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Biodiversity and human health: a scoping review and case studies on underrepresented linkages

Jake M. Robinson[a,b*], Andrew C. Breed[c,d], Araceli Camargo[e], Nicole Redvers[b,f], Martin F. Breed[a]

[a]College of Science and Engineering, Flinders University, Bedford Park, SA, Australia.

[b]inVIVO Planetary Health, New Jersey, USA

[c]Epidemiology and One Health Section, Department of Agriculture, Water, and the Environment, Canberra, ACT, Australia

[d]School of Veterinary Science, University of Queensland, Gatton, Qld, Australia

[e]Centric Lab, London, United Kingdom

[f]Department of Family & Community Medicine, University of North Dakota School of Medicine & Health Sciences, Grand Forks, North Dakota, USA

***Corresponding author**: Jake M. Robinson, jake.robinson@flinders.edu.au

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ORCIDs: JMR 0000-0001-8108-3271; NR 0000-0001-8521-2130; ACB 0000-0002-3439-9510; MFB 0000-0001-7810-9696

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Abstract

Mounting evidence supports the connections between exposure to environment types—such as green spaces and biodiversity—and human health. However, the mechanistic links that connect biodiversity (the variety of life) and human health, plus the level of supporting evidence, are less clear. Here, we undertook a scoping review to map the links between biodiversity and human health, and summarise the levels of associated evidence using an established weight of evidence framework. Distinct from other reviews, we provide additional context regarding the environment-microbiome-health axis, evaluate the environmental buffering pathway (e.g., biodiversity impacts on air pollution), and draw upon expert opinion to provide case studies on three underrepresented linkages. The case studies include (1) biodiversity and Indigenous Peoples' health, (2) biodiversity and urban social equity, and (3) biodiversity and COVID-19. We observed a moderate level of evidence to support the environmental microbiota-human health pathway and a moderate-high level of evidence to support broader nature pathways (e.g., green space) to various health outcomes, from stress reduction to enhanced wellbeing and improved social cohesion. However, studies of broader nature pathways did not typically include specific biodiversity metrics, indicating clear research gaps. Further research is required to understand the connections and causative pathways between biodiversity (e.g., using metrics such as taxonomy, diversity/richness, structure, and function) and health outcomes. There are well-established frameworks to assess the effects of broad classifications of nature on human health. These can assist future research in linking biodiversity metrics to human health outcomes. Our case studies on underrepresented linkages highlight the roles of biodiversity and its loss on urban lived experiences, infectious diseases, and Indigenous Peoples' sovereignty and livelihoods. More research and awareness of these socioecological interconnections are needed.

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INTRODUCTION

Human health and well-being have been linked at a variety of spatial and temporal scales to exposure to green spaces (terrestrial environments with vegetation), blue spaces (aquatic environments) (Robinson et al. 2021; White et al. 2021), as well as biodiversity (the variety of life in a given environment) (Romanelli et al. 2015; Flandroy et al. 2018; Marselle et al. 2021; Wabnitz et al. 2020). However, the literature on these links generally lacks a clear interpretation and synthesis of the mechanisms involved and the levels of supporting evidence. Here, we produce a scoping review of the links between biodiversity, green spaces, and blue spaces and human health and the levels of supporting evidence via an established weight of evidence framework. Distinct from previous reviews (e.g., Lovell et al. 2014; Aerts et al. 2018; Houlden et al. 2021), we provide additional context regarding the environment-microbiome-health axis, evaluation of the environmental buffering pathway (e.g., biodiversity impacts on air pollution and urban heat island effects), and comparative green space data. We also draw upon expert opinion to provide three case studies on underrepresented linkages in the literature. The linkages include (1) biodiversity and Indigenous Peoples' health, (2) biodiversity and urban social equity, and (3) biodiversity and COVID-19.

Definitions

Biodiversity, green space, and blue space

The term "biodiversity" is a contraction of "biotic diversity" or "biological diversity" and refers to the variety of life on Earth; from the diversity in genes and traits to species- and ecosystem-level diversity. The term was popularised in the mid-1980s by the late evolutionary biologist E.O. Wilson's 1988 book *Biodiversity*. The International Union for the Conservation of Nature (IUCN 1980) summarised early notions of the variety of life as providing both investment and insurance benefits. The focus on the importance of the variety of life for ecosystems and human health and wellbeing was echoed later in the Convention on Biological Diversity's (CBD) definition of "biodiversity" and more recently in the Intergovernmental Platform on Biodiversity and Ecosystem Services (IPBES, 2019).

The term "green space" is slightly more ambiguous and has been defined as "*an area of grass, trees, or other vegetation set apart for recreational or aesthetic purposes in an otherwise urban environment*" (Oxford Languages, 2021). However, Taylor and Hochuli (2017) found in their review of 125 studies that two broad interpretations of green spaces are generally used: (a) green space as synonymous with nature (which itself is challenging to define), and (b) green space as explicitly urban vegetation. The term "blue space" is defined as "*outdoor environments – either natural or manmade – that prominently feature water and are accessible to humans either proximally (being in, on, or near water) or distally (being able to see, hear or otherwise sense water)*" (Grellier et al. 2017). While this scoping review focuses primarily on biodiversity, many of the studies we included consider human health and wellbeing associations using green and/or blue space typologies. Therefore, a considerable amount of literature also covers these elements. The skewed abundance of studies using only broad environmental typologies further highlights the lack of biodiversity metrics used in health-association studies, which is a valuable insight in and of itself.

Mechanisms and pathways

For this scoping review, "mechanisms" refer to the individual or set of interactions that occur between a stimulus (i.e., a particular component of biodiversity, such as trees or microbiota) and the health-associated response (e.g., immune regulation). We categorise these mechanisms into five broad nature-health pathways, whilst recognising there is a degree of interconnectedness:

a) Biological (e.g., physical interactions between humans and other biological constituents of the natural world, such as microbiota or plant volatile organic compounds)
b) Psychological (e.g., interactions between stimuli in natural environments and the human affective and cognitive systems)
c) Social (e.g., features, spaces, and interactions that promote social activities)
d) Physical activity (e.g., features, spaces, and interactions that facilitate physical exercise)
e) Environmental buffering (e.g., features and interactions in the natural world that physically buffer the adverse effects of pollution)

It is important to note that in addition to health benefits, there are also health dis-benefits (i.e., elements of nature exposure that cause harm). These will also be highlighted and summarised in this review.

Health outcomes

Health outcomes measure a change in the health status of a person, which can be attributed to the given mechanism within the broad pathways as defined above. Table 1 shows an example of a health outcome for each nature-health pathway.

Table 1. Example of a health outcome for each nature-health pathway.

Pathway	**Health outcome example**
Biological	*Immune regulation* as a result of exposure to diverse environmental microbiota.
Psychological	*Reduced anxiety* as a result of exposure to calming and restorative environments.

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Social	*Reduced all-cause mortality risk* as a result of social cohesion and conviviality (social isolation is an important risk factor for mortality).
Physical activity	*Improved cardiovascular functioning* as a result of physical activity in natural environments that are conducive to exercise.
Environmental buffering	*Respiratory system benefits* as a result of reduced air pollution by natural features such as trees.

Evidence level

Appraising the quality of the evidence is a vital part of research syntheses and evidence-based practice. The hierarchy of evidence is typically represented as a pyramid, with the weaker level of evidence near the base of the pyramid, and systematic reviews, meta-analyses, and clinical evidence-based guidelines at the top with higher validity (Pandis, 2011). We have adapted the evidence pyramid and included a scoring system that corresponds to the level of evidence (Fig. 1), which we use in this scoping review to weigh the summary of evidence for each study (Table 2). It is important to note that appropriate methodologies are required in any study, regardless of its level of evidence. However, the quality of methods is not incorporated by the pyramid of evidence and instead is evaluated during the assessment of each study identified by the review process.

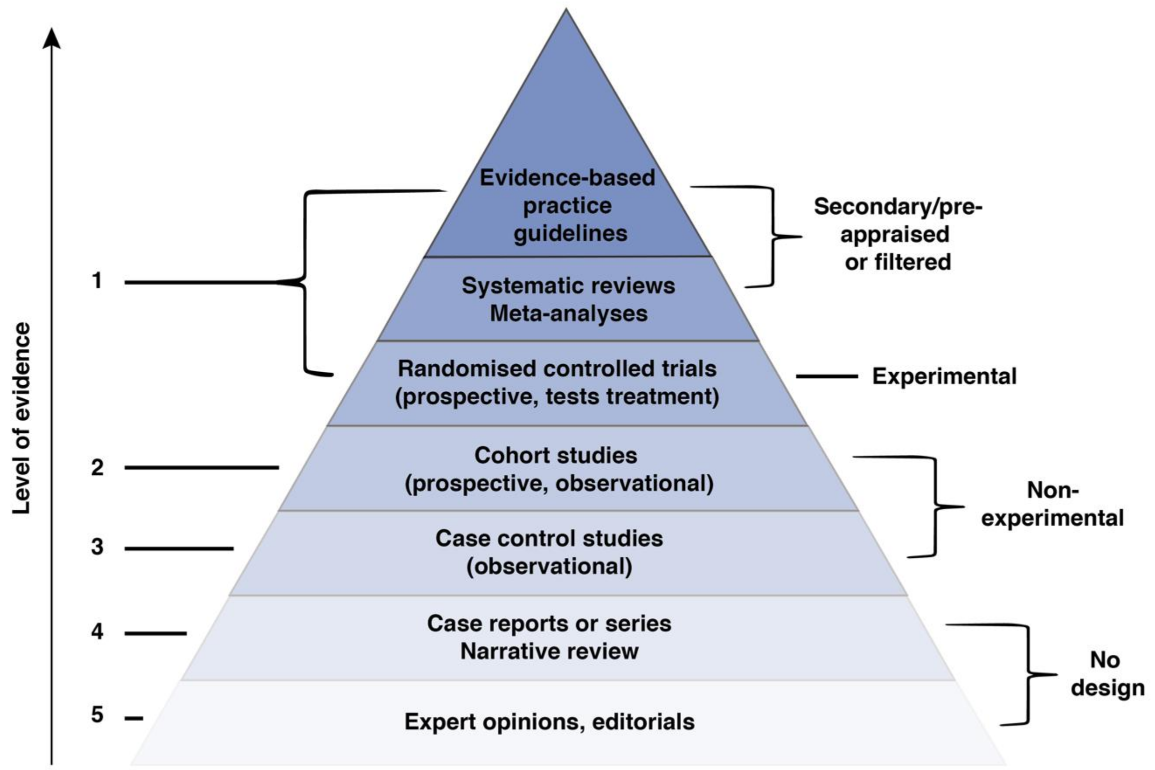

Fig. 1. Research evidence pyramid, where 1 is the highest level of evidence and 5 is the lowest. Refer to Table 2 for a summary and level of evidence. Adapted from Forrest and Miller, 2001.

