

## Mitigating the impact of air pollution on dementia and brain health

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## Review article

## Mitigating the impact of air pollution on dementia and brain health: Setting the policy agenda

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## ABSTRACT

**Background:** Emerging research suggests exposure to high levels of air pollution at critical points in the life-course is detrimental to brain health, including cognitive decline and dementia. Social determinants play a significant role, including socio-economic deprivation, environmental factors and heightened health and social inequalities. Policies have been proposed more generally, but their benefits for brain health have yet to be fully explored.

**Objective and methods:** Over the course of two years, we worked as a consortium of 20+ academics in a participatory and consensus method to develop the first policy agenda for mitigating air pollution's impact on brain health and dementia, including an umbrella review and engaging 11 stakeholder organisations.

**Results:** We identified three policy domains and 14 priority areas. Research and Funding included: (1) embracing a complexities of place approach that (2) highlights vulnerable populations; (3) details the impact of ambient PM<sub>2.5</sub> on brain health, including current and historical high-resolution exposure models; (4) emphasises the importance of indoor air pollution; (5) catalogues the multiple pathways to disease for brain health and dementia, including those most at risk; (6) embraces a life course perspective; and (7) radically rethinks funding. Education and Awareness included: (8) making this unrecognised public health issue known; (9) developing educational products; (10) attaching air pollution and brain health to existing strategies and campaigns; and (11) providing publicly available monitoring, assessment and screening tools. Policy Evaluation included: (12)

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conducting complex systems evaluation; (13) engaging in co-production; and (14) evaluating air quality policies for their brain health benefits.

**Conclusion:** Given the pressing issues of brain health, dementia and air pollution, setting a policy agenda is crucial. Policy needs to be matched by scientific evidence and appropriate guidelines, including bespoke strategies to optimise impact and mitigate unintended consequences. The agenda provided here is the first step toward such a plan.

## 1. Introduction

New research shows exposure to high levels of air pollutants at critical points in our lives, particularly in early life, is detrimental to brain health across the life course and increases the risk of dementia syndrome and related disorders (e.g., Delgado-Saborit et al., 2021; Guzmán et al., 2022; Ran et al., 2021; Wang et al., 2022; Younan et al., 2022). Examples include global cognition and neurodegenerative disorders, learning in childhood and stroke-related brain damage, and reduction in white matter and neuroinflammation (Chandra et al., 2022; Gartland et al., 2022; Guxens et al., 2018; Killin et al., 2016; Russ et al., 2021).

A key component of air pollution is fine particulate matter (particulate matter with an aerodynamic diameter of  $\leq 2.5 \mu\text{m}$ ,  $\text{PM}_{2.5}$ ). The World Health Organization (WHO) estimates that the combined impact of ambient air pollution and household air pollution is linked to roughly seven million premature deaths annually.<sup>1</sup> In addition to bioaerosols and other natural and biogenic materials,  $\text{PM}_{2.5}$  includes a wide range of primary and secondary particle sources from fossil fuel and domestic wood combustion and non-combustion sources such as tyre and brake wear and cooking aerosols. By definition,  $\text{PM}_{2.5}$  incorporates the particle size class of ultrafine particles (UFP) less than  $0.1 \mu\text{m}$  or  $100 \text{ nm}$  in diameter which contribute only marginally to the PM total mass – while representing a large fraction of particle number. The magnitude of exposure-response relationship that  $\text{PM}_{2.5}$  and other air pollutants have with brain health, while not yet precisely quantified, meets many of the Bradford-Hill criteria guidelines for a causal factor (Delgado-Saborit et al., 2021).

Given the global impact of air pollution and  $\text{PM}_{2.5}$  on brain health and dementia, prevention through air quality improvement could lead to better-quality health outcomes, improve productivity and quality of life, and reduce health-related costs<sup>2</sup> (e.g., Calderón-Garcidueñas et al., 2015; Chandra et al., 2022; Chen and Kan, 2022). The WHO estimates that roughly 55 million people have dementia worldwide, at a global cost of roughly \$1.3 trillion; and this figure is expected to rise to 139 million by 2050, with an estimated global cost of \$2.8 trillion.<sup>3</sup> Even a modest reduction in those costs would have substantial societal and financial benefits, reducing pressures on the health and social care sectors and improving the lives of individuals, families, and carers. Zissimopoulos et al. (2014) found that delaying the onset of Alzheimer's Disease for 5 years would result in 41% lower prevalence and 40% lower cost of the disease in 2050.

Social determinants of health play a major role in air pollution's impact on brain health and dementia (Alegría et al., 2018; Marmot and Bell, 2019). They do so through their complex intersection (including feedback loops), which creates the larger, emergent systems in which people are born, live, work and age (e.g., Castellani et al., 2015; Penn et al., 2022). Public health experts call this “systems” impact the “effects of place” (Cummins et al., 2007). Examples include how the causal loop between poverty, living near an industrial air pollution source, and social inequalities across the life course impact cognitive decline and

neurodegenerative disorders in older, urban populations (e.g., Chandra et al., 2022; Delgado-Saborit et al., 2021; Shou et al., 2019). Or, how air pollution exposure in early-life impacts adolescent global cognition, due to poor health behaviours, limited access to green space, living in congested housing with poor indoor air quality, and walking to school on highly trafficked roads (e.g., An et al., 2021; Gartland et al., 2022; Johnson et al., 2021; Lopuszanska and Samardakiewicz, 2020; Stenson et al., 2021). The places people live create the air quality inequalities and brain health vulnerabilities they experience.

Such a complex public health challenge requires innovative systems approaches to policy and practice (Bicket et al., 2020; Skivington et al., 2021). The challenge is that, while strategies have been proposed to address the impact that air pollution has on public health more generally, their benefits for brain health and dementia are only just beginning to be explored (e.g., Calderón-Garcidueñas et al., 2015; Chen and Kan, 2022). This lack of policy development is an immediate public health concern, given the gravity of the links between place, air pollution, brain health, and dementia (Chen and Kan, 2022; Russ et al., 2019) and the need for a continuous evaluation of policies to target interventions more effectively and possibly downregulate less effective practice.

This paper is the first to outline a policy agenda for addressing the impact of air pollution on brain health and dementia. Across a two-year period, we engaged our consortium of 20+ academics and 11 cross-sector stakeholder organisations in a series of participatory and consensus-building workshops, meetings, and working groups, as well as conducted an umbrella review for the last ten years of research on the topic. Our goal was to identify the major domains and priority areas in research, policy and practice needed to inform a policy agenda on the impact of air pollution on brain health and dementia across the life course.

## 2. Method

### 2.1. Developing an air quality and brain health consortium

In spring 2020 we began a two-year process of developing InSPIRE, a UK policy and research consortium for mitigating the impact that places have on air quality and brain health across the life course. The impetus was a consortium development grant to address the need for a knowledge hub/network that brings together research, practice, and policy guidance to co-produce solutions, tools, and translational materials, and to develop innovative research on this topic. A strategic priority was to develop the first policy agenda for mitigating air pollution's impact on brain health and dementia.

**Consortium Academics:** Our initial team of 20+ academics were selected to ensure expertise across the key areas of research in this field. Over the course of two years, the composition of the team evolved, including several new experts joining. Expertise included cognitive psychology and neuroscience, dementia and ageing research, early childhood development and cognitive science, atmospheric chemistry transport modelling and environmental and exposure science, complexity science and computational modelling, co-production and policy evaluation in complex systems, environmental epidemiology and cohort studies, Bayesian statistics and geospatial modelling, and sociology and public health.

**Stakeholders:** In 2020, we recruited 20+ UK community, local government, public and third-sector organisations to form our stakeholder

<sup>1</sup> <https://www.who.int/health-topics/air-pollution#tab=tab2>.

<sup>2</sup> See Air pollution: cognitive decline and dementia. A report by the Committee on the Medical Effects of Air Pollutants (COMEAP). <https://www.gov.uk/government/publications/air-pollution-cognitive-decline-and-dementia>.

