Cities, biodiversity, and health: We need healthy urban microbiome initiatives

Flies, E.J[1*]., Skelly, C[2]., Lovell, R.[3], Breed, M.F.[4], Phillips, D.[2] and Weinstein, P.[4]

[1]School of Natural Sciences, University of Tasmania, Hobart, Australia 7001

[2]Public Health Dorset, Dorchester, UK DT11TP

[3]European Centre for Environment and Human Health, University of Exeter Medical School, Truro, UK TR1 3HD

[4]School of Biological Sciences and the Environment Institute, University of Adelaide, SA 5005 Australia

*Corresponding author – Emily.flies@utas.edu.au

Abstract

Current evidence suggests that diverse environmental microbiomes contribute positively to human health, and could account for known associations between urban green space and improved health. We summarise the state of knowledge that could inform the development of healthy urban microbiome initiatives (HUMI) to re-connect urban populations to biodiverse microbial communities.

In his seminal book “On Airs, Water and Places”, Hippocrates - the ‘father of Western medicine’ - wrote of the importance of healthy places for healthy humans (Hippocrates & Translated by Francis Adams, 400BC). Many of the major public health advances in urban areas over the last centuries have emerged from the recognition that clean water, clean air and unpolluted environments prevent communicable diseases. This is particularly evident in developed countries where cholera, plague and tuberculosis have been all but eliminated due to sanitation and housing upgrades. The world now faces a pandemic of non-communicable disease and, despite the resurgence of ‘socio-ecological’ models of public health (Lang & Rayner, 2012), which explicitly link people and place, the focus has largely been on individual risks and behaviours rather than environmental conditions.

The World Health Organisation (WHO) listed ‘a stable ecosystem’ as a prerequisite for health in their Ottawa Charter (1986), and more than 1000 cities have signed up to promote “healthy [physical and social] environs” in the Healthy Cities program (WHO, 2018). Despite these ambitions, few comprehensive and systematic programmes exist to achieve healthy people in healthy places. When they do exist, initiatives are often localised, sporadic or risk/exposure specific without any clear theory of change underpinning the approaches taken. The lack of strategic planning is problematic as the relationships between environmental and human health are multifactorial, indirect and complex (Fig. 1). The putatively causal associations often lack a quantified ‘dose response’ effect and are influenced by powerful countervailing interests (e.g. commercial or governmental pressures) in maintaining the current responsive, rather than preventative, health measures (Mindell, Reynolds, Cohen, & McKee, 2012). Despite the uncertainty in what works, where and for whom, there is general agreement that urban green spaces can play an important role in creating healthy cities (WHO & Europe, 2016).

[Insert Figure 1 here]

The term ‘urban green space’ has been used to represent a variety of ecosystems and land use types. Here, we use it to loosely refer to any vegetated area in a town or city to which people may be exposed. They include the public or private parks, forests, riparian zones, gardens, sport fields and playgrounds that urban lives intersect with on a daily basis. Green spaces can include places for commuting (e.g. paths for walking or cycling; Fig. 2), places for recreation, domestic spaces, and places of work for certain professions (e.g. professional sports people, landscapers/gardeners).

[Insert Figure 2 here]

The last few decades have seen a rise in the percent of the population residing in cities (urbanicity), a drop in infectious disease rates, and a rise in rates for many non-communicable diseases. It is well known that physical and social environments impact on population-level health of a city (Rydin et al., 2012). Broken windows, congested traffic, unmanaged waste and overcrowding can lead to a physically and mentally unhealthy population. Biodiverse urban green spaces have been identified as an important contributory factor in improving many aspects of public health, but the mechanisms are often not clear. In this editorial, we focus on the role that microbially diverse urban green spaces can have on urban health (Flies et al., 2017), and the need for a systematic, global, healthy urban microbiome initiative (HUMI) to maximise the health gain from exposure to microbial ‘old friends’ (Rook, 2013).

What do we know about the green space contribution to health?

