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Review article

Expert perspectives on exposure-response functions for urban health policy: Lessons from a UBDPolicy workshop

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A B S T R A C T

Policy-makers require robust, quantitative evidence in order to better align urban and transport planning practices with public health goals. Epidemiologically derived exposure-response functions can quantify the association between urban health determinants and human health outcomes. They are therefore a crucial input in quantitative health risk assessments, providing to policy-makers actionable evidence on how healthier, more sustainable cities may be achieved.

The Urban Burden of Disease Policy (UBDPolicy) project convened a two-day workshop to discuss recent developments, ongoing challenges, and future directions for exposure-response functions and their application to quantitative health risk assessment. The workshop discussions centred around air pollution, transport noise, non-optimal temperature, greenspace and physical activity as primary pathways through which urban and transport planning impact human health. Based on this workshop, we provide an expert-guided perspective on how to enhance both our conceptual understanding of exposure-response functions and their practical application in urban health risk assessment. We also identify pathway-specific as well as cross-cutting (e.g., quantifying multiple exposures, need for population sub-group evidence) research needs relevant to environmental health more broadly. We propose several future research directions as an agenda for advancing urban environmental health.

1. Introduction

Suboptimal urban and transport planning can result in increased exposure to air pollution, noise, and excess heat, resulting in large but preventable mortality and morbidity burdens (Khomenko et al., 2021, 2022; Iungman et al., 2023). Conversely, by increasing access to greenspace and levels of physical activity (e.g., by expanding cycling and pedestrian networks), a large number of premature deaths could be prevented annually (Barboza et al., 2021; Mueller et al., 2018). Better urban and transport planning practices can improve public health (Nieuwenhuijsen, 2021), however, in order to take effective action, decision-makers require robust evidence aligning health needs and outcomes with social, environmental, economic and commercial determinants (WHO, 2023).

Quantitative evidence on the population health impact of environmental factors, exposures, policies or programmes can be produced through a quantitative health risk assessment, such as a burden of disease study or a health impact assessment (HIA) (Rigaud et al., 2024). In Europe, quantitative HIAs have previously demonstrated 8–20% of annual mortality burdens to be associated with urban and transport planning related determinants (Khomenko et al., 2020; Mueller et al., 2017). To conduct a quantitative HIA, an external factor must first be deemed causally or likely to influence human health, and an exposure-response function (ERF), representing the quantitative association between an exposure and health outcome, must be available (Rigaud et al., 2024). The choice of the ERF is a key step in the HIA process (Mueller et al., 2023) and an important factor influencing the range of outcomes, meaning it is critical to select the most appropriate ERF for its intended purpose.

In September 2024, UBDPolicy (https://ubdpolicy.eu/) convened an

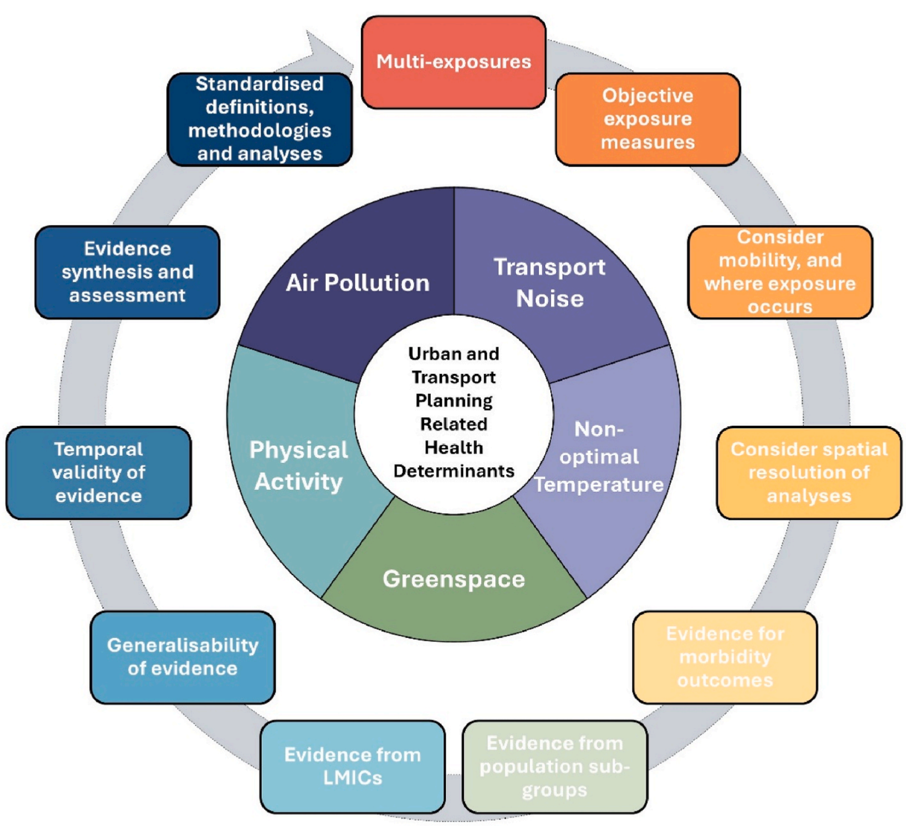

Fig. 1. Overview of urban and transport planning related health pathways included in commentary, along with cross-cutting research needs identified.

international and multidisciplinary group of experts and stakeholders to explore recent advancements, current challenges, remaining gaps, and future directions for ERF research, and their implications for urban HIA. This manuscript details the content and discussions of this workshop into a comprehensive research agenda that aims to re-orient researchers toward enhancing both our conceptual understanding of ERFs, and their effective and practical application in HIAs. Through doing so, we aim to advance the confidence in quantitative evidence that supports more effective urban and transport planning practices to protect and improve public health. Previous reviews (Woodcock et al., 2025; Rigaud et al., 2024; Forastiere et al., 2024) have provided discussion on ERFs, but only within the broader context of quantitative health risk assessment where they are discussed alongside other relevant inputs and modelling assumptions and choices. We instead offer an in-depth focus on the estimation and application of ERFs given their significance in environmental health research, practice, and policy, providing actionable recommendations for researchers to apply in ongoing and future work.

The discussions were structured as follows. First, we identified pathway-specific research needs, focussing on ambient air pollution, transport noise, non-optimal temperature, lack of greenspace and physical activity as key pathways through which suboptimal urban and transport planning may influence public health and where the evidence now allows for quantification (e.g., Glazener et al., 2021). Second, we identified several cross-cutting research needs (Fig. 1) applicable to all pathways and environmental health research more broadly. Finally, we considered how ERFs inform the HIA process, and implications for policy processes. We use the term ERF throughout due to its widespread applicability and use. However, when relevant, we also refer to other related terms (Table 1). Key themes were derived from expert-led

Table 1
Relevant definitions of exposure-response, concentration-response and dose-response functions.

Term	Definition	Uses
Exposure-response function (ERF)	ERFs relate a health outcome to the level of exposure to a specific health determinant. Exposure in this context can represent the total contact, as a product of intensity, duration and frequency to account for when, where, and how much exposure occurs.	*air pollution, noise, non-optimal temperature, greenspace*
Concentration-response function (CRF)	CRFs relate a health outcome to the concentration of a health determinant in the environment (often employed as a surrogate for exposure).	*air pollution*
Dose-response function (DRF)	DRFs relate a health outcome to the dose* of a health determinant received. * *For air pollution, the term dose commonly represents the amount of air pollution inhaled by subjects or participants, as a product of pollutant exposure and minute ventilation.* * *For physical activity, the term dose represents the amount of physical activity performed by subjects or participants and therefore, the DRF refers to the relationship between activity dose and human health outcomes.* * *For greenspace, the term dose usually represents the amount of greenspace experienced by subjects or participants, reflecting contact with and use of greenspace and differing from proximity to greenspace.*	*air pollution, physical activity, greenspace*

Table 2
Summary of open research questions and proposed research directions based on pathway-specific discussion of research needs.

Pathway	Open Research Questions and Proposed Research Directions
Air pollution	• Are recently observed associations between $PM_{2.5}$ and mortality stronger? If so, why? • What factors influence the shape of the $PM_{2.5}$ exposure-response curve? Does it vary by region? • Are certain components of $PM_{2.5}$ more harmful? And to what extent do the reported associations represent a causal effect, or the effects caused by other correlated pollutants? • And what will be the effect of changing compositions including in the context of a changing climate? • What are the health effects of air pollutant mixtures? And how can we measure the extent to which associations reported for one pollutant represent a causal effect, and to what extent do they represent effects caused by other correlated pollutants? • Do gaseous pollutants (O_3, NO_2) modify $PM_{2.5}$ toxicity? Are their effects additive, synergistic, or antagonistic? • How do different ERF shapes (e.g., linear, supra-linear, sub-linear) impact HIA, especially at low-to-moderate concentrations? • What new statistical approaches can robustly resolve multipollutant exposures, incorporate omics data, and support integration with experimental toxicology?
Noise	• How do different noise exposure-estimation methods influence observed effects? • Are different sources of noise associated with different effects? And in what circumstances is it suitable to use pooled (e.g. transport) estimates in lieu of source-specific estimates (e.g. construction)? • How do noise sources and characteristics vary by setting? How generalisable is the current evidence base, that is largely derived from European studies? • What scalable methods (e.g., land-use regression) can be applied to develop fit-for-purpose noise exposure maps especially in low- and middle-income countries? • How do multiple noise sources interact in affecting health? • What is the relationship between transportation noise and air pollution? How best can studies account for potential effect transfer?
Greenspace	• How can we better define greenspace, and what metrics or measurements best represent specific outcomes or pathways? • How do different mechanistic pathways, or contexts, influence specific health outcomes? • How do spatial resolution and measurement choice influence ERFs, and what aligns best with specific mechanistic pathways? What is the evidence for other landscapes, or nature characteristics (e.g., biodiversity, naturalness), and how can these be better captured and incorporated in research? • To what extent do subjective perceptions versus objective greenness metrics differentially affect health outcomes? How do culturally and contextually relevant perceptions modify greenspace impacts? • What mediators (e.g., physical activity, social cohesion, stress reduction) and moderators (e.g., socioeconomic status, age, gender) affect greenspace–health associations? • How does seasonality or temporal exposure (e.g., summer peaks) influence greenspace-associated benefits?
Non-optimal temperature	• How do populations adapt to non-optimal temperatures, and can long-term effects be disentangled from this? • How do health risks associated with non-optimal temperatures vary across different climates, geographies, and population subgroups? • How do we account for climate change in current modelling approaches, to capture processes such as population adaptation, and incorporate elements of climate justice? • How does temperature interact with other environmental exposures and modify their health effects? • What are the long-term health effects of chronic exposure to non-optimal temperatures?

(*continued on next page*)

Table 2 (*continued*)

Pathway	Open Research Questions and Proposed Research Directions
	• What are the best practices for projecting future temperature-related health burdens under varying climate, demographic, and adaptation scenarios?
Physical activity	• How do associations of physical activity vary by intensities or domains not routinely captured? • How can objective measurements best capture physical activity associations, and how comparable are these results to traditional approaches? • What are the trade-offs of using device-based versus self-reported measures, and how should we align dose-response functions (DRFs) accordingly in HIAs? • How do environmental exposures (e.g., air pollution, temperature extremes, greenspace, noise) interact with physical activity behaviours and their health effects? • How do activity timing, intensity, and location modify the interaction between physical activity and environmental risks?

discussions before and during the workshop and iteratively refined while drafting the manuscript. While no formal consensus method was applied, thematic agreement was reached by prioritising recurrent points of discussion and peer-review comments, with broad multidisciplinary agreement and refinement across 30+ co-authors and multiple revision rounds.

Importantly, we acknowledge this work as an unexhaustive, non-systematic account of a large and expanding evidence base. However, by leveraging participants' subject-matter expertise to build upon workshop discussions, we highlight several prominent knowledge gaps and research needs (Table 2). This work additionally serves to encourage holistic consideration of a diverse body of evidence often discussed in isolation, to the detriment of integrated evidence assessment and application.