<sup>3</sup> <https://www.who.int/news-room/fact-sheets/detail/dementia>.

ecosystem. All were initially engaged via email and informed about the project and, after dialogue with members of our academic team, joined the consortium. The COVID pandemic made public engagement very challenging. We were able to engage in one or more online meetings with 11 of our stakeholder organisations, which included representation from the dementia and ageing communities, schools and urban planning, third-sector organisations and community activist groups,

healthcare and brain health, and local and national government, including civil servants involved in policy for air quality and public health.

## 2.2. Developing a policy agenda

Table 1 shows the 14 priority areas identified by our work as a

**Table 1**  
Setting the policy agenda.

Domains and Priority Areas	Source for identifying priority area	Actionable Items
<b>Domain A: Research and Funding</b>		
1. Embracing a 'complexities of place' approach	Consortium Academics Stakeholders N = 6 Policy Papers	<ul style="list-style-type: none"> <li>Applying a complex systems perspective of air quality and brain health</li> <li>Drawing from the complexities of place literature in public health</li> <li>Augmenting conventional statistics with computational science and Bayesian modelling</li> <li>Taking an interdisciplinary methods approach to modelling</li> <li>Exploring feedback loops and complex configurations of factors to make sense of causality</li> </ul>
2. Focusing on vulnerable populations in places	Consortium Academics Umbrella Review	<ul style="list-style-type: none"> <li>Exploring the role that health inequalities play in the impact air pollution has on brain health.</li> <li>Examining how places create brain health vulnerabilities, such that certain populations are more at risk from air pollution than others.</li> <li>Studying how vulnerable populations may respond to exposure to different levels of air pollution, even levels considered otherwise health.</li> </ul>
3. Modelling the impact of ambient PM <sub>2.5</sub>	Consortium Academics Umbrella Review	<ul style="list-style-type: none"> <li>Building high resolution, long-term exposure models</li> <li>Developing more comprehensive current models for linking aspects of PM<sub>2.5</sub> source types and composition to specific health outcomes</li> <li>Helping to develop current and historical models for those parts of the world where such models are significantly underdeveloped</li> </ul>
4. Studying indoor air pollution	Umbrella Review	<ul style="list-style-type: none"> <li>Drawing on the wider literature linking indoor air quality to public health</li> <li>Focusing on this issue for school zones, populations living near busy roads or in cities, and for those vulnerable to even mild air quality issues</li> </ul>
5. Making breakthroughs in pathways to disease for brain health	Consortium Academics Umbrella Review	<ul style="list-style-type: none"> <li>Exploring new and multiple pathways to disease beyond just the blood-brain barrier</li> <li>Improving study design and research methods</li> <li>Detailing pathways to disease links and how they are associated with specific forms of brain disease and cognitive impairment</li> </ul>
6. Embracing a life course perspective	Consortium Academics	<ul style="list-style-type: none"> <li>Identifying exposure dose levels and stages in the life course critical to brain health</li> <li>Grounding current and future research in a life-course and developmental framing</li> </ul>
7. Radically rethinking funding	Consortium Academics	<ul style="list-style-type: none"> <li>Developing and studying cohort studies</li> <li>Restructuring research funding mechanisms</li> <li>Supporting high-risk, high-payoff science</li> </ul>
<b>Domain B: Education and Awareness</b>		
8. Making this unrecognised public health issue a known concern	Stakeholders N = 6 Policy Papers	<ul style="list-style-type: none"> <li>Developing a global and national agenda to make the unrecognised impact of air pollution on brain health known to the public, government officials, researchers, funding organisations, third-sector organisations, community groups, and business and industry.</li> <li>Initiating local, national, and international awareness campaigns</li> </ul>
9. Developing educational products	Stakeholders	<ul style="list-style-type: none"> <li>Getting the word out to colleagues in public health and air quality through academic channels</li> <li>Developing lesson plans for primary and secondary schools</li> <li>Co-creating educational products to improve public engagement and collective corrective action</li> </ul>
10. Attaching air pollution and brain health to existing strategies and campaigns	Stakeholders	<ul style="list-style-type: none"> <li>Making sure messages are empowering, given that diseases like dementia have no cure</li> <li>Adding air pollution to existing stakeholder campaigns for brain health and dementia</li> <li>Including brain health to current stakeholder strategies around air quality improvement</li> <li>Highlighting known links between air quality and brain health and climate change, as well as the sustainable development goals and strategies</li> </ul>
11. Providing publicly available monitoring, assessment, and screening tools	Stakeholders Consortium Academics N = 6 Policy Papers	<ul style="list-style-type: none"> <li>Using current evidence on air quality and brain health to bolster existing air quality or brain health campaigns and to demonstrate co-benefits</li> <li>Translating historical and current ambient and indoor air quality datasets, dashboards, and models into useable, publicly accessible resources for citizens, healthcare providers, governments, and third-sector and private sector organisations.</li> <li>Developing screening and assessment tools for individual exposure, particularly during early life and at critical points in the life course where air pollution exposure is most impactful.</li> <li>Developing tools for assessing health behaviours, pre-existing conditions, or co-morbid conditions that prevent, slowdown, or exacerbate the impact of air pollution on brain health, including the progression of dementia post-diagnosis</li> </ul>
<b>Domain C: Policy Evaluation</b>		
12. Conducting complex systems evaluation	Consortium Academics N = 6 Policy Papers	<ul style="list-style-type: none"> <li>Embracing a complex systems perspective of evaluation for air quality and brain health</li> <li>Drawing from the complexity turn in public policy evaluation to adopt best practices</li> <li>Augmenting conventional evaluation methods with participatory systems mapping, etc.</li> <li>mapping barriers and incentives to change and counterfactuals</li> <li>Engaging in policy evaluation via co-production</li> </ul>
13. Engaging in co-production	Stakeholders Consortium Academics	<ul style="list-style-type: none"> <li>Drawing from the wider climate change and air pollution literature on co-production</li> <li>Recognising there are multiple approaches to engagement and co-production</li> <li>Articulating and improving the rigor of the engagement approach used</li> <li>Considering the influence regional, national, and international differences on engagement, as for example countries in the global south versus the global north</li> </ul>
14. Evaluating current air quality policies for their brain health benefits	Stakeholders	<ul style="list-style-type: none"> <li>Drawing on existing policies for air quality and public health in general to develop, in the short-term, a catalogue of useful policy guidelines</li> <li>Exploring wider policy needs beyond just emissions reduction</li> </ul>

consortium and the three policy domains to which they belong, as well as their primary source. We explain the five steps we took to obtain this list, including which domains and priority areas emerged from each step.

**Step 1 Engaging consortium academics:** The first step was to bring together our team of consortium academics through a series of meetings and workshops. The COVID pandemic required all meetings to be online. Meetings were of two types and took place over an eight-month period, starting spring 2020. Consensus building monthly large group meetings and workshops were used to develop our consortium's vision and division of labour, learn about interdisciplinary expertise and co-production with stakeholders, and develop a theory of change model. Weekly to monthly small group meetings (which sometimes included stakeholders) focused on the priority areas of policy and research we would develop. From our work as a consortium, the Research and Funding policy domain emerged, including all of its priority areas, except Priority 4 on indoor air pollution. The Policy Evaluation domain also took shape, as well as Priority Areas 11, 12 and 13.