A growing body of evidence has demonstrated that green spaces are key components of healthy places, contributing directly and indirectly to population health and to the quality of life of citizens. Urban green spaces indirectly impact human health through ecosystem services including mitigating heat island effects, air pollution and noise (MEA & Millennium Ecosystem Assessment, 2005; WHO & Europe, 2016). Urban green spaces, of all types, also provide crucial reservoirs of biodiversity underpinning ecosystem services and functions in urban areas.

Much of the research linking exposure to urban green spaces directly to health has come from the developed west (Lai et al. in press) and has focused on exploring relatively simple exposures and outcomes (Hartig, Mitchell, de Vries, & Frumkin, 2014). Syntheses of this predominantly cross-sectional epidemiological evidence suggests that green spaces in urban residential areas are linked to lower obesity, cardio-vascular disease and mortality and to greater overall self-reported health (Gascon et al., 2016; Lachowycz & Jones, 2011; Twohig-Bennett & Jones, 2018; World Health Organization & Convention on Biological Diversity, 2015), among other benefits. The strongest evidence is perhaps for green space positively impacting mental health and wellbeing, including reductions in stress, fatigue, anxiety and rates of depression (Gascon et al., 2015). These benefits appear to be most significant for marginalised groups; in Europe, socioeconomic inequalities in mental wellbeing have been found to be narrower in greener urban areas (Gascon et al., 2015; Hartig et al., 2014; Mitchell et al., 2008). The greater use of longitudinal data has strengthened the reliability of these outcomes and furthered our understanding of the connection between environment and health through the lifecourse (T Sanders, Feng, Fahey, Lonsdale, & Astell-Burt, 2015; Taren Sanders, Feng, Fahey, Lonsdale, & Astell-Burt, 2015; Weimann et al., 2015). Improved quality of life, increased physical activity and enhanced social interactions have been identified as potential mechanisms connecting green space to improvements in health and wellbeing outcomes.

The associations are not, however, universal. The health benefits from urban green spaces appear to be context dependent, with varying patterns of effect depending on the geographical and socio-cultural location, climate, urban form, and other such factors. We also see variation in outcomes according to individual and population level factors such as gender, age and social economic status (Alcock, White, Wheeler, Fleming, & Depledge, 2014; Astell-Burt, Mitchell, & Hartig, 2014; van den Berg et al., 2015).

Our understanding of health benefits of urban green space is limited for a number of reasons. First, much of the evidence relates only to the residential environment, ignoring green spaces around the work-place or other locations to which people are regularly exposed (e.g. commuter routes). Second, often crude assessments and characterisations of the environment are used, classifying spaces on a continuum of ‘green’ to ‘not green’ with little consideration of the biodiversity, quality, state and type of green spaces (Wheeler et al., 2015). Third, assessments of green space exposure are limited by assumptions of exposure, typically based on a person’s residential proximity to green space, rather than actual assessment of green space exposure age, frequency, duration, and type. Finally, there is substantial variation in the design of studies into green space health benefits (Ekkel & de Vries, 2017). Few studies have made use of designs that examine causative, rather than associative, factors driving the observed benefits.

Given the overwhelming evidence for green space health benefits, some governments (e.g. the United Kingdom; Ham & Alderwick, 2015; NHS, 2014) have begun developing policy to harness the potential of urban green spaces (See Solutions Box). However, there is still a need to better understand the mechanisms driving green space health benefits so that green spaces can be designed, restored, or used more effectively to benefit both the environment and human health concurrently. One of the promising mechanisms is that exposure to biodiverse environmental microbiota causes a cascade of upstream health benefits (Fig. 1; Flies et al., 2017; Kuo, 2015; World Health Organization & Convention on Biological Diversity, 2015).

[insert Solutions Box here]

Mechanisms for health benefits from microbially diverse green space

We could easily be considered to be in the decade of the microbiome; hardly a day goes by without another connection forged between the human microbiome and health. For example, in neonatology it has been found that cesarean births, antenatal antibiotics and bottle feeding alter microbial colonization, and are associated with immune dysfunction (Mueller, Bakacs, Combellick, Grigoryan, & Dominguez-Bello, 2015). Immunotherapy studies have found that anti-cancer treatments (CTLA-4 blockade) are only effective if certain gut microbes are present (Vétizou et al., 2015). Gastroenterology studies have discovered that fecal transplants from healthy individuals can reduce inflammatory bowel disorders (Costello et al., 2017).