2. Discussion

2.1. Pathway-specific research needs

2.1.1. Air pollution

Ambient air pollution remains a primary environmental contributor to mortality and morbidity worldwide (Kasdagli et al., 2024; Orellano et al., 2024; Forastiere et al., 2024a) with broad consensus based on decades of scientific literature confirming air pollution as a major global public health risk factor (Brauer et al., 2024; Boogaard et al., 2019). Most workshop discussions centred around fine particulate matter ($PM_{2.5}$) due to its public health significance, however we recognise that other ambient air pollutants including black carbon (BC), ozone (O_3) and nitrogen dioxide (NO_2) also contribute to the global disease burden (Strak et al., 2021; Brauer et al., 2024). Based on substantive epidemiological evidence for major health outcomes, well-established ERFs are available, however, several important and unresolved questions remain (Boogaard et al., 2024; Forastiere et al., 2024b) that we discuss here.

2.1.1.1. Evolving risks (stronger recent effects for $PM_{2.5}$). Recently published meta-analyses (Orellano et al., 2024) show moderately stronger associations between $PM_{2.5}$ and all-cause or non-accidental mortality, indicating that the already large current burdens of air pollution might be underestimated when using previous ERFs (Chen and Hoek, 2020; Hoek et al., 2013). The epidemiological evidence published between the systematic reviews by Hoek et al. (2013) and Orellano et al. (2024) results in an estimated relative risk (RR) for all-cause mortality per 10 μg/m^3 increase in $PM_{2.5}$ exposure that is 50 % higher (relatively) than the previous estimate (RR = 1.062 vs. 1.095, respectively). Orellano et al. (2024) also found higher $PM_{2.5}$ summary estimates for all-cause mortality than those reported by Chen and Hoek (2020) (RR = 1.095 vs. 1.08), albeit with wider 95 % confidence intervals due to the large increase in the number of recent studies (60 additional studies). This difference may be explained by several possible reasons. Improved resolution of air quality data might have allowed for better capturing of exposure contrasts, and likely less exposure measurement error. It is often assumed that exposure measurement error would bias the associations towards the null, albeit exposure measurement error may be complex (Samoli and Butland, 2017; Sheppard et al., 2012). It may also be explained by other factors such as changes in $PM_{2.5}$ composition over time, in the pollutant mixture correlated with $PM_{2.5}$ concentrations and/or by more recent studies in settings such as Europe and North America where air pollution levels are relatively low, which paired with a supra-linear ERF curve results in a larger relative effect per additional exposure unit at low compared to higher concentrations (Boogaard et al., 2024).

In contrast, the risk estimate for NO_2 has not exhibited an increasing trend, with estimates not changing between recent comparable systematic reviews and meta-analyses conducted in 2013 (Hoek et al., 2013) and 2024 (Kasdagli et al., 2024) (RR = 1.05 and 1.045 per 10 μg/m^3, respectively), and a notably smaller RR in a 2020 review (RR = 1.02 per 10 μg/m^3) (Huangfu and Atkinson, 2020). This difference in trend warrants further examination to help clarify the factors that may affect associations between specific air pollutants and health outcomes, and the extent of this influence.

2.1.1.2. Unknown heterogeneity (shape of the $PM_{2.5}$ exposure-response curve). While there is consensus that current epidemiological studies have not provided evidence of a threshold concentration below which no effect occurs (Orellano et al., 2024), recent research has highlighted substantial heterogeneity in the shape of the CRF for $PM_{2.5}$ at low levels (Fig. 2), with different shapes observed in different regional cohorts (near linear in the U.S., and supra-linear in Europe and Canada) (Boogaard et al., 2024). Somewhat surprisingly, the variability in the magnitude and shape of the association across the Canadian, U.S. and European studies was reduced only slightly in a harmonized analysis (Chen et al., 2023a). Similarly, there is some evidence of heterogeneity in the shape within regions (e.g., between different European cohorts) (Brunekreef et al., 2021).

It is not yet clear to what extent these results may be due to sampling variability, differences in populations and their responses, the toxicity of the air pollution mixture, and/or the statistical methods used, and therefore warrant further examination, particularly when considering the significant implications that a supra-linear CRF could have for quantifying health effects at low-levels of exposure (Weichenthal et al., 2022). For now however (as suggested by the UK Committee on the Medical Effects of Air Pollutants (COMEAP)), the current evidence remains insufficient to recommend any change from the current assumption of a linear CRF relationship when quantifying the impacts associated with long-term exposure to $PM_{2.5}$, although there is value, in research settings, to investigate the influence of using different CRF shapes, as sensitivity analyses (COMEAP 2025 (in preparation)).

2.1.1.3. Drivers of heterogeneity ($PM_{2.5}$ components). $PM_{2.5}$ is heterogenous, varying by source, size and chemical composition across regions (McDuffie et al., 2021; van Donkelaar et al. 2019). Research suggests that a wide range of $PM_{2.5}$ components are associated with adverse health effects (Hao et al., 2023; COMEAP, 2022b), and varying exposure-response curves (Chen et al., 2024a). Despite this heterogeneity, epidemiological studies have found consistent associations with mortality and morbidity in very different settings globally (Chen and Hoek, 2020), with such evidence underpinning the World Health Organization's (WHO's) 2021 revised guidelines for $PM_{2.5}$ (WHO, 2021). Relatedly, the consistency of adverse effects observed across diverse settings provides support for the usefulness of $PM_{2.5}$ mass concentrations as a metric for ambient particles, which remains useful for quantitative HIAs (COMEAP, 2022a). As concluded by the United States

Environmental Protection Agency (U.S. EPA) in their 2019 Integrated Science Assessment (ISA) for particulate matter, there is currently insufficient evidence for different PM components being more closely related to health outcomes than $PM_{2.5}$ mass and no individual $PM_{2.5}$ component or source is a better predictor of mortality than $PM_{2.5}$ mass (US EPA, 2019), although this evidence needs updated synthesis and assessment. Future studies should explore how $PM_{2.5}$ sources and composition are evolving in response to anthropogenic changes, particularly to transport decarbonisation and electrification, climate change, and wildfires (Xu et al., 2023; COMEAP, 2020). Source apportionment studies may help further elucidate sources of PM and its components, with practical application for epidemiology and HIA (Shan et al., 2024).

Similarly, $PM_{2.5}$ occurs within a mixture of other pollutants such as volatile organic compounds (VOCs), and O_3 and NO_2 gases, that not only interact with and impact $PM_{2.5}$ toxicity (e.g., Weichenthal et al., 2017), but are themselves associated with well-established independent health effects. Owing to substantial evidence delineating these independent health effects, WHO updated recommendations on air quality guideline levels for gaseous pollutants, primarily NO_2 and O_3 in 2021. These gaseous pollutants also exhibit substantial global variation (McDuffie et al., 2020), and these differing correlations may partly explain observed heterogeneities in the magnitude and shape of reported single pollutant $PM_{2.5}$ ERFs. These complexities benefit from more advanced approaches (e.g., the pollutant mixture complexity index) to better separate risks of $PM_{2.5}$ from risks of gaseous pollutants on mortality (Masselot et al., 2024) or delineate additive, synergistic or antagonistic effects which remain largely unknown. The development of multi-pollutant statistical approaches (e.g., Chen et al. (2024b) discussed in more detail later) remains an active area of research. While numerous advanced approaches have been developed, particularly for omics analyses and in studies of the exposome (Stafoggia et al., 2017; Agier et al., 2016; Chadeau-Hyam et al., 2013), further progress remains necessary, especially in the analysis of complex pollutant mixtures, and in the integration of epidemiological and toxicological data to better interpret intricate exposure patterns and their health effects (Savitz and Hattersley, 2023).

2.1.2. Noise

Transport noise - primarily from road traffic, railway and aircraft - is a significant environmental risk factor for which the epidemiological evidence of adverse health effects continues to grow. As highlighted in both a recent European Environment Agency (EEA) report (EEA, 2025; Engelmann et al., 2023) and systematic review (Pershagen et al., 2025), consistent associations are now observed for long term health effects including all-cause mortality, incidence of cardiovascular diseases and diabetes. Adverse effects start below current WHO Environmental noise guidelines for Europe (WHO, 2018), and emerging evidence indicates road and railway noise may increase risks for dementia, breast cancer and tinnitus (EEA, 2025; Sørensen et al., 2023).

2.1.2.1. Assessment methods (noise exposure-estimation). The current state of the art for noise exposure assessment are source-specific emissions plus propagation methods that estimate exposure at façade points

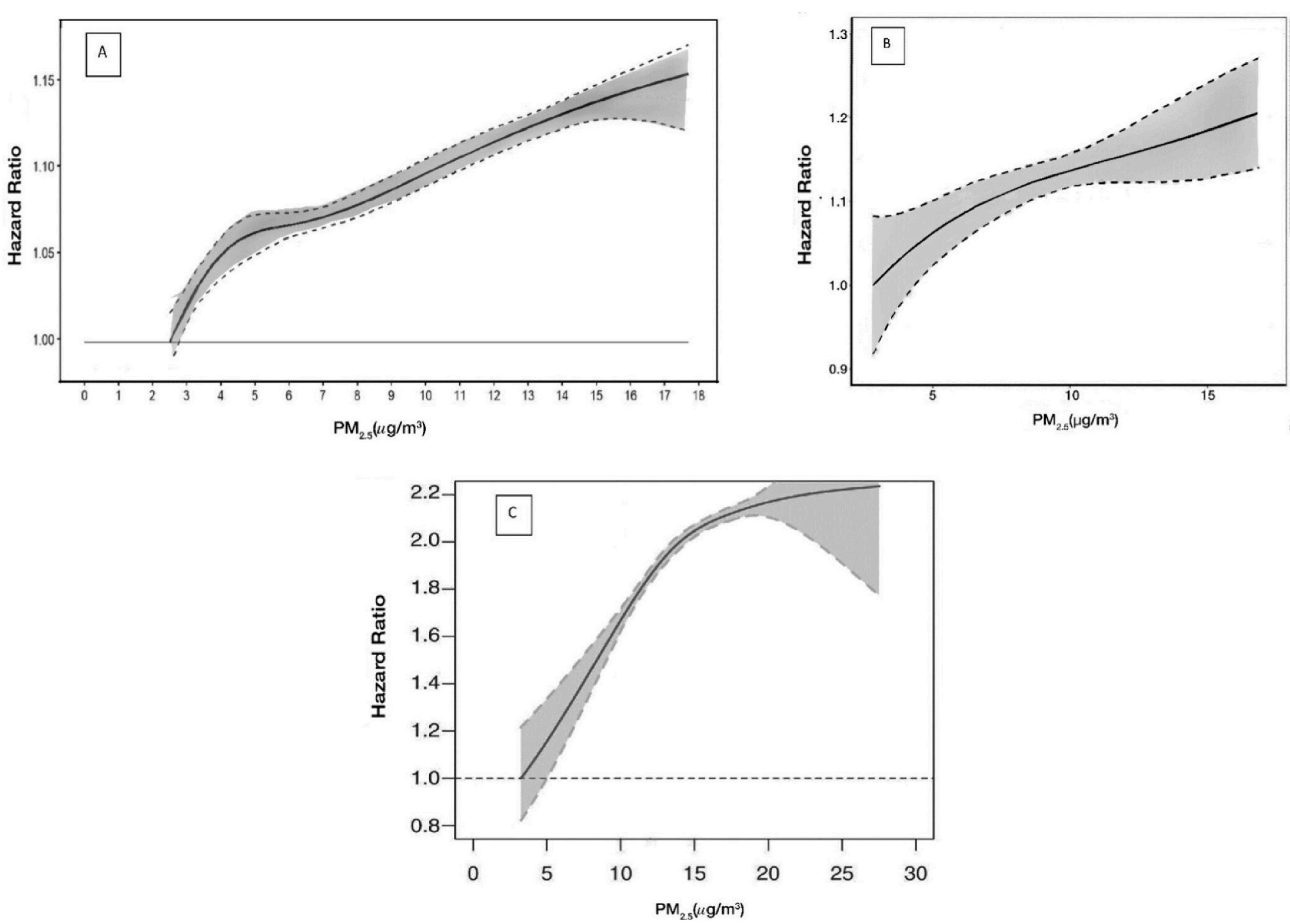

Fig. 2. CRFs for associations between long-term exposure to $PM_{2.5}$ and all-cause or nonaccidental mortality in (A) the Canadian MAPLE study; (B) U.S. Medicare study; and (C) European ELAPSE Pooled cohort. Shaded area corresponds to the 95 % CI. From Boogaard et al. (2024).

on buildings or a fine lattice. These models consider noise emissions from different vehicle types, volumes and speeds, together with sound absorption and reflections from ground terrain, buildings and other structures such as noise barriers - see for example the Nord2000 method (Kragh et al., 2023). Within agglomerations of more than 100,000 persons and near major roads, railways and airports, strategic noise mapping by transportation source is mandatory for European countries under the Environmental Noise Directive (END). However, historically, strategic noise maps developed under END differ substantially across countries, due to different exposure assessment methods and variations in the resolution of input data, resulting in many being of low quality (Khomenko et al., 2022). Similarly, few noise maps employ continuous noise exposure ranges, more frequently categorising by 5-dB noise bands that may misclassify exposure levels and increase uncertainty (Khomenko et al., 2022). Burden of disease estimates based on END strategic noise maps, that only consider agglomerations and major noise sources (e.g., major roads, railways and airports) and do not include lower levels of noise exposure, may be underestimated (EEA, 2025; Aasvang et al., 2023; Jephcote et al., 2023).