Scoping review process and structure

We carried out a literature search using four databases and literature search engines, including Web of Science, Scopus, PubMed, and Google Scholar (particularly for grey literature). The date of the original literature search was July 2021 and was updated in February 2022. A list of key search terms was developed (e.g., “biodiversity” AND “health” “nature” AND “wellbeing” “biodiversity” AND “air quality” “green space” AND “wellbeing” “biodiversity” AND “physical activity”). These were refined and entered into the literature databases and search engines using Boolean operators to acquire relevant scientific literature for the review. The search identified 8,524 studies as potentially relevant. When sufficient literature was collated, and duplicates were removed, the title and abstract of each

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potentially relevant article were screened. The links between biodiversity, green space, and blue space with human health and wellbeing were then evaluated, along with the level of supporting evidence and methodologies used. Papers were considered for detailed evaluation if they were written in English and if they mentioned aspects of biodiversity on physical and psychological health outcomes. This resulted in 79 studies being included in this review. The full papers for each study were acquired for evaluation. The results of this data collation and evaluation process formed the basis of the scoping review. Drawing upon our socioecological backgrounds, we also identified three areas that were seemingly underrepresented in the literature: (a) biodiversity and Indigenous Peoples' health, (b) biodiversity and urban social equity, and (c) biodiversity and COVID-19. We invited three relevant experts to provide opinions for case studies in these areas. The case studies explore the roles of biodiversity and biodiversity loss in these socioecological domains.

RESULTS

We begin by highlighting the first of three underrepresented case studies—biodiversity and Indigenous Peoples' health (Box 1). This case study is likely relevant to all five of the biodiversity-health pathways (Fig. 3). Moreover, ensuring the sovereignty and rights of Indigenous Peoples represents an unparalleled pathway to protecting biodiversity for all people.

Box 1. Biodiversity and Indigenous Peoples' health case study

Despite Indigenous Peoples inhabiting only twenty-two percent of the Earth's surface, eighty percent of the world's remaining biodiversity is currently stewarded by Indigenous Nations (Tauli-Corpuz, 2016). Indigenous Peoples are fundamentally connected to the Country and Lands they have stewarded for thousands of years (Fletcher et al. 2021). This

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environmental stewardship role is increasingly being recognized as important to "meeting local and global conservation goals" (Garnett et al. 2018) in preventing biodiversity loss as well as meeting climate-change targets. Indigenous Peoples' access to and protection of their Lands' biodiversity is also a fundamental determinant of their own health in addition to the planet's health (Redvers et al. 2022). Indigenous Peoples' traditional foods, medicines, and cultures are rooted within relationships to the surrounding environment, and any disconnection and disruption of the relationship to the environment (including biodiversity loss) serve to perpetuate the substantial health disparities already felt within Indigenous communities globally (Alves and Rosa, 2007; Penafiel et al. 2016; Cunsolo and Ellis, 2018; Cunsolo et al. 2020).

Land and Nature serve as conduits for overall resilience and well-being for both rural and urban Indigenous Peoples (Hatala et al. 2020). Land and Country access is a direct tool for facilitated healing within Indigenous communities (Schultz et al. 2018; Redvers, 2020; Redvers et al. 2021), and a loss of Land removes the ability of communities to collectively take care of themselves and the planet. Yet, there has been a history of relocating Indigenous communities in the name of conservation and ecotourism (Notess, 2018) despite Indigenous-managed lands having demonstrated equal-or-higher biodiversity than government "protected areas" (Schuster et al. 2019; Fletcher et al. 2021). With this, for the protection of Indigenous Peoples' health and the planet's rich biodiversity, Indigenous Peoples' and their traditional knowledges need urgent acknowledgment while actively making space for Indigenous leadership on all levels of biodiversity protection. Indigenous land tenure rights; protection of Indigenous traditional languages, which hold traditionally defined taxonomies; ancestral personhood designations supporting the rights of Nature; and a prioritization of Indigenous Peoples' health as the stewards of the remaining key biodiversity areas in the world are necessary steps to reduce the likelihood of further species loss, and further human-caused degradation of key environmental areas (Redvers et al. 2022).

Biological pathway

Environment-microbiome-health axis

Our scoping review identified 23 environmental microbiome studies, including both experimental and non-experimental studies. Mounting evidence suggests that exposure to a diverse range of microbiota from the environment is essential for the regulation of the human immune system (Rook, 2013; Roslund et al. 2021). The biodiversity hypothesis (Haahtela, 2019) posits that the recent global decline in biodiversity and the social barriers that restrict exposure to the remaining biodiversity leads to microbial deprivation, which causes a disturbed immune response and subsequent inflammatory diseases (Fig. 2). Incidentally, biodiversity loss has also been linked to an increased incidence of infectious disease outbreaks, such as COVID-19 (Mishra et al. 2021; Platto et al. 2021) (Box 2).

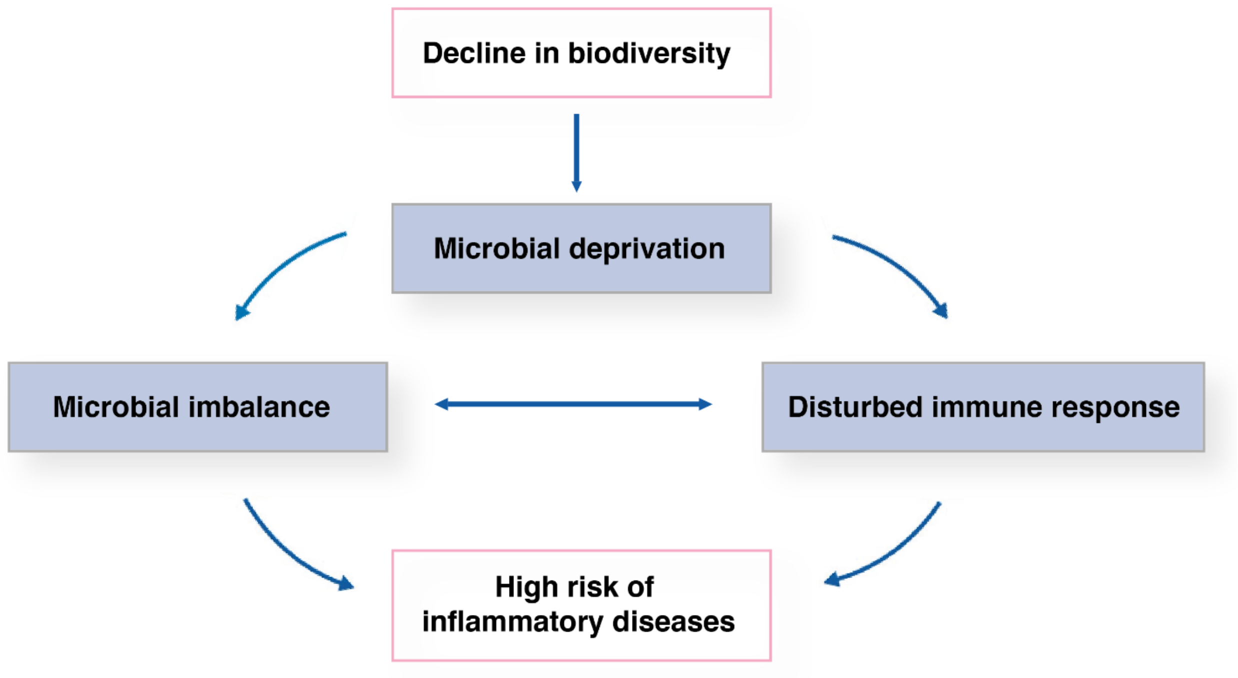

Fig. 2. The biodiversity hypothesis (Adapted from Haahtela, 2019).

Support for the biodiversity hypothesis includes three key strands of evidence: (a) experimental lab-based (randomised controlled trial) animal model studies; (b) cohort studies on human participants (observational); and (c) human case-control studies (observational). As Table 2 indicates, there is moderate evidence based on animal randomised controlled trials, human cohort studies, and human case-controlled studies, but a deficiency in randomised controlled studies on humans.

<u>Observational studies</u>

Ruokolainen et al. (2017) compared changes in allergies from school age to adults in Finnish and Russian Karelian populations. Allergies are more common in Finnish schoolchildren compared to those in Russian Karelia. The authors randomly selected children from Finland (*n* = 98) and Russian Karelia (*n* = 82) and analysed allergy symptoms and allergen sensitisation. The skin and nasal microbiota of the participants were also collected. The authors found that allergies and atopic sensitisation were 3-10 x more common in the Finland population. Skin microbiota and bacterial and fungal communities in the nasal mucosa differed between the populations, with bacterial diversity being significantly higher among Russian Karelian subjects. These results suggest that a potential microbially-mediated mechanism explains the health outcomes, thus supporting the biodiversity hypothesis. The difference in bacterial alpha diversity in this study is thought to be attributed to levels of surrounding biodiversity and exposure to it. This is supported by several studies based in rural areas demonstrating that being in closer contact with rural environments, and particularly to animals, soil and vegetation (e.g. animal farming vs. urban living), likely increases the diversity of microbiota transferred onto and into the human body (Hanski et al. 2012; Shukla et al. 2017; Kraemer et al. 2018; Chen et al. 2019).