However, the environmental source of the human microbiome, and the role of *natural environmental* microbiomes in human health has largely been neglected. It is clearly possible that there are broader health benefits of exposure to the microbiomes of biodiverse green spaces (Flandroy et al., 2018; Flies et al., 2017; Mills et al., 2017) but these have largely been unexplored experimentally or even epidemiologically.

The environment within which humans evolved was biodiverse (faunistically, floristically, and microbially; Kellert & Wilson, 1993), so a negative health effect of reduced exposure to biological diversity is somewhat intuitive and serves as the foundation for the 'old friends' hypothesis (Rook, 2013). However, fundamental research gaps remain in revealing the human health benefits from urban green spaces (Craig, Logan, & Prescott, 2016; Flies et al., 2017; Liddicoat, Waycott, & Weinstein, 2016). Could exposure to biodiverse microbiomes in urban green spaces provide better immune priming and health outcomes (Mills et al., 2017)? If so, it remains unclear how the *quality* of urban green spaces would affect such a relationship. Such *quality* indicators would include plant, animal, or structural diversity (Fig. 3), which associate with microbial diversity and therefore exposure to a 'healthy' environmental microbiome. If such a relationship can be substantiated and quantified, a significant reduction in disease burden could potentially be achieved by including high *quality*, biodiverse urban green space in city planning.

[Insert Figure 3 here]

What do we know about environmental microbiomes?

As of yet we still know very little about the microbiomes in urban green spaces. We know urban green microbiomes are different than those in built environments (Mhuireach et al., 2016) and can harbour great diversity of microbial species (Ramirez et al., 2014). There are four main components to the environmental microbiome relevant to urban green spaces: substrate, air, water, and plant-dependent microbes (Table 1; Fig. 4). Much is known about each of these microbiomes in different contexts; how soil microbiota interact with plants in ecological (Bissett et al., 2016; Bulgarelli et al., 2012; Urbina et al., 2018) or agricultural settings (Bakker, Otto-hanson, Lange, Bradeen, & Kinkel, 2013; Rousk et al., 2010), or how aerial microbes relate to land use (Bowers, McLetchie, Knight, & Fierer, 2011; Mhuireach et al., 2016), for example. We also know that it is possible to restore microbiomes from a degraded or artificial state to one that represents wild, native areas (Cavagnaro, Cunningham, & Fitzpatrick, 2016; Gellie, Mills, Breed, & Lowe, 2017; Yan et al., 2018). But despite the potential for positive health impact (Charlop-Powers et al., 2016), the microbiomes in urban green spaces remain poorly studied.

[Insert Figure 4 here]

There is also a lack of knowledge of the microbiomes associated with human structures (e.g. benches, paths) in these green spaces, and how environmental microbiomes fluctuate through time (e.g. diurnally, daily, seasonally, yearly), external urban influences (e.g. pollution, traffic, surrounding land use), and across micro- (within-green spaces) and macro-geographic (e.g. latitude, biome, human development index) scales.

[insert Table 1 here]

Rothschild et al. (2018) clearly showed that people's environment has an stronger influence on their gut microbiomes than people's genetic background. However, 'environment' in this context refers to anything non-inherited, including diet, lifestyle, and pharmaceuticals. Very little is known of the influence that the outdoor environment has on human microbiomes. Consequently, very few studies have directly linked non-diet environmental microbiomes to human health (but see Liddicoat et al., 2018). However, there is a large body of evidence that supports the inference that environmental microbiomes could potentially impact on human health (Flandroy et al., 2018; Rook, 2013; von Hertzen et al., 2015). Therefore, there is the potential to improve human health by designing microbially rich, biodiverse, heathy urban green spaces.

