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Abstract

Poor air quality is associated with poor health. Little attention is given to the complex array of environmental exposures and air pollutants that impact mental health during the life course. We attend to this oversight by gathering expert opinions and undertaking a rapid scoping review. We summarise the key scientific findings, and identify knowledge gaps and methodological challenges. We propose future research priorities and the optimal methods to address them. There is emerging evidence of associations between poor air quality, both indoors and outdoors, and poor mental health and specific mental disorders. Evidence of critical periods in exposures among children and adolescents argue for more longitudinal data as the basis of early prevention policies. Particulate matter including bioaerosols are implicated but form part of a complex exposome influenced by geography, deprivation, socio-economic conditions, and biological and individual vulnerabilities. The findings call for dedicated action to address critical knowledge gaps and design interventions for mitigation and prevention, reflecting ever-changing sources of air pollution. In the interim, the existing evidence base can help motivate the efforts of researchers, practitioners, policy-makers, industry, community groups, and campaigners to raise awareness and take informed action. Such work necessarily requires collaboration between a wide range of experts and specialists. There are knowledge gaps and a need for developing a more substantial evidence base, for example, around bioaerosols exposure and mental health impacts.

1. Aim and Scope

The purpose of this rapid scoping paper is to gather expert opinions and summarise the existing body of knowledge on air quality and mental health, whilst highlighting methodological challenges, knowledge gaps and future research directions. The perspective we take is broad, interdisciplinary, and adopts a 'life-course' approach; considering psychiatric, cognitive, and neurodevelopmental pathways; and a wide spectrum of both indoor and outdoor air pollutants, including bioaerosols, heavy metal ions, non-organic PM, and gaseous pollutants.

2. The Health Burden of Air Pollution

The World Health Organization (WHO) has ranked air pollution as one of the major environmental risks, and the single biggest environmental threat to human health.[1] Worldwide, it is estimated that 4.2 million and 3.8 million premature deaths were attributable to outdoor and indoor air pollution, respectively.[1] The WHO guidelines implicate particulate matter (PM) with aerodynamic diameters of ≤2.5μm ($PM_{2.5}$) and ≤10μm (PM_{10}), ozone, nitrogen dioxide, sulphur dioxide and carbon monoxide. Among different air pollutants, PM is a major public health concern.[2] PM has diverse sources (natural/anthropogenic, indoor/outdoor), formation processes, composition (organic/inorganic) and sizes:

- Ultrafine: $PM_{0.1}$ – particles that are less than 0.1 μm in diameter
- Fine: $PM_{2.5}$, particles that are less than 2.5 μm in diameter
- Coarse: PM_{10}, particles that are greater than 2.5 μm and less than 10 μm in diameter

The particle size and duration of exposure and chemical composition are key determinants of adverse health effects; smaller particles can be inhaled more deeply into the lung. The strongest evidence for adverse effects on health is for $PM_{2.5}$, with an extensive body of evidence linking outdoor $PM_{2.5}$ exposure to mortality, cardiovascular diseases and pulmonary diseases, and cancer.[2] [3] The body of evidence is so extensive that PM is now classed as a group 1 carcinogen by the International Agency for Research on Cancer (IARC).[4] Given the high levels of incident serious mental illness in urban areas, where air pollution is greatest, and the reverse causal relationships between cancer and serious mental illness (that we later discuss), there may be common aetiological and mutually reinforcing pathways of risk involving air pollution and inflammation.

Bioaerosols are the biological fraction of PM (called BioPM), and are a complex mixture of bacteria, viruses, and fungi, or parts of living organisms, like pollen, spores, endotoxims from bacterial cells or mycotoxins from fung.[5] [6] Bioaerosol exposure is associated with chronic and acute respiratory illness (via both atopic and non-atopic allergic mechanisms, and non-allergic pathways like infection), and other diseases including gastrointestinal disturbance, dermatological conditions, general malaise and fatigue.[5] [6] However, the role of BioPM in health burden, their mechanisms of toxicity, and impact on human health and wellbeing across the indoor-outdoor continuum of exposure is not yet clear. Conclusive evidence linking the exact mode of action between pollution, including bioaerosol exposure and its related toxicity, is lacking. However, airway inflammation and oxidative stress are recognised as major mechanisms of the diseases due to PM and associated microbe expsosure.[7] [8] In particular, bacterial endotoxin (lipopolysaccharides; LPS) and fungi are linked with inflammatory responses and hypersensitivity in airway models.[8] [9] Inflammation is implicated in the aetiology and progression of an illness, and important for mental and physical conditions with shared aetiologies, showing reverse causality, and co-morbidities.[10] [11] [12] Although the exact process by which inflammation (peripheral and brain tissue) leads to neurotoxic effects is dynamic, complex and subject to numerous self-reglatory processes,[13] if shared mechanisms of disease atiology are established, there is hope for new forms of prevention and treatment by targetting inflammation.[14] For example, these aetiological processes may be amenable to anti-inflammatory medication. Furthemore, the design of environments and buildings to reduce inflammatory responses may be an important public health intervention. In areas of high deprivation and urbanicity, poverty and lack of affordable housing, unemployment and lack of green space, and unsafe neighbourhoods are common. These chronic adversities as well as other traumatic incidents are associated with inflammation and poor physical and mental health.[15] [16] As a ubiquitous exposure, poor air quality in indoor and outdoor environments could be a prime modifiable target to reduce the population-level burden of poor mental health, and to improve the quality of life of those already suffering poor mental health.

