-2012)	Wave 5 (2013)	Wave 6 (2015)	Wave 7 (2017)
Total no. of observations per wave	6,866		6,082	5,389	4,730	3,855
Gender, No. (%)						
Female	3,538 (51.53)		3,127 (51.41)	2,804 (52.03)	2,479 (52.41)	2,044 (53.02)
Male	3,328 (48.47)		2,955 (48.59)	2,585 (47.97)	2,251 (47.59)	1,811 (46.98)
Age						
50-64	3,989 (58.10)	3,392 (49.40)	1,952 (32.09)	1,383 (25.66)	857 (18.12)	385 (9.99)
65-79	2,566 (37.37)	2,958 (43.08)	3,137 (51.28)	2,999 (55.65)	2,868 (60.63)	2,539 (65.86)
80+	311 (4.53)	516 (7.52)	993 (16.33)	1,007 (18.69)	1,005 (21.25)	931 (24.15)
Area deprivation, No. (%)						
Non-deprived	3,076 (44.80)		2,721 (44.74)	2,962 (54.96)	2,496 (52.77)	2,114 (54.84)
Deprived	2,367 (34.47)		2,119 (34.84)	2,261 (41.96)	1,818 (38.44)	1,467 (38.05)
Missing value	1,423 (20.73)		1,242 (20.42)	166 (3.08)	416 (8.79)	274 (7.11)
Urban or rural area, No. (%)						
Urban	4,896 (71.31)		4,306 (70.80)	3,894 (72.26)	3,398 (71.84)	2,730 (70.82)
Rural	1,911 (27.83)		1,728 (28.41)	1,453 (26.96)	1,291 (27.29)	1,097 (28.46)
Missing value	59 (0.86)		48 (0.79)	42 (0.78)	41 (0.87)	28 (0.73)
Prevalent late-life depression (LLD)						
No, free of LLD	5,600 (81.56)	5,571 (81.14)	4,689 (77.10)	4,111 (76.29)	3,584 (75.77)	2,900 (75.23)
Yes, prevalent LLD	1,266 (18.44)	1,295 (18.86)	1,393 (22.90)	1,278 (23.71)	1,146 (24.23)	955 (24.77)

Notes: [a] Numbers and percentages of time-constant variables were identical in wave 1 and wave 2 due to the study design (valid outcome measure in both waves conducted before the Great Recession had started)

3.2 Prevalent and incident cases of late-life depression from 2004 to 2017

Starting with the prevalent cases (**Figure 2A**) in the study population, a general and continuously existing higher level of LLD was present for participants who were living in deprived areas compared to those living in non-deprived area. In 2004/05, the prevalence of LLD tends to be higher in deprived areas (21.68%, 95% CI: 16.18-20.18) compared to participants from non-deprived areas (18.18%, 95% CI: 16.18-20.18).

Figure 2. Age-standardised prevalent (A) and incident (B) cases of late-life depression by area deprivation among study participants ages 50 and older from 9 European SHARE countries (2004–2017)



An increasing prevalence from 2004 to 2011 was visible for both deprived and non-deprived areas. However, the increase in LLD prevalence was stronger for deprived areas during this main period of the GR. In 2013, the prevalence rate showed then a decreasing trend for non-deprived areas (17.89%, 95% CI: 16.39-19.38), whereby the proportion of people with prevalent LLD has increased further to its all-time maximum of 25.93% (95% CI: 23.93-27.92) in deprived areas. In 2015, the two prevalence rates started to converge, but still with a higher level of prevalent LLD in deprived areas (26.04%, 95% CI: 23.47-28.62) compared to non-deprived areas (19.21%, 95% CI: 17.32-21.09).

Turning to the incidence rates (**Figure 2B**), deprived areas tend to have a general higher level of incident LLD, but with a convergence of both incidence rates in 2017. An increasing trend was found for both non-deprived (11.28%, 95% CI: 10.03-12.53) and deprived (12.98%, 95% CI: 11.49-14.48) areas in 2011, the year with the highest incidence rates for both groups. Thereafter, the incident cases showed a slight but constant decreasing trend for people from deprived areas. In non-deprived areas, there was a marked decrease in LLD incidence in 2013 (9.03%, 95% CI: 7.91-10.16), but with a subsequent increasing trend.

All in all, prevalence and incidence of late-life depression was generally higher in deprived than in non-deprived areas, and these differences in prevalence and incidence increased during the Great Recession.

3.3 The short- and long-term effects of Great Recession on LDD in dependency of area deprivation

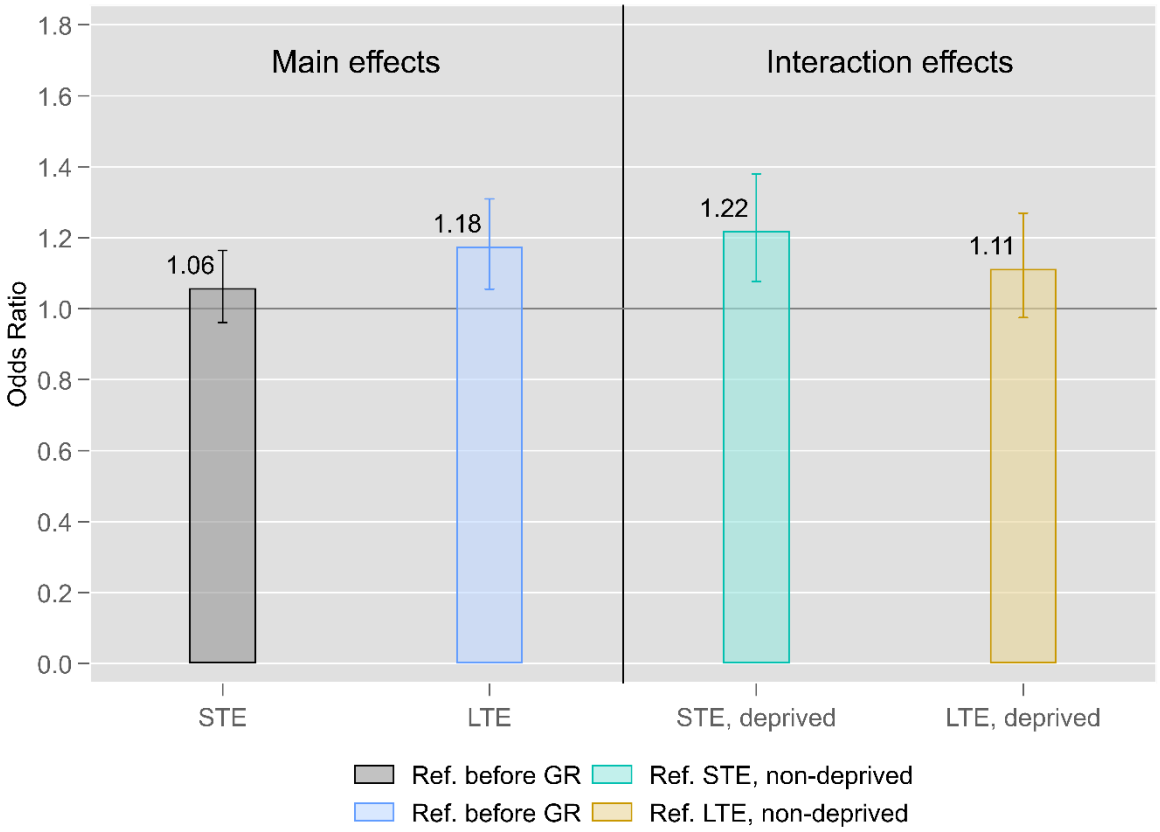
Panel fixed effects modelling showed no (stat. significant) general short-term effect (STE) by the Great Recession (GR) on late-life depression (LLD), but a stat. significant interaction between the STE and area deprivation on the risk of LLD (**Figure 3**).

In fact, participants living in deprived areas, had a 22% higher short-term risk (OR: 1.22, CI: 1.02-1.46) of prevalent LLD compared to participants living in non-deprived areas.

Turning to the long-term effects of the GR, there was a general 23% (main effect LTE: OR: 1.23, CI: 1.05-1.44) higher risk of prevalent LLD, but no additional interaction effect, suggesting that the GR had the same negative LTE on LLD for participants from non-deprived and deprived areas. See **Table 2** for the complete model results.

The different sensitivity analyses confirmed the observed findings from the main model and showed that area deprivation did not reflect only the differences between urban and rural areas. The first sensitivity analysis among non-household respondents only (Supplementary Table S2, Model 1) confirmed the findings of a general LTE from the main model. The STE for people from deprived areas lost significance due to a very low number of remaining observations (846 participants with 4,533 observations). However, the point estimator also suggested a higher (non-significant) STE on LLD for people from deprived areas (OR: 1.13, 0.81-1.56).

Figure 3. Sensitivity model 9 using the degree of depression as outcome: the role of area deprivation in the short- (STE) and long-term (LTE) effects of the Great Recession (GR) on the risk of late-life depression among study participants ages 50 and older from 9 European SHARE countries (2004–2017)



Sensitivity models 2 to 4 (**Supplementary Table S2, Model 2-4**) revealed that, due to the inclusion of the interaction between GR and area deprivation, the general negative STE disappeared (see **Supplementary Table S2, Model 2** without interaction terms). The models underlined that participants from rural areas suffered more from the negative STE than did participants from urban areas (OR: 1.23, CI: 1.03-1.48) (**Supplementary Table S2, Model 3**). However, the inclusion of the interaction between the GR and urban/ rural area did not explain the interaction effect between GR and area deprivation (**Supplementary Table S2, Model 4**). This underlined that area deprivation did not reflect only the differences between urban and rural areas.

Table 2. Complete results of the main model: the risk of late-life depression among study participants ages 50 and older from 9 European SHARE countries (2004-2017)

Variable	Odds Ratio	95% CI
Great Recession		
Before Recession	Ref.	
Short-term effect	1.07	0.93-1.23
Long-term effect	**1.23**	1.05-1.44
Area deprivation x Great Recession		
Deprived, short-term effect (STE)	**1.22**	1.02-1.46
Deprived, long-term effect (LTE)	1.16	0.97-1.40
Age		
50-64	Ref.	
65-79	1.02	0.89-1.18
80+	1.09	0.86-1.38
Job status, No. (%)		
Retired	Ref.	
Employed or self-employed	**1.26**	1.06-1.50
Unemployed	**1.50**	1.10-2.07
Permanently sick or disabled	1.22	0.88-1.69
Homemaker	1.11	0.90-1.29
Body mass index, No. (%)		
Below 18.5 (underweight)	1.52	0.99-2.34
18.5-24.9 (normal weight)	Ref.	
25-29.9 (overweight)	**0.81**	0.70-0.92
30 and above (obesity)	**0.81**	0.66-0.98
Physical activity, No. (%)		
Active, at least one activity per week	Ref.	
Inactive, no activity per week	**1.46**	1.28-1.66
Cognitive functioning (recall of a 10-word list), No. (%)		
Zero to three words recall	Ref.	
Four to five words recall	**0.78**	0.70-0.87
Six or more words recall	**0.67**	0.58-0.77
Grip strength in kilogram of the stronger hand		
1. Quantile (lowest)	Ref.	
2. Quantile	**0.85**	0.75-0.97
3. Quantile	**0.72**	0.61-0.85
4. Quantile (highest)	**0.60**	0.48-0.76
Number of chronic diseases, No. (%)		
None	Ref.	
One	**1.29**	1.13-1.46
Two or more	**1.71**	1.49-1.96
Number of prevalent limitations in IADL, No. (%)		
None	Ref.	
One or more	**2.10**	1.88-2.35
Partner living in same household (household-level), No. (%)		
No	Ref.	
Yes	**0.64**	0.48-0.84
Household size (household-level), No. (%)		
One household member	Ref.	
Two household members	1.13	0.87-1.47
Three household members	1.24	0.91-1.69
Four or more household members	1.35	0.96-1.92

Notes: Bold values denote significant results ($p < 0.05$). Ref. denotes the reference group. Area deprivation = fixed effect.

Also, the sensitivity model 5 among participants with at least four instead of three LLD observations (**Supplementary Table S2, Model 5**), model 6 (**Supplementary Table S2, Model 6**) among participants aged 65 and older, and sensitivity model 7 (mixed effects) using random intercepts for countries, households and participants confirmed the results of the main model (**Supplementary Figure S4**).

The models using the number of depressive symptoms (sensitivity model 8, **Supplementary Table S3**) or the degree of depression as outcome (sensitivity model 9, **Supplementary Table S3**) also confirmed the results from the main model. That is a 18% (OR: 1.18, CI: 1.06-1.31) higher risk of (more severe) depression in the long-run of the Great Recession and a 22% (OR: 1.22, CI: 1.07-1.38) higher short-term risk of (more severe) depression among participants living in deprived areas (ref. non-deprived areas) (**Figure 3**).

4. DISCUSSION

4.1 Summary of the findings

This study found that the age-standardised prevalence and incidence rates of late-life depression tended to be generally higher in deprived than in non-deprived areas among adults aged 50 and older in Europe from 2004 to 2017. Trends in late-life depression prevalence suggested that the Great Recession was associated with a dispersion of prevalent late-life depression between participants from deprived and non-deprived areas. The panel fixed effects regression models confirmed this finding showing, in line with the first hypothesis, a general negative long-term effect (not short-term effect) by the Recession leading to a higher risk of late-life depression compared to the pre-recession period from 2004 to 2007. The interaction for area deprivation and the Recession showed, related to the second hypothesis, that people from deprived areas had a higher risk of late-life depression in the short run – but not in the long run - compared to people from non-deprived areas. The findings from the regression models were confirmed when the different degrees of depression or the number of depressive symptoms were used as outcomes.

4.2 Interpretation and comparison of the findings

The first interesting result of this study was that people from deprived areas had a higher risk of late-life depression in the short-run compared to people from non-deprived areas.

This is in line with previous research on the effects of the Great Recession on health inequalities in Europe (Bacigalupe et al. 2016, Hoynes et al. 2012, Margerison-Zilko et al. 2016, Reibling et al. 2017, Rugh et al. 2010). These previous studies found that especially groups, which are characterised by precarious or vulnerable determinants, were immediately affected by the financial crisis. People with precarious socio-economic, life style and health characteristics are, beyond this, more likely to live in unfavourable and deprived neighbourhoods (Jokela 2014). Previous studies have already explored possible mediation paths of how area deprivation might amplify the impact of a recession on the onset of depression in later life over individual-level characteristics (potential mediators). There is evidence that the perceived job insecurity of socio-economic vulnerable groups, which more likely live in deprived areas than in non-deprived areas (Jokela 2014), may have already increased in the short-term of the Great Recession (Burgard et al. 2012). This was especially the case for the oldest workers, who felt much more insecure than middle-aged workers (Kuroki 2015). A longitudinal study based on the European Social Survey found that particularly poor mental health increased among inactive and precariously employed people (Reibling et al. 2017). Our results showed a higher risk of late-life depression for inactive people as well. A critical literature review on the health impacts of the Great Recession concluded that especially men and racial/ ethnic minorities were severely hit by the crisis (Margerison-Zilko et al. 2016). We also know that the youngest and oldest workers with low levels of education have experienced disproportionate losses (Hoynes et al. 2012).

These existing studies, however, explored only individual-level factors and did not show that area-level characteristics have a (moderating) impact on the relationship between a Recession and late-life depression. And, this effect moderation by area deprivation was still visible in our study when the impact of important individual-level pathways was eliminated. One potential explanation for this finding is that entry barriers to (potentially new) jobs and perceived financial insecurity are generally higher in deprived areas. We know that people with disadvantaged socio-economic, life style, and health characteristics often perceive their jobs as being insecure (Khubchandani & Price 2017) and these people are more likely to live in deprived areas (Jokela 2014). In this study, deprived areas were characterised by longer distances to stores and a lack of public services, which may also be accompanied by worse job opportunities in the immediate surrounding. Beyond this,

previous research found that the recession-induced perceived financial insecurity in the neighbourhood, e.g. caused by foreclosures, may have contributed to the onset of depression in the long-term (Cagney et al. 2014). It could have lasted longer, until perceived financial insecurity also reached people who were living in non-deprived areas, perhaps due to higher job security among higher-educated people. This would explain why this study found that in the short-run the Great recession was related to late-life depression among participants from deprived areas only, but in the long-run among both people from non-deprived and deprived areas. Another explanation is that a higher quality of the living environment (higher social cohesion, more green spaces, more recreational opportunities) in non-deprived areas promotes coping strategies to deal with an increase of anxiety and stress, especially during a financial crisis. Non-deprived areas offer more resources to promote stress reduction, so that the negative short-term effect of a financial crisis can (at least partially) be cushioned. It is accordingly well documented that area deprivation per se erodes social cohesion (Becares et al. 2011), and higher levels of social cohesion are in turn related to a lower risk of late-life depression (Yamaguchi et al. 2019). In addition to social cohesion, less deprived and favourable areas provide green spaces for recovery and physiological stress reduction (Hedblom et al. 2019), and are less often characterised by food insecurity (Jessiman-Perreault & McIntyre 2017). Moreover, people from deprived areas may have worse labour market accessibility, which could strengthen the effect of perceived job insecurity and a potential job loss (Damm 2014).

The finding that the Great Recession is related to a higher long-term risk of late-life depression is in line with previous studies, which found negative long-term effects of recessions on different (changing) mental health outcomes, e.g. depression, anxiety or general mental health (Bacigalupe et al. 2016, Banks et al. 2020, Marshall 2020, Witteveen & Velthorst 2020). In this, the pathway over (over time cumulated) self-perceived financial insecurity, which may, among others, be affected by spillover effects of the social environment, could also play an important role. Furthermore, perceived unemployment and income downturns in the family could also explain the increased long-term risk of depression caused by recessions (Ström 2003), which had already been shown in a panel study among adults in Australia (Bubonya et al. 2017). In analogy to the family stress theory (Conger et al. 1994), but in a reversed fashion, unemployment and income downturns of one's own children may promote (inter-) parental conflicts and anxieties, subsequently

leading to a higher risk of depression. Stressful life events in the family pose one directly-related major risk factor of depression (Caspi et al. 2003) and can bring on anxiety disorder (Taher et al. 2015). Due to the higher (perceived) job security of family members, this effect may have been only observed in the long-term for people from non-deprived areas (Esser & Olsen 2011). As an epidemiological pathway, existing research suggests that stressful life events lead to a reduction in hippocampal volume and thus to a higher risk of depression (Zannas et al. 2013).

4.3 Strengths and limitations

This is one of the first studies to explore the role of area characteristics in the relationship between an economic crisis and depression, and it has some important strengths.

First, our outcome of interest, late-life depression measured by the EURO-D scale, is a widely (and cross-cultural) validated measure (Castro-Costa et al. 2008, Guerra et al. 2015, Larraga et al. 2006), which was developed specifically to measure depression among participants in older ages, and thus fitted well for the older SHARE population. In contrast to using depression diagnoses by a doctor, as has been done in studies using administrative/ claims data (Steffen et al. 2020, Wulsin et al. 2015), EURO-D also pinpoints undetected depression among participants who did not consult a doctor and thus did not receive a diagnosis. There is evidence that these latter data suffer from undercoding and underreporting of depression prevalence (Doktorchik et al. 2019).

Second, country-specific durations of the Great Recession were examined by using time series and country-specific GDP and unemployment data, and were additionally validated by calculations conducted by Eurostat based on EU-SILC data (OECD 2018). Previous studies have mainly compared changed health between pre- and post-recession periods (Reeves et al. 2014, Riumallo-Herl et al. 2014).

Third, the measure used for area deprivation was country-specific standardized and thus of a relative nature, so that varying levels of perceived area deprivation between countries were considered.

Despite the strengths of this study, there are some limitations.

First, the SHARE data were surveyed only every two years. This came with limitation of a (potential) certain delay between the true country-specific durations of the Great Recession and the SHARE data. Beyond this, wave 3, which was conducted from 2008 to 2009 when the Great Recession had its climax, did not contain information on LLD. It was thus not possible to include the very short-term effects of the Great Recession between 2008 and 2009 in the analyses.

Second, same source bias is especially relevant when using self-rated/ perceived environmental characteristics in combination with mental health outcomes, e.g. depression. Depressed people are more likely to rate their environment negatively; people without depression more positively. Sensitivity model 1 (**Table 2, model 1**) among non-household respondents only (= those not answering the environmental questions) confirmed the findings of the main model, but the interaction effect for the Great Recession and area deprivation lost significance due to the small number of observations. To deal further with this limitation, an interaction model (results not shown) was calculated, including a 3-way interaction term for Great Recession, area deprivation and a variable indicating whether a participant was the household respondent, from whom the information on area deprivation came or not. There was no difference in the effect between household respondents and other household members, suggesting that same source bias plays a subordinate role. Beyond this, previous research showed that subjective neighbourhood characteristics are more relevant for mental health than objectively measured features (Zhang et al. 2019), why perceived area determinants are of high interest.

Third, area deprivation was measured only in SHARE wave 5 (year 2013), when the climax of the Great Recession had already passed so that a post-treatment moderator was used. Post-treatment moderator bias occurs when the moderator is a consequence of the treatment (Montgomery et al. 2018). To attempt to address this issue, area deprivation as a time-constant variable was used. This was possible by focusing on participants who had not relocated over time to keep area deprivation stable as possible. Previous research suggests that local areas have a high degree of stability/ persistency in their relative position and thus their relative deprivation over time (Dorling et al. 2007). However, this bias cannot be ruled out.

Fourth, this observational study was able to disentangle the temporal directionality of cause, e.g. the Great Recession, and outcome, e.g. the risk of depression, by using panel data and a natural-experimental design. However, due to the explained methodological limitations and potentially omitted time-varying confounding variables, this study is not able to unveil causality of these effects assuredly.

4.4 Potential future directions

This study suggests that people living in deprived areas suffered more from the negative effects on late-life depression in the short run, but it is not able to unveil real causality due to the explained methodological limitations. This study is rather a building block in establishing causal inference and experimental designs are needed to ensure internal validity. Future observational studies may focus more on underlying pathways why people living in deprived environment are more susceptible to negative mental health effects of economic crises. Having worse coping strategies and less social, economic and cultural capital could be important disadvantages of people living in deprived areas (Conger et al. 1994, Damm 2014, Hedblom et al. 2019, Khubchandani & Price 2017, Yamaguchi et al. 2019), which should be evaluated as potential mediators in subsequent research.

5. CONCLUSION

An advantaged living environment may provide protective resources for mental health, even in times of economic insecurity. Public attention on better area and living environment quality is important to avoid increasing mental health inequalities. The findings are particularly relevant given the contemporary COVID-19 recession, and warrant particular attention for those people living in deprived areas.