Stein et al. (2016) studied environmental exposures, genetic ancestry, and immune profiles among 60 Amish and Hutterite children in the USA. The authors measured levels of allergens and endotoxins and assessed the microbiota composition of indoor dust samples between the two populations. The authors found that despite the genetic and lifestyle similarities between the Amish and Hutterite populations, the prevalence of asthma and allergies was 4-6 x lower in the Amish population. Importantly, endotoxin levels in Amish house dust were >6 x higher than in Hutterite homes. The authors also observed differences in microbial composition in the dust samples. In a subsequent experimental mouse model, the instillation of dust extracts from Amish but not Hutterite homes significantly inhibited airway hyperreactivity and eosinophilia. This suggests a key role of bacterial endotoxins in regulating the immune system, thus further supporting the biodiversity hypothesis.

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Several other studies show differences in human microbiome composition between urban and rural dwellers, particularly in relative abundances of certain taxonomic groups (Lehtimaki et al. 2017; McCall et al. 2020; Lehtimaki et al. 2021). However, further research is required to determine the potential significance of these compositional differences on downstream health outcomes.

Donovan et al. (2021) tested whether exposure to plant diversity (as a proxy for microbial diversity) protected against childhood acute lymphoblastic leukaemia by promoting immune maturation (*n* = 899,126). The authors suggested that plant-diversity metrics based on the maximum number of genera a child was exposed to between the age of 0-2 years were protective of acute lymphoblastic leukaemia. Exposure to the highest tertile of plant diversity was associated with a reduction in acute lymphoblastic leukaemia risk of 35% (95% CI: 11%-53%).

<u>Experimental animal studies</u>

At least five studies have examined the effect of direct soil exposure or indirect soil exposure (trace-level dust) in mouse models. Ottman et al. (2019) found that over 6 weeks, there were significant differences in mouse microbiota (*n* = 32) between two groups, whereby one group was exposed to soil, and the other group was not exposed to soil (control). Differences in bacterial composition were observed, confirming that the environmental exposures had differentially influenced the gut microbiota composition. This is supported by Liddicoat et al. (2020), who found that exposure to trace levels of soil dust modulated the mouse gut microbiome (*n* = 54). They used soils from the Mt Bold Reservoir in South Australia to show that high biodiversity soil exposure facilitated the supply of likely butyrate-producing bacteria important in regulating inflammation and potentially associated conditions such as anxiety. Indeed, this study showed reduced anxiety-like behaviour in the mice with higher levels of a particular soil-derived butyrate-producing bacterium in their caeca. Zhou et al. (2015) also found that exposure to soil, house dust and decaying plant material enhances gut microbiome diversity and innate immunity in mice.

More recently, Liu et al. (2021) used shotgun metagenomics (as opposed to bacterial 16S rRNA amplicon sequencing as used in the studies mentioned above) and found that exposure to soil environments during earlier life stages is distinguishable in the gut microbiome of adult mice. Li et al. (2021) also found that dust exposure prevented the reduction in gut microbiota diversity following antibiotic treatment in mice. Additionally, in this study, dust exposure accelerated the recovery of the gut microbiota following antibiotic treatment.

A wide range of studies now supports the notion that the human microbiome is essential for human health and wellbeing, by, for example, roles in regulating immunity (Rook, 2013), digestion (Lawrence and Hyde, 2017), reducing inflammation (Blander et al. 2017), and cell signalling (Jameson et al. 2020). The observational and experimental studies focusing on the transmission and effects of the environmental microbiome support the biodiversity hypothesis and reframe health from a holistic systems perspective.

Intervention studies

Recently, several human trials have investigated the transference of microbiota from the environment to the human body. For example, Nurminen et al. (2018) conducted an intervention study on 14 participants by assigning one study group to a soil and plant-based compost-rubbing activity (i.e., rubbing their hands) and the other group to a control (i.e., no intervention) for 20 s, and 3 x per day for 14 days. They found that alpha diversity and the relative abundance of phylum *Bacteroides* in participants' faecal samples significantly increased after 14 days. However, once the intervention ceased, there were no significant differences in gut microbiota diversity at day 35 of the study, suggesting that continued exposure to biodiversity is important.

This concept of microbiota transmission from the environment with subsequent modulation of host microbiota is supported by at least four other recent studies (Grönroos et al. 2019; Hui et al. 2019; Selway et al. 2020; Roslund et al. 2020). Selway et al. (2020) showed that spending a short period in a green space (15 mins to 1.5 hours) can significantly increase skin and nasal microbiota diversity (n = 2 to 3).

One of the weaknesses of these studies is the low sample sizes (n = 2 to 14). This means the results can only be taken as indicative and strong inferences cannot be made. However, two recent intervention (non-randomised cluster controlled) trials by Roslund et al. (2020 and 2021) (n = 75) provide more substantial evidence of the biodiversity exposure—microbiota transfer—human health link. They found that after 28 days of children playing in a yard with local biodiverse materials (e.g., forest floor), skin microbiota had significantly increased compared to the control group (i.e., no intervention). Furthermore, specific bacteria were subsequently linked to biomarkers indicating enhanced immunoregulation, supporting the biodiversity and old friends hypotheses (Rook, 2013; Haahtela, 2019). Moreover, a recent follow-up study found that the impacts of this intervention were long-term, with the suppression of potentially pathogenic bacteria on the skin of children after 2-years (Roslund et al. 2021).

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Plant-derived organic compounds

Our scoping review identified eight studies relevant to phytoncide (= plant-derived volatile organic compounds) exposure, along with one plant diversity and acute lymphoblastic leukaemia study, nine relevant forest bathing studies and one systematic review – these included both experimental and non-experimental studies. Interactions between humans and organic plant-based compounds called *phytoncides* is a proposed health-promoting mechanism in the biological pathway. Phytoncides are plant-based volatile organic compounds with antimicrobial properties and can stimulate human immune cells. A recent review on the evidence of the immune function-enhancing effects of phytoncides focused on "forest bathing" experiences (Peterfalvi et al. 2019). The review found that 2-hour long forest walks were associated with significant increases in, and activity of, natural killer cells (= white blood cells of the innate immune system), which can last for days after the experience, both in healthy participants and in individuals with cancer-associated pain.

A series of studies by Li et al. (2006-2010) have highlighted the potential immune-regulating effect of phytoncides. However, the study sample sizes were modest (n = 25), and the possible role of mediators such as other sensory or non-sensory stimulators was not well-controlled. As such, the field-based evidence is moderate and correlational but is supported by results of preclinical controlled lab experiments on human cells and animal models (Li et al. 2006; Li et al. 2009). Although biodiversity metrics were not explicitly included, the phytoncide α-pinene was assessed, which is primarily derived from coniferous trees.

Plant-derived organic compounds have been shown to reduce locomotor activity and increase muscle relaxation, with subsequent improvements in sleep (by >3 times) (Do Vale et al. 2002; Woo and Lee, 2020), stress (Cheng et al. 2009), and anxiety in randomised controlled experiments on mice (Silva et al. 2007). A recent systematic review of 22 clinical studies investigating the effects of "forest bathing" on human stress responses found that salivary cortisol levels were significantly lower in forest participants than in control groups (Antonelli et al. 2019). Forest bathing can significantly influence cortisol levels in the short term in such a way as to reduce stress. This is likely the result of an integrated stimulation of the five senses, whereby plant organic compounds contribute.

Box 2. COVID-19 case study: the importance of biodiversity

The existence of linkages between biodiversity and emergence of infectious diseases has been apparent for decades (Daszack et al. 2000), but there has been less progress on the elucidation of causal pathways and mechanisms for observed associations and effects. Interest in the origins of the COVID-19 pandemic and consideration of how to respond in a sustainable and responsible way to future pandemic threats have intensified the need for the application of science to this issue (Plowright et al. 2021). Biodiversity is recognised as being both a source of, and potentially a protective factor against, pandemics such as COVID-19 (Keesing et al. 2010; Morand et al. 2014). The concept of a 'dilution effect', whereby increased species diversity reduces disease risk is likely an oversimplification of the processes involved as applied to disease emergence and pandemic prevention (Randolph and Dobson, 2012; Ostfeld, 2013; Salkeld et al. 2013).

While there is a lack of evidence from appropriate studies to measure how human activities influence disease emergence (Gottdenker et al. 2014), activities that contribute to biodiversity loss (e.g., land-use change, intensive livestock production, wildlife trade, and climate change) are often implicated. Indeed, wild animal species known to carry zoonotic pathogens are more abundant and comprise a greater proportion of the host species diversity at sites under substantial human use (e.g., urban and agricultural systems) compared to nearby undisturbed habitats (Gibb et al. 2020). In a 'post-COVID' world, so called 'ecological countermeasures' have been proposed to apply ecological restoration to maintain or increase biodiversity and reduce zoonotic disease risk and disease emergence (Breed et al. 2021; Reaser et al. 2021). Conversely, potential positive feedback loops have been identified whereby response policies to COVID-19 could promote future zoonotic disease outbreaks, for example, economic recovery policies that subsidise mining and forestry while postponing climate change mitigation (Lawler et al. 2021).