3. Mental Health And Air Pollution

Half of the adults with mental illnesses show signs and symptoms by the age of 11, and 75% do so by the age of 24;[17 18] so prevention of mental health problems in young people is a major public health priority. In addition to the human suffering and functional impairment caused by chronic mental health problems, people with mental illnesses are also at risk of premature mortality due to cancer, heart disease, lung disease, and obesity-related conditions.[19-21] Identifying modifiable risk factors for mental health problems is, therefore, a crucial research challenge of the 21st century.

Alongside cardiovascular and respiratory health effects, there is emerging evidence that exposure to air pollutants (both indoors and outdoors) may lead to neurocognitive disorders and affect mental health (directly and indirectly) through a range of potentially causal pathways.[22 23 24 25 26 27] Observational evidence has implicated outdoor air pollutants as risk factors for a variety of mental health problems, including depression, anxiety, personality disorder, and schizophrenia.[28-32] In contrast, there is little research on the mental health impacts of indoor air quality and exposures to air pollutants.

Much of the existing literature on outdoor air pollution and mental health is based on cross-sectional observations, aggregated air quality data, and studies of adults. In addition, studies often do not rule out alternative interpretations such as individuals with a greater liability to mental health problems self-selecting into neighbourhoods with poorer air quality or not being able to leave those areas. Furthermore, other disadvantageous aspects of the environment are associated with poor air quality and poor mental health, such as deprivation, crime, and noise, which might each also affect mental health. However, to understand the role of air pollution in the development of mental health problems, longitudinal studies are needed to ensure exposure to air pollution occurs before the emergence of mental health problems. Ideally these studies should collect information on individual- and neighbourhood-level deprivation. Causal inferences are strengthened by such designs, although confounding influences do still need consideration.

Since a great proportion of time is spent indoors, it is reasonable to assume that some of the effects attributed to outdoor air pollutants result from indoor exposures.[33] Indoor environments can have diverse pollutants (PM, NO_2, CO) of outdoor and indoor origin and highly varying source strength per area for each pollutant across different indoor environments. Yet indoor environments may be a more significant source of specific chemical exposures (e.g. volatile and semi-volatlie organic compounds; called VOCs and SVOCs). Much built environment research is model-based, with less real world sampling in diverse geographical contexts. The health evidence often lacks housing and geolocation information making it difficult to review historical data for causal trends retrospectively. Both would benefit from greater interaction with chemists so that we can better understand pollutants, the potential webs of causation. The impact of cooking emissions on human and environmental health can be reduced by better-designed research that might help to reconsider open plan kitchen and living spaces that are popular.[34] Different factors related to design, construction and occupants' activities can implicate occupants exposure to different pollutants indoors.[35] Additionally, the growing focus on energy-efficient built environments may lead to increased exposure to an array of air pollutants of indoor origin, due to the decreased ventilation.[36] Sound insulation may also influence ventilation; hence there is a need for building designs that tackle multiple environmental factors. These design features may explain low grade fatigue and poor mental health found in certain buildings and work environments which lack ventilation, daylight, and good air quality; thus 'sick building syndrome' may be partially explained by air quality. [37] [38]

The Royal College of Paediatrics and Child Health, together with the Royal College of Physicians considered indoor air quality and found that emissions from construction materials, building design (e.g., ventilation and heating systems) and activities inside buildings (e.g. cooking, fireplaces, cleaning products, moisture production) all impact on indoor air quality and affect health.[39] Some activities can lead to elevated moisture levels indoors, resulting in dampness and related pollutants such as mould and house dust mites, which in turn affect health. Whilst this report did not specifically consider mental health outcomes, the underpinning studies found links between poor indoor air quality and neurological and psychological symptoms with cognitive and behavioural effects. For example, higher CO_2 levels can be associated with poorer cognitive function and concentration. Of course, other indoor air pollutants that accumulate with CO_2 may be responsible. There is ongoing research and debate on the effects of CO_2 concentrations on cognitive performance in settings such as schools and offices.[40] [41]

Some researchers have also emphasised that fossil fuel combustion “is driving indoor CO_2 towards levels harmful to human cognition”.[42] Some studies have also examined associations between cognitive performance and indoor levels of CO_2, and VOCs independent of ventilation rates.[41] A recent systematic review raises significant questions about the quality of the evidence, and whether any associations between CO_2 and health can yet be inferred, although several studies suggested high concentrations of CO_2 did require more mental effort and led to fatigue.[43]