Acknowledgements

I thank SHARE-ERIC for providing the data and their support, and Renée Lüskow for her language editing. The author would also like to thank Gabriele Doblhammer and Fanny Janssen, who advised him on the statistical analysis and writing. No conflict of interest to declare.

Highlights

- Living environment is important in older ages but its role during crises is unknown.
- Great Recession is related to a generally higher risk of depression in the long run.
- People from deprived areas suffered more from the short-term effects on depression.
- Better area quality is important to avoid increasing mental health inequalities.

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III. SUPPLEMENTARY MATERIAL

Additional description to Table 2. The influence of individual-level factors on the associations between the Great Recession and late-life depression

In addition to the finding that area-level factors moderated the effect of the Recession on LLD, this study also backs up results on individual-level risk factors from earlier studies and identified similar vulnerable social groups. Starting with individual-level job status, which were already identified as a main driver explaining the negative effect of a financial crisis at macro-level on depression, this study found that being employed/ self-employed (OR: 1.25, 95% CI: 1.06-1.50, ref. retired) or unemployed (OR: 1.50, 95% CI: 1.10-2.07, ref. retired) were associated with a higher risk of LLD (**Table 2**). Another factor pertaining to older people who have higher vulnerability to the negative effects of macro-level crisis is living without a partner. As expected, living together with a partner in the same household was associated with a lower risk of LLD also in this study (OR: 0.64, 95% CI: 0.48-0.84). A lower risk of LLD was also related to several health-related factors. One was more words recall than 0 to 3, so better than worst cognition (OR 4-5 words recall: 0.78, 95% CI: 0.70-0.87; OR 6+ words recall: 0.67, 95% CI: 0.58-0.77). Another was grip strength better than the lowest quantile (2. quantile OR: 0.85, 95% CI: 0.75-0.97; 3. quantile OR: 0.72, 95% CI: 0.61-0.85; 4. Quantile OR: 0.60, 95% CI: 0.48-0.76), and another was living together with a partner in the same household (OR: 0.64, 95% CI: 0.48-0.84). Surprisingly, being overweight (OR: 0.81, 95% CI: 0.70-0.92) and obese (OR 0.81, 95% CI: 0.66-0.98) were correlated with a lower risk of LLD when compared to participants with normal weight (BMI 18.5-24-9), while underweight people (OR 1.52, 95% CI: 0.99-2.34; p-value: 0.057) showed a borderline significantly higher risk of LLD. As expected, a higher number of chronic diseases (OR one disease: 1.29, 95% CI: 1.13-1.46; OR two or more diseases: 1.71, 95% CI: 1.49-1.96), prevalent limitations in ADL (OR 2.10, 95% CI: 1.88-2.35), inactivity (OR: 1.46, 95% CI: 1.28-1.66), being employed/ self-employed (OR: 1.25, 95% CI: 1.06-1.50, ref. retired) or unemployed (OR: 1.50, 95% CI: 1.10-2.07, ref. retired) were associated with a higher risk of LLD. Being overweight and obesity were, surprisingly, related to a lower risk of LLD in this study. This has, however, already been shown in previous research, e.g. in a longitudinal study for late-life depression in the US (Chang et al. 2017). One potential explanation is that appetite decreases and weight loss, and not weight gain, are early manifestations of late-life depression (Potter et al. 2014, Unützer 2007).

Supplementary Table S1. Complete descriptive statistics of all variables during the observation time from 2004 to 2017

Characteristic	Wave 1[a] (2004-2005)	Wave 2[a] (2006-2007)	Wave 4 (2011-2012)	Wave 5 (2013)	Wave 6 (2015)	Wave 7 (2017)
Total no. of observations per wave	6,866		6,082	5,389	4,730	3,855
Gender, No. (%)						
Female	3,538 (51.53)		3,127 (51.41)	2,804 (52.03)	2,479 (52.41)	2,044 (53.02)
Male	3,328 (48.47)		2,955 (48.59)	2,585 (47.97)	2,251 (47.59)	1,811 (46.98)
Age						
50-64	3,989 (58.10)	3,392 (49.40)	1,952 (32.09)	1,383 (25.66)	857 (18.12)	385 (9.99)
65-79	2,566 (37.37)	2,958 (43.08)	3,137 (51.28)	2,999 (55.65)	2,868 (60.63)	2,539 (65.86)
80+	311 (4.53)	516 (7.52)	993 (16.33)	1,007 (18.69)	1,005 (21.25)	931 (24.15)
Country of residence, No. (%)						
Austria	537 (7.82)		425 (6.99)	400 (7.42)	351 (7.42)	259 (6.72)
Germany	715 (10.41)		686 (11.28)	477 (8.85)	423 (8.94)	348 (9.03)
Sweden	931 (13.56)		757 (12.45)	718 (13.32)	670 (14.16)	464 (12.04)
Spain	752 (10.95)		655 (10.77)	637 (11.82)	545 (11.52)	447 (11.60)
Italy	915 (13.33)		807 (13.27)	724 (13.43)	663 (14.02)	584 (15.15)
France	838 (12.21)		743 (12.22)	634 (11.76)	483 (10.21)	402 (10.43)
Denmark	525 (7.65)		478 (7.86)	444 (8.24)	384 (8.12)	313 (8.12)
Switzerland	309 (4.50)		286 (4.70)	242 (4.49)	229 (4.84)	200 (5.19)
Belgium	1,344 (19.57)		1,245 (20.47)	1,113 (20.65)	982 (20.76)	838 (21.74)
Education (based on ISCED-1997)						
None/ (pre-)primary education or first stage of basic education	2,242 (32.65)		1,950 (32.06)	1,741 (32.31)	1,484 (31.37)	1,173 (30.43)
Lower/ upper secondary edu. or second stage of basic education	1,123 (16.36)		1,002 (16.47)	878 (16.29)	788 (16.66)	647 (16.78)
Post-secondary non-tertiary education	2,094 (30.50)		1,867 (30.70)	1,635 (30.34)	1,421 (30.04)	1,156 (29.99)
First/ second stage of tertiary education	1,407 (20.49)		1,263 (20.77)	1,135 (21.06)	1,037 (21.92)	879 (22.80)
Job status, No. (%)						
Retired	3,402 (49.55)	3,833 (55.83)	4,198 (69.02)	3,889 (72.17)	3,655 (77.27)	3,159 (81.95)
Employed or self-employed	2,104 (30.64)	1,763 (25.68)	924 (15.19)	644 (11.95)	382 (8.08)	181 (4.70)
Unemployed	227 (3.31)	168 (2.45)	93 (1.53)	73 (1.35)	43 (0.91)	22 (0.57)
Permanently sick or disabled	120 (1.75)	141 (2.05)	106 (1.74)	88 (1.63)	51 (1.08)	33 (0.86)
Homemaker	923 (13.44)	883 (12.86)	688 (11.31)	559 (10.37)	466 (9.85)	348 (9.03)
Other or missing value	90 (1.31)	78 (1.14)	73 (1.20)	136 (2.52)	133 (2.81)	112 (2.91)
Body mass index, No. (%)						
Below 18.5 (underweight)	56 (0.82)	62 (0.90)	78 (1.28)	63 (1.17)	60 (1.27)	45 (1.17)
18.5-24.9 (normal weight)	2,629 (38.29)	2,548 (37.11)	2,277 (37.44)	1,952 (36.22)	1,716 (36.28)	1,403 (36.39)
25-29.9 (overweight)	2,867 (41.76)	2,850 (41.51)	2,466 (40.55)	2,169 (40.25)	1,906 (40.30)	1,556 (40.36)

30 and above (obesity)	1,233 (17.96)	1,292 (18.82)	1,145 (18.53)	1,045 (19.39)	934 (19.75)	740 (19.20)
Missing value	81 (1.18)	114 (1.66)	116 (1.91)	160 (2.97)	114 (2.41)	111 (2.88)
Physical activity, No. (%)						
Active, at least one activity per week	6,458 (94.06)	6,380 (92.92)	5,395 (88.70)	4,735 (87.86)	4,155 (87.84)	3,320 (86.12)
Inactive, no activity per week	408 (5.94)	486 (7.08)	687 (11.30)	654 (12.14)	575 (12.16)	535 (13.88)
Cognitive functioning (recall of a 10-word list), No. (%)						
Zero to three words recall	1,230 (17.91)	1,122 (16.34)	1,068 (17.56)	948 (17.59)	858 (18.14)	693 (17.98)
Four to five words recall	2,875 (41.87)	2,838 (41.33)	2,487 (40.89)	2,141 (39.73)	1,835 (38.79)	1,589 (41.22)
Six or more words recall	2,746 (39.99)	2,891 (42.11)	2,500 (41.10)	2,256 (41.86)	1,995 (42.18)	1,540 (39.95)
Missing value	15 (0.22)	15 (0.22)	27 (0.44)	44 (0.82)	42 (0.89)	33 (0.86)
Grip strength in kilogram of the stronger hand						
1. Quantile (lowest)	1,571 (22.88)	1,689 (24.60)	1,771 (29.12)	1,735 (32.20)	1,589 (33.59)	1,391 (36.08)
2. Quantile	1,348 (19.63)	1,359 (19.79)	1,272 (20.91)	1,103 (20.47)	974 (20.59)	798 (20.70)
3. Quantile	1,779 (25.91)	1,694 (24.67)	1,496 (24.60)	1,249 (23.18)	1,113 (23.53)	913 (23.68)
4. Quantile (highest)	2,168 (31.58)	2,124 (30.94)	1,543 (25.37)	1,302 (24.16)	1,054 (22.28)	753 (19.53)
Number of chronic diseases, No. (%)						
None	1,905 (27.75)	1,875 (27.31)	1,383 (22.74)	1,101 (20.43)	892 (18.86)	691 (17.92)
One	2,340 (34.08)	2,174 (31.66)	1,847 (30.37)	1,562 (28.98)	1,376 (29.09)	1,019 (26.43)
Two or more	2,621 (38.17)	2,817 (41.03)	2,852 (46.89)	2,726 (50.58)	2,462 (52.05)	2,145 (55.64)
Number of prevalent limitations in IADL, No. (%)						
None	6,256 (91.12)	6,127 (89.24)	5,117 (84.13)	4,434 (82.28)	3,828 (80.93)	3,046 (79.01)
One or more	610 (8.88)	739 (10.76)	965 (15.87)	955 (17.72)	902 (19.07)	809 (20.99)
Partner living in same household (household-level), No. (%)						
No	1,402 (20.42)	1,508 (21.96)	1,556 (25.58)	1,523 (28.26)	1,392 (29.43)	1,200 (31.13)
Yes	5,464 (79.58)	5,358 (78.04)	4,526 (74.42)	3,866 (71.74)	3,338 (70.57)	2,655 (68.87)
Household size (household-level), No. (%)						
One household member	1,097 (15.98)	1,175 (17.11)	1,277 (21.00)	1,265 (23.47)	1,168 (24.69)	1,026 (26.61)
Two household members	4,033 (58.74)	4,055 (59.06)	3,911 (64.30)	3,403 (63.15)	3,031 (64.08)	2,457 (63.74)
Three household members	979 (14.26)	928 (13.52)	623 (10.24)	521 (9.67)	376 (7.95)	265 (6.87)
Four or more household members	757 (11.03)	708 (10.31)	271 (4.46)	200 (3.71)	155 (3.28)	107 (2.78)
Area deprivation, No. (%)						
Non-deprived	3,076 (44.80)		2,721 (44.74)	2,962 (54.96)	2,496 (52.77)	2,114 (54.84)
Deprived	2,367 (34.47)		2,119 (34.84)	2,261 (41.96)	1,818 (38.44)	1,467 (38.05)
Missing value	1,423 (20.73)		1,242 (20.42)	166 (3.08)	416 (8.79)	274 (7.11)
Urban or rural area, No. (%)						
Urban	4,896 (71.31)		4,306 (70.80)	3,894 (72.26)	3,398 (71.84)	2,730 (70.82)
Rural	1,911 (27.83)		1,728 (28.41)	1,453 (26.96)	1,291 (27.29)	1,097 (28.46)
Missing value	59 (0.86)		48 (0.79)	42 (0.78)	41 (0.87)	28 (0.73)

Prevalent late-life depression (LLD)						
No, free of LLD	5,600 (81.56)	5,571 (81.14)	4,689 (77.10)	4,111 (76.29)	3,584 (75.77)	2,900 (75.23)
Yes, prevalent LLD	1,266 (18.44)	1,295 (18.86)	1,393 (22.90)	1,278 (23.71)	1,146 (24.23)	955 (24.77)

Notes: [a] Numbers and percentages of time-constant variables were identical in wave 1 and wave 2 due to the study design (valid outcome measure in both waves conducted before the Great Recession had started)

Supplementary Table S2. Sensitivity models part 1: the short- (STE) and long-term (LTE) effects of the Great Recession (GR) on late-life depression among study participants ages 50 and older from 9 European SHARE countries (2004-2017)

	Sensitivity Model 1: Full model among non-household respondents only		**Sensitivity Model 2**: GR only		**Sensitivity Model 3**: GR x area deprivation		**Sensitivity Model 4**: GR x area deprivation & GR x rurality		**Sensitivity Model 5**: GR x area deprivation & GR x rurality among participants with at least 4 observations		**Sensitivity Model 6**: GR x area deprivation & GR x rurality among participants aged 65+	
No. of participants (observations)	846 (4,533)		3,114 (15,677)		3,114 (15,677)		3,114 (15,677)		2,637 (14,246)		1,443 (6,927)	
	OR	95% CI	OR	95% CI	OR	95% CI	OR	95% CI	OR	95% CI	OR	95% CI
STE (ref. before GR)	1.11	0.86-1.44	**1.29**	1.17-1.42	1.12	0.98-1.28	1.07	0.93-1.23	1.08	0.93-1.25	1.03	0.83-1.29
LTE (ref. before GR)	**1.50**	1.12-2.00	**1.41**	1.25-1.59	**1.27**	1.09-1.48	**1.23**	1.05-1.44	**1.23**	1.04-1.45	**1.40**	1.08-1.80
STE deprived areas (ref. STE non-deprived areas)	1.13	0.81-1.56			**1.24**	1.03-1.48	**1.22**	1.02-1.46	**1.23**	1.02-1.48	**1.39**	1.05-1.84
LTE deprived areas (ref. LTE non-deprived areas)	1.16	0.83-1.62			1.17	0.97-1.41	1.16	0.96-1.40	1.17	0.97-1.41	1.23	0.91-1.65
STE rural areas (ref. STE urban areas)	1.43	0.99-2.05					**1.23**	1.03-1.48	1.18	0.97-1.44	**1.34**	1.01-1.78
LTE rural areas (ref. LTE urban areas)	1.08	0.75-1.57					1.13	0.93-1.38	1.13	0.92-1.38	1.23	0.91-1.65

Notes: The models shown were estimated by performing binary logistic fixed effects panel regression models based on the SHARE waves 1, 2, 4, 5, 6, and 7. Models were controlled for time-varying age, partner in household, household size, limitations in activities of daily living, physical inactivity, BMI, job status, grip strength, cognition, and number of chronic diseases. Bold values show point estimators that are significantly different from 1 ($p < 0.05$). Models 1 to 3 were conducted stepwise. The right column contains the 95% confidence interval of the point estimators.

Supplementary Table S3. Sensitivity models part 2: the short- (STE) and long-term (LTE) effects of the Great Recession (GR) on late-life depression among study participants ages 50 and older from 9 European SHARE countries (2004-2017)

	Sensitivity Model 7: Linear panel fixed effects model using depressive symptoms as outcome		**Sensitivity Model 8**: Ordered logit panel fixed effects model using degrees of depression as outcome	
No. of participants	6,866		6,866	
	Coefficient	95% CI	Coefficient (logit)	95% CI
STE (ref. before GR)	0.03	-0.04-0.11	0.06	-0.04-0.15
LTE (ref. before GR)	**0.11**	0.03-0.19	**0.16**	0.05-0.27
STE deprived areas (ref. STE non-deprived areas)	**0.15**	0.05-0.24	**0.19**	0.07-0.32
LTE deprived areas (ref. LTE non-deprived areas)	0.09	-0.01-0.19	0.11	-0.03-0.24
STE rural areas (ref. STE urban areas)	0.08	-0.01-0.18	0.08	-0.04-0.20
LTE rural areas (ref. LTE urban areas)	0.06	-0.04-0.16	0.08	-0.05-0.22

Notes: Model 7 used the number of depressive symptoms as outcome and was estimated by performing linear fixed effects panel regression with robust standard errors based on the SHARE waves 1, 2, 4, 5, 6, and 7. Model 8 used the degree of depression as outcome (0 symptoms = no depression [no. obs = 8,377], 1 symptom = very less depression [no. obs = 7,858], 2-3 symptoms = less depression [no. obs = 10,220], 4-5 symptoms = moderate depression [no. obs = 4,801], 6 symptoms = severe depression [no. obs = 1,087], 7+ symptoms = very severe depression [no. obs = 1,445]) and was estimated by performing ordered logit fixed effects panel regression (BUC estimator by Baetschmann et al. 2014, Stata package feologit (Baetschmann et al. 2020)) based on the SHARE waves 1, 2, 4, 5, 6, and 7. Both models were controlled for time-varying age, partner in household, household size, limitations in activities of daily living, physical inactivity, BMI, job status, grip strength, cognition, and number of chronic diseases. Bold values show point estimators that are significantly different from 1 ($p < 0.05$). The right column contains the 95% confidence interval of the point estimators.

Supplementary Table S4. The explorative factor analysis (EFA) for the used area deprivation index variables based on the SHARE population

Factor	**Eigenvalue**	**Variance** (after promax rotation)	**Proportion** (after promax rotation)
Factor 1 (social and built environment)	3.01	3.01	0.87
Factor 2 (access to local services)	0.97	1.03	0.30

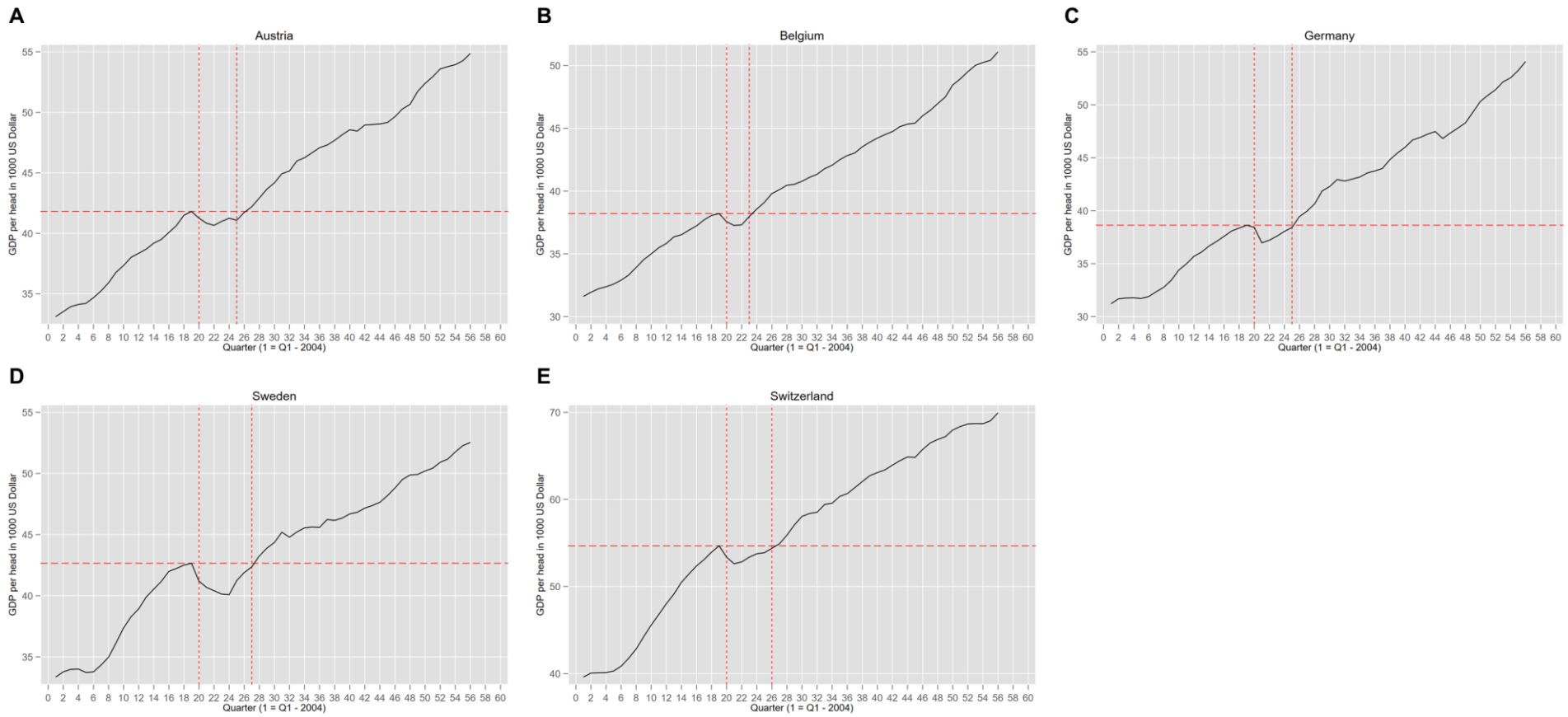
Variable	**Factor loadings** factor 1 (after promax rotation)	**Factor loadings** factor 2 (after promax rotation)	**Uniquness** (after promax rotation)
Feeling part of the area	0.01	0.50	0.75
Vandalism is a big problem	< -0.01	0.41	0.79
Area is kept clean	< -0.01	0.52	0.71
Helpful people in the area	-0.01	0.53	0.72
Easy to get to the nearest bank/ cash point	0.86	0.01	0.28
Easy to get to the grocery shop/ supermarket	0.86	-0.01	0.26
Easy to get to the nearest general practitioner or the health centre	0.84	0.03	0.28
Easy to get to the pharmacy	0.90	-0.03	0.19

Notes: KMO = 0.83, correlation between factor 1 and factor 2 with r = 0.13.