Fernández et al. (2020) investigated whether environmental pollution and biodiversity levels were associated with the spread and mortality of COVID-19. The authors created a global database using daily case reports from the World Health Organisation, in combination with spatiotemporal models to identify the influence of biodiversity and other variables on the spread and mortality of COVID-19. They found a significant association between COVID-19 infection and the national biodiversity index and air quality. In particular, there was a significant relationship between the loss of biodiversity, and diminished air quality, with COVID-19 spread and mortality. While further research is required, these results are consistent with the biodiversity hypothesis. Many other factors can contribute to the spread of disease and mortality, which need to be considered in future research.

Indeed, microbiota in the human gut appear to play a role in regulating the severity of COVID-19 through the modulation of host immune responses (Yeoh et al. 2021), which is influenced by exposure to environmental microbiota (Liddicoat et al. 2020; Roslund et al. 2021). Environmental microbiota-associated immune training can enhance protection

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against both pathogen infection and auto-immune diseases (Rook, 2013), and could therefore potentially improve immune-mediated responses to the multifaceted impacts of COVID-19.

Psychological pathway

Our scoping review identified 21 studies on reductions in stress and improved positive emotions and one systematic review; five studies on increased attention restoration; two studies on nature connectedness, including one systematic review; and eight studies on reductions in anxiety and depression – including both experimental and non-experimental studies. However, only ten studies included specific biodiversity metrics (including one perceived biodiversity). Several purported psychological factors are involved in the nature-human health nexus, which also involves physiological processes. As such, this category is perhaps better viewed as a 'psycho-physiological' pathway. The main psycho-physiological elements for which evidence supports clear mechanisms include: (a) stress reduction and positive affect; (b) depression and anxiety reduction; (c) attention restoration; and (d) nature connectedness.

Stress reduction

Corazon et al. (2019) carried out a systematic review on the effects of engaging with nature on the human stress response. They found that of the 36 studies assessed, 30 were considered low quality (based on factors such as sample sizes, lack of proper controls, and selection bias), 6 were moderate quality, and none were high quality. Of these studies, three were conducted as randomised controlled trials. Sample sizes varied widely, ranging from 9 to 935 subjects. The most common research setup entailed comparing an intervention in a natural environment (e.g., a forest or park) to an intervention in a highly urbanised setting. The most common activity was simply walking in nature. Eight studies included measures of self-perceived stress. Four of these found a significant difference between the intervention and control (nature > control) (Kjellgren et al. 2010; Bird, 2015; Im et al. 2016; Largo-Wight et al. 2017). Eight studies reported a significant effect of the nature-based intervention on positive affect (positive emotional responses linked to stress reduction) (Van Den Berg and Custers, 2011; Berman et al. 2012; Duvall and Kaplan, 2014; Marselle et al. 2014; Passmore and Howell, 2014; Tyrväinen et al. 2014; Marselle et al. 2016; Fuegen and Breitenbecher, 2018). Classifications of surrounding biodiversity characteristics (e.g. taxonomy, structure, diversity/richness) in these interventions were absent.

A recent study in the UK investigated aspects of biodiversity on participants' positive affect (n = 228) (Cameron et al. 2020). The results showed a strong association between levels of bird biodiversity within a green space and human emotional response to that space. Respondents reported being happier in sites with greater bird diversity (r = 0.78) and a greater variety of habitats (r = 0.72). These relationships were strengthened when emotions were connected to perceptions of overall biodiversity (r = 0.89). To summarise, participants who considered a given site to be rich in wildlife reported more positive emotions associated with stress reduction. This is supported by another recent study (n = 121) that showed that animal diversity was positively associated with increased positive affect and decreased negative affect (Nghiem et al. 2021). Also corroborating these results is a study by Wolf et al. (2016), who ran a controlled study (with randomly assigned low and high exposures) showing that watching videos of nature scenes with greater species (in birds and trees) richness consistently led to higher mental wellbeing (via measures of positive effects) outcomes in participants (n = 140).

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Anxiety and depression

Marselle et al. (2020) found that the abundance of street trees, but not species richness, significantly reduced the risk of antidepressant prescriptions for individuals (*n* = 9,751) with low socio-economic status in Leipzig. This abundance - but not richness - trend was corroborated by Cox et al. (2017), who found that higher bird abundances in the afternoon, but not species richness, were associated with less depression and anxiety in the UK (*n* = 263). Contra to these studies, Methorst et al. (2021) recently found no link between bird abundance and mental health outcomes but found a significant association with bird species richness. Mavoa et al. (2019a) explored the effects of neighbourhood green space and biodiversity on the emotional wellbeing of adolescents in New Zealand (n = 4,575). The results showed a significant relationship between reduced depressive symptoms and mean greenness, presence of native vegetation, and having a higher nature availability index. They estimated vegetation diversity using landcover datasets. Another study by Mavoa et al. (2019b) found statistically significant relationships between subjective wellbeing and both fauna and flora species richness across different neighbourhood scales when species richness measures were modelled independently. However, the relationships were not significant when fauna and flora species richness were included in the same model as overall greenness.

Four other studies included specific tests for anxiety (Sahlin et al. 2015; Song et al. 2015; Niedermeier et al. 2017; Yu et al. 2017). All demonstrated reductions in reported anxiety as a result of nature-based interventions. However, none explicitly used specific biodiversity metrics, i.e., only the broad environment type was considered (such as a woodland or park).

Attention restoration

Few studies have investigated the relationship between biodiversity and psychological restoration. Fuller et al. (2007) showed that green spaces with higher plant, bird and habitat richness were significantly associated with attention restoration metrics (e.g., recovery from fatigue and ability to gain perspective) in green space users (n = 312). The authors noted that participants had more accurate perceptions of plant species richness than bird or butterfly species richness, which are typically less easily observed. This result was corroborated by Young et al. (2020), who showed that garden biodiversity increased the perceived restorativeness of gardens (n = 193). Johansson et al. (2014) demonstrated that nature-based images containing higher levels of biodiversity were associated with brain activity patterns suggestive of greater attention (n = 35). Carrus et al. (2015) also established an association between plant diversity and perceived psychological restorativeness (n = 569). One study showed no association between actual biodiversity and wellbeing (including attention restoration) but reported a positive association between wellbeing and perceived species richness of birds, butterflies, and plants (Dallimer et al. 2012).

Nature connectedness

Nature connectedness — also known as nature relatedness — is a validated psychological construct that measures a person's emotional, cognitive, and experiential connection with the natural world. Importantly, nature connectedness has been linked to wellbeing (Capaldi et al. 2017). Broadly, engaging with nature has been shown to enhance a person's nature connectedness (Richardson et al. 2018; Pritchard et al. 2020). Studies also show that a population's nature orientation tends to be higher in 'greener' neighbourhoods (Shanahan et al. 2017). However, few studies have explicitly investigated the role of specific biodiversity metrics (e.g., taxonomy, diversity/richness, structure) on a person's level of nature connectedness. This highlights a clear research gap that needs to be addressed. Luck et al. (2011) found that nature connectedness was weakly associated with species richness (coefficient = 0.009, p = <0.01). They also found that personal wellbeing was positively related to species richness and abundance and vegetation cover and negatively related to urban development. In this cross-sectional study (n = 1,043), the odds that a household had a higher level of personal wellbeing increased by 20% (1–45%) as species richness increased.

Social and physical activity pathway

Our scoping review identified two studies on increased wellbeing and social cohesion and twelve studies and two systematic reviews on improved cardiovascular function as a result of physical exercise. These included both experimental and non-experimental studies. Natural environments are considered by many to be spaces that are conducive to social activities and physical exercise, i.e., 'supportive environments'. This facilitatory role is thought to indirectly lead to various health and wellbeing benefits by, for example, improving social cohesion and cardiovascular functioning. Wan et al. (2021) recently conducted a systematic review (of 51 studies) on the relationship between urban green spaces and social cohesion. They found that physical characteristics and perceptions of green spaces directly influenced social cohesion. Tilove et al. (2017) found that participants *(n* = 652) living in a greener environment and close to high-quality green spaces reported significantly higher perceived social cohesion in the neighbourhood. This is corroborated by a cross-sectional study by Van Den Berg et al. (2017), who showed that, through single mediation analysis, social cohesion was a mediator of the association between time spent visiting green spaces and mental health (*n* = 3,948).

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Schipperijn et al. (2013) found positive associations between physical activity and certain features of outdoor environments, including size, walking/cycling routes, wooded areas and water features (n = 1,305). Klompmaker et al. (2018) conducted a cross-sectional study using a Dutch national health survey (n = 387,195). They found that the level of surrounding greenness (measured using the normalised difference vegetation index; NDVI) significantly decreased the odds of being overweight and increased odds for physical activity. This is corroborated by Mytton et al. (2012), which found a positive association between green space and physical activity levels (95% CI: 1.13–1.44). This study took green space measures from the generalised land use database (GLUD) and digital ordnance survey land use maps. Several other studies support these green space–physical activity results (Coutts et al. 2013; McEachan et al. 2016; Akpinar and Cankurt, 2017; Benjamin-Neelon et al. 2019; Wang et al. 2019).

Thompson-Coon et al. (2011) conducted a systematic review comparing physical activity indoors vs in outdoor natural environments on the mental wellbeing of participants. Eleven trials (n = 833) were included. The majority of trials (n = 9) reported improvements in mental wellbeing on the outcome measures. Another multi-study analysis by Barton and Pretty (2010) assessed the level of exposure to 'green' exercise required to improve mental health. They included 10 UK studies (n = 1,252). The overall effect size for improved self-esteem using the Cohen's d statistic was d = 0.46 (CI 0.34−0.59, p < 0.01) and for mood d = 0.54 (CI 0.38−0.69, p < 0.01). Effect sizes can be interpreted as small (d = 0.2), medium (d = 0.5), and large (d = 0.8). All natural environments improved both self-esteem and mood, but the presence of a water body resulted in greater effects.