There is limited evidence on the impact of indoor air quality on mental health; some studies have found an association between depression and dampness and mould in the home, suggesting that the underlying mechanism leading to poor health is a lack of control over the home environment.[44] Furthermore, poverty and roach infestations are associated with elevated levels of endotoxins, also leading to inflammatory responses.[45] A recent report by an NGO in the UK called Shelter concluded that 23% of households complain of significant dampness, mould and condensation. Associations between mould exposure and various non-specific symptoms such as fatigue, ‘brain fog’ and anxiety have been reported. Yet, overall, the evidence is mixed, and underlying mechanisms are not clear. More recently, studies using animal models suggested an impact of mould inhalation on the central nervous system and immune activation with concomitant neural effects and cognitive, emotional, and behavioural symptoms.[46 47]

Poor socio-economic status is known to be associated with both poor mental health and with poor living conditions, including overcrowding, unstable housing, dampness, poor nutrition and health risk behaviours such as smoking, alcohol use, substance misuse and adverse childhood experiences including poverty, loss events and neglect.[48 49] The exposures to poor indoor air quality vary by low and high income settings; in low income settings burning unclean and solid biomas fuels dominates.[50] All of these might combine to create a pro-inflammatory exposome including poor air quality that impact on health – both in the onset of new illnesses as well as in the compounding of existing disabilities for pre-existing illnesses. Linking the associations with mechanisms is challenging (see Figures 1 and 2 for potential explanations). Yet, there are plausible pathways from pollution to poor health and poor mental health, especially if inflammatory processes are triggered as these are implicated in mental and physical health. One approach to understanding prevention and care is to look at the individual life-course, from pregnancy to youth, adulthood, and old age.

4. Air Quality and Mental Health over the Life-Course

4.1 Pregnancy and Early Years

Studies of associations between early exposure to air pollution and mental health are scarce and the findings are somewhat mixed. Pre-natal air pollution exposure has been linked with cognitive impairments at age 5, [51] but there is no greater risk of anxiety and depressive symptoms.[52] In a Spanish study of 1,889 children, exposure to NO_2 and benzene were inversely associated with mental development, but this did not remain a statistically significant finding after adjusting for confounders.[53] There are some details of relevance: stronger inverse associations were estimated for pollutants among infants whose mothers reported low intakes of fruits/vegetables during pregnancy, in non-breast-fed infants and infants with low maternal vitamin D; however, these interesting interactions were not statistically significant. During pregnancy, exposure to PM_{10}, $PM_{2.5}$, NO_2, and nitrogen oxides ($NO_{x)}$ were associated with a 29%–74% increased odds of unspecified mental disorders that complicated pregnancy.[54] Exposure pathways in utero and early childhood also differ from those in adulthood. In utero, neo-natal and infancy related pathways include ingestion (non-nutritional as well as nutrition), inhalation, transplacental, transdermal, and breast feeding.[50]

4.2 Adolescents

A long-standing finding that has not been fully explained is the higher incident rates of psychoses in inner-city and urban areas. Could air quality be a relevant aetiological factor? Among 2063 adolescents, psychotic experiences were significantly more common among adolescents with the highest (top quartile) level of annual exposure to NO_2, and $PM_{2.5}$.[55] Together, NO_2 and NO_X explained 60% of the variance. There was no evidence of confounding by family socio-economic status, family psychiatric history, maternal psychosis, childhood psychotic symptoms, adolescent smoking and substance dependence. There is also evidence of associations with depression[56]. In the Environmental-Risk Longitudinal Twin Study of a total of 2039 participants, after adjustment for family and individual factors, interquartile range increments in NO_X

exposure were associated with 1.40-point increases in general psychopathology.[57] There was no association between continuously measured $PM_{2.5}$ and general psychopathology. However, those in the highest quartile of $PM_{2.5}$ exposure scored higher than those in the bottom 3 quartiles. NO_X alone was significant in these significant findings. NO_X exposure was associated with all secondary outcomes, but associations were weakest for internalising and strongest for thought disorder symptoms. Studies to replicate this and evaluate the source of these differential impacts are needed. Despite NO_X concentrations being highest in neighbourhoods with worse physical, social, and economic conditions, adjusting estimates for neighbourhood characteristics did not change the results. Consistent with this finding, and contrary to popular views on the role of socio-economic factors, a Swedish study did not find that stressors (usually linked with socio-economic factors and mental health problems) increased susceptibility to air pollution-related asthma.[58]