Healthy urban microbiome initiatives

Microbiome science is rapidly delivering new understanding of the microbial mechanisms of health but it has yet to be linked to contact with natural environments. A Healthy Urban Microbiome Initiative (HUMI) has now emerged to examine these connections specifically, providing the basis for a public health intervention in the form of healthy urban greenspace exposure (see Solutions Box).

Microbial abundance and diversity have been identified as one of the reasons rural farming populations experience less inflammatory related diseases and immune dysfunction (Ege et al., 2011; Hanski et al., 2012; Riedler et al., 2001; Stein et al., 2016; von Mutius & Radon, 2008), but the relationship is complex. If we can identify the species, ecological communities or routes of exposure for environmental microbiomes that are most conducive to health, green space public health interventions such as HUMI can be more effective.

In doing so, we have the potential to improve the health and wellbeing of urban populations by modifying their environment; regreening cities and restoring biodiversity into urban green spaces, which may then provide human and environmental health co-benefits in ways that we could not have conceived of before the rise of microbiome science (Mills et al., 2017). This creates the possibility of a future in which green spaces are no longer considered an economic burden, due to forgone development and maintenance costs, but rather as an essential component of urban design that provides benefits to physical, mental wellbeing – and the associated economic benefits.

Conclusions

Urban green spaces have a clear benefit to both environmental and human health. The mechanisms behind this connection are not yet clear, but exposure to biodiverse environmental microbiomes provides one possible explanation with tremendous promise for public health applications. If we can identify the characteristics of health-giving urban microbiomes, we can then manipulate aspects of the environment to promote microbial biodiversity (e.g. urban spaces with a diverse structure, flora, and fauna), and promote the types of interactions that put people in contact with these beneficial environmental microbiomes.

To achieve this, however, we will need to makes some fundamental changes to how we think. We need more place-based, preventative, wellness-focused healthcare systems that interact with urban planners, environmental managers, and politicians to promote healthy urban designs and living. We need greater evidence of the mechanisms, and characteristics connecting green spaces to health. Finally, we need better decision-making frameworks (e.g.

integration of ecological networks or complexity science) to support the trade-offs surrounding healthy urban design (Rydin et al., 2012). Given the rapid rate and scale of global urbanisation and current non-communicable disease trends, the development of a new public health tool – healthy urban microbiomes – could not come at a better time. A global healthy urban microbiome initiative (HUMI) that capitalises on this potential could mitigate the adverse effects of our otherwise increasing isolation from biodiverse environments.

Acknowledgements: EJF is funded by Australian Research Council grant FL160100101.

Works Cited

Alcock, I., White, M. P., Wheeler, B. W., Fleming, L. E., & Depledge, M. H. (2014). Longitudinal Effects on Mental Health of Moving to Greener and Less Green Urban Areas. *Environmental Science & Technology*, *48*(2), 1247–1255. https://doi.org/10.1021/es403688w

Astell-Burt, T., Mitchell, R., & Hartig, T. (2014). The association between green space and mental health varies across the lifecourse. A longitudinal study. *Journal of Epidemiology and Community Health*, *68*(6), 578–583. https://doi.org/10.1136/jech-2013-203767

Bakker, M. G., Otto-hanson, L., Lange, A. J., Bradeen, J. M., & Kinkel, L. L. (2013). Plant monocultures produce more antagonistic soil Streptomyces communities than high-diversity plant communities. *Soil Biology and Biochemistry*, *65*, 304–312. https://doi.org/10.1016/j.soilbio.2013.06.007

Bissett, A., Fitzgerald, A., Meintjes, T., Mele, P. M., Reith, F., Dennis, P. G., … Richardson, K. (2016). Introducing BASE: the Biomes of Australian Soil Environments soil microbial diversity database. *GigaScience*, *5*(1), 21. https://doi.org/10.1186/s13742-016-0126-5

Bowers, R. M., McLetchie, S., Knight, R., & Fierer, N. (2011). Spatial variability in airborne bacterial communities across land-use types and their relationship to the bacterial communities of potential source environments. *The ISME Journal*, *5*(4), 601–612. https://doi.org/10.1038/ismej.2010.167