**Step 2 Stakeholder Engagement:** The second step was engagement with 11 of our stakeholder organisations, which co-occurred with Step 1 but then extended over the course of the second year of consortium development. There are multiple approaches to engagement and co-production (Oliver et al., 2019; Williams et al., 2020); including literatures for air pollution and climate change (e.g., Bremer and Meisch, 2017; Howarth et al., 2022; Jerneck and Olsson, 2013; Sarr et al., 2021). Following the framework outlined by Fransman (2018), we engaged stakeholders as collaborators in developing a policy agenda, including identifying, from their diverse perspectives, key priority areas and strategies for its implementation. We also embraced Fransman's (2018) research engagement as affect approach, which sees engagement as something that cannot be planned and controlled from the outset, but instead unfolds and changes through our work with stakeholders. Stakeholder meetings involved interview teams of two to four academics, including the Director. Initial meetings with stakeholders were 1+ hour in duration and took place between June and November 2020. All meetings were online due to the pandemic. From our online meetings with stakeholders, the Education and Awareness policy domain and its four priority areas emerged, and the Policy Evaluation domain was further refined, including the addition of Priority Area 13 on co-production.

**Step 3 Year-2 Stakeholder engagement:** In Year-2 we took a more active approach to co-production, working directly with two third-sector organisations devoted to dementia and brain health and one government organisation involved with the UK National Health Service (NHS). The lead for Academic Health Science Network, North East and North Cumbria had time to be an author on this paper; the other two did not have time, but provided comments. These three organisations were selected because they have extensive stakeholder networks and because they (a) work directly with disadvantaged communities across the life course, (b) promote brain health in early life and adolescence, (c) focus on dementia, or (d) work on behalf or directly with those living with dementia, including giving them voice in the policy and practice process.

In Year-2 we also ran a 2-h participatory system mapping workshop to explore and develop our emerging policy agenda. Participants included several consortium academics and three members from our year-2 stakeholder organisations.

Participatory Systems Mapping involves a group of stakeholders and researchers collaboratively developing one or more 'complex system maps' of a topic (Barbrook-Johnson and Penn, 2021, 2022; Penn et al., 2022). The maps represent what participants variously believe to be the causal and influence structure of the topic at hand. Systems mapping a topic helps explore and identify unintended policy consequences, trade-offs, and synergies, and develop consensus amongst stakeholders and researchers (Barbrook-Johnson and Penn, 2021, 2022; Penn et al., 2022). Fig. 1 is the map from the workshop. It was created using the Participatory System Mapper (PRSM) online programme<sup>4</sup> that allows users to swarm, in real-time, around the map's development, making for a highly collaborative process. During the workshop, after an initial list of policy factors was identified, the group organised them into clusters, which corroborated several of the priority areas identified in the first two steps, including 1, 3–4, 8, and 10–11.

**Step 4 Umbrella Review:** While several literature reviews were conducted during the two years of consortium building, as a final exercise we conducted an umbrella review (Aromataris et al., 2015) of existing reviews for the last ten years, using Web of Science Core Collection, PubMed, and Google Scholar. The umbrella review was used both to corroborate (where possible) and add to the priority areas identified through our engagement with consortium academics and stakeholders. Articles included mapping reviews, systematic reviews, other umbrella reviews, integrated reviews, and rapid reviews. The keywords used were air pollution, PM<sub>2.5</sub>, brain health, cognition, cognitive function, cognitive decline, dementia, Alzheimer's disease, neurodegenerative disease, stroke, and inflammatory disease. In May–June 2022, using the general search terms 'review' and 'air pollution or PM<sub>2.5</sub> or air quality' in the Web of Science Core Collection, we identified N = 714 results, which we then filtered using the above key words as all-field terms. This reduced our search to N = 50 articles. Additional articles were identified on PubMed and Google Scholar using the same set of search terms, resulting in N = 77 total publications (End date of search: 2 June 2022). Four consortium experts read the abstracts of the N = 77 articles to filter out any reviews not directly focused on brain health. The result was the N = 38 articles in Table 2.

The umbrella review supported most priority areas in Research and Funding, including the addition of Priority 4, Studying Indoor Air Pollution. The reviews did not have a lot to say about Priority Area 1 or about the policy domains of Education and Awareness or Policy Evaluation. As such, we added to our umbrella review any published opinions, policy papers, and invited perspectives directly or indirectly related to policy or evaluation for air pollution and brain health. Exploring the Web of Science Core Collection, PubMed, and Google Scholar, we identified a total of N = 6 publications (See Table 1). These papers corroborated Education and Awareness and Policy Evaluation, as well as priority areas 1–2, 8, 12, and 13.

**Step 5 Writing this paper:** This last step was vital, as it required us to complete our policy agenda. The paper was written over the course of ten months. To create an open and transparent environment for writing and consensus building, the paper was uploaded during the first week of writing as a Google document and worked on by all authors over the next several months. All authors were each asked to comment on the priority areas relative to their expertise and on the paper overall. Thematic analysis was used by the lead author to arrive at the final names of the three policy domains and the 14 priority areas (Braun and Clarke, 2014; Clarke et al., 2015).

<sup>4</sup> <https://prsm.uk/>.



**Table 2**  
Umbrella review.

N = 38 REVIEW articles on air pollution and brain health							
An et al., 2021	A review of the effect of traffic-related air pollution around schools on student health and its mitigation	JOURNAL OF TRANSPORT & HEALTH	DEC	2021	23	10.1016/j.jth.2021.101249	
Avellaneda Gómez et al., 2021	Recognition of air pollution as a risk factor for stroke in clinical practice guidelines: a literature review	NEUROLOGIA	JUL-AUG	2021	36	10.1016/j.nrl.2020.08.003	
Bé jot et al., 2018	A review of epidemiological research on stroke and dementia and exposure to air pollution	INTERNATIONAL JOURNAL OF STROKE	OCT	2018	13	10.1177/1747493018772800	
Bergmann et al., 2020	Effect modification of the short-term effects of air pollution on morbidity by season: A systematic review and meta-analysis	SCIENCE OF THE TOTAL ENVIRONMENT	MAY 10	2020	716	10.1016/j.scitotenv.2020.136985	
Chandra et al., 2022	Air pollution and cognitive impairment across the life course in humans: A systematic review with specific focus on income level of study area	INTERNATIONAL JOURNAL OF ENVIRONMENTAL RESEARCH AND PUBLIC HEALTH	FEB	2022	19	10.3390/ijerph19031405	
Chen et al., 2021	The association between ambient air pollution and atrial fibrillation: A systematic review and meta-analysis	INTERNATIONAL HEART JOURNAL	MAR	2021	62	10.1536/ihj.20-523	
Cristaldi et al., 2022	Possible association between PM2.5 and neurodegenerative diseases: A systematic review	ENVIRONMENTAL RESEARCH	MAY 15	2022	208	10.1016/j.envres.2021.112581	
Clifford et al., 2016	Exposure to air pollution and cognitive functioning across the life course—a systematic literature review	ENVIRONMENTAL RESEARCH	MAY	2016	147	10.1016/j.envres.2016.01.018.	
de Bont et al., 2022	Ambient air pollution and cardiovascular diseases: An umbrella review of systematic reviews and meta-analyses	JOURNAL OF INTERNAL MEDICINE	JUN	2022	291	10.1111/joim.13467	
Delgado-Saborit et al., 2021	A critical review of the epidemiological evidence of effects of air pollution on dementia, cognitive function and cognitive decline in adult population	SCIENCE OF THE TOTAL ENVIRONMENT	FEB 25	2021	757	10.1016/j.scitotenv.2020.143734	
de Prado Bert et al., 2018	The effects of air pollution on the brain: a review of studies interfacing environmental epidemiology and neuroimaging	CURRENT ENVIRONMENTAL HEALTH REPORTS	SEP	2018	5	10.1007/s40572-018-0209-9	
Dillon et al., 2020	The modifying effects of obesity on the association between air pollution and stroke: A systematic review	JOURNAL OF EPIDEMIOLOGY AND COMMUNITY HEALTH	SEP	2020	74	10.1136/jech-2020-SSMabstracts.115	
Dominski et al., 2021	Effects of air pollution on health: A mapping review of systematic reviews and meta-analyses	ENVIRONMENTAL RESEARCH	OCT	2021	201	10.1016/j.envres.2021.111487	
Editor's Editorial, 2018	Air pollution and brain health: an emerging issue	LANCET NEUROLOGY	FEB	2018	17	10.1016/S1474-4422(17)30462-3	
Fu and Yung, 2020	Air pollution and Alzheimer's Disease: A systematic review and meta-analysis	JOURNAL OF ALZHEIMERS DISEASE		2020	77	10.3233/JAD-200483	
Gartland et al., 2022	The effects of traffic air pollution in and around schools on executive function and academic performance in children: A rapid review	INTERNATIONAL JOURNAL OF ENVIRONMENTAL RESEARCH AND PUBLIC HEALTH	JAN	2022	19	10.3390/ijerph19020749	
Han et al., 2020	The impact of long-term exposure to ambient air pollution and second-hand smoke on the onset of Parkinson disease: a review and meta-analysis	PUBLIC HEALTH	FEB	2020	179	10.1016/j.puhe.2019.09.020	
Herting et al., 2019	Outdoor air pollution and brain structure and function from across childhood to young adulthood: A methodological review of brain MRI studies	FRONTIERS IN PUBLIC HEALTH	DEC 6	2019	7	10.3389/fpubh.2019.00332	
Isaevska et al., 2021	Exposure to ambient air pollution in the first 1000 days of life and alterations in the DNA methylome and telomere length in children: A systematic review	ENVIRONMENTAL RESEARCH	FEB	2021	193	10.1016/j.envres.2020.110504	
Johnson et al., 2021	Air pollution and children's health—a review of adverse effects associated with prenatal exposure from fine to ultrafine particulate matter	ENVIRONMENTAL HEALTH AND PREVENTIVE MEDICINE	DEC	2021	26	10.1186/s12199-021-00995-5	
Killin et al., 2016	Environmental risk factors for Dementia: a systematic review.	BMC GERIATRICS	OCT	2016	16	10.1186/s12877-016-0342-y	
Kim et al., 2020	Air pollution and central nervous system Disease: A review of the impact of fine particulate matter on neurological disorders	FRONTIERS IN PUBLIC HEALTH	DEC 16	2020	8	10.3389/fpubh.2020.575330	
Konduracka and Rostoff, 2022	Links between chronic exposure to outdoor air pollution and cardiovascular diseases: a review	ENVIRONMENTAL CHEMISTRY LETTERS	APRIL	2022	2	10.1007/s10311-022-01450-9	
Lin et al., 2022	The epidemiological evidence linking exposure to ambient particulate matter with neurodevelopmental disorders: A systematic review and meta-analysis	ENVIRONMENTAL RESEARCH	JUN	2022	209	10.1016/j.envres.2022.112876	
Lopuszanska and Samardakiewicz, 2020	The relationship between air pollution and cognitive functions in children and adolescents: A systematic review	COGNITIVE AND BEHAVIORAL NEUROLOGY	SEP	2020	33	10.1097/WNN.0000000000000235	
Murata et al., 2022	Air pollution and the risk of Parkinson's Disease: A review	MOVEMENT DISORDERS	JAN	2022	37	10.1002/mds.28922	
Niu et al., 2021	Association between exposure to ambient air pollution and hospital admission, incidence, and mortality of stroke: an updated systematic review and meta-analysis of more than 23 million participants	ENVIRONMENTAL HEALTH AND PREVENTIVE MEDICINE	JAN 26	2021	26	10.1186/s12199-021-00937-1	
Oudin, 2020			MAR	2020	134		