4.3 Adults

A study in USA and Denmark demonstrated air pollution (measured on an air quality index of 87 potential air pollutants in the USA and 14 in Denmark; including PM_{10} and $PM_{2.5}$, diesel emissions and NO_2, and organic substances such as polycyclic aromatic hydrocarbons) was significantly associated with increased risk of psychiatric disorders.[59] The country-specific data showed pollution exposure associated with bipolar disease in both countries, and depression, schizophrenia, and personality disorder in Denmark. A number of studies show associations between air pollution and service use for mental disorders.[22 60-62] A recent systematic review and meta-analysis showed associations of $PM_{2.5}$ and PM_{10} with depression, anxiety, bipolar disorder, psychosis, and suicide in adults. The most apparent association was between long-term (> 6 months) exposure to $PM_{2.5}$ and depression.[63] Depression and suicide were the most studied outcomes; however, there were no studies of long-term PM exposure and suicide, nor of PM exposure and bipolar disorder. The review highlighted a need for larger-scale longitudinal studies using representative samples, improved adjustment for an area-level factor such as traffic noise, access to green space, and socio-economic status to help better understand potential causality in observed associations. Further research is needed on the mechanisms involved in the observed associations.

5. Methodological Issues In Air Pollution & Mental Health Research

Outdoor air pollution can be measured and estimated in numerous ways.[64] [65] Here we describe some of the main methods used in the field of air pollution and mental health, in roughly chronological order. Dating back to the seminal work by Faris and Dunham (1939),[66] a precursor to the air pollution and mental health field is the body of research demonstrating associations between the urban environment and mental health, often by using population density or urban-rural comparisons. Air pollution has been speculated as a potential driver of this relationship.[67] However, cities are complex environments comprising multiple correlated risk factors that could impact mental health, making urbanicity only a crude proxy for air quality. Nevertheless, a series of comparative studies based in Mexico used a similar design, comparing Mexico City to less polluted areas. Among these, one post-mortem study[68] compared prefrontal white matter between children and teenagers who had lived in Mexico City versus a less urbanised area and found that ultrafine PM was found in the former but not the latter group's brain cells.

Among the earliest studies are also those exploring the association between people's *perceptions* of air pollution and mental health. For example, Evans et al. (1986)[69] asked residents of Los Angeles to rate the level of smog that day, from 1 (no smog) to 10 (heavy smog), and examined correlations of these responses with depression, anxiety and hostility. Though relatively economical to conduct and enabling individual-level analysis, this type of design examines a different question than the potentially direct, biological impacts of air pollution on the brain. In addition, this design is only suited to air pollutants that can be seen or smelled, which excludes many types such as carbon monoxide, which can have impacts on neurological functions. Research on the self-reported perception of indoor air quality also shows that factors other than indoor pollutant concentrations can affect perceptions, for example, occupational status or thermal sensation. Similar findings exist for environmental noise (in particular traffic noise)[70,71] and various components of air pollution (in particular, PM), which cluster with poor air quality.[72] Thus, it is difficult to separate the effects of noise and air pollution. Noise can increase the risk of mental disorders such as depression, anxiety disorders, psychoses and suicide.[73] The place effects of these and other different potential causal factors need to be considered in future studies.

Proximity to roads has also been used as a proxy for air pollution exposure and noise.[74] [75] For instance, using data from the Danish Civil Registration System, Pedersen et al (2006)[75] examined the association between distance to major roads and schizophrenia. The authors used official classifications of road types and Geographic Information System software to calculate the distance between households and the nearest major road. This innovative methodology still does not factor in other sources of air pollution, meteorological patterns, nor urban morphometric features (e.g., pockets of air pollution trapped between high-rise buildings).

One of the most common methods is to measure air pollution concentrations directly at monitoring sites, often using passive diffusion tubes. Some studies have also set up monitoring stations at the locations of interest to measure real-time concentrations. For instance, Wang et al (2009)[76] installed NO_2 and PM_{10} monitors at various locations within two schools in Quanzhou, China, and examined associations with neurologic functioning. The most common design is to use data from existing, permanent monitoring stations, often in conjunction with a time-series analysis design. For instance, Gu et al (2020)[77] obtained data on daily average pollution concentrations for 75 Chinese cities, from China's National Air Quality Monitoring System, and examined correlations with daily hospital admissions for depression. Though this time-series design is powerful in terms of understanding potential short-term effects of air pollution, monitoring stations are often very sparse, making it inappropriate to infer individual-level exposure from the data.