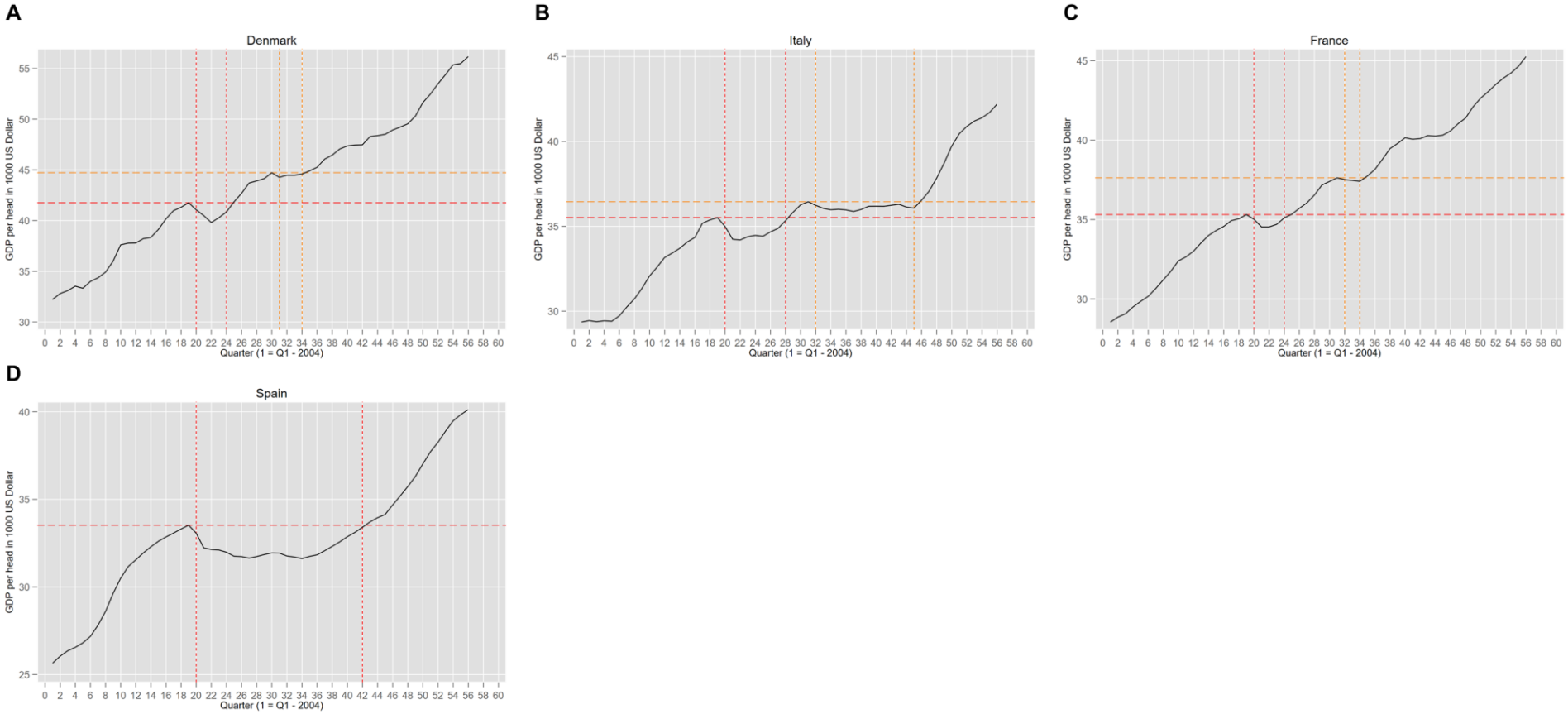
Description to Supplementary Table S4. The explorative factor analysis (EFA) for the used area deprivation index variables

To uncover the underlying structure of the SHARE variables used to compute the area deprivation index (ADI), exploratory factor analysis (EFA) was performed for the entire SHARE population. The Kaiser-Meyer-Olkin (KMO) measure was 0.83 showing that the given data is well-suited for conducting an EFA. Two relevant factors, factor 1 and factor 2 were detected, which show a between-factor correlation of 0.13. Given the factor loadings illustrated in **Supplementary Table S4** the variables "feeling part of the area", vandalism is a big problem", "area is kept clean", and "helpful people in the area" load especially on factor 1 (factor loadings > 0.4), while the variables "easy to get to the nearest bank/ cash point", "easy to get to the grocery shop/ supermarket", "easy to get to the nearest general practitioner or the health centre", and "easy to get to the pharmacy" load especially on factor 2 (factor loadings > 0.8). Factor 1 was, evaluated based on the content of these items, assumed to measure the latent construct "social and built environment" and factor 2 the construct "access to local services". These two dimensions were already shown to be relevant area deprivation features (Allik et al. 2020). The scores allocated to these eight items were tallied to yield an additive area deprivation index (ADI) for each household. Cronbach's alpha ($\alpha = 0.74$) showed an acceptable internal consistency of the used ADI.

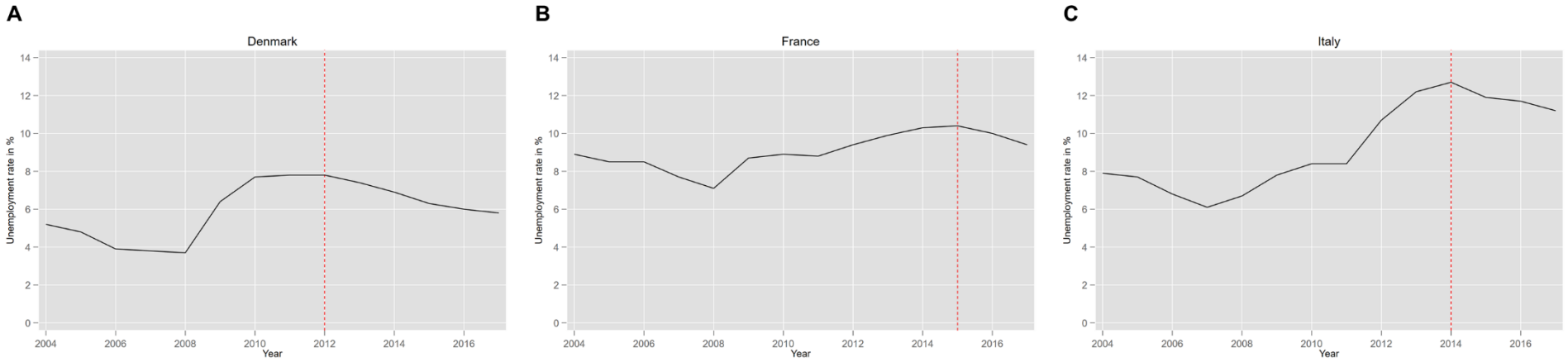
Supplementary Figure S1. Country-specific durations of the Great Recession used in the study calculated by using quarterly GDP data (2004 to 2017) for Austria (A), Belgium (B), Germany (C), Sweden (D), and Switzerland (E)



Supplementary Figure S2. Country-specific durations of the Great Recession used in the study calculated by using quarterly GDP data (2004 to 2017) for Denmark (A), Italy (B), France, and Spain (D)



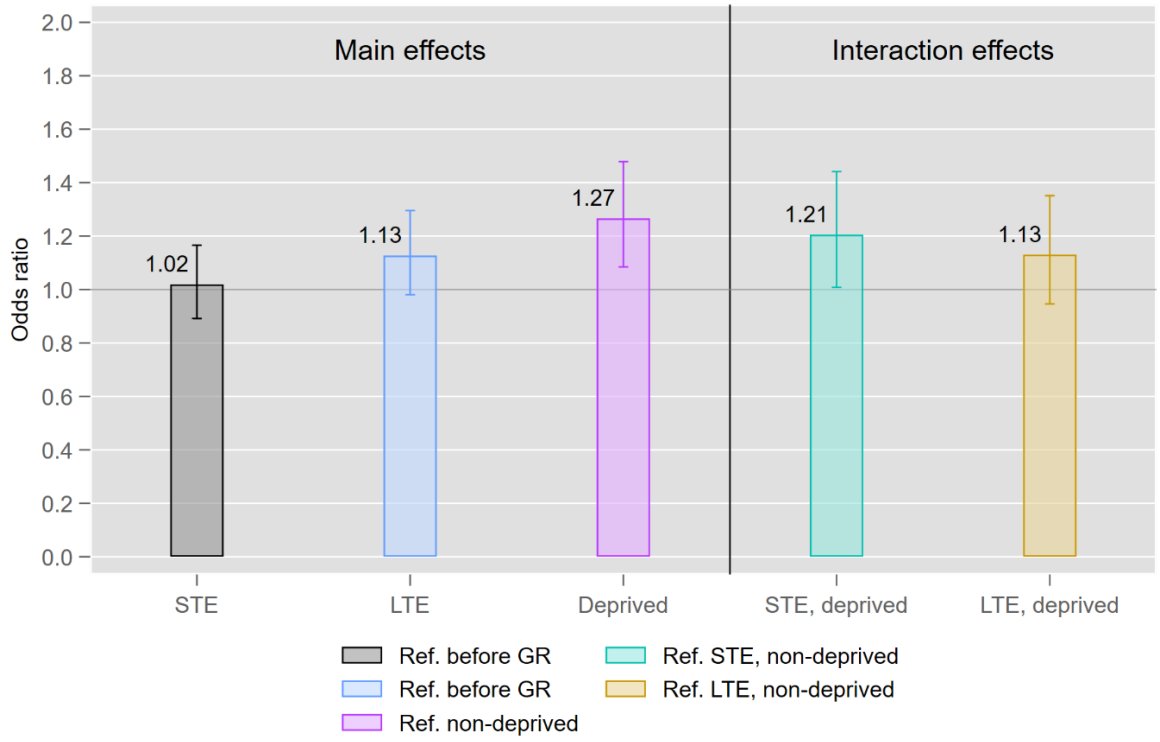
Supplementary Figure S3. Country-specific yearly unemployment rates between 2004 and 2017 to validate the total duration of the Great Recession in Denmark (A), France (B), and Italy (C) with follow-up recessions after the main recession from 2008 to 2009



Description to Supplementary Figures S1-S3. The country-specific durations of the Great Recession

A recession is defined as two consecutive quarters of negative economic growth compared to a basis quarter (Gaski 2012). Economic growth was thereby measured by a country's gross domestic product (GDP) in a quarter-to-quarter comparison. A basis quarter is the quarter immediately prior to the two or more declining GDP quarters. The end of a recession is specified as the return of GDP to (at least) the amount of the basis quarter. To deal with cases of potential follow-up recessions after a main recession, time-series (yearly) data on unemployment rates were explored. The main recession and a follow-up recession were considered as one coherent recession period when the unemployment rates between the main and the follow-up recession showed an increasing trend (following in these cases the US NBER definition of a recession, see Leamer 2008). The (quarterly) developments of the national GDPs from 2004 to 2017 were illustrated for each country in **Supplementary Figures S1** and **Supplementary Figure S2**. The main recession was illustrated by using red lines, while follow-up recessions were shown by orange lines. Austria (Q1 2010), Belgium (Q3 2009), Germany (Q1 2010), Sweden (Q3 2010), and Switzerland (Q2 2010) were defined as countries without a follow-up recession and a STE in 2011 only (**Supplementary Figure S1**, end of the recessions in brackets). The other waves (5, 6, 7) were treated as LTE observations. For Spain, a coherent recession up to Q2 2014 was determined, so that the SHARE waves through wave 6 in 2015 were defined as STE observations. Denmark (Q2 2012), Italy (Q1 2015), and France (Q2 2012) were found to have experienced a follow-up recession (**Supplementary Figure S2**, end of the follow-up recessions in brackets), which is why the UE rates were additionally investigated in these cases. The UE rates showed an increasing trend until 2012 for Denmark, until 2015 for France, and until 2014 for Italy, so that in each of these three countries the UE rates between the main and the follow-up recession had an increasing trend. Accordingly, the years 2011 (wave 4) and 2013 (wave 5) were specified as STE observations for Denmark and France, and the years 2015 (wave 6) and 2017 (wave 7) as LTE observations. For Italy and Spain, the years 2011 (wave 4), 2013 (wave 5), and 2015 (wave 6) were defined as STE observations and only 2017 (wave 7) as a LTE observation. An overview of the country-specific crisis durations is illustrated in **Figure 1**. The findings gathered in this explorative analysis are in line with the classification of economic recovery since 2008 calculated by Eurostat based on EU-SILC data (OECD 2018).

Supplementary Figure S4. Sensitivity model 7 (ME): the role of area deprivation in the short- (STE) and long-term (LTE) effects of the Great Recession (GR) on the risk of late-life depression among study participants ages 50 and older from 9 European SHARE countries (2004-2017)



Notes: Shown point estimators (Odds ratios) were estimated by performing logistic mixed effects regressions with random intercepts for countries, households, and individuals based on the SHARE waves 1, 2, 4, 5, 6, and 7. The vertical lines in the bars illustrate the 95% confidence intervals of the point estimators. Models were controlled for time-varying age, partner in household, household size, limitations in activities of daily living, physical inactivity, BMI, job status, grip strength, cognition, number of chronic diseases, and interaction between the Great Recession and rurality

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6

Discussion

6.1 Summary of the main findings

With this thesis, I have investigated how different environmental living conditions are linked to physical and mental health among European adults in the twenty-first century, and, for its two sub-objectives, analyzed the underlying spatial patterns and pathways.
In general, I found strong connections between physical and mental health outcomes in Europe in the twenty-first century and various chronic, stable and changing environmental living conditions in the built, natural, economic, and community environment. I also found significant spatial patterns in health and regional differences in the associations between local infrastructure and the macro-level economy with health, and uncovered important mediating and moderating pathways.
The spatial approach found that obesity prevalence was, in the univariate analysis, higher in urban regions than in suburban and rural settings. However, when the effects of demographic, socioeconomic, and food infrastructure variables were eliminated, obesity prevalence was higher in suburban regions compared to urban regions. Significant clusters of obesity were also mainly observed in suburban and rural areas. Furthermore, limited accessibility to unhealthy local food infrastructure was linked to lower obesity prevalence, but the relationship was especially pronounced in urban and suburban areas than in rural areas; fresh food was thus only relevant for urban areas. Throughout, the wider food access conditions (food environment) were more relevant than the immediate environment. Moreover, a macro-level financial crisis was found to increase the short-term risk of depression in people living in rural areas, but not those living in urban areas.
The pathway approach showed that stable detrimental environmental living conditions, such as higher levels of environmental pollution and poor housing conditions, are associated with worse short-term physical or mental health. This was true for worse general physical health, reduced lung function, and worse cognitive functioning. However, not only stable but also short-term changes in environmental living conditions, namely increased environmental pollution, deteriorated local infrastructure, and poorer housing conditions were associated with worse health in the short term. Further, the health of people who experienced improved conditions did not differ from the people living under the stable best conditions. The approach also showed that, although air pollution and

mental health are mainly directly linked, the association is in part mediated by lung function, which is a physical health outcome.

When we observed health in the long term, stable higher exposure to environmental pollution, and worsened or increased pollution, and stable worse local infrastructure were found to be connected to physical health deteriorations over time, while a macro-level financial crisis was found to be related to a higher risk of depression and thus worse mental health. We also found two interesting interactions suggesting that there are subpopulations which are more vulnerable than others. The first showed that men were more susceptible to worsened pollution than women. The second revealed that a macro-level financial crisis increased the general long and short-term risk of depression, but only for people living in deprived or rural areas.

In sum, this thesis underlines the special health importance of the local infrastructure, environmental pollution, housing conditions, general area deprivation, and the macro-level economy, and found interesting temporal, moderating, and mediating pathways as well as spatial patterns. Long-term (chronic) health impacts result primarily from poor local infrastructure, environmental pollution, and economic downturns, but not from housing conditions. Additionally, interesting vulnerabilities and patterns emerge which differ between the environmental living conditions: unhealthy food infrastructure was particularly important for health in urban regions; living in deprived or rural regions is disadvantageous in times of economic downturns; men's health was more susceptible to environmental pollution than women's; and air pollution may not only affect physical but also mental health on direct or indirect pathways.

6.2 Summary of the individual studies conducted

This subsection provides a more detailed overview of the main findings of the individual studies conducted for this thesis.

6.2.1 Local food environment and obesity (Study I)

The study presented in Chapter 2 asked how healthy and unhealthy local food infrastructure is spatially related to obesity prevalence in the Netherlands (aged 19+). I explored

global associations and regional differences, and assessed the relevance of the immediate and wider food surroundings.

Obesity prevalence was slightly higher in urban areas (14.61%) compared to suburban (14.19%) and rural (14.09%) areas. Regional clusters of high obesity were observed in selected areas in the north-east, south-west, and south-east of the country, which are characterized by lower population density and are mainly rural. When we controlled for food accessibility, sociodemographic and socioeconomic determinants, obesity prevalence proved significantly higher in suburban (1.03, $p < 0.01$) than in urban areas.

A higher average distance to unhealthy fast food (= limited accessibility) was globally associated with lower obesity prevalence across the entire Netherlands (-0.15, $p = 0.02$), but there were no associations with healthy food accessibility.

Regarding the local differences in the associations, we found significant interactions between the regional location and health and unhealthy food accessibility. In the models confined to urban, suburban, and rural areas, I found that limited accessibility to unhealthy fast food was associated with lower obesity prevalence in urban (-2.94, $p < 0.01$), suburban (-0.65, $p = 0.03$), and rural (-5.03, $p < 0.01$) areas. Limited access to fresh food stores was only relevant for obesity in urban settings (+3.71, $p < 0.01$), and was related to higher obesity prevalence. Local regressions for associations between unhealthy fast food accessibility and obesity showed the strongest relationships for the Randstad, one of the largest metropolitan regions in Europe. Across all areas, the contributions of the wider food access surroundings (= food access conditions in bordering neighborhoods) on obesity were more important (≥ 66% of the total effects) than the contributions of the immediate food access surroundings.

6.2.2 Changing and stable living environments, and physical health (Study II)

Chapter 3 presents a study that investigated how improved, deteriorated, and stable perceived environmental living conditions are temporally associated with physical health among non-movers in Germany (aged 18+). This study considered both health levels (Level Models) and subsequent health changes (Change Model).

Fifteen-point-six percent experienced changing local infrastructure, 14.91% experienced differences in environmental pollution, and 19.0% changes in housing conditions. I included 16,076 PCS observations, which resulted in 11,475 changes in PCS over time (4,980 health improvements and 6,495 health deteriorations). PCS changes ranged between -46.24 and 40.46, with an average decline of -1.49 in overall PCS changes and stronger average declines for women (-1.56) than men (-1.41) over time.

In the multivariate models, I used changing physical health, which was measured using a composite score (PCS) from the 12-items Short-Form Survey of people living under stable best conditions as the reference group throughout.

In the Level Model worsened local infrastructure (-0.77; 95% CI: -1.53, -0.01), environmental pollution (-1.21; 95% CI: -2.11, -0.31), and housing conditions (-1.00; 95% CI: -1.75, -0.24) were related to worse health at baseline. People living under stable moderate (-1.04; 95% CI: -1.56, -0.51) and stable worst pollution (-0.72; 95% CI: -1.29, -0.14), and under stable worst (-0.97; 95% CI: -1.54, -0.39) housing conditions also showed lower PCS scores at baseline.

In the Change Model stable worst local infrastructure (-0.84; 95% CI: -1.33, -0.35), and stable moderate (-0.75; 95% CI: -1.18, -0.31) and worst (-0.66; 95% CI: -1.15, -0.17) environmental pollution were associated with health deterioration. In addition, worsened pollution (-0.86; 95% CI: -1.64, -0.08) was found to be connected with negative health changes. We also found an interesting interaction between environmental pollution and sex in the Change Model. The stratified models confined to men and women showed that men were more susceptible to worsened pollution (-1.73; 95% CI: -2.86, -0.60) than women (-0.48; 95% CI: -1.54, 0.58). Across the studied population, the changing PCS of respondents living under improved conditions did not differ significantly from those with stable best conditions.

6.2.3 Fine particulate matter and its pathway to mental health (Study III)

The study presented in Chapter 4 asked how fine particulate matter – the most dangerous environmental pollution hazard in the living environment – is linked to physical and mental health among adults (aged 18+). This pathway analysis assumes two main lung func-

tion measures (FEV_1, FVC) as physical health mediators, and cognitive performance (Cognitive Processing Time) as a mental health outcome. The direct effect represents the direct route for air pollutants to affect the brain assumed through the olfactory nerve or the blood stream, and the indirect effect is the indirect route through affecting lung function. Of the 49,705 participants, 25,915 (52.14%) had faster (CPT) and 23,790 (47.86%) slower CPT than the mean. The average exposure to PM2.5 was 14.92μg/m^3, and 1.22μg/m^3 to BC. For lung function, the average FEV_1 was 3.50 L (96.54% predicted) and FVC 4.56 L (100.78% predicted).

Higher exposure to $PM_{2.5}$ was significantly related to slower CPT (= worse cognitive performance) even when we controlled for both lung function mediators. An increase in $PM_{2.5}$ exposure of one μg/m^3 was accordingly related to an increase in cognitive processing time of 1.93% (95% CI: 1.32-2.54).

The direct effects of $PM_{2.5}$ on CPT were observed even when we controlled for lung function measures. No significant direct effects were found for BC. We observed mediation for both $PM_{2.5}$ and BC by both lung function measures (FEV_1, $PM_{2.5}$ = 1.32%; FVC, $PM_{2.5}$ = 2.05%; FEV_1, BC = 7.01%; FVC, BC = 13.82%). However, the potential direct route for $PM_{2.5}$ through the olfactory nerve or blood stream showed substantially higher relevance (> 97%).

6.2.4 Area deprivation as a moderator: an economic crisis and depression (Study IV)

Chapter 5 presented a study that asked how the associations between the Great Recession and the risk of depression differ between people from deprived and non-deprived areas. This was conducted on a transnational European sample consisting of people aged over 50 – this was done because they are assumed to have more stable employment and income conditions.

Seven thousand three hundred and thirty-three participants (21.70%) experienced at least one time-prevalent late-life depression (LLD) episode during the observation period from 2004 to 2017. The proportion of participants with LLD increased in each SHARE wave from 18.44% in 2004–2005 to 24.77% in 2017. At baseline (2004–2005), 34.47% of the participants lived in deprived, 71.31% in urban, and 27.83% in rural areas.

The age-standardized prevalent cases of LLD increased from 2004 to 2011 for both deprived and non-deprived areas, but the increase was greater for deprived areas during this main period of the Great Recession. In 2013 prevalence showed a decreasing trend for non-deprived areas (17.89%, 95% CI: 16.39–19.38), while the proportion of people with prevalent LLD increased further to its all-time maximum of 25.93% (95% CI: 23.93–27.92) in deprived areas.

The age-standardized incident LLD cases showed that people from deprived areas tend to have a generally higher level of incident LLD. Only non-deprived areas showed a marked decrease in incident LLD cases in 2013 (9.03%, 95% CI: 7.91–10.16).