(continued on next page)

Table 2 (continued)

N = 38 REVIEW articles on air pollution and brain health							
	Short review: Air pollution, noise and lack of greenness as risk factors for Alzheimer's disease epidemiologic and experimental evidence	NEUROCHEMISTRY INTERNATIONAL					10.1016/j.neuint.2019.104646
Peters et al., 2019	Air Pollution and Dementia: A systematic review	JOURNAL OF ALZHEIMERS DISEASE		2019	70		10.3233/JAD-180631
Power et al., 2016	Exposure to air pollution as a potential contributor to cognitive function, cognitive decline, brain imaging, and dementia: A systematic review of epidemiologic research	NEUROTOXICOLOGY	SEP	2016	56		10.1016/j.neuro.2016.06.004
Ru et al., 2021	Exploration of the global burden of dementia attributable to PM2.5: What do we know based on current evidence?	GEOHEALTH	MAY	2021	5		10.1029/2020GH000356
Russ et al., 2019	Air pollution and brain health: defining the research agenda	CURRENT OPINION IN PSYCHIATRY	MAR	2019	32		10.1097/YCO.0000000000000480
Shou et al., 2019	A review of the possible associations between ambient PM2.5 exposures and the development of Alzheimer's disease	ECOTOXICOLOGY AND ENVIRONMENTAL SAFETY	JUN 15	2019	174		10.1016/j.ecoenv.2019.02.086
Stenson et al., 2021	The impact of traffic-related air pollution on child and adolescent academic performance: A systematic review	ENVIRONMENT INTERNATIONAL	OCT	2021	155		10.1016/j.envint.2021.106696
Tan et al., 2021, Tan et al., 2022	Association between exposure to air pollution and late-life neurodegenerative disorders: An umbrella review	ENVIRONMENT INTERNATIONAL	JAN	2022	158		10.1016/j.envint.2021.106956
Volk et al., 2021	Prenatal air pollution exposure and neurodevelopment: A review and blueprint for a harmonized approach within ECHO	ENVIRONMENTAL RESEARCH	MAY	2021	196		10.1016/j.envres.2020.110320
Wang et al., 2021	How indoor environmental quality affects occupants' cognitive functions: A systematic review	BUILDING AND ENVIRONMENT	APR 15	2021	193		10.1016/j.buildenv.2021.107647
Weuve et al., 2021	Exposure to air pollution in relation to risk of dementia and related outcomes: An updated systematic review of the epidemiological literature	ENVIRONMENTAL HEALTH PERSPECTIVES	SEP	2021	129		10.1289/EHP8716
N = 6 OPINIONS, POLICY PAPERS AND INVITED PERSPECTIVES							
Penn et al., 2022	Adopting a whole systems approach to transport decarbonisation, air quality and health: An online participatory systems mapping case study in the UK	ATMOSPHERE	MAR	2022	13		10.3390/atmos13030492
Chen and Kan, 2022	Preventing cognitive impairment by reducing air pollution	LANCET HEALTHY LONGEVITY	FEB	2022	3		10.1016/S2666-7568(22)00006-X
Yao et al., 2022	The effect of China's Clean Air Act on cognitive function in older adults: a population-based, quasi-experimental study	LANCET HEALTHY LONGEVITY	FEB	2022	3		10.1016/S2666-7568(22)00004-6
Riley et al., 2021	How do we effectively communicate air pollution to change public attitudes and behaviours? A review	SUSTAINABILITY SCIENCE	NOV	2021	16		10.1007/s11625-021-01038-2
Ritz and Yu, 2021	Invited perspective: Air pollution and dementia: challenges and opportunities	ENVIRONMENTAL HEALTH PERSPECTIVES	AUG	2021	129		10.1289/EHP9605
Calderón-Garcidueñas et al., 2013	Air pollution and your brain: what do you need to know right now	PRIMARY HEALTH CARE RESEARCH AND DEVELOPMENT	JUL	2015	16		10.1017/S146342361400036X

### 3. Results

As shown in Table 1, based on the five steps involved in developing our policy agenda (see Methods), we arrived at three policy domains: Research and Funding, Education and Awareness and Policy Evaluation. Within these three domains there are 14 priority areas.

#### 3.1. Domain A: Research and Funding

Priority Area 1. Thinking about the complexities of place. This priority area came from discussions amongst consortium academics on the role that places play in mitigating the impact of air pollution on brain health. We agree with the place and health literature (Castellani et al., 2015; Cummins et al., 2007) that people live in complex socio-ecological systems, which emerge out of the nexus of wider social determinants, including city environments, housing density, green spaces, transportation systems, socio-economic deprivation, public health inequalities, location of industrial air pollution sources, school zones. These social determinants, in turn, intersect with environmental exposure profiles – such as historical air quality for a city or region – or what researchers call the exposome: which is where the complex chemistry of indoor and outdoor air pollution meets the complexities of human biology and public health (e.g., Vermeulen et al., 2020; Wild, 2012). Given this complex intersection, the air quality and brain health of any

given person or population is best determined, theoretically and methodologically speaking, by modelling these place-based factors in configuration and as a complex system.