The measurements techniques used for sampling outdoor pollution can also be used in indoor settings.[65] Usually, measurements from static loggers and/or passive samplers placed within representative rooms and/or locations within a room are used as proxy of exposure to indoor pollutants. Some industry and ISO standards exist for the monitoring of specific indoor air pollutants.[78] Pollutants such as CO_2 or TVOCs (total volatile organic compounds) are sometimes used as a proxy of air quality and ventilation in indoor settings. Indoor concentrations can differ even when building layout/location is similar due to variations in indoor sources and activities. Therefore, it is not always possible to deduce indoor pollution levels via limited sampling sites. Overall, monitoring indoor air quality at scale can be time-consuming and relatively expensive, requiring access to several properties/participants. On the other hand, low-cost sensing technologies also have the potential to provide high-density spatial-temporal information on air quality across the indoor-outdoor continuum, although accuracies can vary. [79] [80] Better assessment of air quality indoors requires standardised and validated measures of built design with expertise from engineers.[81] Furthermore, flame retardants and plasticizers are common in indoor environments and can cause adverse neurological effects and negative behavioural outcomes including impaired learning and spatial memory.[82] [83]

Recently, more sophisticated methods of modelling outdoor air pollution concentrations have enabled much higher resolution estimates to be achieved, thereby facilitating more precise, individual-level exposure based on, for example, residential addresses. One method is land-use regression modelling, which factors in environmental characteristics with predictable influences on pollution concentrations, such as road, factories, forests, etc., to estimate pollution concentrations in a given area.[84] Another method, dispersion modelling, additionally factors in the atmospheric chemistry of air pollutants, together with meteorological data, to estimate pollution concentrations.[85] Dispersion models now achieve good predictions against ground-based measurements, as well as high temporal (e.g., hourly) and spatial (e.g., 20 x 20 metre) precision.[86]

The power of these models for understanding links between outdoor air quality and mental health lies in the ability to link this exposure data with large-scale epidemiological cohort studies. There are several important benefits of this large multidisciplinary consortium approach. First, the large sample sizes afford the statistical power to detect small effects which may be needed in contexts (such as Europe and the USA) where pollution levels and variability are relatively low.[63] Second, together with their large samples, the comprehensive assessment of a wide range of measures provides a valuable opportunity to adjust for multiple confounders and rule out threats to causal inference. These approaches can enable investigations of the role of important social and biological factors as mediators or moderators of associations, including psychosocial adversity, social deprivation, noise pollution, genetic risk, and inflammation. Third, the prospective longitudinal design of cohort studies can help establish the temporality of associations and therefore move the research on from reliance on cross-sectional observations that severely limit causal inference. Fourth, depending on the age and duration of the particular cohort, the impact of outdoor air pollutants on mental health can be explored across developmental periods, residential mobility shaping geographical contexts, and ultimately, across the life course. However, there is a need for more research focused on early life exposure because in-utero and childhood may be a time of particular vulnerability due to the developing lungs, brain and immune system. Indeed, a focus on such early pollution exposure to understand later effects is particularly necessary to elucidate its role in the development of mental health problems given the common onset of symptoms in childhood and adolescence.[87]

In the UK, birth cohort studies such as the Avon Longitudinal Study of Parents and Children (ALSPAC) and the Environmental-Risk (E-Risk) Longitudinal Twin Study have linked high-resolution air pollution models to their data.[55 57 88-90] Combining epidemiological approaches with air pollution modelling in this way has yielded important insights. However, this methodology is not without limitations. Exposure estimates are modelled rather than measured directly. Typically, these are linked to just one (or a few) addresses commonly visited by the study participants (e.g., home, school/college, shops). To better quantify levels of air pollution exposure, multiple different locations are needed as well as several different time-points.

Although some data on indoor/outdoor ratios exist for some pollutants, indoor concentrations are not solely driven by outdoor levels. Therefore, air pollution modelling of outdoor levels could be combined with indoor modelling (or monitoring), to better understand patterns of exposure. Various approaches to modelling indoor air quality exist, including mass balance or CFD models.[78] These can be used to estimate respectively pollutant concentrations and their spatial distribution and can be combined with meta-models of the building stock to estimate indoor air quality at scale.[91] However, models of indoor air quality rely on assumptions about indoor sources and human behaviours, for which there are limited empirical data.

Wearable, personal monitoring devices that measure pollutant concentrations close to the person's breathing zone offer a promising alternative. These enable individuals' exposure to be directly measured in real-time while they go about their usual activity. As people spend time in and move between spaces with varying concentrations of pollution, these devices more accurately capture their unique exposure. Although currently a cumbersome and expensive method – prohibitively so for large samples – future studies should consider utilising new technologies that allow personal monitoring to move towards accurately capturing air pollution exposure in everyday life. The emergence of low-cost sensing technologies has the potential to provide high-density spatial-temporal information on air quality and personal exposure across indoor-outdoor continuum.[92] [93]

6. Research Gaps and Challenges

In the early phase of the BioAirNet (https://bioairnet.co.uk/) research network, we held a sandpit event involving multidisciplinary experts and a range of stakeholders. This sought to identify key knowledge gaps and methodological challenges. The findings were relevant to pollution research and defining complex exposomes, and measurement, analytic approaches and interpretive paradigms for causal inference. The following priority research questions and knowledge gaps were identified:

Could exposure and inflammatory mechanisms explain:

  - Higher rates of mental illnesses (psychoses and affective disorders) in urban areas?
  - And do these effects vary by age, gender, sexuality, ethnicity, and by deprivation?
  - Greater risk for chronic health conditions into adulthood, including psychoses, common mental illnesses, and co-morbid medical conditions.
- What future environmental designs and practices (outdoor, indoor, buildings and institutions) might investigate mechanisms in specific at-risk populations?