Sanders et al. (2015) studied the effects of neighbourhood green space on children's physical activity in Australia using longitudinal data (n = 4,983). They found that boys living in areas with 10 % more neighbourhood green space had a 7 % (95 % CI = 1.02, 1.13) greater odds of having physical activity-based pastimes and an 8 % (95 % CI = 0.85, 1.00) lower odds of not enjoying physical activity. No significant results were observed for girls. The authors conclude that more research is needed to explore what green spaces promote active lifestyles. Mueller et al. (2021) found that more strenuous walking and cycling activities occurred with more green space. Still, levels of residential green space did not have a clear link with outdoor moderate to vigorous physical activity.

Finally, recent evidence suggests that green spaces are important from a recreational perspective, especially for people during COVID-19 lockdowns when social distancing measures were in place. For example, Venter et al. (2020) found that outdoor recreational activity increased by 291% during lockdown relative to a 3-year average. Walking, running, hiking, and cycling intensified on trails with greater tree canopy cover, and the level of increase was positively associated with trail remoteness. Robinson et al. (2021) also found that people used green spaces such as woodlands, parks, lakes, and meadows more often and for longer during the COVID-19 lockdowns (mean 106 mins and 5 visits per week) compared to before (mean 66 mins and 4 visits per week), and often for physical activity purposes. While there is substantial literature assessing the effects of green space on sociality and physical activity, no original research papers were identified that directly investigate the connection between biodiversity metrics (e.g. taxonomy, diversity/richness, structure) and these health-promoting pathways. This suggests that the evidence base is inadequate to comprehensively inform biodiversity conservation and public health policy. There is also an important social equity issue to address when considering urban biodiversity and human health. Many people simply do not have access to quality natural environments (Robinson and Jorgensen, 2020). Therefore, health benefits and disbenefits are likely to be unequally distributed (Box 3).

Box 3. Biodiversity and urban social equity case study

Towns and cities are places of dense industrial outputs and human activity which result in environmental stressors (e.g., noise, artificial light, air pollution) (Wang et al. 2020; Robinson et al. 2021). An environmental stressor in this case is a change in the environment that causes humans to engage a wide range of adaptive responses, mitigated by the hypothalamic-pituitary-axis (HPA-Axis) (Maniam et al. 2014). The HPA-axis is a neuroendocrine system that communicates with the digestive, circulatory, and immune systems to allow the human body to maintain an equilibrium or stability during environmental change (Savastano et al. 1994; Hiller-Sturmhöfel and Bartke, 1998; Sudo, 2012). However, when the body is required to constantly adapt, as it is in cities due to these diverse and continuous stressors, the body can experience a process now identified as 'allostatic overload' (Fava et al. 2019; Camargo et al. 2020). Allostatic load is linked to oxidative stress and inflammation, which are part of the pathology for various chronic diseases (McEwen, 1998).

This review has highlighted various mediators of health in respect of accessing nature. This is especially important given the high levels of stress that urban environments place on our biological systems. However, access to green spaces is not equitable for various reasons. The most well-known reason for this inequity is location, as many low-income neighbourhoods lack quality green spaces (Wen et al. 2013; Astell-Burt, 2014). There is also an assumption that if green spaces are created, people will automatically engage with

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them (Wolch et al. 2014). Yet, this is often not the case due to factors such as safety and time. Many people who live in low-income areas work disproportionately high levels of shift work, multiple jobs, or have zero-hour contracts (Blumberg et al. 2019; Bapuji et al. 2020). These employment types can create time poverty, meaning this demographic has less free time to engage in activities of self-care, such as visiting an urban park (Chatzitheochari et al. 2012). For example, people may work during the daytime, often at weekends and sometimes need to supplement their salary with other work (Schleith et al. 2014). This leaves only limited time for accessing green spaces. This is also significant in understanding the racialisation factors that can contribute to inequitable access to green spaces, as many Peoples who are racialised as Black, Afro-Indigenous, and Indigenous often experience time poverty at a disproportionate rate to weather white counterparts (Kalenkoski et al. 2011., Ribeiro, et al. 2012). Another aspect is safety; not everyone feels safe around nature, especially if they have not been exposed to natural environments throughout their lifetime (Ryan, 2005). Another consideration is that marginalised groups may feel unsafe in parks or other green spaces due to harassment (Lopez et al. 2021; Koprowska et al. 2020).

There are at least two learnings from this: (1) Those who may benefit the most from the health benefits of biodiversity are often the least able to access it (Chatzitheochari et al. 2012; Lopez et al. 2021); and (2) creating natural environments does not guarantee engagement due to various socio-economic and socio-cultural barriers (Reichl, 2016; Cronin-de-Chavez et al. 2019).

Given these factors, three recommendations are proposed here:

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1. Integrate new green spaces via community-led initiatives. For example, a new allotment could be paired with a childcare centre to teach young children about growing food. This could have multifactorial health benefits, exposing children to a diverse microbiome and other health-promoting biogenic compounds, enhancing muscular-skeletal and cognitive development, and reducing stress (Roslund et al. 2020; Robinson et al. 2021).
2. Distributing biodiversity throughout a city rather than just in pockets of green spaces could increase equitability and environmental justice. This means using all urban spaces such as rooftops, bus stops, sidewalks, train stations, street medians, and roundabouts.
3.Prioritising nature-based prescriptions in areas where communities experience disproportionate stress levels (i.e., biological inequity) (Camargo et al. 2020). This could involve increasing biodiversity (and engagement activities) in these areas and creating programmes to explore natural environments outside of the city, enabling people to experience as many healing pathways as possible (Robinson and Breed, 2019).

Environmental buffering pathway

Our scoping review identified four studies on reducing the impacts of urban heat island effects and two studies on the potential to improve respiratory function (e.g., reduced asthma) as a result of reduced air pollution. These include both experimental and non-experimental studies. In addition to the vast array of provisioning services the natural environment provides to humans, such as resources, it also provides some fundamental regulating services that buffer the effects of environmental or anthropogenic processes on human health and wellbeing.

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Urban heat island effects

The urban heat island effect is when urban areas replace the natural land cover with dense concentrations of buildings, pavements and other infrastructure that absorb and retain heat. This leads to a localised climate change with detrimental impacts to human health, for example, by increasing heat-related illnesses such as respiratory difficulties, heat exhaustion, and in some cases, death (Heaviside et al. 2016; Huang et al. 2019).

Balany et al. (2020) conducted a review on the impacts of urban green infrastructure on urban heat island effects. They found that from 71 studies, the majority were conducted on a limited spatial scale and focused on temperature and human thermal comfort. Moreover, >95% of the studies reviewed the cooling effects of trees as opposed to other green infrastructure. Human thermal comfort has been shown to be enhanced by tree quantity (Perini et al. 2017; Yahia et al. 2018; Kong et al. 2019; Rui et al. 2019).

Wang et al. (2021) recently investigated the impacts of green spaces on urban heat island effects. In particular, they were interested in the tree community structure within green spaces. They sampled n = 156 plots across n = 15 green spaces in China. They found that tree species richness (a biodiversity metric) and canopy coverage positively correlated with the magnitude of temperature drop amplitude (i.e., cooling). Although these results are correlational, tree species diversity explained up to 59% of the variation in cooling (p = <0.01). The authors point out considerable differences between tree species in their ability to provide urban cooling. Tree canopies with high leaf area and transpiration rates are the most effective at cooling (Rahman et al., 2018), corroborated by Park et al. (2019).

Francoeur et al. (2021) found that adding vegetation complexity to urban lawns (i.e., increasing structure and diversity) significantly reduced surface temperatures (n = 48 plots). All three habitat types – namely, flower meadows, hedgerows, and shrubs – were found to have higher cooling abilities over standard lawns. Shafiee et al. (2020) conducted an experiment over 24 hours for 10 days to test the effects of green living walls on ambient urban heat. They found that walls with plants installed (*Gazania sp., Petunia sp., Liriope sp.* and Cactus) can reduce ambient air temperature by up to 8.7 ^{o}C. A key limitation to this study is the small spatial scale (<10m^2).

None of these studies directly investigate the link between biodiversity metrics and their potential effects on human health via urban heat island effects. As mentioned, Wang et al. (2021) found tree diversity associated with greater cooling but did not assess potential downstream health impacts. However, several studies apply a form of human thermal comfort index, which provides a score of comfort/discomfort. Further research investigating potential health outcomes resulting from biodiversity interventions to regulate urban heat is required.

Air and water quality

<u>Trees and air quality</u>

Trees can remove air pollution through deposition processes (Riondato et al. 2020). These depend upon forest structure, climatic conditions, and air quality, which vary across space and time (Hirabayashi and Nowak, 2016). Nowak et al. (2013) modelled the effects of trees on particulate matter 2.5 microns (PM2.5) concentrations and human health for 10 cities in the US. The annual amount of PM2.5 removed by trees varied between 4.7 tonnes in Syracuse to 64.5 tonnes in Atlanta. Mortality reductions were typically around 1 person per

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year per city but were as high as 7.6 people per year in New York City. However, Lai and Kontokosta (2019) analysed the impact of the spatial distribution of street trees (*n* = 652,169) in the US by combining crowd-sourced tree census data on street trees – with pollen activity, allergen severity, and neighbourhood demographic data, asthma hospitalisation and emergency department visit rates and air quality data (PM2.5). They investigated how street trees impact local air quality and the prevalence of acute respiratory illness and found that although a greater concentration of trees contributed to better local air quality, certain species with higher allergenicity could increase local asthma rates in vulnerable populations.

Although species-specific factors were not considered in the study by Rao et al. (2014), the authors created a land use regression model (R^2 0.70) based on NO_2 measured at *n* = 144 sites in Oregon, US, and estimated every 10 ha of tree canopy within 400 m of a site was associated with a 0.57 ppb decrease in NO_2. Contra to this, Nemitz et al. (2020) found that urban tree planting in the UK was forecast to increase urban NO_2 concentrations due to chemical interaction with changes in volatile organic compound emissions and O_3, but the details depend on tree species selection. This again highlights the importance of studying the effects of tree species on air quality (Sicard et al. 2018).