Brodie, E. L., DeSantis, T. Z., Parker, J. P. M., Zubietta, I. X., Piceno, Y. M., & Andersen, G. L. (2007). Urban aerosols harbor diverse and dynamic bacterial populations. *Proceedings of the National Academy of Sciences*, *104*(1), 299–304. https://doi.org/10.1073/pnas.0608255104

Bulgarelli, D., Rott, M., Schlaeppi, K., Ver Loren van Themaat, E., Ahmadinejad, N., Assenza, F., … Schulze-Lefert, P. (2012). Revealing structure and assembly cues for Arabidopsis root-inhabiting bacterial microbiota. *Nature*, *488*(7409), 91–95. https://doi.org/10.1038/nature11336

Burrows, S. M., Elbert, W., Lawrence, M. G., & Pöschl, U. (2009). Bacteria in the global atmosphere – Part 1: Review and synthesis of literature data for different ecosystems. *Atmos. Chem. Phys. Atmospheric Chemistry and Physics*, *9*, 9263–9280. Retrieved from www.atmos-chem-phys.net/9/9263/2009/

Cavagnaro, T. R., Cunningham, S. C., & Fitzpatrick, S. (2016). Pastures to woodlands: changes in soil microbial communities and carbon following reforestation. *Applied Soil Ecology*, *107*, 24–32. https://doi.org/10.1016/J.APSOIL.2016.05.003

Charlop-Powers, Z., Pregitzer, C. C., Lemetre, C., Ternei, M. A., Maniko, J., Hover, B. M., … Brady, S. F. (2016). Urban park soil microbiomes are a rich reservoir of natural product biosynthetic diversity. *Proceedings of the National Academy of Sciences*, *113*(51), 14811–14816. https://doi.org/10.1073/pnas.1615581113

Costello, S. P., Waters, O., Bryant, R. V., Katsikeros, R., Makanyanga, J., Schoeman, M., … Andrews, J. M. (2017). Short duration, low intensity, pooled fecal microbiota transplantation induces remission in patients with mild-moderately active ulcerative colitis: A randomised controlled trial. *Gastroenterology*, *152*(5), S198–S199. https://doi.org/10.1016/S0016-5085(17)30969-1

Craig, J. M., Logan, A. C., & Prescott, S. L. (2016). Natural environments , nature relatedness and the ecological theater : connecting satellites and sequencing to shinrin-yoku. *Journal of Physiological Anthropology*, *35*(1), 1–10. https://doi.org/10.1186/s40101-016-0083-9

Ege, M. J., Mayer, M., Ph, D., Normand, A., Ph, D., Genuneit, J., … Group, S. (2011). Exposure to environmental microorganisms and childhood asthma. *New England Journal of Medicine*, *364*(8), 701–709.

Ekkel, E. D., & de Vries, S. (2017). Nearby green space and human health: Evaluating accessibility metrics. *Landscape and Urban Planning*, *157*, 214–220. https://doi.org/10.1016/J.LANDURBPLAN.2016.06.008

Flandroy, L., Poutahidis, T., Berg, G., Clarke, G., Dao, M.-C., Decaestecker, E., … Rook, G. (2018). The impact of human activities and lifestyles on the interlinked microbiota and health of humans and of ecosystems. *Science of The Total Environment*, *627*, 1018–1038. https://doi.org/10.1016/J.SCITOTENV.2018.01.288

Flies, E. J., Skelly, C., Negi, S. S., Prabhakaran, P., Liu, Q., Liu, K., … Weinstein, P. (2017). Biodiverse green spaces: a prescription for global urban health. *Frontiers in Ecology and the Environment*, *15*(9), 510–516. https://doi.org/10.1002/fee.1630

Gascon, M., Triguero-Mas, M., Martinez, D., Dadvand, P., Forns, J., Plasencia, A., & Nieuwenhuijsen, M. J. (2015). Mental health benefits of long-term exposure to residential green and blue spaces: a systematic review. *International Journal of Environmental Research and Public Health*, *12*(4), 4354–4379. https://doi.org/10.3390/ijerph120404354