- How might specific design interventions be developed tested for impact on the mechanisms?
- What constitutes an ‘anti-inflammatory’ environment that benefits:
    - Young people in their worlds?
    - Adults at risk of or already suffering mental illnesses and other health conditions?
- What role do social and behavioural factors have for:
    - Creating or concentrating a harmful exposomes in specific places and indoor environments?
    - Mitigating these drivers of poor health?
- How do structural (socio-economic, deprivation, poverty, geographical) and behavioural influences interact to promote or militate against a harmful exposome?
- How is child health and mental health affected, and what are the impacts over the life course?
- How are specific high-risk groups affected: those with early psychoses, chronic depression, multimorbidity, including poor mental health?
- What are the implications for care environments for children and for those with mental illness?

In addition, *specific approaches and methodologies* were identified to better *quantify levels of exposure* to indoor/outdoor pollution and links with health impacts in different scenarios (see Annex 1); *approaches and methodologies* to understand the *mechanisms* of harm to human health and wellbeing (see Annex 2); and the need to specify more carefully which health conditions and causal models were being investigated (Annex 3).

These recommendations are broadly aligned with the six priorities proposed in a recent review of environmental science and mental health,, including over 200 publications and six case studies: Five areas of opportunity were identified, which consider both the research approach and topics warranting further investigation:

- Exploit large-scale datasets
- Longitudinal approaches
- Integrative complex systems research
- Mixed methods approach

- Community of practice

6 Research Design For A Way Forward

The priority areas require advances in complex systems and mixed-methods research and more capability to collect, analyse and use new data for policy actions. Research in this area needs to be interdisciplinary, and the methodologies selected will also need careful co-design and review to address all the research questions and gaps. The following is a list of potential study designs and recruitment venues for interdisciplinary research with health outcomes.

7.1 School studies

Experience-based sampling is possible through mobile phone applications and wearable devices or by websites and self-report measures. The volume of data would not be sufficiently high, perhaps compared with school-based studies where young people usually complete the questionnaires in PHSE classes. A whole-school approach to support studies will be needed to ensure data quality, engagement and participation, and to ensure the research process itself is of value and beneficial and aligned with other priorities in schools.

Establishing partnerships and rapport with schools and HEIs, alongside developing appropriate teacher, community and parent panels, will support recruitment into studies and offer information about the acceptability of potential interventions and policy options.

The balance between entire school surveys versus recruitment of young people experiencing specific conditions or vulnerabilities needs some debate; there are tensions in terms of acceptability, the ethical process for recruitment and consent, concerns about stigma and confidentiality, and methodological challenges of screening people into specific studies. A whole-school approach would permit a series of nested case-control studies for specific conditions and contexts.

Research studies will need appropriate ethical and safeguarding frameworks, especially for young people, but generally for any proposed intervention studies.

Some young people will not be in school, or will have been excluded, perhaps directly due to health problems and linked with adverse social circumstances that are likely to affect their health status; these groups may well be those most likely to be exposed to poor air quality. Thus, additional samples of excluded groups will need to be considered, alongside creative and innovative methods for including them. There are likely to be age, gender, sexuality, and ethnicity related intersectional forces that are associated with exclusion and with poor mental health. Specific consultation and sampling strategies will need to be devised.

7.2 Longitudinal cohort studies with linkage

There are a number of existing cohorts that can be linked to data on air pollution. These offer opportunities to measure pollutants and mental health outcomes at multiple time points, resolving the temporal ordering and identifying critical periods for exposures and specific outcomes; the approach can also identify variation across multiple venues, and test generalisability and causal effects where exposures vary by geography. The linkage process takes time, yet some research groups have successfully done so and are generating new evidence in real-time and gathering evidence on the entire exposome (e.g. Equal-Life EU funded programme). The alternative approach is to design and establish new cohorts, with appropriate measures of air quality as well as the total hypothesised exposome.

7.3 In-depth qualitative cohorts

This study design may be especially suited to exploring complex social, psychological and spatial mechanisms, generating new hypotheses and in-depth information about contexts and health status. Realist methodologies and ethnographies, for example, may reveal context, mechanism, outcome relationships, which can be tested in epidemiological cohorts. The approach is also suited to recruiting those at risk of not being represented in surveys and population, school-based, and cohort studies. Obviously, this approach may not help identify or verify biological mechanisms unless bio-data are collected alongside. Such data could include functional brain scans, inflammation, epigenetic effects and genetic liability through polygenic risk scores.