Having modelled noise exposure at the façade on the floor of residence vs. using a spatial grid for residential exposure assessment can also substantially influence health estimates (Vienneau et al., 2019). While the preferred façade exposure estimates have been utilised in settings such as Denmark and Switzerland to produce high resolution datasets, such spatially resolved models are not widely available and remain underutilised more widely (Vienneau and Wunderli 2023). More broadly there remains a paucity of exposure data outside Europe (The Lancet Regional Health - Europe 2023), though geospatial approaches (e.g., land-use regression) using monitoring data may be suited to scale up noise exposure assessment in epidemiological studies (Roscoe et al., 2023), particularly for low- and middle-income countries (Chen et al., 2023b).

2.1.2.2. Expanding classifications (source-specific transport noise). In a typical urban environment, people are exposed to multiple noise sources (e.g., transport, construction, commercial, entertainment). Transport noise, for which most evidence is available, is typically further evaluated by source, for which the most compelling evidence comes from road traffic, at least partly related to the number of studies (Engelmann et al., 2023). In lieu of source-specific noise ERFs for all outcomes, which are necessary to reflect the different acoustic characteristics of sources (Wunderli et al., 2016), discussions on the appropriateness of applying pooled estimates representing total transport noise remain ongoing. Based on the assumption that the biological mechanisms involved may be similar for different noise sources (Sørensen et al., 2023), in some circumstances estimates pooling different noise sources may be appropriate. For example, a recent EEA report proposes the use of a pooled effect estimate for transport noise to estimate cardiovascular risks of rail and aircraft noise for which the evidence is inadequate (Engelmann et al., 2023). This however is not appropriate for all sources nor all outcomes (e.g. annoyance, for which source-specific curves are available).

While the effects of environmental (including transportation) and occupational noise exposure are relatively well researched, some noise sources are better studied than others (SheikhMozafari et al., 2025), and new sources continue to emerge (Willis et al., 2024). More is known, for example, about the broad range of effects of road traffic noise, that affects nearly everyone, compared to railway noise. Compared to, for example, the more advanced work on source apportionment that has been undergone for air pollution, more effort is needed to identify sound sources if using measurements instead of engineering models as a basis for exposure assessment. This may be of particular policy relevance given, for example, the potentially beneficial effects of pleasant and calm soundscapes for health and wellbeing (Kong and Han, 2024). Additionally, there is a need to recognise that the sources and characteristics of transportation noise likely differ by study setting and, therefore, the current evidence base that is largely derived from European studies may not be generalisable to other study settings with differing noise profiles. For example, in low- and middle-income country cities daytime and night-time noise levels can frequently exceed those in European cities (Chen et al., 2023c), and additional evidence from sub-Saharan Africa based on measurements highlights heterogeneous noise sources and unique soundscapes (Clark et al., 2021; Osei and Effah, 2022). Further research is also needed to better understand how other contextual factors (e.g., built environments, population densities, underlying population and health characteristics) may influence noise characteristics and their effects.

In recognition that individuals can be exposed to multiple sources of transportation noise (e.g., road, railway, aircraft) simultaneously, there is also a need for studies to investigate the health effects of combined noise exposure for which less is known, and to determine which models are best suited to predict combined risks (Sørensen et al., 2023; Seidler et al., 2019).

2.1.2.3. Confounding and effect modification (noise and air pollution). Given that transport represents a major source of both noise and air pollution, research on transport noise published in the last decades almost always considers air pollution at least as a potential confounder. Very few studies have looked at interactions (Eminson et al., 2023). Generally, studies have found that associations between noise and health outcomes are independent of air pollution (Eminson et al., 2023). For example, in the Swiss National Cohort, Héritier et al. (2019) find transport noise to be independently associated with myocardial infarction mortality, even after adjustment for NO_2 and/or $PM_{2.5}$. This is not observed in all contexts (e.g., in analysis of the UK Biobank, Hao et al. (2022) consistently find noise effect estimates reducing after adjustment for $PM_{2.5}$). When considering the reverse, the evidence is mixed, with some studies observing associations with traffic-related air pollution to be attenuated after adjustment for noise, and some observing no change in air pollution effect estimates (Rugel and Brauer, 2020). Many studies on air pollution however do not adjust for confounding by noise at all. Future research should explore the possible occurrence of effect transfer, which can arise when exposure is less accurately estimated for one exposure compared to another (Evangelopoulos et al., 2021). This may be particularly relevant for noise, considering that advanced sound propagation models are available in only a limited number of settings.

2.1.3. Greenspace

Current available evidence for the extent of local greenspace indicates protective effects for a growing number of long-term health outcomes (e.g., all-cause and stroke mortality, CVD morbidity, mental health), but remains limited or inconclusive for many others (Sakhvidi et al., 2023; Yang et al., 2021; Rojas-Rueda et al., 2019). Generally, greenspace ERFs exhibit heterogeneity (varying substantially by type of greenspace, outcome examined, and contexts) and are consequently a significant source of uncertainty in greenspace HIA (Barboza et al., 2021).

2.1.3.1. Defining and categorising greenspace. Greenspace, which itself exhibits significant variability, lacks a common unifying definition, with definitions often changing between disciplines (Taylor and Hochuli, 2017). The definition of greenspace used can alter observed outcomes (e.g., Klompmaker et al., 2018). Furthermore, greenspace can be represented by a variety of different metrics and indicators, all measuring different aspects of the environment (e.g., greenness, vegetation type and cover, access to and use of open spaces) (Liu et al., 2023; Vilcins et al., 2024a,b), and the way in which greenspace is measured and classified can impact statistical associations (Mitchell et al., 2011). The substantial variation in what is considered greenspace and qualities therein (Kondo et al., 2018) have important implications for HIA, as the definition of greenspace used to derive a particular ERF may not necessarily match definitions used in policies and HIA. While definitional decisions will depend on the research question and intended application, researchers should still aim to provide a meaningful definition that both qualifies and quantifies how greenspace is defined (e.g., examples presented by Taylor and Hochuli, 2017), for which construct-based approaches may be additionally useful (Lee et al., 2025). For future research, it is feasible to obtain and evaluate typologically-distinct and context-specific metrics of greenspaces across many urban areas (e.g., canopy and grasses within or proximate to residential, near-road, and park contexts) (Browning et al., 2024).

To date, HIAs have primarily relied on normalised difference vegetation index (NDVI) as a simple and inexpensive metric of vegetation extent despite its many limitations such as the inability to accurately characterise how individuals access, interact with and experience greenspace (Donovan et al., 2022; Holland et al., 2021). For some outcomes, contact with and use of greenspace may be more important predictors of health than NDVI or proximity-based metrics (Holland et al., 2021; Kruize et al., 2020; White et al., 2021), therefore more ERFs should be derived using metrics that more accurately reflect them (e.g., White et al., 2019). Importantly, NDVI also lacks specificity to differentiate fundamental aspects of green cover such as trees, grasses, quality, and visibility, and does not differentiate between publicly accessible and private greenspace. Such aspects can influence observed health effects, and are therefore necessary to consider to enable targeted health intervention (Yi et al., 2025; Odebeatu et al., 2024). Future research needs more sophisticated and precise exposure metrics. This is partially due to a need to consider which metrics may more accurately reflect specific mechanistic pathways of interest (for example when addressing noise attenuation, biomass metric may be more appropriate than NDVI). This will further require greater consideration of characteristics of greenspace morphology, including quality, size, shape, fragmentation, connectedness, aggregation, and diversity (Wang et al., 2024). Spatial resolution, which can differ substantially (e.g., NDVI resolution from MODIS (250 m^2) and Landsat 8 (30 m^2)), should also be considered, and decisions made based on context-relevant pathways (Jimenez et al., 2022).

There is a further need to consider potential differences between objectively measured and perceived metrics of exposure, which do not always align (Marselle et al., 2021; Leslie et al., 2010). Some evidence indicates perception may matter more for certain pathways (e.g., Dzhambov et al. (2018) found associations of mental health to vary depending on whether subjective or objective measurements of greenspace were used). Alternative metrics that more accurately capture how greenspace is perceived by individuals may therefore be better suited (e.g., Viewshed Greenness Visibility Index (VGVI) (Labib et al., 2021), when metrics relevant to harm mitigation are not being considered. Perceptions of greenspace quality (e.g., attractiveness, cleanliness, and safety) may also impact health outcomes (Knobel et al., 2021) with differing patterns of associations depending on outcome (Nguyen et al., 2021). Yet, perceptions of quality may also vary based on individual and community-level culture and values. Evidence is lacking for other qualities, particularly the identification of needs-specific or culturally appropriate amenities, and there is a need for more longitudinal and experimental studies (Nguyen et al., 2021).

2.1.3.2. Drivers of heterogeneity (pathway- and context-specific greenspace). Greenspace, and nature more broadly, impacts health and wellbeing through four mechanistic pathway domains (each comprised of many individual pathways) (Fig. 3). These mechanistic pathways may be important drivers behind varying greenspace-health associations that further differ by context. For example, in an urban environment the effects of greenspace may be more driven through mitigation (e.g., reducing harm from heat, air pollution, noise) than in rural contexts (Browning et al., 2022). HIAs should therefore attempt to separate out different fundamental contexts (e.g., high burden urban environments, low burden urban environments, rural). Further research may also improve our understanding of how ERFs differ between environmental contexts and how they may further differ among sub-groups of the population. These different pathways and contexts are further complicated by the numerous concurrent mediators and moderators operating at all social and spatial levels (Marselle et al., 2021; Dzhambov et al., 2020) that are increasingly complex to model and incorporate within HIA. For example, sex and gender may modify the association between greenspace and health (Sillman et al., 2022) however more robust empirical studies are required to grow the evidence base for this and many other moderators/mediators for which less is known (e.g., modifications by personal traits, or mediation by physical activity) (Sakhvidi et al., 2023). There are many seemingly important moderators/mediators for which there is yet no consensus on whether they are essential to measure, such as nature-relatedness (i.e., people's connection to nature) (Dean et al., 2018), or nature contact during commuting to (Zijlema et al., 2018) or during work (Lygum et al., 2023). Research on greenspace, and nature more broadly, continues to evolve, incorporating new evidence (e.g., the recently proposed biopsychosocial resilience framework (White et al., 2023)) as it emerges. Overall, greenspace research more routinely integrates pathway analyses to statistically disentangle the role of different mediators, which should also be replicated for other environmental exposures where it received less attention (Dzhambov et al., 2020).