The other rather consistent theme amongst our discussions was that the causal pathways by which places impact air quality and brain health across the life course create an intricate web of causal connections that are, at once, dynamic, nonlinear, interdependent, overlapping, and circular, and which often lead to outcomes that (from a public health perspective) are unknown, unanticipated, or unintended (as in the case of negative consequences). The challenge, then, is how best to model this complexity, because lacking a whole-system view makes targeting the right policy interventions and practice strategies difficult.

We therefore advocate, as a first priority, a theoretical and methodological shift to a complex systems perspective, which is consistent with wider trends in public health (Castellani et al., 2015; McGill et al., 2021; Rutter et al., 2017; Skivington et al., 2021). As actionable items, we recommend drawing from the complexities of place literature in public health; augmenting conventional statistics with the latest development in computational modelling (e.g., agent-based modelling, complex networks, case-based modelling) and Bayesian statistics for multi-level modelling (e.g., Blangiardo et al., 2019); taking an interdisciplinary methods approach to modelling; and exploring feedback loops and complex configurations of factors to make sense of causality.

2. Focusing on vulnerable populations. Vulnerability as a priority

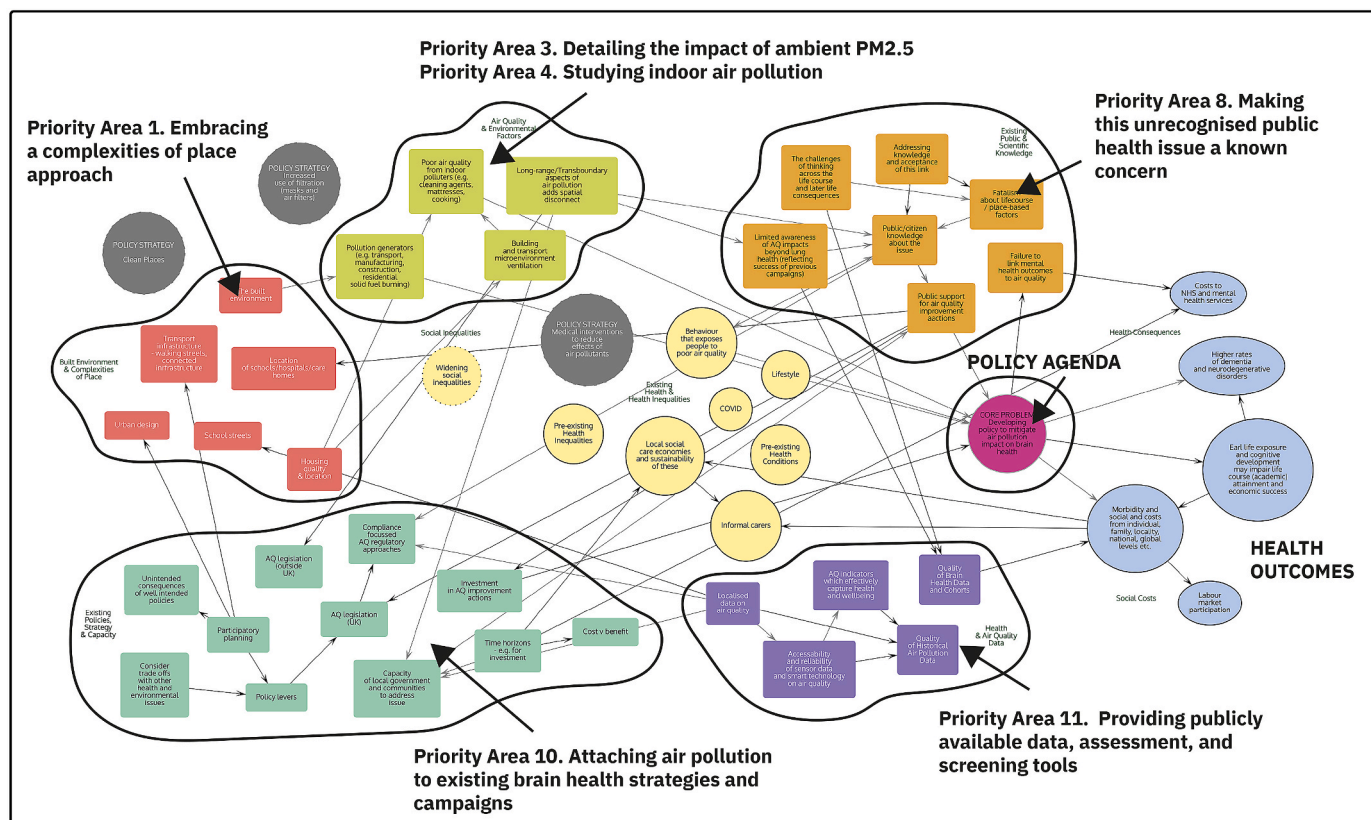


Fig. 1. Participatory Systems Map developed during 2-h workshop with consortium stakeholders and academics

This working map provides an example of the visual outcome from a 2-h participatory systems mapping event. Each cluster constitutes a Priority Area identified during the workshop, which were grouped based on the workshop members' analysis of this public health issue.

emerged out of two distinct but interconnected discussions amongst consortium academics. The first, initiated by our sociologists and public health experts, focused on the role that socio-economic and health inequalities play in the impact air pollution has on brain health. Our concern here is how places create brain health vulnerabilities, such that certain populations are more at risk from air pollution than others. Our concern is consistent with the wider literature on air quality and public health, which suggests that health inequalities worsen the impact that air pollution has on public health (Ailshire and Brown, 2021; Ferguson et al., 2021; Hajat et al., 2015; Tessum et al., 2021; Zhao et al., 2019). Research on air pollution and brain health is starting to explore this form of vulnerability, as in the case of income inequalities (e.g., Chandra et al., 2022), but based on our umbrella review (in particular, the  $N = 6$  policy papers) evidence is presently lacking (e.g., Delgado-Saborit et al., 2021). This form of vulnerability needs to be a priority.

Our second discussion, which links to the first, involved a fundamental rethink of how air pollution and health inequalities impact vulnerable populations. Most place-based approaches focus on cleaning up highly polluted areas where inequalities and high levels of deprivation are known to exist. While this has significant value, based on two recent studies by Deryugina et al. (2021a, 2021b), a more useful strategy may be to focus on serving vulnerable populations living in any area, be it polluted or otherwise. For vulnerable populations, such as those struggling with asthma or cardiovascular disease or pre-existing health inequalities, even low levels of air pollution in an otherwise 'clean air' environment can trigger or exacerbate ill health (e.g., Dominici et al., 2019; Strak et al., 2021); or, in comparison to more affluent populations living in the same air polluted environment, vulnerable populations (particularly the poor) still experience worse health outcomes (Hajat et al., 2015). The same may very well be true for brain health and dementia. Certain forms of existing health inequalities or cognitive

vulnerabilities may make even low dose thresholds concerning, including speeding the progression of dementia and other neurodegenerative disorders.

Given these two discussions and the current lack of literature in this area for brain health, we advocate, as a second priority, concentrating on the issue of vulnerability. As actionable items, we recommend widening the study of vulnerability to determine to what extent socio-economic and health inequalities and places create brain health susceptibilities for certain populations, as well as exploring how vulnerable populations may respond differently to exposure to different levels of air pollution, even levels considered otherwise healthy.