8. Conclusions

Air pollution and mental health are both major challenges that the world must grapple with, now and for years to come. This makes their intersection a doubly vital public health priority. This paper outlines evidence on the importance of indoor and outdoor air quality on mental health, research needs, challenges, and future directions. There remain methodological challenges that must be overcome to provide insights into critical time points, place-based hot spots for poor air quality; as well as biological, psychological and social mechanisms, and strategies for prevention and mitigation. The clinical, public health, societal (wellbeing and economic) impacts need to be modelled. Better quality primary research and longitudinal cohorts, especially for young people at critical points of maturation, are needed alongside well specified systematic reviews and network analyses. Specifically, foci include evidence of links between bioaerosols and mental health, better exposure measurement. An important subject that need separate consideration is climate change. The pathways between global warming, poor air quality, climate change and poor mental health may be mediated through natural disasters and social disruption, biodiversity loss, ecosystem destruction.[50] Engagement of policy stakeholders from diverse sectors is necessary to translate emergent findings into actions. We hope this paper and related publications from a number of networks will bridge knowledge gaps to foster a new wave of research, practice and policy actions. This will allow us to better understand the complexity and connectivity among people, air pollution exposure, and resultant health and wellbeing impacts under ever-changing air pollution sources and exposure patterns. The resultant knowledge should seek to inform policies on air pollution interventions, urban and built environment design, land use planning and behaviour change.

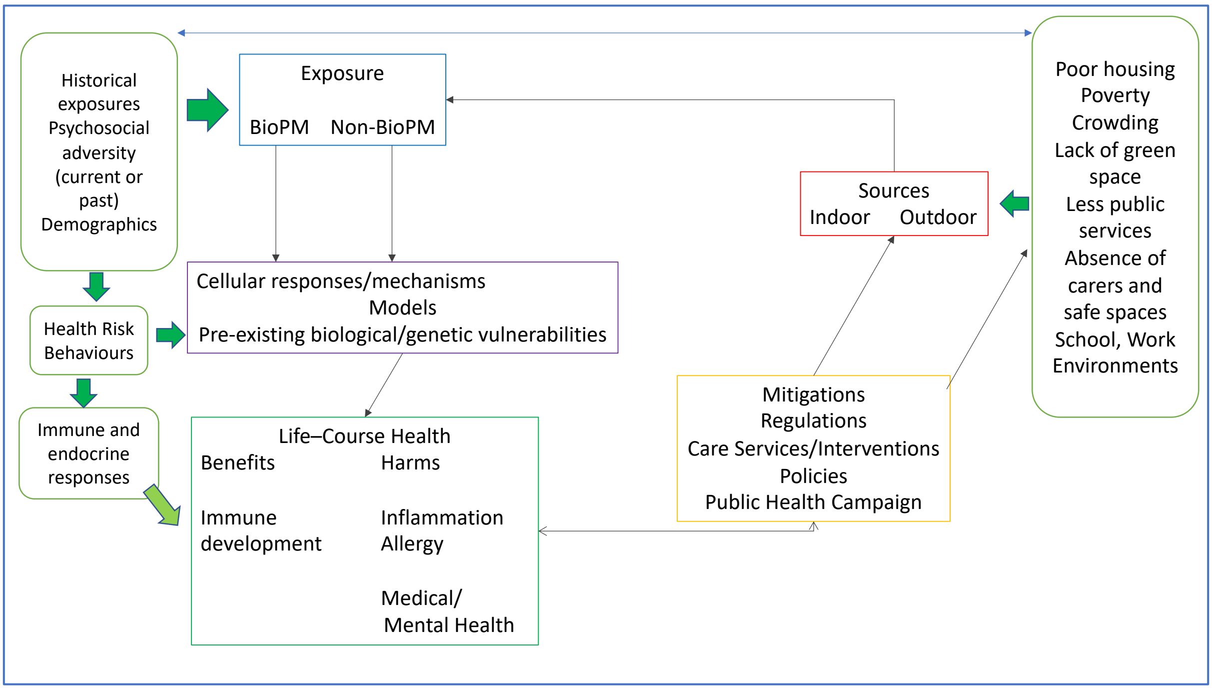
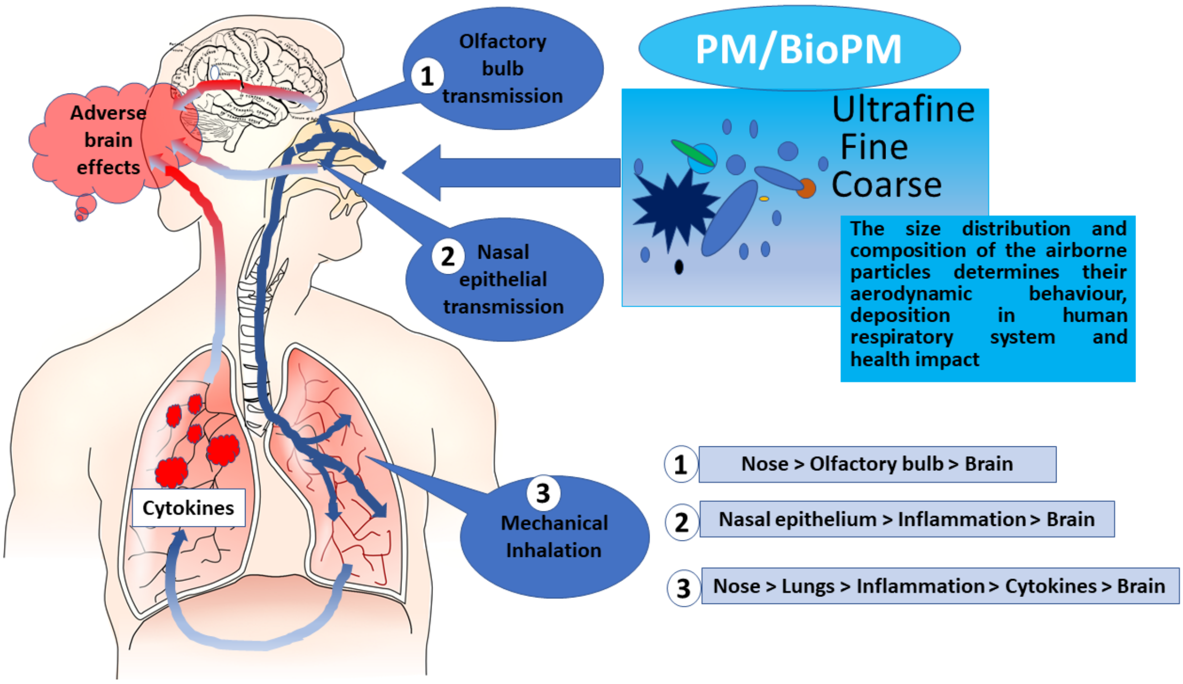