No general short-term effect was found for the Great Recession on late-life depression. However, a statistically significant interaction between the Great Recession and area deprivation on the risk of late-life depression was observed in the short run: participants living in deprived areas had a 22% higher short-term risk of prevalent LLD (OR: 1.22, CI: 1.02–1.46) compared to participants living in non-deprived areas. Turning to the long-term effects of the Great Recession, there was a general 23% higher risk of prevalent LLD (OR: 1.23, CI: 1.05–1.44), but no effect moderation by area deprivation.

6.3 Reflections on the main findings

The substantial spatial patterns and pathways between environmental living conditions and health observed in this thesis can be explained by different mechanisms relating to human social behaviors, social stratification, and underlying salutogenic as well as pathogenic pathways. The main findings of this thesis will be discussed in the following sections by referring to potential existing hypotheses and theories, which build upon the theoretical background set out in the introduction.

6.3.1 The important role of environmental living conditions for health

This thesis generally found that environmental living conditions were of high importance for health and health inequalities among adults in Europe in the twenty-first century.

In doing so, this thesis confirmed existing environmental health theories which construct the overall theoretical of frame for this thesis, such as the Health Map to Local Human

Habitat (Barton & Grant 2006), the Health Development Model (Bauer et al. 2006), and the Environmental Press Theory (Lawton et al. 1978). More precisely, this thesis emphasizes that the following aspects are of high relevance when exploring the health consequences of environmental living conditions:

- a holistic, multi-level theoretical approach to environmental health;
- the combination and synthesis of interdisciplinary perspectives;
- the inclusion of at least four dimensions of living environmental conditions, such as the built environment, the natural environment, the local and macro-level economy, and the local social community;
- stable and chronic exposure measures, and changing living environments;
- a comprehensive understanding of health regarding pathogenic and salutogenic outcomes;
- the multidimensionality of health and the relevance of physical health and mental health, as well as their interrelations;
- the underlying moderating and mediating pathways; and
- spatial patterns and regional differences in health and their associations with environmental living conditions.

This thesis is novel because it adds new evidence to the field of environmental health by revealing significant spatial patterns and pathways, and thus provides interesting answers to the question of how environmental living conditions are linked to physical and mental health among European adults in the twenty-first century. This research highlights that environmental living conditions play a substantial role in determining population health, alongside demographic, socioeconomic, and lifestyle determinants.

6.3.2 General spatial patterns in health: Urban, suburban, and rural differences

My findings reveal significant general spatial patterns in health. Obesity prevalence was observed to be more prevalent in urban areas than in suburban and rural areas, in the univariate analysis. However, when the effects of demographic, socioeconomic, and food infrastructure variables were eliminated, obesity was found to be more prevalent in suburban areas compared to urban areas. Significant clusters of obesity were mainly observed in suburban and rural areas.

Prior research has shown mixed results and does not coherently show a significant uniform spatial pattern for health in more or less urbanized areas. However, comparison with prior research is difficult due to the different use and operationalization of location. Most studies only regarded the urban-rural dichotomy and neglected the suburban category. Studies have found for the US, Germany, and various European countries taken together, that health was better in urban than in more remote, deprived, or less densely populated regions (Castillo-Reinado et al. 2020, Kobo et al. 2022, Marques et al. 2018). In contrast, there is also evidence from the UK and the US that moving to live among older people is related to worse health per se – people are assumed to be motivated by a desire to live near facilities not available in their previous places of residence, when they decide to move to regions characterized by better infrastructure (Larson et al. 2004). It was found for Europe that urbanization was linked to a higher risk of mental disorder (Kovess-Masféty et al. 2005, Verheij et al. 2008). There are various possible explanations for why health differs between areas.

One explanation is that migration selection by healthy individuals contributed to the health differences between urban, suburban, and rural regions. This can for example be the case if younger and healthier people relocate from the countryside to urban areas to access better education (Verheij et al. 1998). An important determinant of this is local infrastructure making areas more or less attractive for living: public services, job opportunities, or food environments were shown to be relevant determinants for residential mobility (Capello et al. 2011, Gareis et al. 2021, Salahodjaev & Mirziyoyeva 2021, Zykiene et al. 2020). Accordingly, research from the UK suggests that positive health migration from deprived into non-deprived regions contributed particularly to health inequalities observed between different areas (Norman 2005). In contrast, research on the Netherlands observed a different picture: people who moved were found to be healthier, especially when they came from regions in decline, but these effects proved non-significant when the researchers controlled for demographic and socioeconomic factors. As a conclusion, the authors explained that health and residential mobility are complexly interrelated with socioeconomic and demographic characteristics (Dijkstra et al. 2015). A study from Finland also found that healthier movers tended to relocate to urban centers, while un-

healthier movers did not relocate to urbanized areas (Vaalavuo et al. 2021). In sum, research on the selective health migration hypothesis does not uniformly support this explanation.

A second explanation follows the findings from the prior research showing that the movers' demographic and socioeconomic determinants contributed to the health differences between urban and rural areas (Dijkstra et al. 2015). Accordingly, this thesis shows that physical health measured by obesity prevalence was found to be worse in the univariate analysis in urban areas than in suburban and rural areas, but the pattern changed after controlling for the demographic, socioeconomic, and food infrastructure variables: suburban areas were then observed to have worse health than urban regions. This suggests that the clusters of obesity prevalence we observed may also be the areas that perform less well on socioeconomic development, and have an older population. However, most prior research controlled for demographic and sociodemographic characteristics in the models applied (except Marques et al. 2017) and still found differences by urbanization. That does not mean that demographic and socioeconomic characteristics did not contribute to the observed regional inequalities, but they are potentially not the only variables that are important to explain the differences.

A third explanation is that the quality of local health services is an important determinant contributing to regional health differences. Worse access to healthcare in rural areas is assumed to be a major determinant contributing to the regional disparities in health (Groenewegen et al. 2020). Researchers found that differences in healthcare staffing, service financing, and legal coverage are the main drivers in terms of health care for the persisting urban-rural differences (The Lancet 2015). This explanation could be relevant in terms of health prevention and promotion – favorable local health services could be an important resource for health screening and monitoring. That would contribute to the early detection and diagnosis of disease, permitting early treatment. This explanation is supported by the Health Development Model presented earlier in this thesis, which underlines the important role of health resources, prevention matters, and health promotion in disease development and health maintenance (Bauer et al. 2006). Local health services should substantially support these pathways assumed from the theory.

A fourth explanation is that differences in the local infrastructure, such as the local food environment, or other environmental living conditions explain the differences between urban, suburban, and rural regions. There is clear evidence in the theoretical literature and empirical observation that detrimental environmental living can affect health, and that the extent of exposure appears differently between regional settings (de Vogli et al. 2011, Elliott & Wartenberg 2004, Mazidi & Speakman 2017). In addition, the other findings drawn from the pathway approach applied in this thesis support the explanation that contextual conditions from the living environment could indeed affect health. Local human habitat theory also supports this explanation, because it describes that environmental determinants and their pathways can differ between places of residence and thus regional settings (Barton & Grant 2006). The analysis of spatial effect variations presented in this thesis shows that access to unhealthy food is more important for urban and suburban than for rural areas.

In sum, it is possible that a combination of all four explanations could contribute to the differences in health between different areas and more research is needed to disentangle the underlying pathways. Because the spatial differences observed were based on a spatial approach and an ecological design, causal inference and the underlying pathways cannot be proved (Loney & Nagelkerke 2014).

6.3.2 Variations in the spatial associations

A first finding in terms of spatial variation in the associations identified was that the association of accessibility to unhealthy local food infrastructure with obesity was more pronounced in urban and suburban areas than in rural areas. Fresh food was only relevant to urban areas.

Even though the prior literature on local effect variations is scarce, research from the US (Michimi & Wimberly 2010) and among children (Salmon et al. 2013) support the findings presented in this thesis observed for European adults.

One explanation is that the average distance to food retail locations are generally shorter and the absolute time costs are lower in more densely populated regions. Travelling and crossing administrative borders is easier, faster, and cheaper in urban areas (Matz et al.

2015). As a result, healthy and unhealthy food retail locations are in competition with each other, which is why longer distances lead to longer relative time costs in urban areas where people have to travel longer to reach the targeted healthier food stores. This could influence people's decisions, as they initially desire healthy food but might then switch to unhealthy food if the places for accessing unhealthy food are closer and the time costs to prepare the food are lower – this would mean lower total opportunity costs (Losada-Rojas et al. 2021, Michimi & Wimberly 2010, Pucher & Renne 2005).

The lower opportunity costs for unhealthy food could also explain why the wider food environment was found to be more important than the immediate surroundings in this study. Unhealthy food has fewer barriers to access in more urbanized areas. Prior research showed that routine travel outside an area, for instance commuting, were particularly relevant for explaining the actual visits of food locations (Shearer et al. 2015). It is also likely that people do not work in their home area given the average commuting distance for European workers of 28.56 kilometers in 2017 (SD Worx 2018), especially when small-area data for a given neighborhood were used.

The wider food environment might also be important due to the presence of food delivery services (Pinho et al. 2020), making the time required to obtain unhealthy fast food virtually nil and increasing the potential radius for the purchase of such food.

However, due to the operationalization by Statistics Netherlands of food infrastructure access used in this thesis, measured by proximity as the average distance to the food locations in a neighborhood, it is not possible to distinguish between potential access, actual visits, and real food consumption. It is also not possible to distinguish between local stores and delivery services as discussed in newer literature (Gebremariam et al. 2017).

A second finding was that fresh food accessibility was only relevant for urban but not for suburban and rural neighborhoods.

One hypothesis is the existence of a certain distance threshold, beyond which the distance to healthy food locations no longer impacts or has diminished impact on obesity, as postulated by Michimi & Wimberly (2010). Rural residents have to travel further for their daily activities (Probst et al. 2006, Pucher & Renne 2005), which means that the relative time and other costs weigh less heavily when deciding whether to travel to a healthier food location, especially if a car is needed for the journey (Zijlstra et al. 2022). Our findings are in line with previous results for the US which found using census data from 2006 at

the county level, relationships between healthy food accessibility and adult obesity prevalence for metropolitan (urban) regions, but not for non-metropolitan (rural) regions (Michimi & Wimberly 2010).

Taking the first two findings of this section together, our study adds further evidence to the existing literature from the US that distinguishing regional subtypes is essential when studying the associations between food accessibility and obesity. This was underlined by both regression types used in the spatial approach, namely the multivariate global regression approach (Spatial Lag of X model) and by the local regression approach (geographically weighted regression). Taking the findings from both regression models together, we can conclude for the Netherlands that unhealthy food plays a special role in the health of people living in high-density and urbanized regions like the Randstad, which is one of the largest metropolitan regions in Europe. Against a background where the urban population is expected to increase in the coming decades in Europe (Adlakha & John 2022) and in the Netherlands (Statistics Netherlands 2019), special attention to food environmental risks, such as unhealthy food, is needed in such highly urbanized regions. This is also in line with the obesogenic environment theory, which assumes that the emergence of obesogenic (food) environments is one of the main drivers of the rapid increase in the obesity prevalence already observed (Egger & Swinburn 1997). The theory hypothesizes that the micro-level food environment can influence people's diets through the physical presence of or access to food. That is, easy access to unhealthy food combined with limited access to healthy food is the pathway linking health to super-nutrition, that is the intake of food with a high proportion of fat, high energy-density etc. It also seems that the obesogenic environment is especially a problem of urban areas (Kirchengast 2021, Townshend & Lake 2009).

Another important aspect linked to these findings is that this thesis used obesity prevalence as a sort of physical health outcome. However, obesity cannot only be regarded as a disease, but also as a risk factor for other diseases, such as cardiovascular or metabolic diseases (Al-Goblan et al. 2014, Bakhtiyari et al. 2022). That would mean that obesity could also act as a mediator in the pathway linking unhealthy food environments with other diseases.

A third finding was that a macro-level financial crisis increased the short-term risk of depression for people living in rural areas, but not in urban areas.

There is little empirical evidence that the effects of macro-level financial crises differ between locales, and the local economy could mediate or moderate the impact on health. Rural areas have structural disadvantages compared to urban areas (Zwiers et al. 2016). One example is that the effect of financial crises on health of people from urban and rural areas can be partially explained by austerity policies in healthcare systems (Recio et al. 2022), which means that communities spend less money on local healthcare infrastructure, especially in rural areas. Another hypothesis is that the effect of economic downturns or other events at the macro-level on health could depend on the quality of the relevant environmental living conditions – rural areas are for example more deprived in terms of local infrastructure. Families from more deprived areas generally show a higher risk of experiencing economic hardships or pressure (Hooper et al. 2022) due to a higher probability of job and even housing loss (Borrell et al. 2014). One study also found that people living in deprived areas had the highest mortality rates when mortality levels before and after a recession were compared (Marí-Dell'Olmo et al. 2015). We controlled for area deprivation and urban–rural residence in this study and both the effects of area deprivation and urbanrural location persisted. But, area deprivation was operationalized by characteristics from the built and social community environment, and not from local socioeconomic determinants, e.g. such as regional education level, employment, and income, as done in prior research. That means that the socioeconomic composition of urban and rural regions could explain the differences in the short-term effect of a financial crisis on the risk of depression between different areas. However, more research is needed here.

6.3.3 Short-term health effects of environmental living conditions

Using the pathway approach, this thesis found that stable or worsened detrimental environmental living conditions such as higher or increased levels of air pollution, detrimental or worsened housing conditions, and worsened local infrastructure are associated with worse short-term physical or mental health. This is true for worse general physical health, reduced lung function, and worse cognitive functioning. Short-term health effects were measured using health levels at one point in time, for instance, from one wave or year. A causal time order was introduced for all the study designs used, from exposure (*t-1*) to outcome (t_0).

One explanation can be derived from the Environmental Press Theory (Lawton et al. 1978), which refers to the short-term health effects of environmental living conditions. The main strain of the theory is that health and the environment are in an ongoing adaptation process. Health is thus the degree of fit between a person's competencies, e.g. physical and functional health as well as cognitive and affective functioning, and the demands of their environment. If a mismatch between environment and competencies occurs, environmental press develops, leading to worse health. However, people are also able to adapt to detrimental environments, and this can happen quite quickly. We know from anthropological evolution theories and empirical studies that humans are able to "occupy" environments characterized by stressful conditions by using behavioral social and physiological adaptations (Frisancho 1993). Because physiological adaptations such as genetic and bodily changes usually take longer to become effective, behavioral social adaptations would appear the more likely mechanism for the operation of changes in perceived physical health. Behavioral plasticity, which is the ability of organisms to change their behavior in response to stimuli (Komers 1997), allows humans to respond rapidly to poor living environmental characteristics (Mathew & Perreault 2015).

Another methodological study argued that short-term health effects measured by health levels, and not by changes in health over time, could simply reflect health disparities that already persisted before the exposure or treatment occurred (Glass et al. 2013). Accordingly, it cannot be excluded that the health levels differed before the observation period for the prospective cohort study had started, regardless the assumed exposure. Interpreted from a counterfactual perspective, we cannot confirm that if the exposure to environmental living conditions had not occurred, health disparities between the living environments would nevertheless not have been observed. One argument against this accusation could be that we observed non-movers only, so that positive health selection into living environments did not play a role during the observation time (1999-2014). Another argument is that we observed that the health of people who experienced improved conditions did not differ from people living under stable best conditions. Worsened environmental living conditions were indeed also related to worse health. These findings underline that changes in exposure can lead to real short-term changes in health. However, the methodological concern about causality cannot be completely ruled out.

6.3.4 Long-term health effects of environmental living conditions

An interesting finding when we observed physical health in the long term was that stable high exposure to environmental pollution and worsened pollution, and stable limited local infrastructure were connected to physical health deterioration over time among adults (aged 18+) in Germany. A financial crisis like the Great Recession was found to increase the general long-term risk of depression among people aged 50 or older from several European countries. There are different potential interpretations for this finding.

First, the observed long-term health effects emphasize that the characteristics of the living environments – such as environmental pollution, local infrastructure, and perceived insecurity due to local unemployment caused by the financial crisis – influence people's bodily conditions and may delay or accelerate the ageing processes in addition to individual age-related factors, as suggested in the literature (Andrews & Phillips 2005). This could lead to permanent health deterioration in the longer run.

Second and from a methodological perspective, the long-term effects could reflect more causal associations than the short-term effects. While the short-term effects were measured using health levels, the long-term effects showed changes in health over time after the occurrence of the exposure. Moreover, the long-term health effects were controlled for the health levels at baseline, which is why it is unlikely that they only reflect health disparities between living environments (selection bias or composition effect) and not real causal contextual effects among the non-movers. However, even when the models controlled for several demographic, socioeconomic, and lifestyle factors at the individual level, there is still the possibility that important third variables confound the associations in the long-term models. One argument supporting potential causality is that the associations for environmental pollution and the local infrastructure were statistically robust in both the short and long term, which was additionally underlined by sensitivity analyses among different sub-populations.

Third, if we assume that both the short and long-term effects on health were indeed causal, then it is interesting that environmental pollution and local infrastructure proved significant throughout, while housing conditions were only relevant in the short term. The Environmental Press Theory (Lawton et al. 1978) and the concept of adaptations between environment and individuum could offer an explanation: the observed associations for

housing conditions, which applied only in the short run, could mean that people adapt quite quickly to detrimental housing conditions, so that negative changes in health in the longer run can be avoided. It is also possible that people who realize that their housing conditions are unhealthy, change or improve them after a period and thus avoid health deteriorations in the longer run. That makes even more sense when we consider the dimension housing conditions refer to: these characteristics are in people's immediate, direct surroundings and they can change them. This is different to the local infrastructure or environmental pollution because these factors cannot be changed by individuals acting alone. Unfortunately, I was not able to prove this explanation because the data on environmental living conditions were not available after baseline – the point in time from which health was observed – so that subsequent changes in the conditions could not be measured. If this explanation is indeed true, the findings would indicate that the local infrastructure, environmental pollution, and economic downturns cause lasting damage to health.

6.3.5 Mediating and moderating pathways

A first finding on the underlying pathways in this thesis was that air pollution and mental health are usually linked directly.

This finding showed that fine particulate matter seems mainly to take a direct route to impair cognitive functioning. This is an important finding because the exact routes by which air pollutants can carry out their neurotoxic effects have barely been tested empirically – there are substantial gaps in the knowledge of the underlying causal mechanisms. An important pathway discussed in the theory is that air pollutants can damage the brain directly by entering through the olfactory nerve or the lung, with subsequent entry into the blood stream (Block & Calderón-Garcidueñas 2009). The relevance of this direct route could be that people cannot be aware of the great danger they are exposed to in their living environments and that air pollution is a chronic invisible danger for mental health over the life course (Verrier et al. 2002). Ulrich Beck (1992) referred to such risks in modern societies in the 1980s with his theory of risk societies. Air pollution is insidious because the danger it causes only becomes visible once disease is already present (Fuller et al. 2022). That is different to lifestyle factors for example, because most people know

about their risks, for instance from smoking, and are able to change their behavior. Air pollution, among other environmental living conditions, is even more complex and difficult, because a meaningful change in behavior would either mean that society as a whole reduces its emissions of air pollutants to care for better air quality, or that an individual would move to a healthier place (Fang et al. 2022). However, research has shown that there remains a lack of information on the dangers of air pollution (Ramírez et al. 2019). Furthermore, this finding on the relevance of the direct pathway also means that particulate matter, as the most important environmental health risk, can directly reach other vital organs beyond the brain (Schraufnagel 2020).

A second finding was that the effect of fine particulate matter on brain health was partly mediated by lung function, a physical health measure. This confirms a second potential pathway assumed in the literature: air pollutants can enter the lungs by inhalation leading to lung impairments, which has a subsequent negative effect on the brain (Block & Calderón-Garcidueñas 2009) This result also confirms many prior studies that have already found that air pollution damages the lungs (Adam et al. 2015), and that lung damage can lead to cognitive impairment (Wang et al. 2022). However, this finding is particularly relevant for the development of prevention and promotion interventions: when the lungs mediate the effect of air pollution on cognitive impairment, prevention interventions addressing lung impairments caused by air pollutants should also consider possible brain impairments as a subsequent consequence (Mrozek et al. 2015).

A third finding was that men's physical health was more susceptible to being affected by increased environmental pollution than women's health.
This finding is also supported by a previous cross-sectional study which found relationships between physical environmental problems (air quality and waste disposal) and subjective health for men only (Sundström et al. 2014). Even while the sex-specific differences in environment health associations remain quite unexplored, three explanations for the sex differences have been discussed. First, men and women perceive or experience their objective surroundings differently, which is why the same characteristics could objectively lead to different effects on perceived health (Ellaway & Macintyre 2001). Second, the factual exposure doses received of the different living environmental characteristics differ between men and women. This could be explained by differences in social roles,

physical activity, and outdoor movement patterns (Xiao & McCright 2015). Third, the bodies of men and women are more or less sensitive to environmental characteristics, suggesting differences in vulnerability (Snow 2008). However, more research is needed on environmental gender medicine to explain the sex differences in the observed effects.

A fourth finding was that the Great Recession increased the general long and short-term risks of depression, but only for people living in deprived or rural areas.
Accordingly, area deprivation or locale (urban or rural) can be understood as moderators for the short-term effects of a financial crisis on depression, and both risk factors combined can act as a cumulative risk factor for mental health. One explanation is that, in line with the theory of local opportunity structures, residents living in deprived areas have acquired coping strategies to deal with the restrictions of their surrounding, for instance the limited access to infrastructure in "normal" times (Bernard et al. 2016, Marotz-Baden & Colvin 1986). However, in times of increased precarity and insecurity these coping strategies might no longer be appropriate and people might not able to adapt to the new living conditions. Based on the Environmental Press Theory by Lawton et al. (1978), a temporary mismatch between a individual's living conditions and personal competencies can lead to worse health in the short run. While people from non-deprived or urban regions could absorb the shock of a financial crisis for a short-period, this was not possible for people from deprived or rural areas due to their limited resources. The higher the quality of the living environment (higher social cohesion, more green spaces, more recreational opportunities, better local economy, and labor market accessibility) in non-deprived or urban areas could promote coping strategies for dealing with an increase of anxiety and stress (Bécares et al. 2011, Damm 2014, Hedblom et al. 2019, Jessiman-Perreault and McIntyre 2017).

6.4 Reflection of the methodological approaches

In summary, the approaches applied in this thesis are innovative in four respects, namely a more holistic, interdisciplinary approach integrating spatial patterns and temporal and other pathways. In the following, the novelties are discussed with regard to their strengths and limitations.