2.1.3.3. Expanding classifications (nature is not always 'green'). Most available evidence for nature focuses on greenspaces, and increasingly blue space (White et al., 2020). However, there is a need to move beyond typical definitions of 'green space' and 'blue space' in recognition that nature is diverse, with emerging research demonstrating other landscapes such as 'white space' (snow-covered) or 'brown space' (rock--covered or deserts) may pose health benefits or risks not currently captured (Li et al., 2023). Further, each of these space categories facilitates exposure to other types of nature such as natural soundscapes,

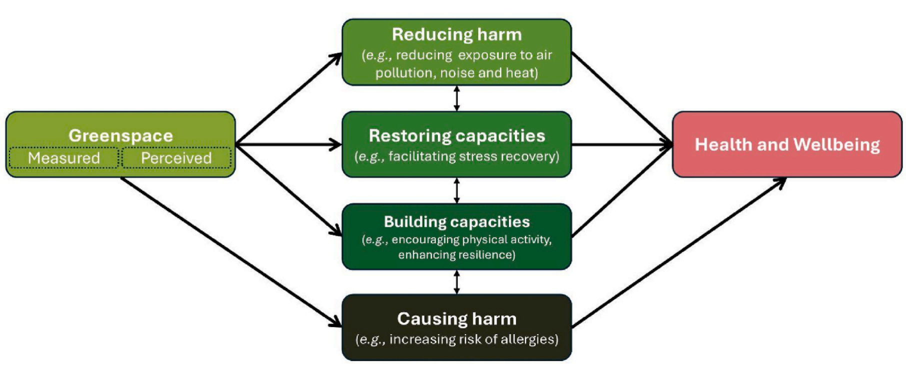

Fig. 3. Pathways linking greenspace to human health. Adapted from Marselle et al. (2021) and Markevych et al. (2017).

microbial colonisation, biogenic chemicals, animal interactions, and many other elements of nature contact. The biodiversity of natural landscapes, which can influence human health but is not as extensively researched (Marselle et al., 2021), requires greater consideration. Individual perceptions of these specific landscapes and contacts may influence health benefits (e.g., deserts can activate restorative pathways among desert residents, but others may view these landscapes as harsh/barren and therefore not receive the same benefit) (Yin et al., 2022). The 'naturalness' of greenspace and other landscapes also requires further consideration, with research demonstrating its importance for improved mental wellbeing (Bressane et al., 2024). Similarly, however, naturalness may be perceived differently by individuals (Hoyle et al., 2019; Hwang and Roscoe, 2017). Seasonality, which can significantly influence the physiognomy of green and other natural environments, is another commonly overlooked dimension (Bell et al., 2017) that can influence health and physical benefits (Zhou et al., 2022). Therefore, the temporality of chosen exposure metric (e.g., summertime maximum or annual average) may influence results, requiring careful consideration on which to select based on the pathways of relevance.

2.1.4. Non-optimal temperature

Non-optimal temperatures (both heat and cold) exert substantial mortality impacts worldwide, though most of the current mortality burden can be attributed to cold (Masselot et al., 2023; Zhao et al., 2021). Due to climate change, heat-related health burdens are expected to increase, and prevailing regional disparities in these burdens will continue to widen (García-León et al., 2024). Differential patterns of risk are also observed according to age, with risk increasing with age, and by cause (e.g., cardiorespiratory causes show stronger effects than non-cardiorespiratory causes) (Scovronick et al., 2024). Health estimates for temperature-related risk vary across cities due to the numerous climatic, environmental, and socio-economic factors which influence vulnerability to heat and cold (Sera et al., 2019). Thus, while the evidence for short-term effects of heat and cold is robust, the use of a meta-analytic summary estimate, as for air pollution, noise and greenspace, is not supported. City or region-specific ERFs should be used in HIA.

2.1.4.1. Assessment methods (modelling complex temperature-related effects). The temperature-mortality relationship comprises the effects of exposure to heat and cold, both of which contribute to excess mortality. The minimum mortality temperature (MMT) is often used to represent the 'optimum' temperature at which the risk of mortality is lowest. It reflects adaptability to local climate, and differs widely across cities (Tobías et al., 2021). Modelling this non-linear (typically J- or U-shaped) temperature-mortality association is complex, characterised by different lag periods, that further vary substantially between populations due to differences in acclimatisation, susceptibility, age structure, access to resources and local public policies (Guo et al., 2014). These complexities require sophisticated statistical approaches and large amounts of historical data (Gasparrini et al., 2015). This is exemplified in Masselot et al. (2023) where an advanced three-stage modelling framework was developed and used to provide comprehensive risk estimates and mortality impact assessment of non-optimal temperature across 854 European urban areas. Their work also offers clear directions for future developments, including Bayesian applications and machine learning to improve risk spatialisation and predictive performances, and the adoption and application of their framework to other environmental stressors.

2.1.4.2. Evolving risks (population adaptation to and long-term effects of non-optimal temperature exposure). The health effects of short-term exposure (days to weeks) to non-optimal temperatures are well established, with robust estimates routinely employed in HIA (Iungman et al., 2025; Khomenko et al., 2025). Conversely, there are very few studies investigating associations between long-term temperature exposure and health (Zafeiratou et al., 2021), and less physiological evidence on what the effects of long-term exposure to non-optimal temperature could be. Establishing the presence of an independent effect of long-term exposure is methodologically challenging due, in large, to population adaptation processes which occur over time (Zafeiratou et al., 2021). These processes, which may be due to behavioural, physiological, or societal adjustments, may lead to the mitigation of long-term health effects, and are likely to vary by context as demonstrated by substantial global variability in the MMT, an important indicator of adaptability to climate (Tobías et al., 2021). A deeper understanding of these adaptive mechanisms is crucial, especially in the context of climate change and projection of future temperature-related health burdens, for which there is limited methodological guidance (Rai et al., 2022). Further research, utilising innovative designs and longer series is warranted.

The current evidence base for long-term exposure to non-optimal temperatures is sparse, and existing studies exhibit substantial heterogeneity regarding study design, outcome considered, temperature metric and exposure duration. Recent evidence from a European-wide small-area study indicates potentially independent effects of long-term exposure to non-optimal warm periods, beyond those of short-term exposure, although these results were again highly heterogeneous across geographic areas and temperature metrics (Zafeiratou et al., 2025). A multi-country study explored the timescale of heat-mortality associations, suggesting that most of the long-term effects can be explained by the cumulation of short-term inputs (Armstrong et al., 2017). However, this question must be clarified by further longitudinal research, particularly through the application of non-ecological, longitudinal cohort studies that cover a range of geographical areas and incorporate individual-specific information (e.g., age, socioeconomic status, pre-existing conditions) as well as area-specific characteristics.

2.1.4.3. Confounding and effect modification. There is strong evidence linking temperature-related mortality and effect modification by individual-level factors such as age, sex, and occupation (Son et al., 2019). Research has also demonstrated how environmental factors such as greenspace and air pollution modify temperature-related effects (Song et al., 2024; Wicki et al., 2024; Stafoggia et al., 2023; Choi et al., 2022) however, the evidence for community-level effect modifiers (e.g., population density, healthcare facilities) is limited and requires further research (Son et al., 2019). Evidence on effect modification is also limited for cause-specific outcomes (Zafeiratou et al., 2023), and more research is needed to understand behavioural responses (Folkerts et al., 2022). Examination of biobanks and electronic health records could also reveal further insight into modifiers such as genetic susceptibility and medication usage, respectively.

2.1.4.4. Evolving risks (climate change and climate justice). Climate change impacts, including unprecedented global warming and extreme events such as heatwaves (IPCC, 2023) and cold spells (Hanna et al., 2024), are likely to worsen worldwide. One third of heat-related deaths have already been attributed to anthropogenic climate change (Vicedo-Cabrera et al., 2021), which is further exacerbating existing heat-related health and economic burdens (García-León et al., 2024; van Daalen et al. 2024). Recent evidence also demonstrates that increases in heat-related deaths consistently exceed any decrease in cold-related deaths, resulting in net temperature-related health burdens increasing, even under scenarios of high mitigation and adaptation (Masselot et al., 2025). Incidentally, the question of population-adaptation remains a substantial source of uncertainty in projections of temperature-related health burdens (Rai et al., 2022). While there are a variety of approaches for quantitatively incorporating adaptation into impact assessments, there remains no best practice (Rai et al., 2022; UK Health Security Agency, 2024). Additionally, methods for including adaptation are often not grounded in empirical evidence (Cordiner et al., 2024), and there remains additional uncertainty relating to the appropriateness of applying current models of adaptation to future impacts that are extending beyond historical experiences (Vanos et al., 2020). The impact of population ageing, a global trend, is also likely to be a crucial driver for future temperature-related risks that will amplify the increasing impacts of extreme heat (Chen et al., 2024c), warranting further research. Beyond the independent physiological effects of heat exposure, long-term changes in heat and other weather patterns may also influence the foundational behavioural and social determinants of health. These include physical activity, transportation, access to facilities and services, greenspace typologies and biodiversity, economic and productivity loss, and social cohesion (Ragavan et al., 2020; Berry et al., 2010; Moser and Hart 2015).

There also remains a need for research into social inequities and environmental injustice of climate on health, moving beyond just physiological characteristics (e.g., age, underlying health conditions). It should consider the underpinning forms of exclusion, oppression and exploitation that are driving unequal health impacts in historically marginalised and minoritised groups who have contributed the least to climate change, are most exposed to its impacts and have the worst access to protective interventions (Kotsila and Anguelovski 2023). Researchers should more closely examine ongoing and intersecting oppressive structures that underpin existing health inequities but also interact with climate change to exacerbate them (Deivanayagam et al., 2023).

2.1.5. Physical activity

Physical activity can be considered a product of built environment and policy decisions, representing a pathway through which human health is influenced by urban and transport planning, as conceptualised through several well-established frameworks (Glazener et al., 2021; Tonne et al., 2021; Nieuwenhuijsen, 2020). For example, compact, mixed-land use design and active transport infrastructure can promote physical activity levels and improve public health (Cerin et al., 2022; Khreis et al., 2024; Kärmeniemi et al., 2018). Similarly, urban interventions such as low-traffic neighbourhoods or 15-min cities aim to simultaneously reduce car usage and improve urban environments by promoting physical activity, enacting multiple co-benefits (Nieuwenhuijsen et al., 2024; Xiao et al., 2024). Participating in regular physical activity results in health benefits across all ages and abilities. Recent systematic reviews have shown non-linear dose-dependent associations between higher physical activity volumes and decreased risk of a wide range of mortality, cardiovascular disease, cancer (Garcia et al., 2023) and mental health outcomes (Pearce et al., 2022).

2.1.5.1. Defining and categorising physical activity

Physical activity is a diverse behaviour, comprising several activity types and domains, varying by intensity, duration and frequency, resulting in heterogeneity in operational definitions across studies (Piggin, 2020). There are also multiple ways to measure and report physical activity, and different decisions and approaches to estimate DRFs. Consequently, many physical activity studies are challenging to compare, indicating a need for comprehensive data harmonisation strategies (Garcia et al., 2023; Pearce et al., 2022; Gates et al., 2017) and standardised methodological decisions and approaches across outcomes.