3. Modelling the impact of PM<sub>2.5</sub>. In terms of air pollution modelling, a key discussion, initiated by our environmental science experts, is the need for high-resolution exposure models of all regulated and traffic-related air pollutants (Chen and Kan, 2022, p. 81). The robust and widespread findings obtained from the academic literature (including our umbrella review) document a level of agreement within the international scientific community that exposure to PM<sub>2.5</sub>, is a measure of health risk stemming from a complex and variable mixture of ambient airborne particles of different chemical composition, numbers, and size classes and that PM<sub>2.5</sub> is linked to a variety of brain health outcomes in biologically plausible ways, including dementia. However, as the umbrella review also makes clear, the much-needed next step, particularly for countries or regions of the world where such models are lacking, is to develop more comprehensive exposure models for linking aspects of PM<sub>2.5</sub> source types and composition to specific brain health outcomes.

This next step is particularly true for historical and long-term simulations. The consortium recognises that building such long-term simulations is a sizeable challenge. But without such models, we are considerably limited in exploring the links between historical air quality and later-life brain health, including dementia, as air pollution



monitoring data going back to the 1970s or later is scarce or nonexistent. If policy is to be developed around dose response relationships and knowledge of air pollution's impact on brain health across the life course and for later-life dementia, scientists need to pioneer historical (multi-decadal) models of PM<sub>2.5</sub> mass concentrations, and its components, at adequately high spatial and temporal resolution (e.g., hourly at 1 km × 1 km), to derive national, regional, and local quantitative population exposure estimates across a range of scales.

We therefore advocate, as a third priority, the advance of air pollution modelling for studying brain health, as well as public health in general. As actionable items, we recommend support, both from funders and institutions, to help scientists develop current and historical models, particularly for those parts of the world where such models are significantly underdeveloped.

4. Studying indoor air pollution. A major insight from our umbrella review is the importance of indoor air pollution for brain health. Most people spend the vast majority of their time indoors (>90%), which can encompass a very wide range of settings including their homes, hospitals, workplace, schools, public transport, and cars (Calderón-Garcidueñas et al., 2015; Krishnamoorthy et al., 2018; Qiu et al., 2019; Sunyer et al., 2015). Indoor air pollutants can originate from both indoor and outdoor sources. Indoor air pollutants include gaseous pollutants (CO, CO<sub>2</sub>, NO<sub>3</sub>, radon), particulates, volatile agents (VOC, formaldehyde), and biological agents (allergens, endotoxin, mould, bacteria). Indoor sources of these pollutants include combustion (heaters, wood burners, smoking, cooking), furniture and building materials, hobbies, cleaning activities, as well as from mould, bacteria, pets, and plants. Infiltration of outdoor traffic pollution can be especially high in homes in cities and near busy roads. Factors such as building design and material and natural and mechanical ventilation will affect the level of indoor air pollutants from indoor and outdoor sources. Also, exposure to air pollution inside cars, particularly for children in the back seat, can be worse than outside the vehicle, although the issues of route variation and mode of commute require a complex array of factors to be considered (Karanasiou et al., 2014; Gilliland et al., 2019; Ma et al., 2020).

Given the impact of indoor air quality on public health in general, we agree that, as part of a policy agenda, evidencing the impact of indoor air pollution on brain health needs to be a priority area, including, as actionable items, drawing on the wider literature on indoor air pollution, and focusing on this issue for schools, housing near busy roads or in cities, and those vulnerable to indoor air quality issues, such as care home residents with dementia.

5. Making breakthroughs in pathways to disease for brain health. For our consortium's experts in dementia, neuroscience, psychiatry, clinical psychology, child development, and ageing and brain health, significant discussions took place around the necessary next step in linking air pollution to brain health. For our consortium and for the literature (based on our umbrella review) this step involves making breakthroughs in pathways to disease for brain health.

While we have used the phrase 'brain health and dementia' in this paper, the latter is just one example of the former. Brain ill health is an umbrella term for a long list of different forms of brain disease and cognitive impairment (Delgado-Saborit et al., 2021). In terms of air pollution, areas of focus include global cognition and specific cognitive domains (e.g., executive function, learning, attention, memory), language, cognitive decline, mild and incident cognitive impairment, dementia and Alzheimer's disease, other neurodegenerative disorders, stroke-related brain damage, reduced white matter, and neuroinflammation (See Table 2).

Since the ground-breaking work of Calderón-Garcidueñas and colleagues in the early aughties, research interest on the impact of air pollution on brain health has developed significantly (See 2008; 2013, 2016). Still, based on our discussions and umbrella review, the necessary next step is to understand more fully the numerous direct and indirect biological pathways and underlying physiological mechanisms by which air pollution impacts brain health, and how these changes are modified

by relevant health, lifestyle, behavioural and social factors.

Making this next step requires addressing several challenges as well as exploring potential opportunities, all of which we identify as actionable items for this priority area. To begin, due to the diversity of the study designs, exposure assessment techniques, cognitive endpoints, and the wide range of confounding factors, major gaps remain in our current understanding of the cognitive effects associated with specific pollutants, which links this issue with Priority Area 3 (See Table 2). Our umbrella review evidences that there is also a lack of understanding about the ways in which air pollution impacts brain health beyond ultrafine particles crossing the blood-brain barrier, due in part to the need for more high-quality laboratory and epidemiological research (e.g., Calderón-Garcidueñas et al., 2008; Wang et al., 2021; Young et al., 2019). Still, there are promising avenues for research. For example, PM<sub>2.5</sub> seems to impact brain health via key biomarkers, inflammatory processes (neuro and vascular) and cardiopulmonary disease; and there is growing research showing that chronic exposure can deteriorate the protective barriers of the brain (e.g., Campbell et al., 2005; Hajipour et al., 2020; Shi et al., 2020). Also, increases in concentrations of beta amyloid and tau proteins associated with plaque build-up and neurofibrillary tangles in dementia seem to be sensitive to PM<sub>2.5</sub> (e.g., Alemany et al., 2021; Calderón-Garcidueñas et al., 2016; Costa et al., 2020). Nevertheless, the time course and contingencies between the mechanisms underlying direct brain health effects and indirect effects through cardiopulmonary impacts need to be elucidated more clearly, alongside differentiating the toxicological effects of specific PM<sub>2.5</sub> components and size fractions (de Bont et al., 2022; Konduracka and Rostoff, 2022). Finally, increased awareness of what aspects of brain and cognitive health are at greater risk is key, as well as knowing at what exposure dose levels and which stages in the life course are critical (Shehab and Pope, 2019).

6. Embracing a life course perspective. Through our discussions, the consortium agreed that, as a priority area, current and future research needs to be grounded in a life course perspective. This priority includes, as actionable items, linking air quality models with existing cohort datasets and developing new cohort studies. Our rationale is as follows. First, current research suggests that later life cognitive decline, dementia and other neurodegenerative disorders result from the cumulative long-term impact of exposure to air pollution (e.g., Russ et al., 2019, 2021). Being able to correlate historical models of air pollution with the life course of individuals, grounded in an environmental epidemiological approach, is therefore critical – which is why cohort studies comprising rigorous measures of cognitive and brain health, as well as reliable proxies, are urgently needed. Second, life course models provide important context for policy and planning, as they chart and analyse the health of people within and across the historical, geographical, social, and environmental contexts in which they live, including wider determinants (Russ et al., 2021). Third, given that breathing high levels of air pollution at critical points in the life-course is detrimental to brain health and cognitive development, particularly in early life and childhood, primary prevention approaches need such vital information to know when intervening is most crucial and cost effective (Chen and Kan, 2022).