6.4.1 A more holistic approach to environmental health

The first novel aspect to this thesis is that it uses a more holistic approach to environmental health and this was shown to have some strengths.

First, it used a more comprehensive understanding of health including both diseases and continuous health outcomes, and thus combined the pathogenic and salutogenic health approach under a single umbrella. The findings confirm that both approaches to health have their added value in understanding and explaining the consequences of exposure to different environmental living conditions. *Study II* (**Chapter 3)** underlines that observing health as an equilibrium, which was subjectively assessed by individuals, is useful because it allows for health improving and deteriorating over time. This is essential because environmental living conditions can also change to improved conditions leading to subsequent improved health. That is of great relevance when assuming a causal relationship between environmental living conditions and health: no-risk or even improved conditions should not affect health or even improve health (Hernán 2004). Having an exclusively pathogenic approach neglects such a perspective – a dichotomous distinction between being ill and not being ill has the disadvantage that important variance in the changes in outcome cannot be observed as well as with the continuous measures. That is particularly the case when studies explore risk factors for the onset of chronic diseases, such as diabetes, dementia, or cardiovascular diseases (Dendup et al. 2018, Killin et al. 2016, Münzel et al. 2022). In these cases, no change back from ill to not ill is possible. That is unfortunate because such an approach cannot explore how favorable or improved living environmental conditions could contribute to disease recovery. *Study IV* (**Chapter 5)** shows that by using late-life depression as the outcome of interest, it is also possible to integrate changes from ill (prevalent depression) to not ill (no prevalent depression anymore) in a pathogenic approach to health. That is also in line with the Health Development Model (Bauer et al. 2006) which suggests that a strict pathogenic perspective considering only chronic diseases no longer corresponds to a modern understanding of environmental health.

Second, this thesis understands health as a multidimensional concept reflecting both physical and mental health: both health dimensions are *per se* relevant when exploring their associations with the environment, but they are also interrelated, which has been shown by *Study III* (**Chapter 4)** and previously suggested in the theory.

Third, this research includes disease as an outcome, despite continuous health measures having their advantages. This has been done because theory and previous studies proposed that diseases are interrelated with perceived physical and mental health (Ohrnberger et al. 2017). The dichotomous operationalization of diseases can be applied without using any survey data: it is thus based on objective conditions, and can more easily be incorporated into the data and variables. This improves the comparability of the findings between the different studies. This is useful for the understanding of how diseases attributable to environmental living conditions contribute to the disease burden in the population and the related demand for healthcare services, which in turn leads to costs in healthcare systems.

Fourth, four different living environment dimensions have been considered and it has been shown that there are indeed similarities, but also differences between their health consequences (unhealthy vs. healthy food accessibility, and housing conditions vs. environmental pollution and local infrastructure). These findings suggest that it is important to compare different environmental living conditions within the same study and design. The problem of the prior studies in the field is, however, that they used various data, operationalizations, and study designs, which is why their results cannot really be compared (Caudeville 2021, Ebi 2021)

Fifth, environmental living conditions can affect health in addition to individual characteristics, which is why the requirements for the data are high. It is accordingly important also to include the third variable at the individual level to control for complexity and diversity in the determinants of health. The studies conducted for this thesis incorporate the individual-level characteristics throughout.

Although it has many strengths, this thesis also has its limitations.

First, it does not combine pathogenic and salutogenic health concepts as well as subjective and objective environmental living conditions in a single study design. It is thus difficult to compare the different underlying pathways and spatial patterns between the health outcomes and environmental characteristics.

Second, this thesis has the strength that it shows how to apply and partially combine different existing data sources (Statistics Netherlands, RIVM, SOEP, Lifelines, OECD, and

SHARE). This "bigger-data-approach" comes simultaneously with a weakness, that due to the more holistic approach to environmental health, the focus of this thesis is relatively broad in terms of the measures used but also the study populations. Populations and countries differ in their composition, policies, and spatial structure. It thus remains open whether the spatial patterns and pathways found can be generalized to specific other European countries which have not been included in this thesis, such as Greece, Poland, or Norway. The results therefore need to be confirmed in further studies to ensure their external validity.

Third, there is no consistent definition of what the living environment is and this shortcoming is also reflected in the theory. This thesis has attempted to interlock three existing theories to build an overall theoretical umbrella. Even though this is a strength of this thesis, this theory as a whole is not derived from previous inductive studies. It is therefore possible that the theory overemphasized specific aspects or omitted important elements. The approach has accordingly no claim to general validity.

Fourth, even though the approach includes many domains from the living environment, important sub-dimensions have been neglected, such as weather conditions and climate change (Rocque et al. 2021, Schnieder & Breitner 2016).

6.4.2 Including an interdisciplinary perspective

A second novel aspect of this thesis is that it combines theory, data, and methods from demography, public health, epidemiology, economy, and geography under the overarching topic of environmental health:

- *Study I* explores the spatial associations between food infrastructure and obesity by applying an ecological design and spatial econometric methods (public health, geography, and demography)
- *Study II* investigates the temporal associations between changing and stable living environments, and physical health, and applied a pathway approach (demography and public health)

- *Study III* focuses on the associations between fine particulate matter, lung function, and cognition, and concentrated especially on epidemiological pathways (epidemiology and demography)
- *Study IV* is interested in the role of area deprivation in the short and long-term associations between a financial crisis and depression among older adults, and integrated urban–rural differences (demography, economy, public health, and geography).

This interdisciplinary perspective is novel because it is an attempt to synthesize and integrate the various disciplines under a single umbrella. Each study has aimed to combine at least two perspectives to create a more comprehensive picture of the reality. That is different to the classical multidisciplinary perspective, which is the exploration of topics from different angles. Multidisciplinary approaches build additive value by showing the contrasts between disciplines (Choi & Pak 2006).

However, the interdisciplinary perspective on environmental health applied in this thesis has its limits.

First, there are other disciplines which have been omitted from this research, although they were known to contribute to the topic substantially, such as ecology, toxicology, or meteorology (Kelley 2008, Shahid et al. 2020).

Second, the studies conducted in this thesis were barely able to include all the disciplines in each design. It therefore difficult to derive the full interdisciplinarity of this thesis's overall approach from a single study, even though *Study IV* attempted to do so in arguably the most integrative manner.

6.4.3 Spatial approach: regarding regional differences

The spatial approach used in this thesis has clear strengths.
First, in the case of spatial data there is no need for sampling because the entire population is reflected in the data used. Second, it has uncovered important spatial clusters of worse health. Third, it includes differences between regional subtypes, e.g. urban, suburban, and rural regions. Fourth, it has allowed us to evaluate the importance of the wider and the immediate environment for health. Fifth, it has provided findings that are highly

relevant for regional policymakers because they reveal regions with particular need for intervention.

However, it is important to note that the approach has weaknesses compared to other approaches at the individual level.
First, causal interpretations are difficult to derive. The reason is that the studies (Study I and partially Study IV) used either a cross-sectional ecological study design (*Study I*), or considered the regional settings as a time-invariant variable (*Study IV*). The studies have therefore not been able to disentangle or control for the underlying pathways, to uncover why unhealthy people live in regions with worse environmental living conditions (composition vs. causal effects). Second, the interpretation of the results from an ecological study cannot be translated to the individual-level, which would lead to an ecological fallacy (Loney & Nagelkerke 2014). Third, the operationalizations used for regional subtypes can differ between studies and populations. Most studies used the urban–rural dichotomy, while this study also includes a suburban category. That makes it difficult to compare the findings between different studies.
Fourth, the spatial data used and the spatial units explored are clustered using administrative boundaries. Which level of aggregation is suitable for an ecological study with a given research question remains relatively open. In *Study I* we chose the neighborhood level (six digits zip codes), which is a very small-area approach. It has the advantage that variances between smaller regions can be measured, but has the disadvantage that estimated small-area data is less reliable.

Overall, this thesis has shown that a spatial approach is very useful for studying the health consequences of environmental living conditions in Europe, despite its limitations. It helps understand global spatial patterns and interrelationships and extends knowledge from individual-level studies by showing where policy interventions are urgently needed.

6.4.4 Pathway approach: considering temporality and mechanisms

The exact pathways for how environmental living conditions can affect health have barely been studied. This thesis has shown important uncovered interesting moderating and mediating pathways, and temporal differences in their effects. Most previous studies either

concentrated on short or long-term associations, and neglected that associations can differ between subpopulations or regional characteristics, or were not able to explore mediating effects due to the methodological approaches used.

A first methodological issue in exploring the effects of environmental living conditions on health is that time-invariant individual characteristics confound the relationships or time-dependent variables intervene in them. This thesis has tried to tackle this issue by eliminating the effect of important time-invariant and time-dependent individual characteristics from the associations, such as lifestyle, employment status, income, in all studies using the pathway approach. Time-invariant variables were considered either by controlling for these third variables in the multivariate models (*Studies II and III*), or by using panel fixed-effects modelling, which controlled for time-constant unobserved heterogeneity within the individuals (*Study IV*). Time-dependent variables were chosen for their relevance as derived from the literature and included as third variables.

A second methodological issue is that many previous studies did not regard the timing of exposure and outcome in their designs. An important requirement for causality is that the exposure (environmental living conditions) precedes the outcome (health). The pathway approach considers this timing throughout by using longer time-series and creating lags. It has thus also partially been possible to distinguish between possible short and long-term effects (*Studies II and IV*), which is necessary to assess the magnitude of the health effects. That is important for deciding whether to establish derived health interventions or promotion programs for a shorter or longer time periods, and how quickly to initiate them. Another important aspect with a view to the timing of health interventions and promotion policies is that this study has observed stable and improved or worsened environmental living conditions over time.

A third methodological problem is that studies often neglect the underlying mechanisms and focus on mere associations, only scratching the surface of the issue. This is unfortunate because mechanisms should be central to the study of causal relationships. Policy measures cannot be implemented in a targeted manner either, without knowing the mechanisms at play. Moderating pathways are important because they reveal which subpopulations are affected most by environmental living conditions. We found that an eco-

nomic crisis is more relevant for people living in deprived than for people from non-deprived areas in the shorter run, and that men's health is more susceptible to be negatively affected by the long-term effects of environmental pollution than women's. Mediating pathways are especially relevant to understanding the process leading to the health consequences caused by the environment – this thesis has shown that physical health is an important intermediary in explaining the neurotoxic effects of air pollution on mental health. While moderating effects can easily be implemented in most regression approaches, special methods are needed to explore the mediating effects based on causal pathway approaches, such as Structural Equation Modelling (SEM), which has also been implemented in this thesis and is thus a strength.

Unfortunately, the pathway approach applied has its limitations due to data restrictions and the study designs used.

First, each study focused either on objective or subjective health and environment data. None of the studies conducted have been able to integrate both kinds of data in a single design to compare the differences and commonalities in these measures. Beyond this, using subjective health and environment data in the same study can lead to a same-source bias, meaning that people who rate the environment worse also assess their health as worse (Diez Roux 2007).

Second, the pathway approach includes the correct time order between exposure and outcome in all cases, but does not consider changes in environments (not considered in *Studies III and IV*) or health (not considered in *Study III*) over time in all the pathway-approach studies. Neglecting changes in health over time brings with it the problem that the differences in health found can only reflect differences in the health levels before the exposure has occurred.

Third, this thesis has used prospective cohort designs for the pathway approach. A potential shortcoming of these approaches is that the internal validity is lower than for experimental designs, for instance for missed third variables or the selection processes in sampling, or the study design. Even when classical experimental designs are difficult to conduct in environmental health research, some approaches are available, including natural experimental designs and those focused only on movers. These longitudinal studies enquired whether changes in the living environments were associated with changes in

health after a move (Jokela 2014, Jokela 2015). However, such studies also come with limitations because of the uncontrolled characteristics that they include on what caused a move that could also affect health. Another point is that the movers may be a special subpopulation *per se* with special characteristics because moves are often caused by external shocks (see for this debate, Oakes 2014). *Studies II* and *IV* pursued a contrasting approach and focused on non-movers only. This subpopulation should be less affected by unobserved external characteristics that might also be affecting health.

Fourth, the observation period used for *Studies II*, *III*, and *IV* is relatively short (8 to 15 years) to observe health effects caused by living environments. We know from many environmental living conditions that they can only have chronic health effects after a long period of exposure (Sexton et al. 1995). Thus, this thesis might have underestimated the effects of environmental living conditions on health. Additionally, this thesis has not been able to derive concrete limit values from which environmental factors become harmful to health.

In sum, the pathway approach has addressed some shortcomings of previous studies interested in the associations between environmental living conditions and health. The strengths of this approach picked up elements from the theory (timing and pathways), but also applied more suitable analytical approach and data with a view to establishing causality, which is why this research implements novelties and reveals new interesting findings.

6.5 Future research directions

The findings from this thesis reveal five possible connecting points for future research on the health consequences of environmental living conditions in modern societies in Europe:

(1) Create more complex and accurate theories about environmental health.
(2) Improve the measures, methods, and estimates.
(3) Extend knowledge about spatial patterns.
(4) Uncover relevant vulnerable subpopulations and pathways.

6.5.1 Create more complex and accurate theories about environmental health

In sum, the holistic approach used in this thesis has proven to be a productive basis for exploring and explaining the health consequences of environmental living conditions. However, more theories are needed to broaden the view on environmental health as a whole in modern societies. That would deliver useful support for further quantitative studies in the field, which could incorporate the assumptions derived from their methodological approaches to check the underlying hypotheses.

This thesis has revealed for example that environmental health associations differ between regional subtypes – the local food environment was more relevant for obesity in urban areas, while an external financial shock was more important for rural and deprived areas in the short run. Even when a relevant theory – such as the health map for human habitat (Barton & Grant 2006) – mentioned that environments differ between areas, exact hypotheses in terms of urban, suburban, and rural regions could not be derived from the theory. Another aspect is that there are barely any theoretical approaches that link the overall macro-perspective on health and environment with the micro-perspective, and that makes it more difficult for quantitative researchers to adopt a suitable approach and targeted hypotheses. The exact underlying pathways for how environments could affect health has barely been incorporated in the Barton & Grant (2006) approach, which is why several "auxiliary theories", such as the Environmental Press theory (Lawton 1978), were needed for this thesis. Simultaneously, quantitative research is needed that integrate the complexity of environmental health in their data, operationalizations, and methods. This calls for a closer collaboration between theory-makers and empirical researchers. Theory-makers could contribute important knowledge to the measures, operationalizations, pathways, and hypotheses employed, while empirical quantitative researchers could prove these concepts in population-based studies and could confirm their results again with the theory-makers. This is also in line with this thesis's approach, which incorporates an interdisciplinary perspective to environmental health and shows that this contributs substantially to understanding the health consequences of environmental living conditions in modern societies. It is accordingly not only important to integrate the work of theory-makers and empirical researchers, but also to synthesize different disciplines. It seems important to formulate a unified framework for close cooperation from the outset,

so that the various disciplines can achieve valuable synergies and have a clear common goal under the same umbrella. The coordination between the different research branches might thus be a challenge, which should be considered when starting such a comprehensive project.

6.5.2 Improve the measures, methods, and estimations

One open question in the research into the effects of living environmental characteristics on health is how measures, methods, and estimates could be improved to capture the complexities between the living environment and health even better.

First, we need more research that compares the commonalities and differences between subjectively and objectively measured exposure and outcome measures, and between the different dimensions of the living environment. It could thus be valuable to combine subjectively measured data with objectively measured exposure data within the same setting and study design. In doing this, it would also be important to incorporate the specific exposure durations to yield even more accurate estimates. The surveys could request participants' general movement patterns and the durations of stays (George & McCurdy 2011). Another promising data source is mobile data from smart devices, which could provide the exact coordinates of the places people visit (Dewulf et al. 2016). Having this information in a longitudinal format, for instance from Google Timelines, and delivered with unique identifiers to link it to health claims data, health surveys, or biobanks, could advance future research substantially. There is little prior research suggesting that there is an interplay between objective and subjective measures of the living environment (Weden et al. 2008). Objective measures could affect perceptions of the environment, and this could subsequently impact health. This would imply that some environmental living conditions only include health effects when they are perceived as positive or negative. That is more unlikely for air pollution, which is a kind of "invisible danger" and should influence perceptions less, but this pathway seems more realistic for the built environment, such as housing conditions, green spaces, safety, or cleanliness.

Second, there is a need for more objective small-area data on environmental living conditions, and in a harmonized longitudinal format. This is important for both types of studies,

individual and the spatial-level. A lot of data is either available at a coarse resolution, such as at the municipality level, or needs to be estimated by using statistic modelling, such as land-use regression models. The coarse resolution of data comes with the problem that the variance within clusters – the spatial units the data refer to – is large, meaning that using same values for each person in a cluster leads to a loss of information and inaccuracy of the environmental–health estimates. Built environment measures can today be better estimated using satellite pictures, whereas air pollution concentrations or weather data have to be estimated using complex statistic prediction models, chemical transport models or numerical weather predictions, including a broad spectrum of regressors which are thus characterized by a relatively high uncertainty (Crippa et al. 2019).

Third, researchers often do not know how long people are indeed exposed to the living environmental characteristics under study when using observational data. Current studies usually use exposure doses or concentrations at the residential or working addresses of people, without regard to how much time people spend outside or in the neighborhood. However, this information is essential because environmental living conditions can affect people's health when they are outside their dwellings, for instance air pollution, the built environment, and green and blue spaces. One solution to obtain more precise and realistic measures of "real" dose–response relationships is thus to regard the factual exposure time in addition to the dose or concentration, as suggested by various authors (e.g. Abrahamowicz et al. 2006). Those time-weighted exposure measures are common in occupational medicine. However, unfortunately the data on the exact exposure time is often missing. A first step to improve the measures could be the combination of time-use survey data and mobile data on the duration of visits to places with objective and subjective exposure and health data.

Fourth, one issue with exploring the effects of living environmental characteristics on health is to distinguish between effects that are caused by positive health selection for specific living environments and the real causal effects of the surrounding. This issue is based on the fact that observational data is essential for studying people in their natural surroundings, and why a randomized assignment to the experimental and control groups in accordance with a correct experimental design principle is difficult. An approach to address this proposed in the recent literature is to apply a quasi-experimental design by

observing changing living environments among movers only, and decompose the associations found into within and between-person effects over time (Jokela 2014, Jokela 2015). However, as already discussed, an approach solely focused on movers also has substantial limitations (Oakes 2014). Hedman & Maarten (2012) argue that it is important first to conduct studies on mobility decisions and their determinants and later to include this information in studies on the contextual effects of living environments on different outcomes. Another proposed approach is to include a comprehensive life-course perspective by using time-series data over a very long period to control for selective residential mobility and the sorting of people into and out of particular living environments (Hedman & Maarten 2012). The life-course approach could be additionally combined with sibling data to control for unmeasured parental and genetic characteristics (Vaalavuo et al. 2021). A classical method to correct for the bias resulting from a non-randomly selected sample is Heckman correction (Heckman 1979), which is rarely used for investigating living environment and neighborhood effects (Ioannides & Zabel 2008). This two-step approach consists of a probit model for selection and a correction factor in the subsequently conducted outcome regression model. In the first step, a selection equation was built using a probit model for the probability of being observed (1 = observed, 0 = not), for instance in the living environment context for living in a specific area. Using the results from the probit model, the inverse Mills Ratio for each observation was calculated. In the second step, the outcome regression model, for example estimated for the contextual effects of the living environments, was then calculated considering the inverse Mills Ratio for the observations as a correction factor. Nevertheless, Heckman correction also has its limitations and is subject to strong assumptions. Oakes (2004) suggests two additional approaches. A first is to focus on the more detailed dependencies between distal determinants and areas, instead of using more sophisticated methods, by using detailed theories on the possible causal mechanisms. This highlights the importance of studying the underlying pathways linking other multi-level variables to health or focusing on approaches that reveal interdependencies between living environmental characteristics and health without assuming directionality. The knowledge that unhealthy persons live in environments characterized by unfavorable factors could somehow be sufficient to derive appropriate policy implications, for instance simply to “improve living environments”. Whether people sorted themselves to these environments due to selective residential mobility or whether

the environment had a real causal effect on health does not violate the conclusion that people should live under beneficial conditions. A second approach suggested by Oakes (2004) is to use community trials. Although experimental studies are rare, some studies can be found. The Chicago's Gatreaux Project and the American Moving to Opportunity program allocated households to flats and living environments quite randomly, which is why such designs overcome the issue of selection bias to a certain extent. However, because these community trials are social programs, they only focus on specific population subgroups. Furthermore, even when the selection process is random, that does not mean that the internal validity is high. Because community trials are integrated into "real world" contexts, and fortunately not in laboratory settings, the effect of confounding variables does still play an important role.

Fifth, this thesis has provided evidence that timing can play an important role in the effects of environmental living conditions on health. That is not only the correct time order between exposure and outcome, but also the duration of health effects. This knowledge is essential to derive suitable policy interventions and to set priorities in the policies. Long-term health effects caused by environmental living conditions as shown for the local infrastructure, environmental pollution, and macro-level shocks in this thesis could be of special societal interest: they could contribute to an increase in the onset of diseases, to sustainable and persisting public health deterioration, and thus pose a substantial challenge for present and future generations.

In sum, more research is needed that tests the suitability of the proposed measures and methods, and that compares their strengths and limitations. This would help develop new approaches uniting, in the best case, several strengths from each of these measures and techniques to obtain even better estimates of environment–health associations.

6.5.3 Extend the knowledge about spatial patterns

Future research should focus more on the spatial patterns of living environmental characteristics and health outcomes. This thesis has shown that there are differences between regional settings concerning the strength and importance of living environment–health associations. The European-wide trend of ongoing urbanization could also be connected to new issues for cities and the periphery (Kompil et al. 2015). For future research it could

be useful to develop interdisciplinary expertise to handle both individual and spatial data, to profit from more detailed multi-level data. Dealing with spatial autocorrelation in regression models such as Spatial Lag of X models, and considering spatial variation in the observed associations, such as by using geographically-weighted regressions, can improve the understanding of regional hotspots and thus the elaboration of policy interventions suitable for specific areas (Rezaeian et al. 2007). This seems to be particularly important in health research, where spatial epidemiology can be profitably applied to investigating environment–health associations because people live in different places with various exposures in the course of their lives (Jia 2019). Spatial analysis techniques have recently attracted more attention as promising future advances in the field (Tatem 2018). However, even though this thesis has shown that the urban, suburban, and rural distinction in the regional subtypes achieve interesting findings in terms of spatial patterns, newer concepts of compiling small-areas into subtypes could also be useful. The functional urban areas (FUA) approach by the OECD for example not only includes population density as an important variable, but also the travel-to-work flows, when distinguishing between cities or cores and their commuting zones. This could serve as a more appropriate measure for comparing regions across countries (OECD 2019). *Study I* has shown, however, that the FUA approach yields very similar results compared to the urban–suburban dichotomy.