Gascon, M., Triguero-Mas, M., Martinez, D., Dadvand, P., Rojas-Rueda, D., Plasencia, A., & Nieuwenhuijsen, M. J. (2016). Residential green spaces and mortality: A systematic review. *Environment International*, *86*, 60–67. https://doi.org/10.1016/j.envint.2015.10.013

Gellie, N. J. C., Mills, J. G., Breed, M. F., & Lowe, A. J. (2017). Revegetation rewilds the soil bacterial microbiome of an old field. *Molecular Ecology*, *26*(11), 2895–2904.

https://doi.org/10.1111/mec.14081

Ham, C., & Alderwick, H. (2015). Place-based systems of care: A way forward for the NHS in England. *King's Fund*, (November).

Hanski, I., von Hertzen, L., Fyhrquist, N., Koskinen, K., Torppa, K., Laatikainen, T., … Haahtela, T. (2012). Environmental biodiversity, human microbiota, and allergy are interrelated. *Proceedings of the National Academy of Sciences*, *109*(21), 8334–8339. https://doi.org/10.1073/pnas.1205624109

Hartig, T., Mitchell, R., de Vries, S., & Frumkin, H. (2014). Nature and Health. *Annual Review of Public Health*, *35*(1), 207–228. https://doi.org/10.1146/annurev-publhealth-032013-182443

Hippocrates, & Translated by Francis Adams. (400BC). *On Airs, Waters, And Places*. Kos, Greece. Retrieved from https://ebooks.adelaide.edu.au/h/hippocrates/airs/

Kellert, S. R., & Wilson, E. O. (Eds.). (1993). *The Biophilia Hypothesis*. Washington, D.C.: Island Press. Retrieved from https://books.google.com.au/books?hl=en&lr=&id=GAO8BwAAQBAJ&oi=fnd&pg=PP6&dq=biophilia+wilson&ots=plqaLGG1x_&sig=CyRZTxbv9__ahyash6eKWXbfars#v=onepage&q=biophilia wilson&f=false

Kuo, M. (2015). How might contact with nature promote human health? Promising mechanisms and a possible central pathway. *Frontiers in Psychology*, *6*(August), 1093–2000. https://doi.org/10.3389/fpsyg.2015.01093

Lachowycz, K., & Jones, A. P. (2011). Greenspace and obesity: a systematic review of the evidence. *Obesity Reviews, 12*(5), e183–e189. https://doi.org/10.1111/j.1467-789X.2010.00827.x

Lang, T., & Rayner, G. (2012). Ecological public health: The 21st century's big idea? An essay by Tim Lang and Geof Rayner. *BMJ (Online), 345*(7872). https://doi.org/10.1136/bmj.e5466

Liddicoat, C., Bi, P., Waycott, M., Glover, J., Breed, M., & Weinstein, P. (2018). Ambient soil cation exchange capacity inversely associates with infectious and parasitic disease risk in regional Australia. *Science of the Total Environment Journal*, *626*, 117–125. https://doi.org/10.1016/j.scitotenv.2018.01.077

Liddicoat, C., Waycott, M., & Weinstein, P. (2016). Environmental Change and Human Health: Can Environmental Proxies Inform the Biodiversity Hypothesis for Protective Microbial–Human Contact? *BioScience*, biw127. https://doi.org/10.1093/biosci/biw127

McLellan, S. L., Fisher, J. C., & Newton, R. J. (2015). The microbiome of urban waters. *International Microbiology : The Official Journal of the Spanish Society for Microbiology*, *18*(3), 141–149. https://doi.org/10.2436/20.1501.01.244

MEA, & Millennium Ecosystem Assessment. (2005). *Synthesis report*. Washington, D.C.: Island Press. Retrieved from https://www.millenniumassessment.org/en/GraphicResources.html

Mhuireach, G., Johnson, B. R., Altrichter, A. E., Ladau, J., Meadow, J. F., Pollard, K. S., & Green, J. L. (2016). Urban greenness influences airborne bacterial community composition. *Science of The Total Environment*, *571*, 680–687. https://doi.org/10.1016/J.SCITOTENV.2016.07.037