7. Rethinking Funding. Consortium members all strongly agreed that, if the above priority areas are to be developed and translated into effective policy and practice guidelines and evaluation, this work needs to be supported monetarily. One of the most striking results of our study was the extent to which funding agencies were not only unaware of the impact that air pollution has on brain health, but also how resistant they were to acknowledge the emerging research in this area, creating a policy gridlock where more funded research outputs were required to inform the major interdisciplinary grant funding applications which are critical to achieve major priority areas in this area. If the priority areas outlined in this domain are going to take place, air pollution and public health funding needs to finance high-risk/high-reward research. To do so, as actionable items, funding agencies and their administrators need

to rethink the policy review process and review panels. Funding agencies also need to support research into evidence-based interventions for preventable and modifiable risk factors, both at the public health and healthcare systems level, to reduce the evidence-to-practice gap (Chong et al., 2021, p. 302). Otherwise developing the evidence necessary to create cost-effective, scalable, high-impact public policy, particularly in terms of the long-term historical impacts that air pollution has on cognitive decline, dementia and later life neurodegenerative diseases will remain intractable.

### 3.2. Education and Awareness

8. Making this unrecognised public health issue a known concern. A key priority area that emerged from our systems mapping workshop (See Methods, Step 3) was the extent to which both stakeholders and consortium academics identified 'awareness raising' as a key issue – see Fig. 1. As suggested by recent headline news (e.g., Carrington 2020), there is a growing mindfulness that air quality may impact brain health. However, the details of this link, including the role of social determinants, are less clear. From the stakeholder side, the issue was that, if the links between air quality and brain health are significant, including early-life cognitive development and later-life dementia, and if the places where people live and work matter, then these linkages need to be made known, as actionable items, to public and third-sector organisations, including dementia and Alzheimer's societies, healthcare organisations, school boards, healthcare practitioners, and government programs and international organisations focused on mitigating air pollution or improving brain health outcomes. The workshop's call for awareness was also put forward by several of our other stakeholder organisations, including a citizen action group. It was also agreed that national and international public awareness campaigns are needed.

On the academic side, the issue raised at the workshop was the extent to which not only funding organisations were oblivious to this issue (see Priority Area 7), but also the extent to which air pollution and public health experts, including colleagues around the world, were unaware. Consortium academics not attending the workshop endorsed this point and, as an actionable item, we recommend the need for researchers in the field to get the message out through various academic outlets. One example is the July 2022 report *Air pollution: Cognitive Decline and Dementia*, released by the UK Committee on the Effects of Air Pollution (COMEAP).<sup>5</sup>

9. Developing educational products. Most of the 11 stakeholder organisations asked that educational outputs be a policy priority area. The proposed outputs ranged from lesson plans on healthy air and happy brains for primary and secondary schools to newsletters and blog posts for those living with or caring for someone with dementia. This expressed priority was consistent with a recent study by Riley et al. (2021) on how to communicate air pollution to change public attitudes and behaviours. As actionable items, they emphasised that education needs to focus on local framings, collective responsibility, and action. It also needs to provide people with positive messages, as well as connect with their emotions, to help overcome disengagement or a sense of powerlessness. This last point is particularly relevant, as dementia presently has no cure. Another actionable item that stakeholders raised, and which Riley et al. (2021) endorsed, is the need to co-produce educational products, because when communities work together it usually leads to collective corrective action (Riley et al., 2021, p. 2027).

10. Attaching air pollution and brain health to existing strategies and campaigns. As an extension of Priority Areas 9 and 10, the public and third sector stakeholder organisations we engaged with all saw the direct benefits of either (a) adding air pollution to their existing campaigns for brain health and dementia or (b) adding brain health to their

current strategies around air quality improvement, climate change, or sustainable development goals. As actionable items, they wanted help making use of current evidence to bolster their campaigns and to demonstrate co-benefits, be it around dementia awareness and brain health or a clean air programme or initiative. Other actionable items included adding current evidence to their newsletters and social media and to their outreach to healthcare practitioners and those living with or caring for someone with a brain health disorder. As a consortium, we endorse this idea, seeing it as a key priority. First, it is an immediate win, as it takes less time and investment to add current evidence to existing air quality or brain health strategies and campaigns. Second, from a policy perspective, these existing campaigns are tried-and-tested and have often established a level of credibility, trustworthiness and authority with the public, government, civil service, third-sector, and private-sector organisations. Third, it gives the field of air quality and brain health time to further develop policy recommendations and strategies, as well as work with stakeholders on policy development and evaluation.

11. Providing publicly available monitoring, screening, and assessment tools. Another key priority area raised in discussions with stakeholders and consortium academics – as well as in a few of the articles in our umbrella review (e.g., Penn et al., 2022; Calderón-Garcidueñas et al., 2015) – is determining what publicly available data and tools are needed to decide where, when, and how interventions can make the most impact, be these interventions at the individual and healthcare level or, in terms of policy, at the community, national or global level. For those involved in these discussions, this priority area is more than raising awareness or education. It is about monitoring, screening, and assessment, to achieve purposeful targeting for positive impact on brain health and health economy in place.

Building on Priority Areas 3 and 4 – and as a first actionable item – an identified need of stakeholders was for ambient and indoor air pollution datasets and models to be translated into useable, publicly accessible resources for citizens, healthcare providers, governments, and third-sector and private sector organisations. Such tools would include a fusion of monitoring data and modelling to provide near-real time air quality exposure information – be they online dashboards or, to address the digital divide, through other public outputs, including television and print media. For governments, public institutions, and healthcare organisations, developing such tools would also help with the identification, assessment and monitoring of cohorts, communities, and places most at risk for brain health (Calderón-Garcidueñas et al., 2015). These data, in turn, could be used to create historical and regularly updated air quality and brain health profiles for countries, regions, cities, communities, schools and even particular streets, available for public consumption.

A second actionable item would be developing screening and assessment tools for individual exposure, particularly during early life and at critical points in the life course where air pollution has the most impact on brain health. This would also include personal and mobile monitors for indoor and outdoor exposure – although we acknowledge issues about the validity and reliability of this technology (e.g., Castell et al., 2017; Crilley et al., 2018; Lewis and Edwards, 2016).

The third actionable item is developing tools for assessing health behaviours, pre-existing conditions, or comorbid health conditions that prevent, slowdown, or exacerbate the impact of air pollution on brain health – although the ethical and legal implications of such public health screening strategies and data collection would need to be addressed, as in the case of genetic testing in early life. It would also include use of these tools to potentially slow the progression of cognitive disorders, cognitive decline and even dementia, post-diagnosis (e.g., Perera et al., 2021; Wang et al., 2022; Younan et al., 2022).

### 3.3. Policy evaluation

12. Conducting complex systems evaluation. Discussions amongst

<sup>5</sup> <https://www.gov.uk/government/publications/air-pollution-cognitive-decline-and-dementia>.

consortium academics about the challenges of evaluation were a direct extension of Priority Area 1. If the air quality and brain health of different populations is directly linked to the complex socio-ecological systems in which they live; and if these systems emerge out of the nexus of wider social determinants and their intersection with exposure profiles and public health across the life course; and if the causal pathways by which places impact air quality and brain health create an intricate web of causal connections, including nonlinear feedback loops and unintended consequences; then any policy evaluation needs to make such ‘complexities of place’ a priority. Concerns about complexity in evaluation were supported by our stakeholders. They wanted to know how to commission, design and manage an evaluation given the issues of complexity, as they recognised the limitations of traditional approaches.

As Moore et al. (2019) explain, however, adopting a complex systems perspective does not necessarily require whole-systems evaluations, which may be unfeasible; neither does it mean that evaluations have to be complex. Instead, it requires the realisation that even the simplest policy or practice strategies take place in complex systems, making outcomes often difficult to predict, guide, manage or control. This realisation is particularly important when making small or large-scale changes to such modifiable social determinants as poverty, transportation, health inequalities and urban planning.

As a priority area, we therefore advocate that policy evaluation for air quality and brain health implement a complex systems approach, consistent with wider trends in public policy evaluation (e.g., Barbrook-Johnson et al., 2021; Bicket et al., 2020; McGill et al., 2021; Moore et al., 2019; Penn et al., 2022; Rigby et al., 2022). As actionable items, we recommend drawing from the highly developed literature on complexity in evaluation to adopt best practices; augmenting conventional evaluation methods with the latest developments in participatory systems mapping, agent-based modelling, and case-based modelling (e.g., Barbrook-Johnson and Carrick, 2021; Rutter et al., 2017; Schimpf et al., 2021); mapping barriers and incentives to change and counterfactuals (e.g., Cox and Barbrook-Johnson, 2021; Hyland and Donnelly, 2015); and embracing a co-production approach to evaluation.