Traditionally, physical activity has been classified using different intensity levels (light, moderate, vigorous) (Fig. 4a). The predominant and most reliable evidence of associations with health outcomes is available for regular moderate-to-vigorous physical activity (i.e., brisk walking, jogging and running) resulting in the WHO recommending adults accumulate 150–300 min of moderate-intensity or 75–150 min of vigorous-intensity physical activity per week to achieve health benefits (WHO, 2020). Conversely, there are currently no WHO recommendations for light-intensity physical activity (e.g., casual walking, light household work), due to comparatively fewer studies, despite the fact that light intensity activity is the main driver of total volume of activity energy expenditure (Lindsay et al., 2019) in the general population. Evidence from experimental and observational studies does however demonstrate associations between light-intensity physical activity and improved cardiometabolic health and reduced mortality risk (Chastin et al., 2019; Ku et al., 2020). Studies employing device-based methods can more accurately reflect low-intensity activities that are difficult to accurately capture using self-reporting methods. Despite the absence of WHO recommendations, light-intensity physical activity presents an opportunity for public health promotion. While more light-intensity physical activity may be required than moderate to vigorous physical activity to lower risk (e.g., 3–4 times higher to reduce risk of premature death (Ekelund et al., 2024a)), light-intensity physical activity is more pervasive (Young et al., 2016) and likely more achievable than moderate-to-vigorous physical activity (Ross et al., 2024).

Physical activity is defined by different domains, typically categorised as leisure-time, occupational, transport or household physical activity (Fig. 4b). Most research typically focuses on leisure-time physical activity (PAGAC, 2018; Beenackers et al., 2012) which observes consistent health benefit. For other domains, the evidence is mixed (Quinn and Gibbs 2023), with largely unknown impacts for household physical activity, and even adverse health effects observed for occupational physical activity (Holtermann et al., 2018). There is also evidence suggesting effect modification by domain (Quinn and Gibbs 2023), and

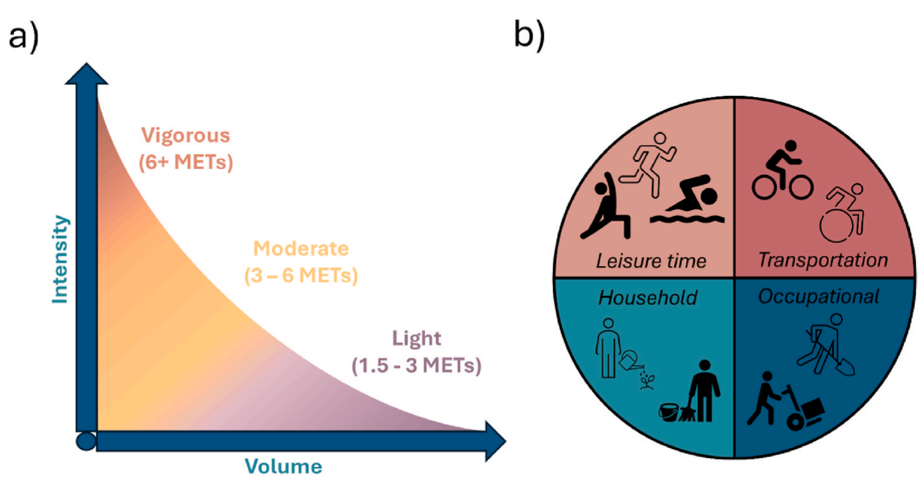

Fig. 4. a) Physical activity intensities, and their interaction with volume for comparable health benefits. Metabolic equivalent of task (MET) represents a physiological measure expressing intensity of physical activity, with one MET being the energy equivalent expended by an individual while seated at rest. b) Physical activity domains.

interactions between them (Prince et al., 2021). Additional studies to measure and examine domain-specific physical activity are needed, and more evidence is also needed on the importance of situational aspects of physical activity (e.g., type and location, and whether it is voluntary), which can be particularly important when considering health inequalities.

2.1.5.2. Assessment methods (objective measurements of physical activity). Physical activity recommendations are based almost entirely on observational studies using self-reported data (WHO, 2020), prone to both recall and social desirability biases often resulting in over-estimation of physical activity levels (Warren et al., 2010). This likely leads to an underestimation of the true association, as evidenced by stronger associations from studies using device-based measurements (Ekelund et al., 2019). Similarly, most observational studies rely on physical activity levels measured only at baseline, again likely under-estimating the true association (Ekelund et al., 2024b). Evidence from a prospective cohort study of Taiwanese adults suggests that associations with all-cause and cardiovascular mortality are stronger when using repeated measures of physical activity (Martinez-Gomez et al., 2022).

Evidence from several large, well-powered studies is now available (e.g., Dempsey et al. (2022), with observed associations orders of magnitude stronger than those using self-report data (Ekelund et al., 2024a). With enhanced granularity (i.e., seconds) allowing short and sporadic bouts of activity to be captured, this evidence-base more accurately reflects the totality of physical activity. This enables a shift from traditionally operationalised and rigid classifications, towards more comprehensive measures including device-measured physical activity energy expenditure (e.g., Strain et al. (2020), or device-measured daily step count, which is more easily understood by the public, and supported as a viable metric for assessing associations between physical activity and health outcomes (PAGAC, 2018). These measures that capture the full spectrum of physical activity more closely align with WHO guidance that "*doing some physical activity is better than doing none*" (WHO, 2020) therefore, observational studies utilising device-based measures are likely to play a prominent role in the development of future physical activity recommendations (Ekelund et al., 2024b). Other methods for assessing physical activity and energy expenditure include, for example, the doubly labelled water method that is considered a gold-standard, or calorimetry approaches, though such methods are expensive and not used in large studies (Ndahimana and Kim, 2017).

The increasing availability of data from smartphones and wearables means device-based measures have the potential to be readily integrated into long-term observational studies. However, many key challenges in the use of device-based measures at the population level remain, including concerns around representative sampling and wear time, validity and reliability, and between-device compatibility (Strain et al., 2022). For example, device-based measures are likely to over-represent privileged populations (Ding and Ekelund 2024). As with traditional measures of physical activity, there is also a need for greater standardisation among the increasing number of consumer wearables providing physical activity measures, which could be achieved through, e.g., advanced harmonisation approaches (Pearce et al., 2020). There is also a need to acknowledge that estimates derived from self-report and device-based measures are ultimately based on conceptually inequivalent approaches (Strain et al., 2022; Welk et al., 2019; Troiano et al., 2014). Consequently, as they cannot be measured on the same scale, it is necessary to pair the right DRF with the right population prevalence measure for correct impact assessment. In order to inform future guidelines, there is an additional need for more device-based evidence for important health outcomes including type 2 diabetes, certain cancers, and mental health (Ekelund et al., 2024a).

Areas of future innovation include integration of biomechanical and physiological data, which may be facilitated by advancements in bioengineering (e.g., skin patches), and the integration of multiple sensors in multiple body locations (Martinez-Gomez et al., 2025). Multi-sensor approaches would allow for better differentiation of activity types and postures, enabling more precise assessments of physical activity compared to approaches based on only one measure. Importantly, it is also recognised that device-based measures may be further complemented by self-report data that may better capture important contextual information (e.g., differentiating leisure time or commuting), allowing for a more accurate total characterisation of physical activity (Martinez-Gomez et al., 2025).

2.1.5.3. Confounding and effect modification (physical activity and environmental exposures). Research has demonstrated how physical activity and air pollution may interact, with physical activity behaviour and health effects potentially moderated by air pollution exposure (Tainio et al., 2021). Evidence from HIAs generally demonstrates health benefits from physical activity outweighing any adverse effects of air pollution exposure (Giallouros et al., 2020; Tainio et al., 2016). In highly polluted areas however this evidence is less certain Lee et al., 2024). The interactions and synergies between physical activity and air pollution are complex, and further stratified evidence (e.g., by time of day, intensity, domain) is needed to increase understanding (Hahad et al., 2023). Research is also limited for other environmental exposures, such as excessive heat or cold that can impact the physiological responses of physical activity (Périard et al., 2021) and may further influence physical activity patterns (Bernard et al., 2021). Also, it has been suggested that performing physical activity in green and blue spaces brings additional health benefits (Yen et al., 2021). Further research is needed to better understand how other environmental exposures may interact with health benefits of physical activity.

2.2. Cross-cutting research needs

Here, we highlight several ongoing challenges and research needs relevant to all pathways and environmental epidemiology more broadly. We focus on multi-exposures and evidence synthesis, that represent two areas of cross-cutting research needs specifically discussed in the workshop, but also highlight several other important cross-cutting topics.

2.2.1. Multi-exposures

The quantification of health impacts of multiple exposures is challenging due to limited ERFs from two or multi-exposure models. ERFs used in HIA are typically derived from single-exposure models. However, populations are simultaneously exposed to multiple stressors and there is growing interest in the investigation of combined effects, and a desire to shift towards a broader exposome paradigm throughout the life-course (Wild, 2005).

Environmental exposures are often correlated (e.g., greenness, air pollution, road traffic noise in Klompmaker et al., 2020)). For example, traffic-related air pollution (TRAP) represents a complex mixture of pollutants, often highly correlated, and it is difficult to assess whether epidemiological associations are due to the direct effects of one pollutant or another, or to the mixture (HEI, 2022). This collinearity (or multi-collinearity when considering multiple exposures) arises due to commonality of sources, such as road traffic, or even meteorological conditions (Gowers et al., 2020). In case of positive correlations and similar directional effects for two exposures, summing the health burden from single-exposure models leads to an overestimation, and is generally avoided in practice (Chen et al., 2024b).

Consequently, several methods and statistical approaches to capture the impact of multiple exposures have been developed (Stafoggia et al., 2017; Maitre et al., 2022), like the 'cumulative risk estimate' (Crouse et al., 2015) or 'g-computation' approaches (Keil et al., 2020). These were employed in epidemiological studies to assess associations of multiple environmental exposures on hypertension (Chen et al., 2024d), stroke incidence (de Bont et al., 2023) and all-cause mortality (Dimakopoulou et al., 2024; Nobile et al., 2024). More studies applied two- or multi-exposure models which adjusted for the confounding effect from the other exposures (Stafoggia et al., 2022; Klompmaker et al., 2019, 2021; Nieuwenhuijsen et al., 2018). Whilst applicable to multiple exposure types, the literature is more developed for air pollution.

A recent study by Chen et al. (2024b) explored how using two-pollutants models can adjust potential under or overestimation of health impacts of air pollutant mixtures. In their work, they found that in two-pollutant models, associations with all-cause mortality for both $PM_{2.5}$ and NO_2 were attenuated compared to single-pollutant models. To demonstrate implications for HIA, they further estimated population attributable fractions (PAFs) using hazard ratios derived from single- and two-pollutant models, finding the former to be 38.6 % larger than the latter (PAF = 0.079 vs. 0.057) (Chen et al., 2024b). They applied the coefficient difference method proposed by COMEAP (COMEAP, 2018), which consists of adjusting coefficients from single-exposure models using coefficient differences for $PM_{2.5}$ and NO_2 from the more limited evidence base of studies with single- and multi-exposure models. They calculated the average coefficient difference between single- and two-pollutant models for $PM_{2.5}$ (0.017) and NO_2 (0.007) and applied this to a more extensive evidence base from the WHO systematic reviews.

While an improvement over single-pollutant models, two- and more complex multi-pollutant models face several challenges (Gowers et al., 2020; Dominici et al., 2010) including: 1) lack of interaction term, 2) multi-collinearity, and 3) transfer of effect. Additionally, relative risks from two-pollutant models, as with single-pollutant models, may also be confounded by other pollutants not routinely assessed (e.g., ultrafine particles, VOCs) (COMEAP, 2018) owing to, e.g., methodological complexity of measurement or limited public health consensus, and therefore whether or not they confound other pollutants cannot yet be accurately assessed. The multi-exposure approach presents many complex challenges, however, it will have significant implications for how we quantify health risks, and how subsequent policies and regulatory standards are designed (Dominici et al., 2010). Future research can also apply the methodology presented by Chen et al. (2024b) to other environmental exposures and outcomes in HIA (Chen et al., 2025). However, applying this methodology or similar to multiple different environmental exposures is likely to introduce complexities related to high-dimensional data, compounding challenges including interaction and multi-collinearity, as well as additional challenges such as nonlinear effects and differing variable types and measurement errors (Yu et al., 2022).