Most studies were based on modelling techniques, and others were relatively small scale (street level) (Riondata et al. 2020). Several studies highlighted the importance of investigating tree species, and Eisenman et al. (2019) found no scientific consensus that urban trees reduce asthma by improving air quality. Collectively, this suggests that considerably more research is required to assess the impacts of trees on air quality and downstream human health outcomes, with a particular focus on the effects of different tree species across different scales.

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Plants and indoor air

Han and Ruan (2020) systematically reviewed the effects of indoor plants on air quality. The authors screened *n* = 95 journal articles and gathered data according to plant species and medium, study design, air quality, and exposure duration. They found that the primary effects of indoor plants on air quality were to reduce pollutant levels — in particular, formaldehyde, benzene, and toluene. *N* = 223 plant species were tested for their impact on air pollution across these 95 studies. The most frequently assessed indoor plant species was Devil's Ivy *Epipremnum aureum*, which appeared 35 times. Of the studies reviewed, only ~19% were conducted in living environments, whereas 76% were laboratory-based experiments, many of which were conducted in small fumigation chambers. Moreover, many studies did not report means and standard deviations. Therefore, a meta-analysis was not possible, and the generalisability of the results is yet to be determined. These studies can be considered poor quality based on inappropriate reporting of their methodology.

Water quality – phytoremediation

Phytoremediation – or using plants and microbes to reduce the toxic effects of contaminants in the environment — is an important and effective environmental restoration method. Sustaining and restoring water quality in both lentic (still) and lotic (flowing) systems is essential for human health and wellbeing. This can manifest directly via exposure and consumption pathways or indirectly via the maintenance of so-called 'ecosystem services' that may be affected by environmental toxins. Aquatic plants can absorb contaminants, including organic and inorganic substances (e.g. heavy metals and pharmaceutical pollutants). Among the aquatic plants, giant salvinia *Salvinia molesta* and water lettuce *Pistia stratiotes* have been widely used to treat agricultural, domestic and industrial wastewater (Mustafa et al. 2021). Turcios et al. (2021) showed that sea aster *Tripolium pannonicum* could uptake and degrade xenobiotics and sulfamethazine, an antibiotic (*n* = 42). The authors conclude that this species is a potential candidate for marine water remediation.

Auchterlonie et al. (2021) investigated the potential for water hyacinth *Pontederia sp.* to be used as a phytoremediation tool to reduce dam eutrophication in South Africa. The results showed that a single plant absorbed up to 7.4 mg of phosphates and 27 mg of nitrates within 11 days. These results suggest that water hyacinth can be applied as a phytoremediation tool to mitigate eutrophication in lentic water bodies. Reducing dam eutrophication has the potential to contribute to human health. Indeed, eutrophication and associated algal blooms of reservoirs have triggered drinking water crises worldwide (Chen and Zhu, 2017). It should be noted that plants considered beneficial in some environments may be invasive in others – for example, water hyacinth is deemed invasive in Australia.

Delgado-González et al. (2021) point out that a variety of plant species exist with water phytoremediation potential, which needs further research to make phytoremediation a viable method for a wide range of aquatic ecosystems. Mangroves have recently been suggested to potentially work as a phytoremediation tool for contaminated waters, such as removing organochlorinated pesticides (OCPs) (Ivorra et al. 2021). Ivorra et al. (2021) evaluated *n* = 73 studies that focused on the accumulation of OCPs in areas with and without mangroves. The authors concluded that mangrove areas tended to have lower OCP amounts than non-mangrove areas, indicating a potential tool to deal with persistent contamination. With their unique structures, the mangroves could trap these compounds and degrade and assimilate them with the possible help of the rhizospheric microbes. Further research is needed to explore this hypothesis. However, this study is corroborated by a recent evaluation by Warykszak et al. (2021). The authors used an Australian case study to investigate the

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capacity of planted mangroves *Avicennia marina* to immobilise petrol hydrocarbons within a small embayment subjected to minor oil spills in the 1980s. By extracting a 1 m sediment core, they revealed that mangroves formed a thick (30 cm) organic layer above the hydrocarbon-contaminated sediments and accumulated ~6.6 mm of contaminated sediment per year. The authors found that levels below this organic layer (30–50 cm) were highly toxic. However, it is unclear whether this is remediation or compartmentalisation of toxins.

Water quality – wetlands

The potential of wetlands to enhance water quality has long been recognised. Indeed, Whigham et al. (1988, p.1) noted, *"there is little doubt that freshwater wetlands can significantly improve water quality and, with few exceptions, most have been shown to perform that function".* Based on experimental systems, Brisson et al. (2020) conducted a meta-analysis on plant diversity effects on water quality in wetlands. They assessed $n = 28$ studies and found no significant effect of plant richness on the removal of total suspended solids, but a positive effect on chemical oxygen demand and total nitrogen removal, and a marginal effect on phosphorous removal. Thus, the results of their meta-analysis were consistent with reports of a positive effect of biodiversity on aquatic ecosystem properties. The authors conclude that although the results need to be confirmed by longitudinal field experiments in natural conditions, the findings could help guide practices in natural wetland restoration, which has important implications for human health and wellbeing.

Human-created wetlands are suggested to be effective at ameliorating the effects of agricultural runoff, which can contaminate water supplies, thereby affecting human health. Kovacic et al. (2006) assessed whether created wetlands could improve water quality in the

US. They found that a wetland of 450 ha would be required in the Lake Bloomington area to reduce nitrogen loading by 46%.

A summary of the biodiversity-human health exposure-outcome pathways is presented in Fig. 3.

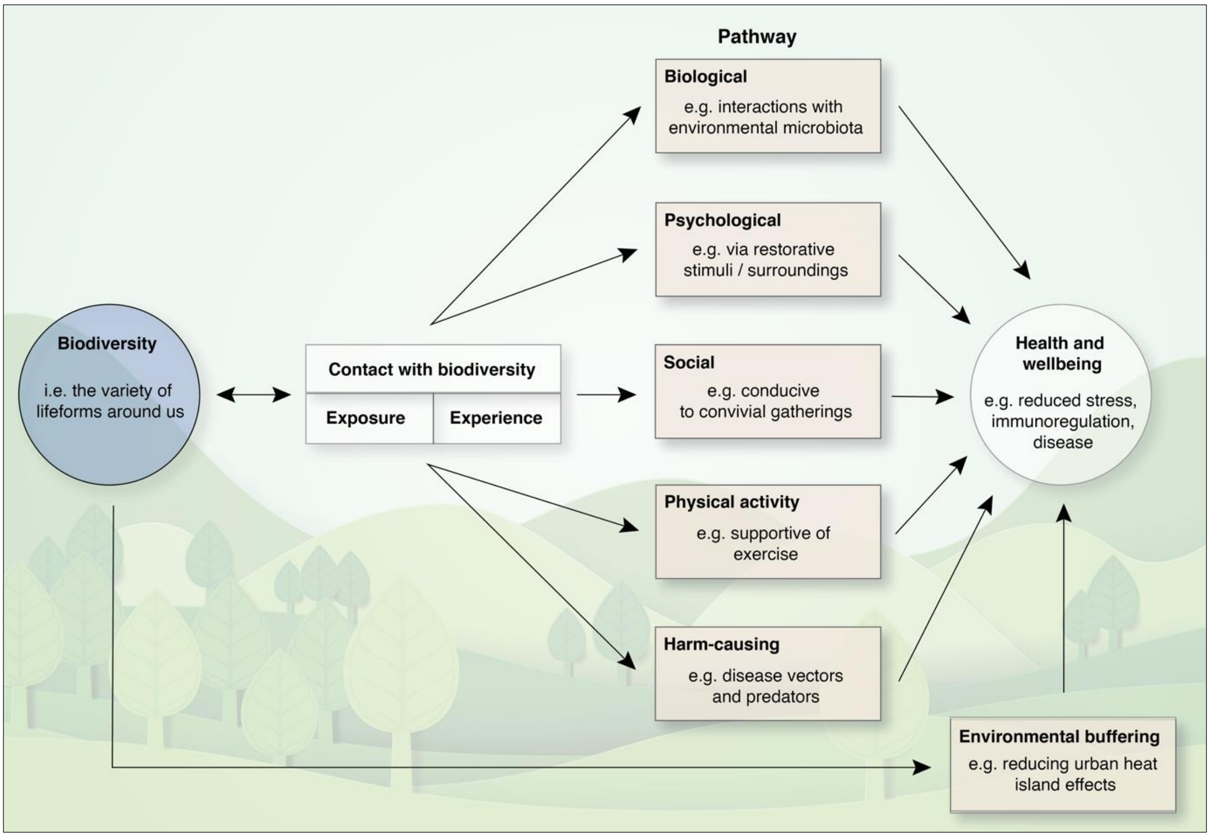

Fig. 3. Summary of the biodiversity-health exposure/experience-outcome pathways (adapted from Marselle et al. 2021).

Harm-causing pathways – health disbenefits

While most of this review has focused on nature-based health-*promoting* pathways, it is also important to acknowledge the potential health-*demoting* pathways. As Marselle et al. (2021) point out, "causing harm" (e.g., dangerous wildlife, zoonotic diseases, allergens) should be considered, as biodiversity can also have a negative influence on human health (Fig. 3). This

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also provides a complete picture of human interrelationships with biodiversity. Indeed, the "causing harm" domain is all the more salient at the moment with SARS-CoV-2, the COVID-19 aetiological agent, being a highly infectious zoonotic virus, and the outbreak is potentially a result of contact with wildlife due to habitat loss (e.g., via deforestation, urbanisation) (IPBES, 2020).