6.5.4 Uncover relevant vulnerable subpopulations and pathways

Prior research has shown that there is already a substantial body of evidence that the different dimensions of the living environment are globally associated with health (WHO 2019). Unfortunately, less is known about (i) subgroups within populations who are more or less susceptible to the adverse effects of the living environment (effect moderations), and (ii) specific pathways for how the living environment characteristics affect health (effect mediations).

Starting with the vulnerabilities, this thesis has shown for example that men were more susceptible to the negative health effects of environmental pollution (**Chapter 3**). Why this is the case remains an open question. One explanation is that the different behaviors of men and women result in variations in the exposure time (Eng et al. 2011). However,

detailed information on specific exposure times is often missing, which is why the actual exposure to pollution cannot be considered. To overcome these research gaps, better data on time-use is needed to obtain information on how long people are indeed exposed to harmful environmental characteristics. However, a more detailed research agenda is also essential, to unite the researchers' specific backgrounds with the research field and recall how a person's own discipline can be used profitably. Future demographic research could focus more closely on differences between the sexes (Bolte et al. 2021 proposed this recently), age groups, or migrants and non-migrants. Future epidemiological research could explore differences in the mechanisms operating between people with a disability, which were shown to be more vulnerable to adverse environmental effects than people without a disability. Future geographical research could consider local variations. Nevertheless, it is also of great interest to combine the focus of one's own discipline with the research agenda from other disciplines: interdisciplinary research could focus on the spatial patterns and regional differences in health by distinguishing between sexes, age groups, and disability status.

Turning to the relevant pathways, this thesis has explored in one study the pathway for air pollution though lung function to affect brain health, and shown the relevance of this indirect mediation pathway but also underlines the relevance of another direct pathway. Because studies on environmental living conditions and their effects on health cannot readily be carried out in laboratory settings and still have high internal validity, considering and developing new strategies and methods is essential to reveal pathogenic pathways and mechanisms in observational study designs. One method used in this thesis is the Causal Pathway Analysis approach, using Structural Equation Modelling. Such methodological approaches open the possibility to investigate causal chains in observational studies, because they permit the inclusion of several endogenous variables (Grace et al. 2015). One strength is that the relevance of the explored pathway compared to the global association found can be estimated. However, causal chain models need a detailed theoretical basis on which the models can be built, because they are not explorative but deterministic in their overall structure (Tarka 2018).

6.6 Policy recommendations and societal implications

The new findings from this thesis have important implications. In general, the findings suggest that policymakers and European society as a whole need to be more aware of detrimental living environments. This is important to protect people's health in their immediate and wider surroundings and to prevent increasing health and social inequalities between regions, which are always characterized by specific environmental living conditions. A sustainable and forward-looking policy strategy should synthesize both environmental and public health policies under a single umbrella, pursuing two overarching goals: improving living environments and population health.

A first principle of such a healthy living environment policy should focus on raising the public's attention to worse living environments and their relevance to health (Peters & Salas 2022). Even though recent research has increased knowledge about the harmful effects of detrimental living environment characteristics, wider society seems to be less well informed (Bianco et al. 2008, Koh 2016). That is especially unfortunate for air pollution, for example, because this is an invisible environmental health hazard which is difficult to perceive, which is why personal behavioral adaptations to prevent ill health are more difficult. A first step is thus to better inform people about the health risks of different living environmental characteristics in their surroundings, such as a lack of green spaces or local infrastructure, or higher exposure to air pollution. Prior research has shown that a multimedia approach, using several channels to distribute information about environmental health risks, is needed to reach the broader public (Fitzpatrick-Lewis et al. 2010).

A second principle refers to the space – the "where" – of environmental living conditions, which is one of the cornerstones of this thesis. To adapt their behaviors – such as their residential mobility, physical activity patterns, and outdoor activities – people need information from policymakers about where (in which areas) they are more or less exposed to environmental health risks. The research on general spatial patterns is therefore essential. Public knowledge and higher priority for healthy living environments would then create incentives for regional policymakers and landlords to provide healthier living environments. Environmental living conditions would become a more valuable and transparent resource on local housing markets. This thesis has shown that food environments are more relevant in urbanized areas, and financial crises have stronger short-term health

relationships in rural and deprived regions. This suggests that environmental living conditions do not have the same health effects across space, meaning that a differentiated policy strategy dependent on the targeted living environment domain and the region is needed. Because of these spatial differences, there is a particular need for targeted municipal policy strategies that could be centrally managed and coordinated.

A third principle refers to the time – the "when" and "how long" – of environmental living conditions. As shown in this thesis, there are differences in the duration of environmental effects on health – environmental pollution, local infrastructure, and financial crisis were shown to include long-term health effects, while general housing conditions and financial crisis were only relevant to deprived and rural regions in the short term. Public health policies should first tackle exposures which produce chronic long-term health effects, and in the meantime prepare plans to combat the short-term effects.

A fourth principle refers to the development of a global strategy including healthy living environments building on modern, sustainable regional policies. This strategy could incorporate for example the move away from a car-oriented transport policy characterized by covering open land and creating parking spaces, to avoid toxic emissions of air pollutants and spaces mainly used for mobility. Instead, this strategy could be oriented towards planning based on greener environments to mitigate the effect of warmer temperatures and longer droughts (Kingsley 2019). In addition, this would include a mobility strategy, especially needed in spaces with a high population density, based on alternative transport with lower emissions of air pollutants, such as public transport or bicycles. Financial incentives to support such vehicles, for instance from government funding or tax relief could be one approach to motivate people to participate in this mobility transition. The vacated space, previously used for mobility purposes, could then serve as recreational space for restorative human activities.

A fifth principle concerns considering vulnerable subpopulations from a public health perspective. Healthy living environment policy should especially protect vulnerable subpopulations against environmental risks to improve population health. This thesis found that a) urban populations showed stronger relationships between the local food and other infrastructure and health, b) men were more susceptible to environmental pollution than women, c) lung function mediates the effect of air pollution on brain health, and d) living

in deprived and rural areas is a short-term risk factor for mental health in times of external shocks at the macro level. These results thus point to a special need of prevention measures for a) the urban population, b) men, c) people with lung diseases or impaired lung function, and d) people from deprived and rural neighborhoods in times of economic crisis. Prior research suggests that there is also a special need for prevention measures for children, pregnant women, older adults, people with lower socioeconomic status, and people with disabilities or chronic disease (Balbus et al. 2009, Luber & McGeehin 2008, Sheffield & Landrigan 2011). However, more research is needed to uncover the exact pathways for how environmental living conditions affect health to develop more suitable prevention and intervention strategies.

A sixth principle refers to explicit prevention, intervention, and promotion measures. Clinicians should first consider that environmental health effects are linked to both physical and mental health. When physical health impairments are diagnosed, then an additional view on the potential mental consequences is important. Mental health problems are more difficult to diagnose because they might only become symptomatic at older ages or after a very long time (Barnes et al. 2015, van der Flier & Scheltens 2005). Clinicians should thus apply a more holistic approach to health when assessing the effects of environmental living conditions on health, and could also consider the beneficial effects of environments, such as good air quality or greenness, when prescribing prevention interventions as health remedies or rehabilitation measures.

6.7 Conclusion

This thesis contributes evidence to the literature that space and time are important for uncovering the effects of environmental living conditions on health in Europe in the twenty-first century, and calls for a more holistic and interdisciplinary approach to environmental health.

Environmental living conditions should be regarded as both important to promoting resources and as risk factors for public health, and they belong on the agenda of regional policymakers, and deserve high priority and public interest now and in future. Policies should consider that environment–health associations can differ between urban, suburban, and rural areas, and a special focus should be on urban regions with a high demand

for policy interventions due tothe more important role of unhealthy food and general higher levels of air pollution there. In times of macro-level external shocks, however, rural or deprived regions might also need rapid help to avoid health deterioration in the short run, which could be caused by poorer local infrastructure in these regions. Public health interventions should be aware of the complex pathways, and especially of the interrelationships between environmental characteristics, physical, and mental health. They should consider that environmental living conditions are not only able to have health effects in the shorter term, but also lasting health consequences in the longer term. The interdisciplinarity and complexity of this field therefore calls for close collaboration between different research disciplines, but also for the need for cross-sectional policy strategies in combating poor living environments.

Future strategies on environmental health should not be limited to specific countries, health outcomes, or environmental domains, but should include a global, holistic, and interdisciplinary perspectives to improve both the quality of our living environments and our health. This is particularly important given the further expected changes to our living environments caused by climate change and global warming.

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E

English summary

Health consequences of exposure to environmental living conditions

Pathways and spatial patterns in Europe

Environmental living conditions are a public health concern in the twentieth and twenty-first centuries. The research of health risk factors alongside individual-level variables is of emerging relevance given that European societies are confronted by additional health-relevant developments in recent years: multimorbidity has increased, and the prevalence has increased of many physical and mental health-related diseases, such as obesity, depression, and dementia. Most European societies are also affected by population aging as a result of the demographic transition characterized by lower birth rates and lower mortality.

Despite its societal importance, there is a lack of detailed understanding in Europe of the impact of different environmental living conditions on health, which is why deriving suitable policy strategies is difficult. This thesis has taken this as its starting point. It has aimed to extend the existing research and asked:

> *How are the different environmental living conditions linked to physical and mental health among European adults in the twenty-first century?*

To answer this question, this thesis has pursued four sub-objectives:

(1) considering a more holistic multilevel approach to environmental health involving physical and mental health and five different dimensions of environmental living conditions, namely the built environment, the natural environment, the local and macro-level economic environment, and the social or community environment;
(2) applying an interdisciplinary approach at the intersection between demography, public health, epidemiology, economy, and geography under a single umbrella;
(3) analyzing general spatial patterns and regional differences in the association between environmental living conditions and health; and
(4) analyzing different temporal, moderating or mediating pathways.

Combining these four novel aspects under a single conceptual umbrella is the novelty of this research. This thesis's analytical approach has pursued, in analogy to the subobjectives 3 and 4, two strategies: first, to explore relevant spatial patterns; second, to test and

reveal important temporal, moderating, and mediating pathways. Newly available spatial and individual data were applied and analyzed using advanced multivariable statistical modelling techniques, such as spatial econometric regressions, panel regressions, and structural equation modelling.

Chapter 1 describes the societal relevance, important definitions, theories, empirical backgrounds, data, and methods used in this thesis. The objective was to summarize existing environmental health theories under a single general theoretical framework for this thesis.

Chapter 2 explores in a cross-sectional ecological study using data from Statistics Netherlands and RIVM the spatial associations between healthy and unhealthy food accessibility and obesity prevalence in the Netherlands.
Limited access to unhealthy fast food was found to be globally associated with lower obesity prevalence across the entire Netherlands, but there were no associations for healthy food accessibility. Limited access to fresh food stores was only relevant for obesity in urban areas (= higher obesity prevalence), while limited access to unhealthy food was relevant for urban, suburban, and rural areas (= lower obesity prevalence). However, local regressions revealed that unhealthy food was most important for obesity prevalence in urban areas. The wider food-access environment was found to be more relevant throughout than the immediate food-access environment.

Chapter 3 investigates in a longitudinal individual-level study based on the SOEP data the short and long-term effects of perceived environmental living conditions on physical health in Germany by considering stable beneficial or worse, improved, and worsened characteristics. Stable higher and worsened environmental pollution, stable poor and worsened housing conditions, and worsened local infrastructure were found to be associated with worse short-term physical health. In the long term, stable high exposure to environmental pollution and worsened pollution, and stable worse local infrastructure were shown to be connected to physical health deterioration over time. Men's health was more susceptible to worsened pollution than women's health.

Chapter 4 focuses on the interrelationships between long-term exposure to air pollution, lung function as a physical health measure, and cognitive performance as a mental health measure, and is based on the Dutch Lifelines data. Using causal pathway analysis, this

study found that fine particulate matter partially takes an indirect route through lung function to affect cognition. However, the main pathway found was direct – a route without the intermediate stage through the lung – which is assumed to be a direct pathway through the blood stream or the olfactory nerve.

Chapter 5 considers the moderating role of meso-level area deprivation on the effects of a macro-level financial crisis on the risk of late-life depression in European countries. The level of age-standardized prevalent and incident cases of depression was generally higher among people from deprived areas compared to people from non-deprived areas. The Great Recession was found generally to increase the long-term risk of depression, both for people from deprived and non-deprived areas. However, only people from deprived areas experienced increased risk of depression in the short-term from the Great Recession.

Chapter 6 summarizes the main results, discusses the main results, and strengths and weaknesses of the thesis, and finally summarizes the policy and societal implications of the results and possible future directions for research in this field.

Overall, this thesis has found strong connections between various chronic or stable and changing environmental living conditions from the built, natural, economic, and community environments, and physical and mental health outcomes in Europe in the twenty-first century. It has added empirical evidence for interesting spatial patterns, regional differences and temporal, moderating, and mediating pathways.

The spatial approach has found that unhealthy food accessibility was relevant for obesity in all regional subtypes, but especially for urban and suburban areas, while healthy food accessibility was only important in urban regions. A macro-level financial crisis was only relevant for depression among the residents of rural areas.

The pathway approach has shown that stable higher exposure to environmental pollution, stable detrimental housing conditions, and worsened pollution, housing conditions, and local infrastructure were associated with worse general physical health, reduced lung function, and worse cognitive functioning. Air pollution and mental health were thereby shown to be mainly directly linked, but the association was in part mediated by lung function – a physical health outcome. In the long term, high stable environmental pollution and worsened pollution, and stable worse local infrastructure were connected to physical

health deterioration over time. The Great Recession was related to a generally higher risk of depression. Men's physical health was found to be more susceptible to worsened pollution and the mental health of people from deprived areas was more susceptible to being affected by the Great Recession.

The findings of this thesis underline the general health relevance of the different dimensions of people's living environment, namely local infrastructure, environmental pollution, housing conditions, and economic conditions, and it has revealed interesting spatial patterns and pathways.

The finding of the spatial approach that associations between environmental living conditions and health differ across space could be caused by two main mechanisms. First, differences in the population composition between urban, suburban, and rural regions could cause the observed spatial variations, for instance due to demographic or socioeconomic characteristics. The demographic or socioeconomic characteristics could also be related to better or worse health. Second, there are indeed differences in the magnitude of the environmental effects on health due to differences in the exposure levels or variations in the available health resources, social behavior, or coping strategies, which is why people can be better or worse at adapting to poor or worsened living environments. This thesis has shown that the differences in the population composition is important, but does not fully explain the spatial variations. The analysis suggests that people might readily adapt to worsened housing conditions in the short term. However, environmental pollution or local infrastructure seemed to have lasting and chronic health effects, which were still observed in the longer term.

The pathway approach has found interesting moderating, mediating, and temporal pathways. The moderating pathways suggest that there could be subpopulations that are more vulnerable to the negative health effects of environmental living conditions, such as men and environmental pollution, and people from deprived areas and macro-level economic downturns. This could be explained by differences in the experienced exposure-dose or exposure-time, in the bodily conditions that make people more or less vulnerable to their environments, or by the resources available to people that promote good health or prevent poor health. Better coping strategies or higher resilience due to beneficial environmental conditions which can be characterized by better social cohesion or better local

infrastructure, are assumed to be some of these positive health resources. As a mediating pathway, this dissertation underlines the relevance of the lungs as an intermediate stage between air pollution exposure and cognitive performance. However, even if lungs play a substantial role, this research suggests that an alternative direct pathway through the bloodstream or olfactory nerve, as assumed in the theory, could play a more important role in the link between air pollution and cognition. The temporal differences found in the associations between the dimensions of the living environment and health suggest that environmental living conditions differ in the magnitude of their effects on health, which is why some lead to temporary effects only, and that people might be better or worse at adapting to the various dimensions of environmental living conditions. They could for example be better at adapting to worse or worsened housing conditions and be worse at adapting to worse or worsened pollution.

The spatial and pathway approaches used in this thesis have taken one step further than previous research and provided new insights into the health consequences of environmental living conditions on health in Europe. This dissertation has shown that the inclusion of a spatial perspective regarding the differences in the associations between regional settings – namely urban, suburban, and rural – can improve the research into environmental effects on health because the relationships do not appear equally across space. This is important when elaborating policies suitable to each area. The inclusion of a pathway perspective can improve our knowledge of environmental health because it considers the cause and temporality of the associations and is thus a valuable tool for exploring and fighting the causes of environmental health inequalities at their root. Both the spatial and the pathway perspectives could yield fruitful analytical strategies for developing appropriate prevention and intervention strategies, not only relevant to policymakers but also to physicians in their daily work with affected people. Future policies could incorporate better strategies for informing the public about unhealthy living environments including “where”, “when”, and “how long” people are exposed to detrimental living conditions in their surroundings or neighborhoods. Environmental living conditions could then emerge as a more valuable factor affecting the local housing markets. Physicians should be aware of the possibility that not only physical health outcomes are affected by unhealthy living environments, but also mental health ones, such a brain health, which is deceptive because the symptoms of cognitive impairment are not directly visible. Another

important aspect is the development of a uniform global environmental policy. This is important because the environment in which people live is not only affected by region or country-specific emissions or exposures, but also by human behavior as regards the environment on the planet as a whole. Raising awareness of the global interaction between the environment, human behavior, and health is thus one of the most important tasks for this and future generations.

N

Nederlandse samenvatting

Gezondheidsgevolgen van blootstelling aan verschillende aspecten van de leefomgeving

Mechanismen en ruimtelijke patronen in Europa

De leefomgeving vormt een belangrijk risico voor de volksgezondheid in de twintigste en eenentwintigste eeuw. Onderzoek naar risicofactoren voor de gezondheid, naast variabelen op individueel niveau, wordt steeds belangrijker, aangezien Europese samenlevingen de afgelopen jaren worden geconfronteerd met extra ontwikkelingen op het gebied van gezondheid: multimorbiditeit is toegenomen en veel fysieke en mentale aandoeningen, zoals obesitas, depressie en dementie, komen steeds vaker voor. De meeste Europese samenlevingen hebben daarnaast te maken met vergrijzing als gevolg van de demografische transitie die wordt gekenmerkt door een afname van het geboortecijfer en een afname van de sterfte.

Ondanks het belang voor de samenleving is er in Europa maar weinig gedetailleerd inzicht in de impact van verschillende aspecten van de leefomgeving op de gezondheid. Hierdoor is het moeilijk om goede beleidsstrategieën te ontwikkelen. Dit vormt het uitgangspunt van dit proefschrift. Het doel van dit proefschrift is om het bestaande onderzoek uit te breiden en de volgende vraag te beantwoorden:

> *Op welke manier zijn verschillende aspecten van de leefomgeving van invloed op de fysieke en mentale gezondheid van Europese volwassenen in de eenentwintigste eeuw?*

Om deze vraag te beantwoorden, zijn er in dit proefschrift vier subdoelen nagestreefd:

(1) het aannemen van een meer holistische, multi-level benadering van milieugerelateerde gezondheid door bet bestuderen van zowel de fysieke als de mentale gezondheid en daarnaast vijf verschillende dimensies van de leefomgeving: de gebouwde omgeving, de natuurlijke omgeving, de economische omgeving op lokaal en op macroniveau, en de sociale of maatschappelijke omgeving;

(2) het toepassen van een interdisciplinaire aanpak op het snijvlak van demografie, volksgezondheid, epidemiologie, economie en geografie onder één paraplu;

(3) het analyseren van zowel algemene ruimtelijke patronen alsook regionale verschillen in het verband tussen aspecten van de leefomgeving en gezondheid; en

(4) het analyseren van verschillende onderliggende mechanismen, waaronder de tijdsdimensie, alsook mediërende en modererende mechanismen / paden.

Het samenbrengen van deze vier nieuwe aspecten onder één conceptuele paraplu vormt de nieuwe insteek van dit onderzoek. De analytische aanpak van dit proefschrift heeft, in overeenstemming met subdoelstellingen 3 en 4, twee strategieën gevolgd: ten eerste, het onderzoeken van ruimtelijke patronen; en ten tweede, het testen en definiëren van belangrijke onderliggende mechanismen. Nieuw beschikbare ruimtelijke en individuele data zijn gebruikt en geanalyseerd met behulp van geavanceerde multivariabele statistische modelleertechnieken, zoals ruimtelijk econometrische regressies, panelregressies en structurele vergelijkingsmodellen.

Hoofdstuk 1 beschrijft de maatschappelijke relevantie, belangrijke definities, theorieën, empirische achtergronden, data en methoden die zijn gebruikt in dit proefschrift. Het doel was om bestaande theorieën rond de milieugerelateerde gezondheid samen te vatten onder één theoretisch kader.

Hoofdstuk 2 onderzoekt in een cross-sectionele ecologische studie, aan de hand van data van het Centraal Bureau voor de Statistiek (CBS) en het Rijksinstituut voor Volksgezondheid en Milieu (RIVM), de ruimtelijke verbanden tussen toegang tot gezonde en ongezonde voeding en het percentage obesitas voor Nederland.
Beperkte toegang tot ongezond fastfood bleek voor Nederland in zijn geheel verband te houden met een lager percentage obesitas, maar voor toegankelijkheid tot gezonde voedingsmiddelen vonden we geen verband. Beperkte toegang tot winkels met verse voedingsmiddelen was alleen relevant voor obesitas in stedelijke gebieden (= hogere percentages), terwijl beperkte toegang tot ongezonde voedingsmiddelen relevant was voor zowel stedelijke, voorstedelijke als landelijke gebieden (= lagere percentages obesitas). Uit lokale regressies bleek echter dat ongezonde voeding het belangrijkste was voor het percentage obesitas in stedelijke gebieden. Over het algemeen bleek de toegankelijkheid tot voeding in de wijdere omgeving relevanter dan de toegankelijkheid van voeding in de directe omgeving.