2.2.2. Evidence synthesis and assessment approaches

Systematic reviews and meta-analyses (SRMAs) are increasingly used to synthesise health-effect studies of environmental determinants (Whaley et al., 2016) providing comprehensive, transparent and reproducible summaries of available evidence that guides policy and public discourse (Cooke et al., 2023). However, whilst often considered the “gold standard” for evidence synthesis, the methodological rigour of SRMAs varies, and poorly conducted reviews are prevalent (Forastiere et al., 2024a; Menon et al., 2022; Sutton et al., 2021). Bridging gaps in methodological and quantitative synthesis approaches (Rigaud et al., 2024), and improving how this evidence is applied in practice (Cooke et al., 2023), is necessary to improve the policy relevance of this epidemiological evidence.

Several frameworks exist for evidence synthesis in environmental health, including OHAT and the Navigation Guide (OHAT, 2019; Woodruff and Sutton, 2014). In a critical interpretive synthesis of current SRMA approaches several domains necessary to guide methodological processes are identified (Senerth et al., 2024), including guidance on selection of appropriate qualitative and quantitative synthesis methods, risk of bias assessment, and on reporting methods and results. Notably there is consensus on the importance of risk of bias assessment which, in face of substantial heterogeneity in key concepts considered and the tools/domains available, should be tailored depending on, for example, intended application or study design. Several risk of bias tools to evaluate observational studies on environmental and occupational exposures exist, such as ROBINS-E (Higgins et al., 2024), however there is no consensus on a best approach in these settings (Steenland et al., 2025; Eick et al., 2020). Additionally, integrating broader, more ‘narrative’ assessment in current evidence synthesis and assessment frameworks could ensure greater alignment with features relevant to, and maximize what can be learned from, observational studies in environmental health. As discussed in a Health Effects Institute commentary, existing formal approaches (e.g., GRADE, OHAT) are more oriented towards evaluating the quality of evidence of studies entering a meta-analysis, and less so towards determining the strength and nature of an association (HEI, 2022; Boogaard et al., 2023). Additionally, they often do not include specific criteria relevant to environmental health studies (Forastiere et al., 2024a). Employing a complementary ‘narrative’ assessment may therefore capture some of the important and complex nuances that may be missed otherwise (Boogaard et al., 2023).

In a recent commentary (Shaffer et al., 2025), U.S. EPA scientists outline several practical suggestions to greater facilitate the integration of epidemiological analysis in HIA, and enhance the value of published research. These include several easily implementable reporting practices (e.g., including null and non-significant results, justifying transformations, providing results on original scale, and reporting detailed exposure distribution information) as well as additional modelling practices (e.g., modelling in the low-exposure range, exploring non-linearity, exploring the influence of confounders with a tiered approach). Further recommendations have been provided elsewhere (Nachman, 2011), particularly for air pollution (Forastiere et al., 2024b; Fann et al., 2011). With increasing methodological complexity of SRMA approaches, pairing concise plain-language summaries with technical documentation and engaging scientific advisors will encourage transparent translation of evidence for decision-makers.

Existing evidence assessment approaches may be better tailored for use in environmental epidemiology, such as the growing adaptation and application of the Navigation Guide methodology for assessing SRMAs (Loomis et al., 2022; Teixeira et al., 2021). Another notable approach is the Burden of Proof methodology developed by the Global Burden of Disease (GBD) (Zheng et al., 2022). It utilises a burden of proof risk function, a novel meta-analytical tool for estimating the level of risk closest to the null hypothesis that is consistent with the available data, and provides a consistent way to understand, evaluate, and summarise the cumulative strength of evidence (Zheng et al., 2022). The GBD meta-analytical approaches may differ from other more ‘conventional’ approaches. For example, the GBD method for estimating temperature-mortality ERFs does not employ distributed non-linear lag models to capture lagged temperature effects. Instead, they assume short-term effects to occur on the day of exposure, a more generalisable and computationally manageable approach suitable for their global assessments, but results in potentially conservative or underestimated burdens (Burkart et al., 2021). Similarly, the current GBD approach for establishing $PM_{2.5}$-mortality ERFs integrates household air pollution (and previously active/secondhand smoking (Brauer et al., 2024)) to extrapolate risks at high exposure. This extends coverage to high-exposure regions with limited epidemiological evidence (e.g., many low- and middle-income countries), however introduces uncertainty (Shaffer et al., 2019).

Umbrella reviews, systematic collections and assessments of SRMAs, are being increasingly undertaken to assess, synthesise, and summarise evidence to better inform decision-making (Ioannidis, 2016; Aromataris et al., 2015). Their limitations however include a lack of standardised methods (Shi and Wallach, 2022), and inability to capture recent evidence absent from SRMAs, which may be overcome through inclusion of recent high-quality individual studies (i.e., an Umbrella + review

(Engelmann et al., 2023)). Umbrella reviews also depend on the quality of existing evidence, risking higher-level propagation of errors and biases. Similarly, whether reviewing primary or secondary studies, it remains challenging to identify informative studies and most likely sources of bias (Brunekreef et al., 2024).

2.2.3. Standardised definitions, methodologies, and analyses

Across all exposure pathways we observe a need for standardised definitions (previously discussed, for example, for greenspace), and for standardised methodologies and analyses to allow for meaningful syntheses and comparisons between studies. This should, however, be balanced to ensure that methodological advancement is not limited and provides contextually nuanced insights. Moreover, observing consistency of associations across a diversity of methods (i.e., triangulation) strengthens the confidence in the evidence (Lawlor et al., 2016).

More broadly, this will require greater data harmonisation and collaboration within the scientific community across international and interdisciplinary studies (Dyer et al., 2024a). There is also a need for more open data sources, allowing access to and exploration of how ERFs are constructed. These are available for, e.g., for physical activity (Garcia et al., 2023), heat (Masselot et al., 2023) and air pollution (IHME, 2024).

2.2.4. Incorporation of objective measurements

Objective measurements obtained from personal/wearable sensors are routinely incorporated in physical activity epidemiology (discussed previously in detail) and are increasingly being utilised in environmental epidemiology, particularly for air pollution. New sensor technologies have immense opportunity for exposure and health outcome assessment, with benefits including enhanced individual-level exposure assessment at high spatiotemporal resolution, integration with behavioural and physiological data, and scope for scalable, low-cost data collation (Tonne et al., 2017). However, several considerable theoretical and methodological challenges hinder their wider application, requiring further technological development and research (Doherty et al., 2021).

Data accuracy remains a critical issue (particularly for low-cost sensors) which may result in substantial bias (Ueberham and Schlink, 2018). Consequently, personal sensors require careful assessment and validation prior to application in research (Khreis et al., 2022; Jerrett et al., 2017). Similarly, while GPS-enabled sensors provide valuable temporal data for health research (Kerr et al., 2011), they are often limited in their ability to determine indoor locations due to signal loss (Asaad and Maghdid 2022) limiting their application for investigation of indoor/outdoor exposure differences. Several other limitations, such as device reliability, participant burden, and meteorological interference, inhibit their wider uptake and application, and are discussed elsewhere (Doherty et al., 2021; Helbig et al., 2021).

2.2.5. Consider mobility, and where exposure occurs

In most epidemiological studies, exposure is measured or modelled based on the participants' residential address. However, this practice fails to fully account for the totality of exposure individuals experience (i.e., exposure misclassification, or measurement error), and thereby introduces uncertainty, potentially leading to biased risk estimates. This wider issue remains a topical area of active research across various environmental exposures (Katsouyanni and Evangelopoulos, 2022; Wei et al., 2022; Wilt et al., 2023). Here, we focus specifically on exposure misclassification relating to individual and population-level mobility, and indoor/outdoor differences.

Exposure estimates based on static measurements largely disregard individual daily mobility, leading to inconsistent or unreliable estimates of individual exposure (Kwan, 2012, 2018) across various environmental factors which depend on mobility (Cai and Kwan, 2024). At the population level however, as highlighted by recent publications which observed similar health effects using residential vs. dynamic exposure assessment of air pollution exposure, the overall bias in epidemiological studies may be small (Hoek et al., 2024; Ntarladima et al., 2021). A large census-based cohort study in Canada reported nearly identical associations with both residential and time-weighted average exposure of residential and work address (Christidis et al., 2021) but such associations may be context-specific. deSouza et al. (2024) found in a health impact study slightly smaller estimates of annual mortality attributable to NO_2 (−2 %) and $PM_{2.5}$ (−0.3 %) when deriving exposure levels based on home, instead of home and workplace locations. More research is necessary to understand the extent residential-based exposure assessment leads to bias for other mobility-dependent environmental exposures, not just air pollution for which there is more information (Hoek et al., 2024).

Additionally, in recognising that individuals typically spend around 80–90 % of their time indoors, there is a need to further consider differences between indoor and outdoor exposures. Temperature-related research rarely incorporates indoor environmental conditions that can greatly differ from outdoor environments (Nazarian and Lee, 2021), as demonstrated in a global study identifying weak-to-moderate relationships between indoor and outdoor temperatures (Hou et al., 2023). This relationship may vary based on ambient conditions (i.e., seasonality), and different epidemiological associations may be observed based on this exposure misclassification (Xia et al., 2024). For transport noise, some studies provide attenuation factors for indoor levels at the population level (Foraster et al., 2014; Locher et al., 2018); however, these can be difficult to apply as they depend on building characteristics and personal behaviours (e.g., window opening), as well as underlying exposure-effect pathways (direct vs. indirect). Even for air pollution, where comparatively more research has been undertaken, many knowledge gaps remain, complicated by the multitude of indoor environments (e.g., homes, schools) and variety of sources therein, as well as personal behaviours that may influence them (e.g., ventilation) (Vilcins et al., 2024a,b). There is also a need to consider factors that may influence the effect of indoor-outdoor relationships such as housing quality (Ferguson et al., 2021).

Future epidemiological research could further integrate studies that account for exposure in other microenvironments, such as in transport or indoor environments (Smith et al., 2016; Ferguson et al., 2023). This may be actualised by capitalising on personal/wearable technologies and smartphone-based mobility data that capture not only what individuals are exposed to, but where this exposure occurs (Birenboim et al., 2021). Other opportunities include microsimulation and agent-based modelling that can characterise individual behaviours and exposures for whole populations with high spatiotemporal and sociodemographic resolution (Staves et al., 2023).

2.2.6. Spatial resolution of analysis

Epidemiological studies exhibit sensitivity to the spatial scale of exposure estimates and in practice, the use of finer spatial resolution is thought to result in a higher effect size and smaller bias (Wei et al., 2022; Vodonos et al., 2018). For example, in a CanCHEC (Canadian Census Health and Environment Cohort) study researchers observed stronger associations between air pollutants and lung cancer and respiratory mortality at smaller spatial scales (e.g., 1 km x 1 km, vs. 10 km x 10 km) (Crouse et al., 2020). Non-accidental and cardiovascular mortality differed less with spatial scale. For noise, as demonstrated in a Swiss study on myocardial infarction mortality, higher resolution estimates (e.g., façade estimates and fine scale noise maps (10 x 10 m)) are preferred to coarser scale estimates which can introduce more bias and attenuate health effect estimates (Vienneau et al., 2019). Similarly for greenspace, map resolution and spatial scale should be considered and may explain observed heterogeneities (Wang et al., 2024).

Relatedly, spatial resolution should be considered when estimating health burdens and impacts. Several air pollution studies have demonstrated how exposure and mortality estimates are sensitive to the spatial resolution of exposure maps (Korhonen et al., 2019; Fenech et al., 2018). In a recent HIA study in Colorado, USA, deSouza et al. (2024)

demonstrated that the use of county-level NO_2 and $PM_{2.5}$ estimates, compared to remotely sensed 1 km x 1 km resolution estimates, resulted in a 50 % and 10 % decrease in attributable mortality, respectively, related to fine-spatial resolution variability of air pollution exposure. The spatial resolution of health data should also be considered in HIAs (Jaikumar et al., 2025). For example, in the U.S. deSouza et al. (2024) demonstrated the use of block-level baseline mortality rates, instead of county-level data, yielded a 10 % higher estimated annual mortality attributable to $PM_{2.5}$ and NO_2. In India, Chowdhury and Dey (2016) similarly demonstrated that the use of a uniform nationwide baseline mortality rate dataset, instead of state-specific baseline mortality rates, resulted in ~15 % lower $PM_{2.5}$ attributable premature mortality estimates. Increased efforts to provide high-resolution exposure, demographic and health data are required, and researchers should prioritize exploring associations at multiple spatial scales (Dyer et al., 2024a; Dyer et al., 2024b; Jaikumar et al., 2025). Moreover, incorporating finer-scale spatial exposure data can help identify localised hotspots, and uncover environmental inequalities, allowing for prioritisation of local interventions (Mitsakou et al., 2019). Spatial scale should also be considered when examining multiple exposures, as these may be measured or modelled with varying precisions, potentially leading to a transfer of effect.