Figure 1: Mechanisms and Pathways of Poor Health Related to Air Quality.



The size distribution and composition of the airborne particles determines their aerodynamic behaviour, deposition in human respiratory system and health impact

Figure 2: Pollution to Inflammation (source: xxx).

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- Datasets – matching (homogeneous) longitudinal exposure and health data sets with comprehensive metadata for confounders
- Models – of exposure – personal vs population
- New technologies – *e.g.* real-time pollution measurement, high throughput sequencing, biosensors, personal devices – to inform exposure assessment
- Proxy/biomarkers of exposure – to inform exposure assessment
- Statistical methods and study designs – for linking exposure(s) to outcome(s) with appropriate power
- Methods of measuring and understanding:
    - The human microbiome – and its role in inducing health outcomes
    - Individual genetic diversity – and potential impact on pollution induced health outcomes
    - Benefits vs harms – which particles are beneficial or harmful and in what contexts?
    - Background levels and exposure thresholds – above which health is impacted
  - Vulnerable populations (*e.g. by* age, respiratory disease).

Annex 3

Measures of outcome for specific medical conditions:

- These may include risk phenotypes of conditions of interest (e.g. low mood, psychosis experiences, ischaemic heart disease, asthma in childhood).
- Outcomes of mental health impacts: individually, in combination with medical conditions; data including the timing of one or the other condition suitable for longitudinal data analyses
- Related and relevant demographic (age/gender/ethnicity), and psychosocial variables (social support, relationships, emotional dysregulation, adversity, poverty, trauma, poorer places and environments)
- Exploring which bio-psycho-social and eco-social and bio-bio interfaces are relevant for creating disease vulnerability to bioparticles as well as which psychosocial variables lead to greater exposure: poorer places have poorer housing, poorer food outlets, more crime, violence, less safety, and smaller houses, less green space). What are the types of interactions between these? To what extent are gene-environmental interactions relevant versus direct toxic effects?
- Which poor health outcomes due to poor air quality can lead to poor mental health: *e.g.* respiratory disease or obesity being associated with depression?
- Multimorbidity tends to occur in poorer places and is driven by both biological vulnerability and psychosocial adversity over the life course and in contemporary environments; how does air quality interact with this causal web of poor health and premature mortality for a sub-set of the population who are most likely to be exposed to poor air quality?
- What is the role of inflammation and oxidative stress?

Annex 2

- Literature reviews – linking exposure(s) to outcome(s)
- Knowledge mobilisation - shared datasets, best practice, multidisciplinary partnerships
- Models of pollution related harms: e.g., in vivo, in vitro, in silico for establishing levels of exposure and exploring biological causation pathways in whole systems *vs* specific mechanisms
- Causally informed Mendelian Randomisation studies
- Interdisciplinary collaboration and communication between exposure scientists, health professionals, toxicologists, government, and industry
- Assessing co-exposures – interactions between distinct air pollutants and the resulting effects on the viability, allergenicity, toxicity and pathogenicity
- What core measurements are required: what, in how much detail, for how long and for what purpose(s)?
- More longitudinal cohorts are needed.