Hoofdstuk 3 onderzoekt in een longitudinale studie op basis van data op individueel niveau van het Duitse Socio-Economic Panel (SOEP) de korte- en langetermijneffecten van waargenomen aspecten van de leefomgeving op de fysieke gezondheid in Duitsland door

te kijken naar stabiele (stabiel gunstige of stabiel slechte), verbeterde en verslechterde kenmerken. Er bleek een verband te zijn tussen stabiel gunstige alsook verslechterde milieuvervuiling, stabiel slechte alsook verslechterde huisvesting en verslechterde lokale infrastructuur enerzijds en slechte fysieke gezondheid op de korte termijn anderzijds. Op de lange termijn bleek er een verband te zijn tussen stabiel hoge blootstelling aan milieuvervuiling en verslechterde milieuvervuiling, en stabiel slechte lokale infrastructuur enerzijds en verslechtering van de fysieke gezondheid over tijd anderzijds. De gezondheid van mannen was vatbaarder voor toenemende milieuvervuiling dan de gezondheid van vrouwen.

Hoofdstuk 4 gaat over de onderlinge verbanden tussen lange-termijn blootstelling aan luchtvervuiling, longfunctie als fysieke gezondheidsmaat, en cognitieve prestaties als mentale gezondheidsheid, gebaseerd op data van Lifelines. Uit dit onderzoek, dat gebruikmaakte van causale padanalyse, bleek dat fijnstof deels een indirecte route volgt via de longfunctie alvorens cognitieve prestaties te kunnen beïnvloeden. Maar de belangrijkste route die werd gevonden was de directe route (een route zonder het tussenstadium via de longen), waarvan wordt aangenomen dat het een directe route via de bloedbaan of de reukzenuw betreft.

Hoofdstuk 5 kijkt naar de modererende rol van achtergestelde gebieden op mesoniveau op de mate waarin een financiële crisis op macroniveau van invloed is op het risico op depressie op latere leeftijd in Europese landen. Het niveau van op leeftijd gestandaardiseerde gevallen en incidenten van depressie was over het algemeen hoger onder mensen uit achtergestelde gebieden vergeleken met mensen uit niet-achtergestelde gebieden. Over het algemeen bleek de Grote Recessie het risico op depressie op de lange termijn te hebben verhoogd, voor mensen uit zowel achtergestelde als niet-achtergestelde gebieden. Alleen mensen uit achtergestelde gebieden ervaarden echter een verhoogd risico op depressie op de korte termijn als gevolg van de Grote Recessie.

In **hoofdstuk 6** worden de belangrijkste resultaten samengevat en bediscussieerd, de sterke en zwakke punten van het proefschrift besproken, en – tot slot – de implicaties van de resultaten voor beleid en de samenleving, alsook aanbevelingen voor verder onderzoek uiteengezet.

Over het algemeen zijn er in dit promotie-onderzoek sterke relaties gevonden tussen verschillende chronische of stabiele en veranderende aspecten van de gebouwde, natuurlijke, economische en maatschappelijke leefomgevingen enerzijds, en de fysieke en mentale gezondheid in Europa in de eenentwintigste eeuw anderzijds. Het proefschrift voegt empirisch bewijs toe voor interessante ruimtelijke patronen, regionale verschillen, alsook verschillende onderliggende mechanismen / paden.

Uit de ruimtelijke aanpak bleek dat in alle regionale subtypes de toegangelijkheid tot ongezonde voeding relevant was voor het percentage obesitas, maar met name voor stedelijke en voorstedelijke gebieden, terwijl de toegangankelijkheid tot gezonde voeding alleen van belang was in stedelijke gebieden. Een financiële crisis op macroniveau bleek alleen relevant voor depressie onder bewoners in landelijke gebieden.

De padanalyse liet zien dat er een verband was tussen stabiel hogere blootstelling aan milieuvervuiling, stabiel slechte huisvesting en verslechterde vervuiling, huisvesting en lokale infrastructuur enerzijds en een slechte algemene fysieke gezondheid, verminderde longfunctie en slecht cognitief functioneren anderzijds. Er bleek hierbij een voornamelijk direct verband tussen luchtvervuiling en mentale gezondheid, maar dit verband werd deels gemedieerd door longfunctie, een fysieke gezondheidsmaat. Op de lange termijn bleek er een verband te zijn tussen stabiel hoge blootstelling aan milieuvervuiling en verslechterde milieuvervuiling, en stabiel slechte lokale infrastructuur enerzijds en verslechtering van de fysieke gezondheid over tijd anderzijds. De Grote Recessie leidde over het algemeen tot een hoger risico op depressie. De fysieke gezondheid van mannen bleek vatbaarder voor verslechterde vervuiling en de mentale gezondheid van mensen in achtergestelde gebieden was vatbaarder voor de gevolgen van de Grote Recessie.

De bevindingen van dit proefschrift onderstrepen de relevantie voor de algehele gezondheid van de verschillende dimensies van de leefomgeving van mensen, te weten de lokale infrastructuur, milieuvervuiling, huisvesting en economische omstandigheden. Het proefschrift onthulde bovendien interessante ruimtelijke patronen en onderliggende mechanismen / paden.

De bevinding van de ruimtelijke aanpak dat verbanden tussen de leefomgeving en gezondheid verschillen in verschillende gebieden kan worden veroorzaakt door twee belangrijke mechanismen. Ten eerste leiden verschillen in de samenstelling van de bevolking in stedelijke, voorstedelijke en landelijke gebieden tot de geobserveerde

ruimtelijke variaties, bijvoorbeeld als gevolg van demografische of sociaal-economische kenmerken. De demografische of sociaal-economische kenmerken kunnen ook te maken hebben met een betere of slechtere gezondheid. Ten tweede zijn er inderdaad verschillen in de omvang van de effecten van de leefomgeving op de gezondheid als gevolg van verschillen in de mate van blootstelling of variaties in beschikbare middelen om de gezondheid te bevorderen, sociaal gedrag of copingstrategieën, waardoor mensen zich beter of juist slechter aanpassen aan een slechte of verslechterde leefomgeving. Dit proefschrift laat zien dat de verschillen in de samenstelling van de bevolking belangrijk zijn, maar de ruimtelijke variaties niet volledig verklaren. De analyse suggereert dat mensen zich waarschijnlijk op de korte termijn snel aanpassen aan verslechterde huisvesting. Milieuvervuiling of lokale infrastructuur leken echter tot blijvende en chronische gevolgen voor de gezondheid te leiden, die ook op de lange termijn nog zichtbaar waren.

De padanalyse heeft interessante modererende, bemiddelende en temporale mechanismen / paden gevonden. De modererende paden suggereren dat er bevolkingsgroepen kunnen zijn die kwetsbaarder zijn voor de negatieve gezondheidseffecten van aspecten van de leefomgeving, zoals mannen voor milieuvervuiling en mensen uit achtergestelde gebieden voor economische crises op macroniveau. Dit zou kunnen worden verklaard door verschillen in de ervaren mate of duur van de blootstelling, door verschillen in lichaamstoestand die mensen meer of minder kwetsbaar maken voor hun omgeving, of door de middelen die mensen tot hun beschikking hebben om gezond te leven en/of ongezondheid te voorkomen. Er wordt aangenomen dat betere copingstrategieën of meer veerkracht als gevolg van een gezonde leefomgeving, zoals betere sociale cohesie of een betere lokale infrastructuur, voorbeelden zijn van deze positieve middelen om de gezondheid te bevorderen. Als een mediërend pad onderstreept dit proefschrift de relevantie van de longen als tussenstadium tussen blootstelling aan luchtvervuiling en cognitieve prestaties. Maar zelfs als de longen een substantiële rol spelen, dan nog suggereert dit onderzoek dat een alternatief direct pad via de bloedbaan of de reukzenuw, zoals wordt aangenomen in de theorie, een belangrijkere rol zou kunnen spelen in het verband tussen luchtvervuiling en cognitie. Het gevonden belang van de tijdsdimensie in de verbanden tussen de leefomgeving en gezondheid suggereren dat verschillende aspecten van de leefomgeving

verschillen in de mate waarin ze van invloed zijn op de gezondheid - en om die reden al dan niet alleen tot tijdelijke effecten leiden - endat mensen beter of slechter kunnen zijn in het aanpassen aan de verschillende dimensies van de leefomgeving. Sommige mensen zijn bijvoorbeeld beter in het aanpassen aan slechte of verslechterde huisvesting en minder goed in het aanpassen aan slechte of verslechterde vervuiling.

De ruimtelijke aanpak en de padanalyses die voor dit proefschrift zijn gebruikt, zijn een stap verder gegaan dan eerder onderzoek en bieden nieuwe inzichten in de gevolgen van de leefomgeving voor de gezondheid in Europa. Dit proefschrift toont aan dat het aannemen van een ruimtelijk perspectief met betrekking tot de verschillen in verbanden tussen gebieden (stedelijk, voorstedelijk en landelijk) het onderzoek naar milieu-effecten op de gezondheid kan verbeteren, omdat deze verbanden ruimtelijk verschillen. Dit is belangrijk voor het uitwerken van geschikt beleid per gebied. Een focus op de onderliggende mechanismen / paden kan de kennis over de milieugerelateerde gezondheid verbeteren omdat rekening wordt gehouden met de oorzaak en de tijdsdimensie van de verbanden. Daarmee is zo'n focus waardevol voor het onderzoeken en bestrijden van de oorzaken van ongelijkheden in de milieugerelateerde gezondheid, daar waar ze ontstaan. Zowel de ruimtelijke benadering als de focus op de onderliggende mechanismen / paden kan nuttige analytische strategieën opleveren om de juiste preventie- en interventiestrategieën te ontwikkelen, die niet alleen relevant zijn voor beleidsmakers, maar ook voor medici in hun dagelijks werk. Toekomstig beleid zou betere strategieën kunnen omvatten voor het informeren van de bevolking over ongezonde leefomgevingen, inclusief 'waar', 'wanneer' en 'hoe lang' mensen zijn blootgesteld aan ongezonde leefomstandigheden in hun omgeving of buurt. De kwaliteit van de leefomgeving zou dan kunnen worden gezien als een waardevollere factor die van invloed is op de lokale huizenmarkt. Artsen zouden meer bewust moeten zijn van de mogelijkheid dat niet alleen de fysieke, maar ook de mentale gezondheid kan worden aangetast door een ongezonde leefomgeving. Te denken valt aan de gezondheid van de hersenen, die heel verraderlijk kan zijn omdat de symptomen van cognitieve stoornissen niet direct zichtbaar zijn. Een ander belangrijk aspect is de ontwikkeling van een uniform, wereldwijd milieubeleid. Dit is belangrijk omdat de leefomgeving van mensen niet alleen wordt beïnvloed door emissies of blootstelling uit de eigen regio of het eigen land, maar ook door wereldwijd menselijk gedrag met betrekking tot het milieu. Bewustzijn creëren

over de wereldwijde interactie tussen omgeving, menselijk gedrag en gezondheid is daarmee één van de belangrijkste taken voor de huidge en toekomstige generaties.

Statutory Declaration

I hereby declare that I have created the present work without the use of unauthorized assistance from third parties and without the use of any means other than those specified; thoughts taken from foreign sources have been clearly marked as such. This work has not been submitted in similar or the same form for examination to any academic institution in the country or abroad for the purpose of obtaining an academic degree.

Rostock, 28 February 2023

Benjamin Aretz

Eidesstattliche Versicherung

Ich erkläre hiermit, dass ich die vorliegende Arbeit ohne unzulässige Hilfe Dritter und ohne Benutzung anderer als der angegebenen Hilfsmittel angefertigt habe; die aus fremden Quellen direkt oder indirekt übernommenen Gedanken sind als solche kenntlich gemacht. Die Arbeit wurde bisher weder im Inland noch im Ausland in gleicher oder ähnlicher Form einer Prüfungsbehörde zur Erlangung eines akademischen Grades vorgelegt.

Rostock, 28. Februar 2023

Benjamin Aretz

Own contributions to publications with co-authors of this thesis

Study I

Aretz, Benjamin; Costa, Rafael; Doblhammer, Gabriele; Janssen, Fanny (2023): The association of unhealthy and healthy food store accessibility with obesity prevalence among adults in the Netherlands: A spatial analysis. *SSM – Population Health*, volume 21. Open Access. DOI: 10.1016/j.ssmph.2022.101332.

Own contribution of Benjamin Aretz:

Formulation of the research question: 50%
Study conception: 60%
Conduct and evaluation of the study: 90%
Writing the text: 60%

I confirm with my signature that the above assessment is true.

Rostock, 28 February 2023

Benjamin Aretz

Study II

Aretz, Benjamin; Doblhammer, Gabriele; Janssen, Fanny (2019): Effects of changes in living environment on physical health: a prospective German cohort study of non-movers. *European Journal of Public Health*, volume 29, issue 6, pp. 1147-1153. Open Access. DOI: 10.1093/eurpub/ckz044.

Own contribution of Benjamin Aretz:

Formulation of the research question: 50%

Study conception: 50%

Conduct and evaluation of the study: 70%

Writing the text: 50%

I confirm with my signature that the above assessment is true.

Rostock, 28 February 2023

Benjamin Aretz

Study III

Aretz, Benjamin; Janssen, Fanny; Vonk, Judith M.; Heneka, Michael T.; Boezen, H. Marike; Doblhammer, Gabriele (2021): Long-term exposure to fine particulate matter, lung function and cognitive performance: A prospective Dutch cohort study on the underlying routes. *Environmental Research*, volume 201. Open Access. DOI: 0.1016/j.envres.2021.111533.

Own contribution of Benjamin Aretz:

Formulation of the research question: 90%

Study conception: 80%

Conduct and evaluation of the study: 0%

Writing the text: 60%

I confirm with my signature that the above assessment is true.

Rostock, 28 February 2023

Benjamin Aretz

About the author

Benjamin Aretz holds a bachelor in Sociology (2015) and a master in Sociology (with distinction, 2017), both from the University of Rostock. During his master studies he focused also on demographic topics and raised, together with two students, a fund for an own student research project (5,000 €). Benjamin was hired for teaching (50%) and researching (50%) at the University of Rostock, Chair of Empirical Social Research and Demography led by Prof. Dr. Gabriele Doblhammer in 10/2017. At the same time, he started his PhD project on "Exposure to living environment and its effect on different health outcomes". From June to August 2018 Benjamin was in addition hired for researching in the project RESPONSE - Partnership for Innovation in Implant Technology led by Prof. Dr. Gabriele Doblhammer. Since 01/2019 Benjamin was also hired as an external PhD student at the University of Groningen, Faculty of Spatial Sciences, Population Research Centre (now Cotutelle PhD student at both institutions, main institution at the University of Rostock). During his PhD project, Benjamin spend two research stays at the Population Research Centre Groningen and one research stay at the Netherlands Interdisciplinary Demographic Institute (NIDI) in The Hague. Benjamin was honored by the Best Poster Award of the German Association for Demography (DGD) in 2018.

During his PhD studies, Benjamin presented his research at various conference with a demographic, public health, and epidemiology focus including the European Population Conferences (EPC) in 2018 & 2022, the annual conference of the German Society for Epidemiology (DGEpi) in 2019 & 2022, the international conference of the DFG priority program 1764 (The German Labor Market in a Globalized World) in 2021, and the annual conference of the German Association for Demography (DGD) in 2017, 2018 & 2019.

To communicate his research to a broader audience, his work was published in, among others, Demographische Forschung aus erster Hand, in Deutsches Ärzteblatt, Sueddeutsche Zeitung, Bildzeitung, and spektrum der Wissenschaft.

In March 2020, Benjamin became father of a son. After finalizing his PhD dissertation Benjamin started as a research scientist (group leader) at the Institute of General Practice at the University of Bonn/ University Hospital Bonn in March 2023.

Curriculum vitae

PERSONAL INFORMATION

Date of birth	16 December 1989
Marital status	married, one child
Address	University of Rostock Faculty of Economics and Social Sciences Institute for Sociology and Demography Chair of Empirical Social Research and Demography Ulmenstr. 69 D-18057 Rostock
✉	benjamin.aretz@uni-rostock.de
☎	+49 381 498 4060
🖷	+49 381 498 4395

EDUCATION

10/2015- 09/2017	Master of Arts, Sociology with distinction (University of Rostock, grade: 1.1, top graduate of the graduation class) Master-Thesis: Changes in Living Environment and Health: A Longitudinal Study Based on the GSOEP (grade: 1.0)
10/2012- 09/2015	Bachelor of Arts, Sociology (University of Rostock, grade 1.4) Bachelor-Thesis: Job Satisfaction in the Second Part of Life: A Cross-Sectional Study Based on the Germany Ageing Survey (grade: 1.1)

FURTHER EDUCATION

09/2022	Fundamentals of Business Administration in Finance and Controlling for Scientists, instructor: Susanne Sievers, 2-day course, Rostock – Graduate Academy
02/2020	Project Management for Academics, instructor: Peter Wagner, 2-day course, Rostock – Graduate Academy
11/2019	Rechtliche Aspekte von Cotutelle und Doppelpromotionen (Legal Aspects of Cotutelle and Double Doctorates), instructor: Ass. iur. Karen Schlüter, Maître en droit, 2-day course, Bonn – International DAAD Academy

09/2019	Causal Inference in Epidemiology: DAGs, g-Methods and Target Trial Emulation - A Tutorial for Researchers and Educators, instructor: Prof. Dr. Uwe Siebert, 4 hours course, Ulm – annual conference of the German Society for Epidemiology 2019
10/2018	Advanced Statistical Data Analysis Using R, instructor: Dr. Friederike de Mol, 2-day course, Rostock – Graduate Academy
10/2017	Introduction to Statistical Data Analysis Using R, instructor: Dr. Friederike de Mol, 2-day course, Rostock – Graduate Academy

WORK EXPERIENCE

Since 03/2023	Scientific researcher and group leader at the Institute of General Practice and Family Medicine, University Hospital Bonn, University of Bonn, Bonn, Germany
Since 01/2019	Doctoral candidate at the Department of Demography, Faculty of Spatial Sciences, University of Groningen
06/2018-09/2018	Research associate in the RESPONSE project: partnership for innovation in implant technology (funded by the BMBF)
Since 10/2017	Doctoral candidate and research associate at the Chair of Empirical Social Research and Demography at the University of Rostock
09/2016-09/2017	Project team member in the student research project "Practices and Orientation Patterns of Peer-to-Peer Sharing in Rostock – Chance to participate or Reproduction of Social Inequalities?
10/2015-09/2017	Student assistant at the Chair of Empirical Social Research and Demography at the University of Rostock

FUNDING

07/2019-09/2023	Scholarship of the University of Groningen for research stays at the Faculty of Spatial Sciences, Department of Demography, funding: 5000 €
09/2016-09/2017	Student research project (University of Rostock) "Practices and Orientation Patterns of Peer-to-Peer Sharing in Rostock – Chance to Participate or Reproduction of Social Inequalities?", together with Martin Achterberg and Paul Samula (supervisor: Dr. Sylvia Keim-Klärner), funded by the HERMES-Junior-Program of the University of Rostock, funding: 4900 €

TEACHING

Supervision	Promoter of more than 20 bachelor and master theses
Since 04/2021	Data analysis with Stata, seminar (BA-Level, 90 minutes per week, each summer semester)
Since 10/2019	Research Colloquium: Sociology II / Demography II – Risk Factors, Risk Behavior, Risk Groups and Health (BA-Level, 90 minutes per week, each winter semester)
Since 04/2019	Research Colloquium: Sociology I / Demography I – Risk Factors, Risk Behavior, Risk Groups and Health (BA-Level, 90 minutes per week, each summer semester)
04/2018-09/2019	Qualitative methods, seminar (BA-Level, 90 minutes per week, each summer semester)
Since 10/2017	Methods and Techniques in Empirical Social Research, exercise (bachelor level, 90 minutes per week, each winter semester)

RESEARCH STAYS

07/2019-09/2019	Department of Demography/ Population Research Centre, Faculty of Spatial Sciences, University of Groningen, Groningen (head of department: Prof. Dr. Clara Mulder)
06/2022-07/2022	Department of Demography/ Population Research Centre, Faculty of Spatial Sciences, University of Groningen, Groningen (head of department: Prof. Dr. Hinke Haisma)
07/2022-08/2022	Netherlands Interdisciplinary Demographic Institute, research group "Ageing & Longevity", The Hague (theme leader: Prof. Dr. Fanny Janssen, director: Prof. Dr. Helga de Valk)

HONORS & PRIZES

- Best Poster Award 2017, annual conference of the German Association for Demography (DGD) 2017. Veränderungen des Lebensumfeldes und Gesundheit: Eine Längsschnittstudie auf Basis des GSOEP
- Annual teaching award for the best course (Data analysis with Stata, BA-Level, result of evaluation 1.1 [possible range 1.0-5.0]) at the Faculty of Economic and Social Sciences, University of Rostock, in the academic year 2020/2021

PUBLICATIONS (PEER-REVIEWED)

- **ARETZ B**, COSTA R, DOBLHAMMER G, JANSSEN F (2022): The association of unhealthy and healthy food store accessibility with obesity prevalence among adults in the Netherlands: A spatial analysis. Submitted for publication.

- **ARETZ B** (2022): The short- and long-term effects of the Great Recession on late-life depression in Europe: The role of area deprivation. *Social Science & Medicine, volume 294.* Open Access. DOI: 10.1016/j.socscimed.2021.114697.

- **ARETZ B**, JANSSEN F, VONK M J, HENEKA MT, BOEZEN HM, DOBLHAMMER G (2021): Long-term exposure to fine particulate matter, lung function and cognitive performance: A prospective Dutch cohort study on the underlying routes. *Environmental Research*, *volume 201*. Open Access. DOI: 0.1016/j.envres.2021.111533.

- **ARETZ B**, DOBLHAMMER G, JANSSEN F (2019): Effects of changes in living environment on physical health: a prospective German cohort study of non-movers. *European Journal of Public Health, volume 29, issue 6, pp. 1147-1153*. Open Access.
  DOI: 10.1093/eurpub/ckz044.

- BARTH A, **ARETZ B**, DOBLHAMMER G (2019): Das Risiko für Erwerbsminderungsrente bei Herz-Kreislauf-Erkrankungen nach medizinischer Rehabilitation: Eine ereignisdatenanalytische Studie auf Basis von Daten der Deutschen Rentenversicherung. *Das Gesundheitswesen*, *volume 82, issue 10. pp. 786-793*. DOI: 10.1055/a-0832-2117.

OTHER PUBLICATIONS

- **ARETZ B**, JANSSEN F, VONK M J, HENEKA MT, BOEZEN HM, DOBLHAMMER G (2020): Long-Term Exposure to Fine Particulate Matter, Lung Function and Cognitive Performance: A Prospective Dutch Cohort Study on the Underlying Routes. Preprint on medRxiv, DOI: https://doi.org/10.1101/2020.10.14.20212506.