2.2.7. Evidence for morbidity outcomes

Traditionally, with the exception of noise, HIA studies have focussed more on mortality impacts than morbidity. For example, air pollution HIAs have largely focussed on all-cause and cause-specific mortality, based on ERFs synthesised from long-term epidemiological evidence (Forastiere et al., 2024b). For some health determinants, this may reflect a lack of epidemiological evidence for morbidity. For example, there are comparatively fewer studies for temperature-related morbidity (Cheng et al., 2019), and while there is evidence for some morbidity outcomes (e.g., emergency hospital admissions), the evidence-base is stronger and more robust for all-cause mortality, with mortality data being more readily accessible (UK Health Security Agency, 2024). Morbidity has significant negative societal and economic impacts, through both direct and indirect costs of illness, including medical expenditures, rehabilitation costs, informal care, and labour productivity losses, and individual loss of utility or welfare cost (OECD, 2019). Morbidity ERFs could therefore allow for more comprehensive assessment of the cost of environmental stressors to inform policy analysis (Ru et al., 2023).

Additionally, there is also a need to consider multimorbidity (the co-occurrence of two or more health conditions in an individual) that impacts a substantial, and likely growing, proportion of the population. Environmental determinants are associated with increased risk for several chronic conditions (such as diseases of the circulatory and respiratory systems, neurological disorders like dementia, and metabolic outcomes like diabetes), and through their accumulation, may be associated with multimorbidity. Research has demonstrated associations between air pollution and multimorbidity, suggesting certain organ systems may be more vulnerable than others (Ronaldson et al., 2022). The evidence base however is sparse, and multifaceted and complex by nature (The Academy of Medical Sciences, 2018), but due to its substantial economic and societal burden (Tran et al., 2022) warrants greater consideration.

2.2.8. Evidence from population sub-groups

Across all exposure pathways, there remains a paucity of sub-group ERFs, thereby meaning HIAs cannot produce stratified estimates, precluding equity-informed policy recommendations (Dyer et al., 2024b). More evidence is needed for specific sub-groups (e.g., stratified by age, sex, race/ethnicity, socioeconomic status, and those with pre-existing health conditions) who may be more susceptible and/or vulnerable to adverse health effects. For example, those of lower socio-economic status (SES) are more likely (though not consistently) to be exposed to higher levels of air pollution, and generally, stronger associations between air pollution and health outcomes are observed (Hajat et al., 2021). Similarly, stronger associations for heat-related mortality and morbidity are found for the elderly, people experiencing homelessness, and low SES groups (Benmarhnia et al., 2015; Noor et al., 2025).

The implications of sub-group ERFs for health estimates have been highlighted. For air pollution, recent analyses from deSouza et al. (2024) showed the use of racial/ethnic-specific CRFs in place of an overall CRF in the U.S. resulted in estimates of mortality attributable to NO_2 differing by as much as a factor of 2.9. Other research in the U.S. has also reported steeper ERFs for $PM_{2.5}$ and mortality for Black persons than White persons (regardless of income) (Josey et al., 2023). However, a systematic assessment of findings across evidence-base is lacking. For temperature-mortality associations, a global study observed significant variations by age, with the oldest age groups almost universally observing higher heat and cold risks/burdens than the youngest (Scovronick et al., 2024). Producing reliable estimates for sub-group specific CRFs, and to explain opportunities for transferability, caveats and limitations, however, requires very large populations to reliably estimate them.

Additionally, research should also assess differences between urban and rural populations. For example, while comprehensive temperature-related mortality assessments are available at the local-area (Gasparrini et al., 2022) and regional scale (Masselot et al., 2023), they are generally restricted to urban populations that typically experience higher levels of temperature stress due to the urban heat island effect (Manoli et al., 2019). Evidence from rural areas is largely still missing, and the existing evidence reveals conflicting results with regard to the effect of urbanisation on heat vulnerability which may relate to a number of factors including access to health care services, greenspace, type and quality of housing, lifestyles and cultural differences (Lee et al., 2022; López-Bueno et al., 2022). Further investigation of urban/rural differences may also help reveal important contextual factors and drivers of health (for example, considering the 'paradox' of high greenspace and poor health in rural Central Appalachian communities (Dong et al., 2024)) that should be considered to ensure targeted interventions achieve expected benefits.

2.2.9. Evidence from low- and middle-income countries

There remains a lack of epidemiological evidence from many low- and middle-income countries (Rogowski et al., 2025; Brauer et al., 2024). Expansive regions including Africa, the Middle East, and South Asia remain poorly represented (Health Effects Institute, 2022; Gasparrini et al., 2024). Expanding research to other regions could help elucidate largely unknown drivers of geographical heterogeneity. Additionally, low- and middle-income countries frequently experience higher levels of harmful environmental exposures, and current epidemiological evidence is often lacking at these higher exposure ranges. To enable research in low- and middle-income countries, there is a need for enhanced and practical exposure assessment, for which low-cost sensors, remote sensing, or land-use regerssion models may be well-suited (Clark et al., 2022; Brum et al., 2024). Additionally, there is a need for more longitudinal studies in low- and middle-income countries (Chen et al., 2023c; Rojas-Rueda et al., 2021). This could be facilitated through better collaboration and development of multinational studies which through mutual contribution, method and data sharing, can advance epidemiology at a global scale (Gasparrini et al., 2024). It will be essential for funders to expand their reach to these regions, which should be done in a way that acknowledges imbalances of power and resources (Charani et al., 2022).

Common research practices such as limiting literature searches to articles published in English, further contributes to a loss of available knowledge from low- and middle-income countries, and may ultimately bias effect estimates in meta-analyses (Neimann Rasmussen and Montgomery, 2018). Review teams should therefore consider resource translation services or collaborative screening when language skills are limited.

By strengthening research capacities in low- and middle-income countries, we may unravel unexplained heterogeneities present across epidemiological studies and better understand risk over global exposure ranges. This process involves building both individual and institutional research capacities in these settings, which relies not just on provision of funding but in fostering research culture and local ownership (Malekzadeh et al., 2020). This capacity building process must also acknowledge and navigate prevailing power asymmetries in the global health research system, and seek, through decolonisation of research practices, to foster more equity-oriented approaches (Kumar et al., 2024).

2.2.10. Generalisability of evidence

An ERF typically synthesises available evidence into a single global estimate, derived from a wide range of participants drawn from various study settings. Applying a single global ERF in a HIA provides several advantages: reduced uncertainty by pooling data from multiple sources, streamlined application while enabling greater comparability, and providing a coherent basis for developing broad polices and recommendations (Forastiere et al., 2024b). Consequently, global ERFs may be recommended for quantitative HIA (COMEAP, 2022a), however in practice, this decision is much more nuanced.

The generalisation of an ERF, derived from one population or context, may introduce systematic biases when applied to another setting which may not share the same characteristics. This issue is particularly acute given that most epidemiological evidence originates from high-income countries, notably Western Europe and North America. For example, ERFs for heat-related risk are primarily derived from studies of temperature regions that are generally high-income with better access to adaptive measures, which may not be representative of low- and middle-income countries in the tropics with higher temperatures and less adaptive capacity (Green et al., 2019). Between different populations, several factors such as susceptibility, baseline health status, diet, or genetic background may differ and influence health risks (Singh et al., 2024; Eisen et al., 2024; Lim et al., 2019; COMEAP, 2025). Relatedly, such factors may also influence each other, as well as influencing both risk and underlying health, introducing further complexity requiring more advanced statistical methods (Lloyd et al., 2023). In place of a single global ERF, a regionally (or locally) derived ERF may be employed that may better represent local population characteristics or environmental conditions, and therefore may be better suited for HIA studies targeting specific populations or regions (Pascal et al., 2016). Ultimately, the decision on whether to employ a global or regional ERF will depend on several factors such as the nature of the assessment, the specific policy question, and the intended application (Forastiere et al., 2024b), as well as the actual presence of regional heterogeneity between summary effect estimates, if known (Lee et al., 2023).

In some cases, ERFs derived from a relevant population may not be available. In many low- and middle-income countries, epidemiological evidence is often scarce, meaning HIA studies must rely on ERFs derived from, primarily, high-income settings resulting in uncertainties in estimated health impacts (Thondoo et al., 2022). Accordingly, there is a need for further research and guidance on the adaptation of epidemiological evidence to different contexts, specifically when epidemiological evidence is presently unavailable. Future research should explore how advanced statistical methods (e.g., Bayesian models) may be utilised to adjust estimates to these contexts and, when applied, uncertainty estimates should be provided (Nethery and Dominici 2019).

Evidence generalisability remains an active area of research (Lesko et al., 2017), encompassing other aspects not discussed here, such as extrapolating estimates beyond observed exposure data (Nethery and Dominici 2019), and non-linearity (Cox, 2020), and requires further consideration to reduce uncertainties introduced.

2.2.11. Temporal validity of evidence

The temporal validity of derived ERFs (i.e., how long published results be expected to remain valid and applicable to HIA) remains a critical issue. Since ERFs from SRMAs represent a snapshot of the available evidence at the time searches were conducted, confidence in their findings may degrade over time as new evidence emerges. For instance, clinical evidence from a report assessing 100 systematic reviews indicated that 23 % of reviews were ‘out of date’ (i.e., substantively changed conclusions relating to statistical significance or effect magnitude) within two years, and 7 % were already outdated at time of publication (Shojania et al., 2007). This however may not hold true in all contexts, and while new studies can always be expected, the emergence of new evidence may not translate to a change in ERFs, particularly when there is already a large body of evidence like for air pollution. Further investigation into the temporal validity of published ERFs in an environmental health setting is therefore warranted, and from this, methodological guidance on if, when, and how evidence syntheses should be updated may be further developed. Existing guidance from the Cochrane Collaboration on systematic reviews of interventions, for example, states all Cochrane Reviews should be periodically assessed to determine whether an update is necessary, for which a decision framework for deciding when and how it should be updated is also available (although a general guideline of every two years is frequently cited) (Cumpston and Flemyng, 2024). Other relevant research directions include the viability, and practicality, of “living” systematic reviews that are continually updated to incorporate new evidence as it emerges (Elliott et al., 2017). Living systematic reviews are particularly well suited when:1) the question is a priority for decision-making, 2) the certainty in existing evidence is low and therefore, new evidence is likely to influence current findings, and 3) new emerging evidence is likely (Elliott et al., 2017). Additionally relevant is the concept of an “exit” meta-analysis, that would signal no further research is needed once a meta-analysis has conclusively addressed a research question (Abdulmajeed et al., 2025).

Temporal validity becomes particularly pertinent when considering the world’s rapidly changing exposure patterns. Already, for example, we have observed the substantial impacts of regulatory and technological interventions on global air pollution emissions (Oreggioni et al., 2022) resulting in changes to the TRAP mixture. Notably, climate change is expected to impact future temperature-related risks (Masselot et al., 2025; UK Health Security Agency, 2024). Elevated temperatures may also influence the vegetation composition of urban greenspaces and the extent to which they confer benefits due to air pollution mitigation (Allen et al., 2010). Elevated temperatures can also accelerate photochemical reactions resulting in higher O_3 concentrations in urban areas and increased biogenic VOC emissions (Chang et al., 2023). Additionally, due to increasing wildfire emissions, climate change is further resulting in changes in air pollution composition (Xu et al., 2023). In order to better understand the temporal validity of current ERFs, it will be necessary to consider changing exposure patterns, co-exposures and modifying factors (Vanos et al., 2020; Zhao et al., 2025).