13. Engaging in co-production and participatory research. Given the immediate need for policy and practice guidelines, stakeholders made clear their need to be more involved in defining the research agenda on this topic and in producing, translating, and sharing evidence. In this way the identified needs of these organisations and of people living with or caring for someone with brain health issues can be kept at the forefront of research and policy. For example, through our engagement with stakeholders, we found that, for those living with dementia, a key concern is how air pollution may accelerate the progression of their disease; in contrast, parents and school systems were concerned with cognitive development, school performance and early-life screening; in turn, local planning boards were focused on the benefits of green urban planning and public transportation; and civil servants were concerned with sustainable development goals and the health burden and economic costs of dementia and other brain conditions over the next two decades.

In each instance, it was critical to calibrate the process of co-production within the operating context of each stakeholder organisation, as each situation required different types of engagement (Fransman, 2018; Oliver et al., 2019; Williams et al., 2020). Being responsive and sensitive to these varied interests is challenging and the best way to provide the evidence necessary is to work with stakeholders to understand and incorporate these nuances from the beginning of the research process. This has been one of the key lessons we learned in this study. It also leads to an important point. Co-production is presently booming in social science and health research and evaluation (Fransman, 2018; Oliver et al., 2019; Williams et al., 2020). This is both promising and problematic. In terms of promise, many co-produced approaches acknowledge and address the role that power and politics play in policy, as well as the challenges of competing and conflicting agendas on what counts as evidence. Many approaches also actively recognise the value

of experience and practical knowledge, the importance of inclusivity and diversity, and the necessity to engage democratically with the identified needs of stakeholders across the entire research process. In terms of problems, the boom has led to a conflation of definitions, shallow engagement with stakeholders, and bad practice (Oliver et al., 2019; Williams et al., 2020).

Given the importance stakeholders placed on being involved in any policy agenda for air quality and brain health, as well as the potentials and pitfalls of this approach, we advocate that co-production be a priority area. As actionable items, we recommend that researchers make use of the wider co-production literature, including work in the area of climate change (e.g., Bremer and Meisch, 2017); clarify their approach to co-production; recognise that not all approaches are the same or of equal value in different situations, and that, in some instances, co-production may not be required; and work to ensure that the approach they use meets best practices. We also recommend that regional, national, and international differences in resources, politics, and culture be taken into consideration, as in the case of addressing air quality and brain health in the global south.

14. Evaluating current air quality policies for brain health benefits. Given the gravity and immediacy of the public health issues at stake, from air pollution to dementia and health inequalities, a point of discussion amongst consortium academics was how to develop, in the short-term, a catalogue of useful policy guidelines. Attention turned to existing policies and practices for improving air quality and public health in general, under the assumption that some of these interventions (similar to Priority Area 10) may have immediate co-benefits for brain health.

We therefore advocate, as a priority area, engagement with current policies for air pollution and public health in general, to evaluate them for their brain health benefits (e.g., Carnell et al., 2019; Grennfelt et al., 2020; Williams, 2004). In terms of actionable items, we recommend evaluating this existing repository straightaway, which would allow policy makers to fast-track guidelines and resources for planning and for prevention across the life course, and at multiple levels. We also recommend exploring wider policy needs beyond just emissions reduction, such as improving public health inequalities, creating dementia-friendly communities, upgrading school zones, improving public transportation, addressing housing congestion, and enhancing climate change reductions, as well as linking air pollution and brain health to legally binding net zero targets, which would provide a unique policy opportunity to deliver ambitious and transformative place-based changes.

#### 4. Conclusion

While research, policy and practice strategies have been proposed to address air pollution's impact on public health more generally, their benefits for brain health, including dementia, remain undeveloped (Calderón-Garcidueñas et al., 2015; Chen and Kan, 2022). This underdevelopment is an urgent public health concern, given the rapid growing evidence of the links between places, air pollution, brain health, and dementia. A policy and practice agenda is greatly needed.

Over the course of two years, we worked as a consortium of 20+ academics to develop the first policy agenda for mitigating air pollution's impact on brain health and dementia, including engaging 11 stakeholder organisations, running a participatory systems mapping workshop, and conducting an umbrella review of  $N = 38$  articles and  $N = 6$  policy papers for the last ten years of research (See Table 2). Our goal was to identify the policy domains and priority areas in research, policy and practice that need to take place to produce a policy agenda. Based on the five steps involved in developing our policy agenda (see Methods), we arrived at the following:

Our policy vision is for everyone in the world to be able to breathe clean air that promotes a healthy brain and cognitive life regardless of where they live. In terms of prevention, we aim at mitigating the impact



air pollution has on brain health across the life course, including early childhood development and dementia in later life, and particularly for vulnerable populations living in major urban areas, so that air pollution is no longer a brain health inequality. Our policy agenda is organised around three policy domains: Research and Funding, Education and Awareness and Policy Evaluation. As Shown in Table 1, across these three domains we identified 14 priority areas, each of which includes a list of actionable items to maximize their potential for impact.

In terms of a theory of change, there is no one way to move forward with this policy agenda. Our fourteen priority areas differ in terms of their urgency, feasibility, and impact, as well as the parties primarily responsible for their enactment, depending upon which stakeholders, researchers, policy makers or funding organisations within and across different countries are considering them. From our perspective, the issues requiring immediate attention are generally difficult to implement and require, for the most part, a considerable effort from all those involved – with the exception of two: raising awareness and attaching air pollution and brain health to existing campaigns and strategies amongst public and third-sector organisations. Both are proximately attainable and can have a significant and immediate impact. We also want to emphasise the need for funding organisations to support these advances, in particular the high risk/high payoff science that is needed to address the complex details of this public health issue.

Issues of local capacity are also of considerable importance, as the populations most negatively impacted by air pollution are often those struggling with the greatest levels of inequality, vulnerability, and political economy, particularly in poor urban environments. We therefore emphasise, again, the importance of local-level co-production and engagement. We also emphasise, again, the importance of outlining the co-benefits and incentives to change linked to improving air quality and brain health, particularly in terms of dementia, early life cognitive development, climate change, sustainable development goals and, where applicable, legally binding net zero targets. Given how fast this field is unfolding (particularly in the last three years) and the gravity of the issues it addresses, any policy agenda needs to be matched by scientific evidence and appropriate guidelines, including bespoke strategies to optimise impact and mitigate unintended consequences. Advances in policy, therefore, be they regional, national, or international, need to be matched by advances in research, evaluation, education, and funding. The agenda provided here is the first step toward such a plan.

#### 4.1. Study limitations

In terms of limitations, because we identified and refined our policy agenda, first, through engagement with United Kingdom consortium academics and stakeholders and then, second, through our umbrella review, it is possible that a different policy agenda, including its policy domains and priority areas, would have been generated if this study had been conducted by a different set of researchers. A different outcome is equally possible had the study been done in another country or region of the world, or with different stakeholders, or a different approach to co-production. Stakeholders were also primarily from the public and third sector, with only a few citizen groups and no private sector stakeholders, which again could affect the resulting list of policy priorities. Our choice of an umbrella review may also have had an impact, as a more in-depth systematic review might have provided more nuanced results. For example, for our review, given differences in aetiological complexity, we excluded review articles on depression, anxiety, and autism spectral disorder, which may have yielded additional priority areas or themes; also, while we drew on the most recent research for all fourteen priority areas, a more systematic review might have revealed further insights. Finally, our list of actionable items is not definitive. There are certainly additional methods for implementation, particularly around barriers and incentives to change. Given these limitations, there may be restrictions in the generalisability, value, or utility of our policy agenda.

#### Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

#### Data availability

No data was used for the research described in the article.

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