Mills, J. G., Weinstein, P., Gellie, N. J. C., Weyrich, L. S., Lowe, A. J., & Breed, M. F. (2017). Urban habitat restoration provides a human health benefit through microbiome rewilding: the Microbiome Rewilding Hypothesis. *Restoration Ecology*, *25*(6), 866–872. https://doi.org/10.1111/rec.12610

Mindell, J. S., Reynolds, L., Cohen, D. L., & McKee, M. (2012). All in this together: the corporate capture of public health. *BMJ (Clinical Research Ed.)*, *345*, e8082. https://doi.org/10.1136/BMJ.E8082

Mitchell, R., Popham, F., Smith, G. D., Shaw, M., Mitchell, R., Dorling, D., … Macintyre, S. (2008). Effect of exposure to natural environment on health inequalities: an observational population study. *Lancet*. https://doi.org/10.1016/S0140-6736(08)61689-X

Mueller, N. T., Bakacs, E., Combellick, J., Grigoryan, Z., & Dominguez-Bello, M. G. (2015). The infant microbiome development: mom matters. *Trends in Molecular Medicine*, *21*(2), 109–117. https://doi.org/10.1016/j.molmed.2014.12.002

NHS. (2014). *Five year forward view*. London. Retrieved from https://www.england.nhs.uk/wp-content/uploads/2014/10/5yfv-web.pdf

Ramirez, K. S., Leff, J. W., Barberán, A., Bates, S. T., Betley, J., Crowther, T. W., … Fierer, N. (2014). Biogeographic patterns in below-ground diversity in New York City's Central Park are similar to those observed globally. *Proceedings. Biological Sciences*, *281*(1795), 20141988. https://doi.org/10.1098/rspb.2014.1988

Riedler, J., Braun-Fahrländer, C., Eder, W., Schreuer, M., Waser, M., Maisch, S., … von Mutius, E. (2001). Exposure to farming in early life and development of asthma and allergy: a cross-sectional survey. *The Lancet*, *358*(9288), 1129–1133. https://doi.org/10.1016/S0140-6736(01)06252-3

Roesch, L. F. W., Fulthorpe, R. R., Riva, A., Casella, G., Hadwin, A. K. M., Kent, A. D., … Triplett, E. W. (2007). Pyrosequencing enumerates and contrasts soil microbial diversity. *The ISME Journal*, *1*(4), 283–290. https://doi.org/10.1038/ismej.2007.53

Rook, G. A. W. (2013). Regulation of the immune system by biodiversity from the natural environment: an ecosystem service essential to health. *Proceedings of the National Academy of Sciences of the United States of America*, *110*(46), 18360–18367. https://doi.org/10.1073/pnas.1313731110

Rothschild, D., Weissbrod, O., Barkan, E., Kurilshikov, A., Korem, T., Zeevi, D., … Segal, E. (2018). Environment dominates over host genetics in shaping human gut microbiota. *Nature*, *555*(7695), 210–215. https://doi.org/10.1038/nature25973

Rousk, J., Bååth, E., Brookes, P. C., Lauber, C. L., Lozupone, C., Caporaso, J. G., … Fierer, N. (2010). Soil bacterial and fungal communities across a pH gradient in an arable soil. *ISME Journal*, *4*(10), 1340–1351. https://doi.org/10.1038/ismej.2010.58

Rydin, Y., Bleahu, A., Davies, M., Davila, J. D., Friel, S., di Grandis, G., … Wilson, J. (2012). Shaping Cities for Health: the complexities of planning urban environments in the 21st century. *The Lancet*, *379*(Special Issue), 2079–2108. https://doi.org/10.1016/S0140-6736(12)60435-8.Shaping

Sanders, T., Feng, X., Fahey, P. P., Lonsdale, C., & Astell-Burt, T. (2015). Greener neighbourhoods, slimmer children? Evidence from 4423 participants aged 6 to 13 years in the Longitudinal Study of Australian children. *International Journal of Obesity (2005)*, *39*(8), 1224–1229. https://doi.org/10.1038/ijo.2015.69