2.3. Implications for quantitative health impact assessment and policy

HIA, or health impact modelling, enables quantitative understanding of the impacts of urban planning and transport scenarios on population health (Nieuwenhuijsen et al., 2019). The basic quantitative HIA process is well-established (WHO, 2016), and typically involves the use of exposure data and baseline health data, combined with ERFs to quantify health effects (Fig. 5). By comparing the health burden of counterfactual exposures to environmental stressors (e.g. air pollution, noise) and behaviours (e.g. physical activity) attributable to a policy or hypothetical scenarios, these assessments are intended to support evidence-informed decision-making. Quantitative risk assessment approaches play a central

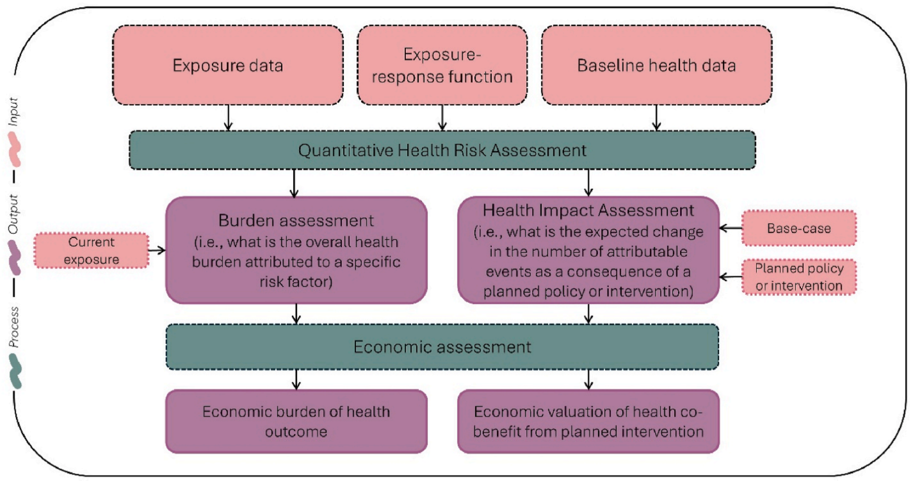

Fig. 5. Simplified schematic of quantitative health risk assessment processes

role in advancing public health and policy. For example, quantitative HIA has played a crucial role in the formulation of air quality guidelines and regulatory criteria in Europe and the U.S. (Forastiere et al., 2024b), and burden of disease approaches like the GBD have provided substantial contribution to the development of global health policy (Murray, 2022). In this section, we further explore the implications of applying ERFs in the HIA process, and present several directions that could lead to more impactful assessments.

2.3.1. ERFs in the HIA process

ERFs are key inputs in quantitative HIAs (Fig. 5), but are often a substantial source of uncertainty, leading to heterogeneity in health impacts (Khomenko et al., 2021; Barboza et al., 2021; Castro et al., 2022; Sohrabi and Khreis, 2020; Malmqvist et al., 2018). In a review of global estimates of mortality attributable to air pollution (Pozzer et al., 2023), the choice of ERF was found to be the most significant factor of disparity between studies. Most evidence comparing uncertainties across different HIAs is available for air pollution. Future studies should explore how HIAs of different environmental health determinants respond to different model inputs. Other inputs and methodological choices associated with differences in estimates include differences in 1) exposure scales, 2) demographic data, and 3) assumptions in exposure range, as well as 4) the choice of counterfactual scenario (Pozzer et al., 2023; EEA, 2022). Importantly, uncertainty persists throughout all phases of quantitative health risk assessment. Differing sources and characteristics of these uncertainties have been described by different frameworks (Knol et al., 2009; Briggs et al., 2009), and may further interact in different ways in their contribution to overall uncertainty (Pozzer et al., 2023). Value of Information approaches can assess where to best invest in filling data and input gaps by mapping impacts of various input parameters on total uncertainty (Schroeder et al., 2025).

2.3.2. Selecting ERFs for application in HIA

ERFs for HIA application are frequently drawn from existing literature (Benavides et al., 2022). Selecting an ERF from the multiplicity of published SRMAs however remains an ongoing challenge (Rigaud et al., 2024), with a growing, heterogeneous body of evidence leading to uncertainty around selecting the most accurate or appropriate ERFs to apply in HIA (Dyer et al., 2024b). For example, city- and age-specific temperature-mortality ERFs developed by Masselot et al. (2023) represent the best available evidence, utilised in several HIA studies (Lungman et al., 2025; Khomenko et al., 2025). Similarly, global-scale studies often employ GBD-derived ERFs which apply consistent methodological approaches with explicit uncertainty quantification, and comprehensive integration techniques to ensure global exposure coverage. The ERF selection process is nuanced, depending on factors including research question and intended purpose, evidence availability, or policy considerations. Accordingly, the process should be proportionate to the scale of anticipated impact, in recognising that not all decisions require the same granularity.

Forastiere et al. (2024a), in a specific attempt to overcome umbrella review limitations, determined reliable ERFs for morbidity outcomes to apply in a HIA on long-term air pollution exposure. Their approach first uses causality determinations provided in the U.S. EPA's ISAs as the basis for pollutant-outcome pair selection. Thus ISAs, representing the most authoritative causal assessment based on comprehensive synthesis and evaluation of available evidence, are leveraged to underpin selection of pollutant-outcome pairs with the most robust scientific evidence available. Then, they undertook a systematic literature search to identify SRMAs of relevant morbidity outcomes, which were then appraised to select those regarded as credible sources of ERFs for use in HIA. If necessary, any identified errors were corrected, and an updated meta-analysis was undertaken. Finally, they provide a classification of outcomes to provide recommendations on the reliability of quantification if applied in HIA. Several ERFs related to the incidence (onset) of disease associated with long-term exposure to $PM_{2.5}$ and NO_2 were proposed and, the study provided information regarding the range of mean exposures for which the uncertainty of a risk assessment is minimised.

Subsequently, Forastiere et al. (2024b) proposed a structured and comprehensive framework for selecting an appropriate ERF (Fig. 6). In this framework, causality determination, methodological quality, and the confidence in the evidence all contribute towards the selection process. However, while we must be certain that a health determinant is causally related to a specific outcome before confidently quantifying its impact, relying solely on ISAs as basis for inclusion may be a conservative approach. Limitations of using ISAs include their currency (e.g., the last assessment for NO_2 was conducted in 2016) that risks omission of emerging hazards (i.e., recently identified determinants or effects) (Rigaud et al., 2024). This framework has since been applied, for example, to analyse the scientific evidence of health risks related to chemicals included in the EU Ambient Air Quality Directive (AAQD) (Orru et al., 2025).

2.3.3. Improving the HIA process and its impact

Ultimately, uncertainties in the HIA process complicate the communication of environmental health risks to policymakers and the public. Crucially, such uncertainties are inherent in all parts of the policy-making process and not HIA; nevertheless the acknowledgement and quantification of this uncertainty, which should be proportionate to

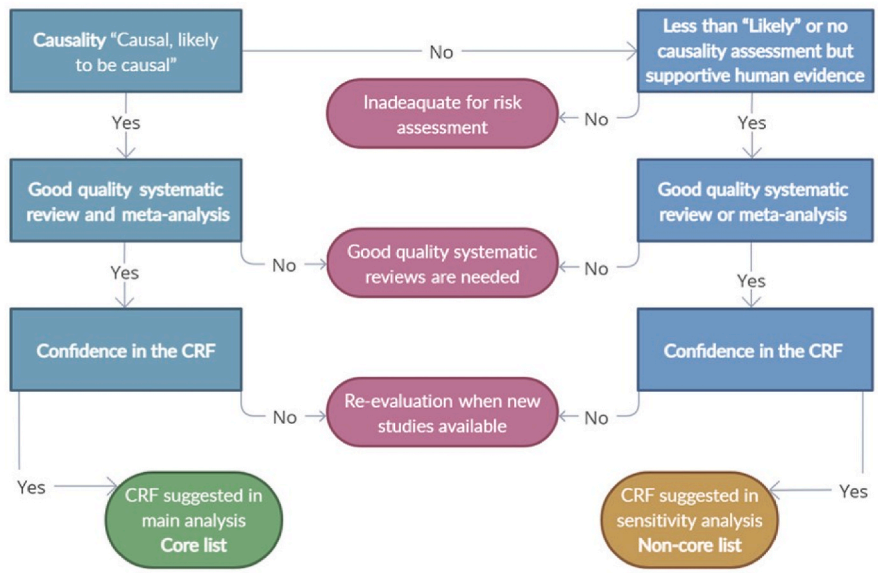

Fig. 6. Schematic representation of the steps in choosing the appropriate concentration-response function (CRF). Figure from Forastiere et al. (2024b), licensed under CC BY-NC-ND 4.0 (http://creativecommons.org/licenses/by-nc-nd/4.0/).

impact and complexity, serves to better support policy-making (Azzini et al., 2020). While there are existing resources to provide guidance and best-practice in conducting HIA, e.g. from WHO (WHO, 2025) or U.S. EPA (US EPA, 2017), there is a pressing need for better, more coordinated resources for improving HIA processes. In addition, increasing fluency of environmental epidemiologists in HIA processes, and vice versa, could facilitate greater consideration of data needs when planning and presenting research (Shaffer et al., 2025). Creating a common understanding among producers and users is essential in avoiding misinterpretation, promoting data collection, and addressing knowledge gaps.

Additionally, we note that the HIA process could more effectively contribute to policy development by integrating health evidence with wider socio-economic considerations. While an HIA can assess physical health impacts associated with environmental stressors, it typically does not account for their broader socio-economic costs, such as the cost of illness, lost productivity, well-being or reduced welfare. Because policy decisions often require cost justification and must balance pragmatism, feasibility, and social acceptability, there is a need for stronger recognition of, and integration between, health impact evidence and socio-economic valuation. Reconciling these outputs would ideally guide the design of more comprehensive and effective policies for improving population health.

Similarly, while a HIA can provide evidence in support of policy or hypothetical scenarios, there remains a need to evaluate the health and equity impacts of policies and interventions more broadly (Garber et al., 2024). This should be conducted at all stages of the policy process (Benavides et al., 2022) and there are methods (e.g., synthetic control methods, difference-in-difference) which can provide valuable evidence on the longitudinal effects of measures accounting for challenges (for example, the frequent co-occurrence of policy measures) (Garber et al., 2024). In order to monitor policy implementation more effectively, measurable policy targets, that are often absent, are also required (Lowe et al., 2022).

Finally, we acknowledge that our focus lies solely on the quantitative aspect of HIA. However, in order to provide a comprehensive assessment, it is essential to also incorporate qualitative and participatory aspects of HIA (Nieuwenhuijsen et al., 2017).

3. Conclusion

We have provided an expert-guided, in-depth discussion focussed on exposure-response functions and their application to quantitative health risk assessment. We critically synthesise and assess a large, disparate and diverse body of literature, mapping knowledge gaps and proposing specific areas for further research. Crucially, we show that the estimation, selection, and application of ERFs is highly nuanced and context-dependent, underscoring the need for critical assessment of their application and more systematic and transparent approaches to strengthen their utility for policy-making. The proposed research agenda is intended to accelerate the translation of scientific knowledge into actionable strategies that support healthier and more sustainable cities through urban and transport planning. Our recommendations draw from an international workshop that convened experts and stakeholders across disciplines, highlighting the importance of continued interdisciplinary collaboration. We encourage similar activities to provide a forum for generating new research ideas, advancing methods, and fostering knowledge exchange across sectors and geographies. Importantly, future efforts must prioritize equity, including participation and perspectives from low- and middle-income countries.

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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.

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Data availability

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

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