- **ARETZ B**, DOBLHAMMER G, JANSSEN F (2019): Schlechtes Lebensumfeld – schlechte Gesundheit. Welche kurzfristigen und längerfristigen gesundheitlichen Auswirkungen haben Umwelt, Infrastruktur und Wohnung? (Bad Living Environment – Bad Health. What short- and long-term health effects do environment, infrastructure and dwelling have?) Demographische Forschung aus Erster Hand (16, 4). https://www.demografische-forschung.org/archiv/defo1904.pdf.

- **ARETZ B**, DOBLHAMMER G, JANSSEN F (2018): Effects of Changes in Living Environment on Physical Health: A Prospective German Cohort Study of Movers and Non-Movers in Germany. *SOEPpapers* (997). https://www.econstor.eu/bitstream/10419/191351/1/1046203460.pdf.

- KNABE A, **ARETZ B**, BIEMANN M, BRAACK MK, HANAUER D, KUNDLER L, SAMULA P, SCHWICHTENBERG N, KLÄRNER A (2018): Die alltägliche Bewältigung von Armut - Individuelle Handlungsstrategien unter der Bedingung materieller Knappheit in städtischen und ländlichen Räumen Mecklenburg-Vorpommerns (Coping with poverty in everyday life – Individual agency of respondents in urban and rural areas of Mecklenburg-Vorpommern). Braunschweig: Johann Heinrich von Thünen-Institut, 56 p, *Thünen Working Paper* (109). DOI:10.3220/WP1541166325000.

WORK IN PROGRESS

- FRENTZ-GÖLLNITZ M, **ARETZ B**, JANSSEN F, DOBLHAMMER G (2021-present): Differences in late-life depression among intra-European migrants: A prospective cohort study.

- **ARETZ B**; HENEKA M, DOBLHAMMER G (2022-present): The inflammatory role of leukocytes in cognitive impairment caused by fine particulate matter: A population-based mediation analysis.

- ODDING C, **ARETZ B**, VONK J, VAN DEN BERG G (2022-): The effect of air pollution on cognitive functioning and the role of genetic variation.

PRESENTATIONS & POSTERS

- **ARETZ B**, COSTA R, DOBLHAMMER G, JANSSEN F (2022): Spatial Patterns of Obesity in the Netherlands, and Its Association with (Un)Healthy Food Store Accessibility (poster at European Population Conference (EPC) 2022, Groningen, 30 June 2022)

- **ARETZ B**: The effect of the Great Recession on late-life depression in Europe: the role of area deprivation. (Presentation on the 6. International conference of the DFG priority program 1764 (The German Labor Market in a Globalized World). Conference topic: Trade, Technology, and Demographics. Online, 11.06.2021).

- **ARETZ B**, JANSSEN F, VONK M J, HENEKA M T, BOEZEN H M, DOBLHAMMER G: Luftverschmutzung, Lungenfunktion, kognitive Beeinträchtigung und die zugrunde liegenden Wirkpfade: Eine prospektive Kohortenstudie in den Niederlanden (presentation at the annual conference of the German Society for Epidemiology (DGEpi) 2019, Ulm, 13 September 2019).

- **ARETZ B**, JANSSEN F, DOBLHAMMER G: Luftverschmutzung und kognitive Beeinträchtigung – Welche Rolle spielt die Lunge? (presentation at the annual conference of the German Association for Demography (DGD) 2019, Bamberg, 14 March 2019).

- **ARETZ B**, DOBLHAMMER G, JANSSEN F: Changes in Living Environment and Physical Health: A Longitudinal Study Based on the German SOEP (presentation at European Population Conference (EPC) 2018, Brussels, 09 June 2018).

- **ARETZ B**, DOBLHAMMER G, JANSSEN F: Changes in Perceived Living Environment and Changes in Physical Health over Time. A Longitudinal Study Based on the German Socio-Economic Panel (presentation at the annual conference of the German Association for Demography (DGD) 2018, Cologne, 16 March 2018).

- **ARETZ B**: Veränderungen des Lebensumfeldes und Gesundheit: Eine Längsschnittstudie auf Basis des GSOEP (poster at the annual interdisciplinary research camp of the University of Rostock 2017, Rostock, 23 November 2017).

- **ARETZ B**: Veränderungen des Lebensumfeldes und Gesundheit: Eine Längsschnittstudie auf Basis des GSOEP (poster at the annual conference of the German Association for Demography (DGD) 2017, Rostock, 20 September 2017).

- ACHTERBERG M, **ARETZ B**, SAMULA P: Praktiken und Orientierungsmuster des Peer-to-Peer Sharings in Rostock – Chance auf Teilhabe oder Reproduktion bestehender Ungleichheiten? (presentation at the 6th Student Congress for Sociology, Chemnitz, 16 September 2017).

- **ARETZ B**, SAMULA P: Bewältigung von Armut im Alltag. Subjektive Handlungsstrategien unter der Bedingung materieller Knappheit. (presentation at the 6th Student Congress for Sociology, Chemnitz, 16 September 2017).

MEDIA PRESENCE (SELECTED)

- spiegel-online: Autos erhöhen das Risiko für Krebs und Demenz – auch mit Elektroantrieb (Cars increase the risk of cancer and dementia - even with electric drives) [27 October 2022]. https://www.spiegel.de/auto/krebs-und-demenz-wie-feinstaub-aus-autos-das-risiko-erhoeht-auch-mit-elektroantrieb-a-27ff5929-a546-461a-9706-998ff5a40a49.

- idw-online.de: Rostocker Forscher finden Einfluss von Feinstaub auf Gehirnleistung (Rostock researchers find influence of fine particulate matter on brain performance) [09 February 2022]. https://idw-online.de/de/news788055.

- spektrum.de: Feinstaub schlägt sich direkt im Gehirn nieder (Fine particles directly affects the brain) [22 November 2021]. https://www.spektrum.de/news/wie-feinstaub-auf-das-gehirn-und-denkvermoegen-schlaegt/1951411.

- aerzteblatt.de: Gesundheitsbeeinträchtigungen durch schlechtes Lebensumfeld (Health impairments due to poor living environment) [11 February 2020]. https://www.aerzteblatt.de/nachrichten/109285/Gesundheitsbeeintraechtigungen-durch-schlechtes-Lebensumfeld.

Reviewer for Journals

- BMC Health Services Research
- BMJ Open Respiratory Research
- Environmental Research
- European Journal of Public Health
- International Journal of Geriatric Psychatry
- Journal of Epidemiology and Community Health (JECH)
- Nature Mental Health
- PLOS ONE
- Scandinavian Journal of Public Health
- Scientific Reports
- Social Science & Medicine (SSM)
- SSM – Population Health

Computer Skills

- Stata, R, SPSS, ArcGIS, GeoDa, QGIS, MS Office, Libre Office, Adobe Illustrator, TYPO3, WordPress

Memberships

- German Society for Demography (Deutsche Gesellschaft für Demographie - DGD)
- German Society for Epidemiology (DGEpi)
- European Association for Population Studies (EAPS)

Other

- 2019: Member of the Nominating Committee for the board of the German Demographic Society (DGD), election period 2019-2022

Acknowledgments

First of all, I want thank the best supervisors I could imagine for my thesis, namely Gabriele Doblhammer and Fanny Janssen. Thank you so much that I could learn from your expertise. Thank you that you always believed in me, sometimes more than I personally believed in me. Thank you for your comforting words, when something went against my plan. And most important for me, thank you for your trust - that you have stood by me in difficult times without knowing if this trust will pay off, that you supported me and gave me the chance to fight for my son. Lennard, Aline, and I will never forget this!

Special thanks go to my other co-authors:

Judith M. Vonk and Marike H. Boezen, University Medical Center Groningen: It was a pleasure to collaborate with you. Especially that you were so open-minded for my research idea and had trust to share your expertise about the Lifelines data was overwhelming!

Michael T. Heneka, Luxembourg Centre for Systems Biomedicine: Thank you so much for your openness and interest in the topic of air pollution and cognition, although it is not your major research focus. Your expertise on neuroinflammation was essential for this paper!

Rafael Costa, Netherlands Interdisciplinary Demographic Institute: The collaboration with you on the spatial approach paper was so great! Thank you so much for your good ideas and your kind and respectful manner – it was fruitful and fun working with you!

I want to thank my colleagues and friends from the Population Research Center, University of Groningen, especially Mark and Stephen: Guys, thank you so much for your always kind welcome and your open nature! I liked so much to laugh with you.

And from the Institute of Sociology and Demography, University of Rostock. Many thanks go especially to my colleagues from the Chair of Empirical Social Research and Demography for your patience, and that you were always there for me: Bärbel Westendorf, Daniela Georges, Anne Fink, Christina Westphal, Elena Rakusa, Sina Jankowiak, Anna-Victoria Holtz, Emma Edel, Thomas Fritze, Constantin Reinke, Alexander Barth, Michael Nerius,

Jonas Mauersberger, and Daniel Kreft. A special thank goes to Daniel Kreft, who have indirectly started my scientific career as he recommended me as a student helper at the chair, and to Renée Lüskow, who was responsible for the English editing of my publications.

Thank you very much to my friends, for your support, your recommendations, the time together! Special thanks go to Kili and Dama – thank you for always standing by me and lend me an ear.

A big thank goes to my family:

Mama and Papa, I will never forget what you have done for me during my childhood, my youth, my studies, my PhD. You prepared the fundament for my life, my career, my PhD. I am proud to be your son!

Janina, Daniela, Franziska, Constantin: It is so great to have so many siblings, to have you around me even when you were not on site. I often remember our great childhood together, our pranks, our mistakes, our discussions, and our poor parents. Thank you for these great memories, and I am looking forward to a great future together with you in Bonn.

Paula, Hannes, Jonas, Lukas, Timo: I appreciate so much that I have gained more brothers and sisters with you.

Gerd and Peter: I will never forget what you did for us. You have supported us unconditionally in the most difficult times. That is family!

Last and most important: The biggest thank goes to the two other parts of my heart, Aline and Lennard. You were the reason why I could achieve this! And, that is the reason why you need more space than these few words…

First and foremost, I would like to express my gratitude to my thesis supervisors, Gabriele Doblhammer and Fanny Janssen, who are the best I could have hoped for. Thank you so much for imparting your expertise and knowledge to me. I am deeply grateful that you always believed in me, even when I doubted myself. Your words of comfort and encouragement meant so much to me, especially during times when things didn't go according to plan. Most importantly, thank you for trusting me and standing by me during difficult times, when there was no guarantee that it would pay off. Your support allowed me to fight for my son, Lennard, and I will always remember and appreciate that.

I would also like to extend special thanks to my co-authors, Judith M. Vonk and Marike H. Boezen from the University Medical Center Groningen. It was an honor to collaborate with you, and I was overwhelmed by your open-mindedness towards my research idea and your willingness to share your expertise about the Lifelines data.

To Michael T. Heneka from the Luxembourg Centre for Systems Biomedicine, I am grateful for your openness and interest in the topic of air pollution and cognition, even though it is not your main research focus. Your expertise on neuroinflammation was essential for this paper.

I must also thank Rafael Costa from the Netherlands Interdisciplinary Demographic Institute for his great collaboration on the spatial approach paper. I appreciate your good ideas and your kind and respectful manner, and it was truly enjoyable to work with you.

To my colleagues and friends from the Population Research Center at the University of Groningen, especially Mark and Stephen, thank you for always being so welcoming and open-hearted. I loved laughing with you.

From the Institute of Sociology and Demography at the University of Rostock, I extend my gratitude to my colleagues from the Chair of Empirical Social Research and Demography, including Bärbel Westendorf, Daniela Georges, Anne Fink, Christina Westphal, Elena Rakusa, Sina Jankowiak, Anna-Victoria Holtz, Emma Edel, Thomas Fritze, Constantin Reinke, Alexander Barth, Michael Nerius, Jonas Mauersberger, and Daniel Kreft. I appreciate your patience and unwavering support, and a special thank you goes to Daniel Kreft, who indirectly kickstarted my scientific career by recommending me as a student helper at the chair, and to Renée Lüskow, who was responsible for editing my publications.

Thank you to my dear friends for your support, recommendations, and time spent together. I must extend special thanks to Kili and Dama for always being there for me and lending me an ear.

To my family, I owe an immense debt of gratitude. Mama and Papa, I will never forget all that you have done for me during my childhood, youth, studies, and PhD. You laid the foundation for my life, my career, and my PhD, and I am proud to be your son. Janina, Daniela, Franziska, and Constantin, having so many siblings is a gift, and I cherish the memories of our childhood pranks, mistakes, discussions, and our long-suffering parents. I am excited for the future we will share together in Bonn.
Paula, Hannes, Jonas, Lukas, and Timo, I appreciate having gained more brothers and sisters with you.

Lastly, and most importantly, the greatest thanks go to the two other parts of my heart, Aline and Lennard. You were the driving force behind my success, and there are no words to express how much I love you both. To at least express my gratitude to you, I need more space…

Für Lennard

In meiner Zeit als Doktorand, das ist die Zeit in der man versucht besonders schlau zu werden oder zumindest so zu wirken, habe ich ganz viel gelernt. Ich habe gelernt wie man ein Forscher oder Wissenschaftler wird, wie man schlaue Texte schreibt, wie man mit viel schlaueren Forscherinnen und Forschern redet und von ihnen lernt, auf meinen Dienstreisen und Auslandsaufenthalten wie andere Kulturen und Traditionen funktionieren, wie man hart und lange arbeitet und man manchmal gar nicht mehr genau weiß wofür. Ich dachte eigentlich, dass man gar nicht mehr lernen kann als in so einer Doktorarbeit. Öfter fragte ich mich trotzdem: Wofür denn das alles? Wen interessiert das eigentlich?

Ich bin nun fast an meinem Ziel. Die Doktorarbeit ist fertig. Ändert es etwas? Nicht wirklich. Will ich den Doktortitel? Ja! Warum? Ich weiß es nicht. Wahrscheinlich, weil einfach so viel Arbeit darin steckt und Papa wollte doch so gerne Forscher werden. Was hat das mit dir zu tun, mein Lenni, mein Sohn, meine Liebe? Es gab Zeiten, da war Papa unsicher. Der Weg schien so unendlich lang und die Kraft so endlich. Papa wusste gar nicht, ob er ein guter Herzkind-Papa sein kann und Forscher.

Manchmal verliert man das Ziel aus den Augen, fragt sich warum, wieso, weshalb. Aber es ergibt immer irgendwann Sinn, man kommt immer zu einem Schluss, zu seinem Ziel. Wenn man es nicht versucht, dann hat man schon verloren. Wenn man ganz fest daran glaubt, wenn man kämpft, auch wenn man in dem Moment noch nicht weiß warum. Es lohnt sich immer. Es ist es wert. Man lernt von und mit anderen. Man wächst.

Und jetzt kommt's, warum das alles eigentlich mit dir zu tun hat, mein Lenni, mein Sohn, meine Liebe. Als du noch in Mamas Bauch warst habe ich zu Mama gesagt, dass wir ganz viel von dir lernen werden. Aber wir waren trotzdem sehr unsicher, ob wir für dich gute Eltern sein werden, ob wir stark genug sind, um mit dir den langen Weg im Krankenhaus zu gehen. Ob wir dem gewachsen sind, was auf uns zukommen würde. Ob wir mit der Angst um dich leben können, damit du leben kannst. Ob wir daran nicht zerbrechen werden. Ich habe oben geschrieben, dass ich nicht wusste, ob ich Papa und gleichzeitig Forscher sein könne. Jetzt weiß ich, dass ich es nur so konnte, weil ich als dein Papa gewachsen bin. Ich habe so viel von dir gelernt. Ich habe so viel mit dir gelernt. Du bist etwas

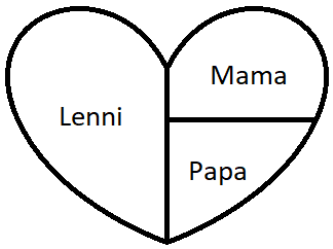
Besonderes, du bist der stärkste Mensch den ich kenne, du bist mein Vorbild, du bist mein Herzenskind, mein Lenni, mein Sohn, meine Liebe:

Lieber Lenni,

Du bist das größte Glück.
Die tägliche Antriebsfeder.
Die pure und ehrliche Freude.
Der Stolz und die Rückbesinnung zum Wichtigsten.
- Familie.

Du bist mein herausforderndstes „Projekt".
Du bist mein Schmerz und mein Leid.
Du bist meine Grenze.
Du bist schwarz und weiß.
- Liebe.

– Du hast kein halbes Herz, du hast das größte Herz überhaupt. –



Ich werde immer für dich da sein!
In Liebe,
dein Papa

Für Aline

Liebe Aline,
meine große Liebe,

Ich erinnere mich an so viele tolle Momente: An die jugendliche Unbekümmertheit, die vielen Momente des Lachens, den gemeinsamen Blödsinn, die Partys und Feiern mit unseren Freunden und der Familie. Aber natürlich sind da auch die Herausforderungen, die wir meistern mussten: Die familiären Probleme, der Umzug ins weit entfernte Rostock, dabei ganz allein auf uns gestellt zu sein, unser geliebter, aber leider schwer kranker Sohn Lennard, um nur einige zu nennen. Manchmal frage ich mich: Wie konnten wir das überhaupt schaffen? Was haben wir nicht alles durchlebt und durchgestanden – ich glaube so ähnlich könnte man unsere letzten gemeinsamen elf Jahre auch beschreiben.

Wahrscheinlich würden wir in Anlehnung an unsere rheinländische Herkunft einfach antworten: „Et kütt wie et kütt." Und: „Et hätt noch immer jot jejange". Nach vorne schauen, nicht aufgeben, kämpfen und lieben. Wir sind immer alles gemeinsam angegangen, wir konnten uns aufeinander verlassen. Früher, also die Zeit vor dir sozusagen, da hätte ich nie für möglich gehalten, dass ich all sowas schaffen kann. Du hast mir gezeigt, wie stark man sein kann, wenn man sich gegenseitig unterstützt und einfach gemeinsam ist. Mit dir war ich erst mutig. Wir sind absolute Familienmenschen und kennen den Mehrwert des Gemeinsamen. Das war vermutlich ein erstes Geheimrezept!

Ein zweites Geheimrezept war glaube ich das Lachen. Gemeinsam Lachen. Das war und ist immer unsere Stärke gewesen. Auch in schlechteren Momenten können wir nicht lange aufeinander böse sein; irgendwer muss immer irgendwann lachen. Wir verlieren nie das Lachen, wir finden im Schlechten immer noch etwas Gutes. Und das ist vor allem auch deine große Stärke – das Glas ist nie halb leer, sondern mindestens halb voll.

Und dann ist da noch das wichtigste Geheimrezept: Vertrauen. Du bist mein Zufluchtsort, wenn es mal nicht läuft, meine größte Unterstützung, ein Grund warum das alles für mich so Sinn macht. Du bist meine Stärke, meine Stütze, mein zuhause, mein Herz, meine große

Liebe! Ich werde dir für immer dankbar sein, wie sehr du mich unterstützt hast während unserer ganzen Jahre, aber auch während meiner Promotion.

Du hast mir den Rücken freigehalten, wenn ich für mehrere Monate in den Niederlanden war. Du musstest abends öfter länger auf mich warten, weil die Arbeit gerufen hat. Du hast mich aufgebaut, wenn ein Artikel in einem Journal abgelehnt wurde. Du hast mir Mut gemacht, dass ich stärker bin als ich denke. Du hast mir das Selbstbewusstsein gegeben daran zu glauben, dass ich das schaffen kann. Ich wusste, dass ich zuhause bei dir meine Sicherheit habe, damit ich an anderer Stelle etwas wagen konnte, mutig sein konnte, etwas riskieren konnte. Du weißt, dass ich selbst mein größter Zweifler bin, dass ich phasenweise denke es ist nicht gut genug. Du kennst meine Schwächen. Du weißt, dass ich selten mit dem zufrieden bin was ich geschafft habe, dass es mir schwer fällt stolz auf mich selbst zu sein. Aber du warst es immer! Du hast an mich geglaubt. Du hast mir vertraut. Du hast mich so genommen wie ich bin. Ich hatte nie das Gefühl du willst mich ändern, aber ich habe immer deine Unterstützung gespürt und gebraucht. Du bist der tollste Mensch den es gibt – daran gibt es keinen Zweifel für mich! Diese Doktorarbeit ist auch dein Verdienst! Ohne dich wäre das nicht möglich gewesen! Und genau deshalb ist es richtig, dass dir die letzten Seiten und Worte in diesem Buch gehören.

Aline, bleib so wie du bist, denn so bist du wundervoll. Ich bin unglaublich stolz auf dich. DU bist das Geheimrezept!

Gemeinsam – Lachen – Vertrauen

Für immer!
In Liebe,
dein Benjamin

Abstract

This dissertation delves into the health consequences of environmental living conditions in Europe, considering both physical and mental health aspects. By adopting a holistic multilevel approach and an interdisciplinary perspective, the research focuses on exploring spatial patterns and temporal pathways between the environment and health outcomes. It specifically investigates various dimensions of the living environment and their influence on physical and mental health. By analyzing data using advanced statistical techniques, this thesis underscores the complex relationship between environmental factors and health.

Several key findings emerge from this research, including the association between food accessibility and obesity, the impact of environmental pollution on physical health, the link between air pollution and cognitive functioning, and the role of living in deprived areas in the onset depression during a macro-level financial crisis. This dissertation underscores the significance of both spatial variations and temporal factors in understanding the impact of environmental living conditions on health outcomes.

The results hold implications for policy formulation, suggesting the need for tailored interventions based on specific spatial and temporal contexts. The findings emphasize the importance of public awareness regarding the global interplay between the environment, human behavior, and health. Furthermore, the research highlights the relevance of considering both physical and mental health in addressing environmental health concerns.

Description of the author

Benjamin Aretz holds a bachelor in Sociology (2015) and a master in Sociology (with distinction, 2017), both from the University of Rostock. During his master studies he focused also on demographic topics and raised, together with two students, a fund for an own student research project (5,000 €). Benjamin was hired for teaching and researching at the University of Rostock, Chair of Empirical Social Research and Demography led by Prof. Dr. Gabriele Doblhammer in 10/2017. At the same time, he started his PhD project. Since 01/2019 Benjamin was additionally hired as an external PhD student at the University of Groningen, Faculty of Spatial Sciences, Population Research Centre (Cotutelle PhD student). During his PhD project, Benjamin spend two research stays at the Population Research Centre Groningen and one research stay at the Netherlands Interdisciplinary Demographic Institute (NIDI) in The Hague. After finalizing his PhD dissertation Benjamin started as a research scientist (group leader) at the Institute of General Practice at the University of Bonn/ University Hospital Bonn in March 2023.