Other infectious diseases such as Ebola, Borna, SARS, and vector-borne diseases such as malaria, zika, schistosomiasis, dengue, leishmaniasis, tick-borne encephalitis and Lyme disease all originate in wild animals (Müller et al. 2019; Ahmad et al. 2020; Niller et al. 2020). Habitat loss, urbanisation and agricultural intensification can increase interactions with wild animals (Barouki et al. 2021). Thus, the destruction of biodiversity and the associated increase in contact can increase the risk of interactions between humans and wild animals, which potentially increases infectious disease spillover events and subsequent outbreaks (Marselle et al. 2021). Vector-borne diseases involve interrelationships between pathogens, vectors (e.g., mosquitoes, tsetse flies, and ticks) and hosts (e.g., humans, rodents, birds) (Marselle et al. 2021). Several studies have investigated the potential link between infectious disease agents and genetic, phenotypic (traits), and species diversity (Ostfeld, 2009; Roberts and Heesterbeek, 2018; Vadell et al. 2020). In many cases, only weak relationships have been found between biodiversity and vector-borne disease prevalence (Ruyts et al. 2018; Stensgaard et al. 2016; Vadell et al. 2020), but with some evidence to support both the dilution hypothesis (Schmidt and Ostfeld, 2001) and the amplification hypothesis (Roiz et al. 2019). The dilution hypothesis posits that an increase in biodiversity reduces the prevalence of vector-borne diseases. Whereas the amplification hypothesis posits that an increase in biodiversity increases the prevalence of vector-borne diseases (Marselle et

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al. 2021). This immense complexity and the contrasting evidence means additional, longitudinal and multiscale research is needed.

Physical and physiological harm can be experienced through encounters with toxic plants and fungi and dangerous animals such as snakes, spiders, and large predators (Methorst et al. 2020). Harmful interactions with biodiversity may also include psychological harm, invoked through fear, and may even inhibit the restorative capacities of nature by causing a person to avoid particular biodiverse environments (Marselle et al. 2021). The emission of biogenic compounds such as spores and pollen and volatile organic compounds from plants can also cause health disbenefits. Some volatile organic compounds can react with other compounds to increase the level of O_3 in the atmosphere under certain conditions (Berezina et al. 2020), and O_3 is known to be a potent lung irritant (Zhang et al. 2019).

While a high abundance of allergenic vegetation (e.g. certain tree species such as alder *Alnus glutinosa*, birch *Betula sp*., hazel *Corylus avellana, and Eucalyptus sp.*) may negatively affect allergic people, a more biodiverse environment is thought to protect through the dilution effect (Marselle et al. 2021). However, it could also increase allergen diversity, depending on the plant species present. Further research is required to assess the optimal configuration of vegetation (e.g. density, species), particularly in urban areas where most of the population reside. There is also some evidence to show that pollution can increase the allergenicity of tree pollen, thereby increasing allergy susceptibility (Beck et al. 2013; Obersteiner et al. 2016; Gilles et al. 2018).

A summary of the biodiversity and human health mechanisms, pathways, and evidence is presented below in Table 2 and Fig. 4.

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Table 2. Summary of biodiversity and human health links with the associated level of supporting evidence (refer to Fig. 1).

Pathway	Mechanism	Measured health outcome	Number and type of studies			
			Human RCT	**Animal model RTC**	**Human cohort**	**Human case-control**
Biological	Exposure to environmental microbiota	Improved immune regulation (reduced disease likelihood and severity); reduced inflammation; improved mental health	Nil	2* (Stein et al. 2016; Liddicoat et al. 2020) Level of evidence = 3	2 (Roslund et al. 2020 & 2021) Level of evidence = 2	2∞ (Ruokolainen et al. 2015; Stein et al. 2016) Level of evidence = 3
Biological	Exposure to phytoncides	Enhanced immune cell activity; enhanced ability to sleep; anti-inflammation effect	Nil	3§ (Cheng et al. 2009; Woo et al. 2019 and 2020) Level of evidence = 3	Nil	5 (Li et al. 2006, 2007, 2008, 2009; Tsao et al. 2018) Level of evidence = 3
Biological	Exposure to plant diversity	Protection against childhood acute lymphoblastic leukaemia	Nil	Nil	1¶ (Donovan et al. 2021) Level of evidence = 2	Nil
Biological	Forest bathing – multi-sensory	Reduction in stress, measured via cortisol	Nil	1 (Antonelli et al. 2019) Level of evidence = 1	Nil	8† (Li et al. 2006; Li et al. 2009; Cheng et al. 2009; Horiuchi et al. 2013; Jung et al.

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						2015; Jia et al. 2016; Dettweiler et al. 2017; Kobayashi et al. 2017) Level of evidence = 3
Psychological	Exposure to calming natural environment	Reductions in stress and improved positive emotions	2 (Grazuleviciene et al. 2016; Razani et al. 2018) Level of evidence = 1	1Δ Level of evidence = 1	Nil	17Δ (Kjellgren et al. 2010; Bird, 2015; Im et al. 2016; Largo-Wight et al. 2017; Van Den Berg and Custers, 2011; Berman et al. 2012; Duvall and Kaplan, 2014; Marselle et al. 2014; Passmore and Howell, 2014; Tyrväinen et al. 2014; Marselle et al. 2016; Wolf et al. 2016; Fuegen and Breitenbecher, 2018; Cameron et al. 2020;

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						Nghiem et al. 2021; Vos et al. 2022; Zhu et al. 2022) Level of evidence = 3
Psychological	Exposure to calming natural environment	Increased attention restoration	Nil	Nil	1 (Johansson et al. 2014) Level of evidence = 3	4Ω (Fuller et al. 2007; Carrus et al. 2015; Young et al. 2020; Dallimer et al. 2012) Level of evidence = 3-4
Psychological	Exposure to the different sights, sounds, and smells of natural environments	Increased nature connectedness and eudaimonic wellbeing	Nil	1£ (Pritchard et al. 2020) Level of evidence = 1	1£ (Richardson et al. 2018) Level of evidence = 2	Nil
Psychological	Exposure to the different sights, sounds, and smells of natural environments	Reduced anxiety and depression	Nil	Nil	1£ (Niedermeier et al. 2017)	8£ (Luck et al. 2011; Sahlin et al. 2015; Song et al. 2015; Cox et al. 2017; Yu et al. 2017; Mavoa et al. 2019; Marselle et al. 2020; Methorst et al. 2021)

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					Level of evidence = 3	Level of evidence = 3-4
Social	Social interactions in natural environments	Increased wellbeing and social cohesion	Nil	1£ (Wan et al. 2021) Level of evidence = 1	Nil	2£ (Tilove et al. 2017; Van Den Berg et al. 2017) Level of evidence = 3-4
Physical activity	Facilitating exercise	Improved physical activity, with potential to support cardiovascular function	Nil	2£ (Barton and Pretty, 2010; Thompson-Coon et al. 2011) Level of evidence = 1	Nil	10£¥ (Mytton et al. 2012; Coutts et al. 2013; Schipperijn et al. 2013; Sanders et al. 2015; McEachan et al. 2016; Akpinar and Cankurt, 2017; Klompmaker et al. 2018; Benjamin-Neelon et al. 2019; Wang et al. 2019; Mueller et al. 2021) Level of evidence = 3-4

Buffering	Urban cooling from trees	Reduced impacts from urban heat island effect	Nil	1√ (Wang et al. 2021) Level of evidence = 1	Nil	4√ Level of evidence = 3-4
Buffering	Reduced air pollution from trees≈	Improved respiratory function (e.g. reduced asthma)	Nil	Nil	Nil	2 (Nowak et al. 2013; Lai and Kontokosta 2019) Level of evidence = 3-4

*4+ animal model studies have confirmed environmental microbiome exposure and colonisation with associated health-promoting traits
∞13+ human cohort or case control studies show changes in microbiome composition that are associated with favourable health outcomes
§Studies investigated ability to enhance sleep via GABA interactions
¶Specifically, exposure to the highest tertile of plant diversity was associated with a reduction in ALL risk of 35%
†See Antonelli et al. (2019); often study aspects of biodiversity, but without specific metrics (e.g. structure, composition, diversity)
∆See Corazon et al. (2019); specific biodiversity metrics were absent (i.e. only broad classifications of nature were used)
ΩUsed bird and plant species diversity
£Specific biodiversity metrics were absent (i.e. only broad classifications of nature were used)
¥Measures of cardiovascular improvements were generally absent
√Only measured 'human comfort index'
≈10+ studies provide evidence of air pollution-reducing abilities of trees, but do not directly assess human health outcomes. Han and Ruan (2020) conducted a systematic review of indoor plants on air quality and found significant improvements such as reduced formaldehyde, benzene, and toluene. However, direct human health outcomes were not assessed.

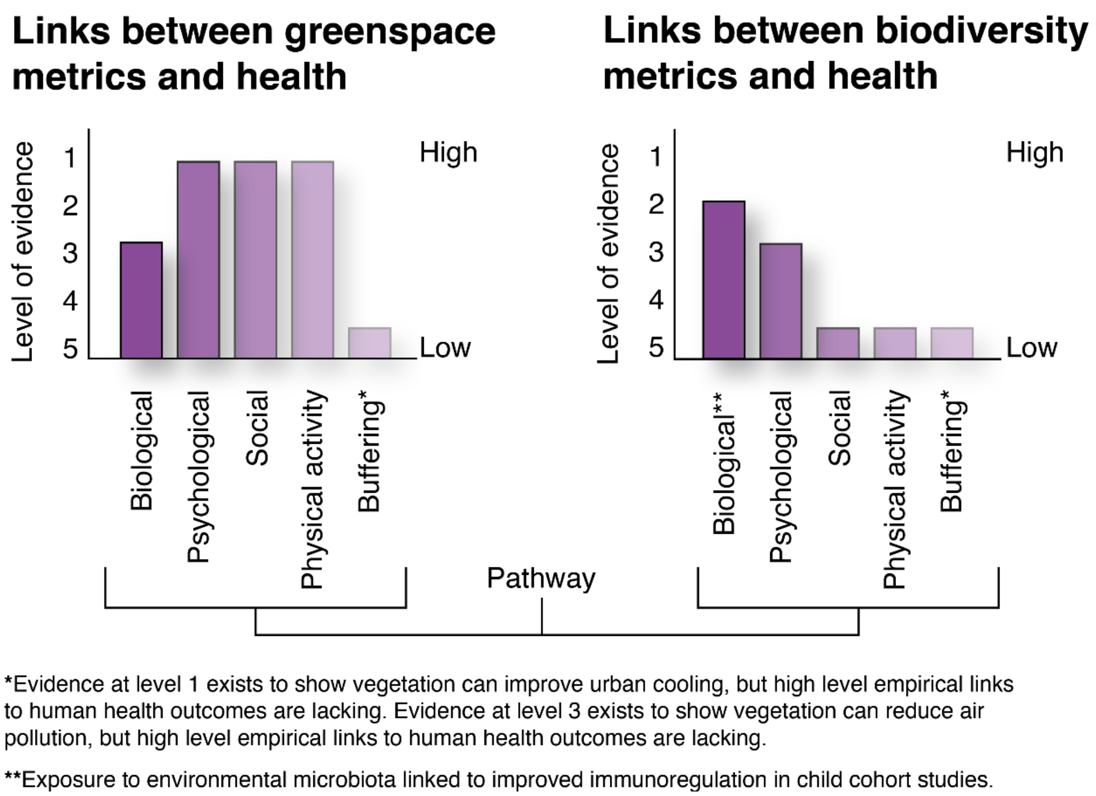

Fig. 4. Summary of the evidence level for the links between greenspace and health and biodiversity and health.

DISCUSSION AND CONCLUSIONS

It is clear that considerably more research is required to better understand the connections and causative pathways between biodiversity (e.g., using metrics such as taxonomy, diversity/richness, structure) and the various health outcomes. We found mixed evidence for positive relationships between biodiversity and human health, which is consistent with other reviews (Aerts et al. 2018, Houlden et al. 2021). A constructive response in this situation would be to support and promote these biodiversity-health research requirements. However, there is also substantial literature assessing the effects of 'green space' and broader classifications of nature on human health, and sufficient evidence overall to act now in terms of implementing strategies and interventions — e.g., conserving, designing and restoring nature and creating nature-based activities along with safe, equitably distributed and accessible open spaces with human health and wellbeing in mind (Robinson and Breed, 2019; Watkins et al. 2021).

To summarise, there is a moderate level of evidence to support the environmental microbiota-human health pathway (**level 2-3**), and a moderate-high level of evidence to support the broader nature classification pathways to various health outcomes, from stress reduction to enhanced wellbeing, and improved social cohesion (**level 1-3**). However, minimal specific biodiversity metrics were used, indicating a clear research gap. There are well-established frameworks to assess the effects of broad classifications of nature on human health and wellbeing (e.g., exploring green space on wellbeing via validated psychological instruments; forest bathing on stress reduction via cortisol analysis). These can assist future studies (see Box 4 for potential areas for future research) in linking biodiversity metrics to human health outcomes.

Our three case studies on underrepresented linkages highlight the roles that biodiversity and its loss have on Indigenous Peoples' sovereignty, urban lived experiences and equity, and infectious diseases such as COVID-19. Prioritising Indigenous Peoples' health as the stewards of the remaining key biodiversity areas in the world is necessary to reduce the likelihood of further biodiversity loss (Redvers et al. 2022). Interconnected with this biodiversity conservation is the conservation of Indigenous languages and knowledges, which in turn, are important determinants of the health and wellbeing of Indigenous communities (Sivak et al. 2019). The second case study suggested that people who may benefit the most from the health benefits of urban biodiversity are often the least able to access it due to various socio-economic and socio-cultural barriers (Cronin-de-Chavez et al. 2019). Addressing this concern must be prioritised in any urban green infrastructure policy.

Otherwise, we risk widening the gaps in social and ecological injustice. It is becoming increasingly clear that biodiversity plays an important role in the containment and outbreak of infectious disease agents and humans' ability to respond to the diseases via immunoregulatory pathways (Robinson et al. 2022). We call for more research and awareness of the socioecological interconnections in these three underrepresented case studies.

Recent calls have been made to consider ecosystem restoration as an effective public health intervention, which can bring several important co-benefits (Breed et al. 2021). For example, the act of restoring biodiverse environments may promote immune regulation through enhanced exposure to diverse microbiota, thereby facilitating the biological pathways to favourable health (Robinson et al. 2022). Restoring nature more broadly (and reversing encroachment) can contribute to reducing the risk of zoonotic spillover by creating habitat for stable populations of disease vectors and restricting human-wildlife interactions (outside of urban environments) (Gibb et al. 2020; Plowright et al. 2021). Moreover, active engagement in ecosystem restoration can be implemented as a restoration-based health intervention (Breed et al. 2021). This 'reciprocal restoration' process can have important psychosocial and physical health benefits whilst giving back to the land and promoting nature connectedness and environmental stewardship.

It should be noted that there are important ethical considerations when it comes to expecting natural environments to ameliorate toxins and adapt to anthropogenic stressors. This is true from both an intrinsic value, where ecosystems and their biodiversity have value in their own right, and an instrumental value perspective, where ecosystems are seen to provide a means to an end or a service that only benefits humans. The latter (instrumental value) is what

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underscores 'ecosystem services'. This concept can be problematic as it reinforces the one-sided relationship between humans and the rest of biodiversity. Whereas, reciprocity is key to restoring and conserving biodiversity and human health.

There is a need for improved policy developments that promote and manage ecosystem restoration as a public health intervention. This should include a greater consideration of the integration of health-biodiversity co-benefits in implementing nature-based solutions and promoting reciprocity with the land.

Box 4. Potential areas for future research.

- Investigate the effects of environmental microbiome exposure on human immune function – cohort studies and randomised controlled trial designs.
- Build upon the plant diversity study (Donovan et al. 2021) and assess potential microbial pathways to protection against acute lymphoblastic leukaemia.
- Assess the effects of general biodiversity metrics (composition, structure, diversity) on stress reduction – e.g., via cortisol analysis and perceived stress scale (PSS).
- Assess the effects of general biodiversity metrics (composition, structure, diversity) on ability to enhance nature connectedness – e.g., via Connectedness to Nature Scale (CNS), or Nature Relatedness scale (NR-6).
- Assess the effects of general biodiversity metrics (composition, structure, diversity) on anxiety, depression and general wellbeing – e.g. via the Warwick-Edinburgh Mental Wellbeing Scale (WEMWBS).
- Assess the effects of general biodiversity metrics (composition, structure, diversity) on social cohesion and physical activity – with specific measures for improvements in cardiovascular function.

- Assess the effects of general biodiversity metrics (composition, structure, diversity) on environmental buffering potential – e.g., air quality, urban heat island, with specific measures for downstream health outcomes.
- For all of the above, it would be prudent to maximise the level of evidence via, for example, cohort studies and randomised controlled trials (see Fig. 1).

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GLOSSARY

Alpha diversity: Species richness in a system (the number of species in a population) and species evenness (the abundance of each species in a population).

Biodiversity hypothesis: Contact with natural environments enriches the human microbiome, promotes immune balance and protects from allergy and inflammatory disorders (Haahtela, 2019).

Biophilia: A hypothesis that proposes humans possess an innate affinity to connect with other forms of life. Edward O. Wilson introduced and popularized the hypothesis in his book, Biophilia (1984).

Dysbiosis: A term used to describe an imbalance or maladaptation in a microbiome (collection of microbial communities in a given environment), typically with adverse effects on animal health.

Ecosystem restoration: The process of assisting the recovery of an ecosystem that has been degraded, damaged, or destroyed. Restoration ecology is the corresponding scientific discipline.

Eudaimonic wellbeing: The subjective experiences associated with eudaimonia or living a life of virtue in pursuit of human excellence.

Forest bathing: A Japanese practice (Shinrin-yoku 森林浴) of immersing oneself in a forest environment – a method of being calm amongst trees for a wellbeing benefit.

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Green Infrastructure: Strategically planned network of natural and semi-natural areas with other environmental features designed and managed to deliver a wide range of ecosystem services' in both rural and urban settings (European Commission's Green Infrastructure Strategy, 2013).

Microbe: Also known as microorganism. Microscopic organisms that exist as unicellular, multicellular or cell clusters. Examples include bacteria, fungi, viruses, archaea, protozoa, and algae.

Microbiome: The entire collection of microorganisms (and their genetic material) in a given environment, their habitat and theatre of activity.

Natural killer cells: White blood cells of the innate immune system. Also known as large granular lymphocytes. They represent 5–20% of all circulating lymphocytes in humans.

Nature connectedness: One's affective, cognitive and experiential connection with the rest of the natural world.

NDVI: Normalised difference vegetation index – a remote sensing measure of relative landcover greenness.

Noncommunicable disease: Chronic, non-infectious diseases such as diabetes and inflammatory bowel disease.

Old Friends hypothesis: An update by Rook et al. (2003) on the hygiene hypothesis (Strachan, 1989)- suggesting that because of our long evolutionary association with certain microorganisms, they are recognised by the innate immune system as harmless or in some cases, treated as "friends" because they are needed for regulation.

Phytoncide: An organic plant-based volatile compound that is antimicrobial and is known to stimulate immune cells and neurotransmitters, with beneficial outcomes.

PM2.5: Refers to particulate matter 2.5 - tiny particles or droplets in the air that are two and one half microns or less in width.