Sanders, T., Feng, X., Fahey, P. P., Lonsdale, C., & Astell-Burt, T. (2015). The influence of neighbourhood green space on children's physical activity and screen time: findings from the longitudinal study of Australian children. *International Journal of Behavioral Nutrition and Physical Activity*, *12*(1), 126. https://doi.org/10.1186/s12966-015-0288-z

Stein, M. M., Hrusch, C. L., Gozdz, J., Igartua, C., Pivniouk, V., Murray, S. E., … Sperling, A. I. (2016). Innate Immunity and Asthma Risk in Amish and Hutterite Farm Children. *New England Journal of Medicine*, *375*(5), 411–421. https://doi.org/10.1056/NEJMoa1508749

Twohig-Bennett, C., & Jones, A. (2018). The health benefits of the great outdoors: a systematic review of greenspace exposure and health outcomes. *Environmental Research*, *166*(February), 628–237. https://doi.org/10.15124/CRD42015025193

Urbina, H., Breed, M. F., Zhao, W., Lakshmi Gurrala, K., Andersson, S. G. E., Ågren, J., … Rosling, A. (2018). Specificity in Arabidopsis thaliana recruitment of root fungal communities from soil and rhizosphere. *Fungal Biology*, *122*(4), 231–240. https://doi.org/10.1016/J.FUNBIO.2017.12.013

Vacher, C., Hampe, A., Porté, A. J., Sauer, U., Compant, S., & Morris, C. E. (2016). The Phyllosphere: Microbial Jungle at the Plant–Climate Interface. *Annual Review of Ecology, Evolution, and Systematics*, *47*(1), 1–24. https://doi.org/10.1146/annurev-ecolsys-121415-032238

van den Berg, M., Wendel-Vos, W., van Poppel, M., Kemper, H., van Mechelen, W., & Maas, J. (2015). Health benefits of green spaces in the living environment: A systematic review of epidemiological studies. *Urban Forestry and Urban Greening*, *14*(4), 806–816. https://doi.org/10.1016/j.ufug.2015.07.008

Vaz-Moreira, I., Nunes, O. C., & Manaia, C. M. (2014). Bacterial diversity and antibiotic resistance in water habitats: searching the links with the human microbiome. *FEMS Microbiology Reviews*, *38*(4), 761–778. https://doi.org/10.1111/1574-6976.12062

Vétizou, M., Pitt, J. M., Daillère, R., Lepage, P., Waldschmitt, N., Flament, C., … Zitvogel, L. (2015). Anticancer immunotherapy by CTLA-4 blockade relies on the gut microbiota. *Science*, *350*(6264), 1079–1084. Journal Article. https://doi.org/10.1126/science.aad1329

von Hertzen, L., Beutler, B., Bienenstock, J., Blaser, M., Cani, P. D., Eriksson, J., … de Vos, W. M. (2015). Helsinki alert of biodiversity and health. *Annals of Medicine*, *47*(3), 1–8. https://doi.org/10.3109/07853890.2015.1010226

von Mutius, E., & Radon, K. (2008). Living on a Farm: Impact on Asthma Induction and Clinical Course. *Immunology and Allergy Clinics of North America*, *28*(3), 631–647. https://doi.org/10.1016/j.iac.2008.03.010

Weimann, H., Rylander, L., Albin, M., Skärbäck, E., Grahn, P., Östergren, P.-O., & Björk, J. (2015). Effects of changing exposure to neighbourhood greenness on general and mental health: A longitudinal study. *Health & Place*, *33*, 48–56. https://doi.org/10.1016/J.HEALTHPLACE.2015.02.003

Wheeler, B. W., Lovell, R., Higgins, S. L., White, M. P., Alcock, I., Osborne, N. J., …

Depledge, M. H. (2015). Beyond greenspace: an ecological study of population general health and indicators of natural environment type and quality. *International Journal of Health Geographics*, *14*, 17. https://doi.org/10.1186/s12942-015-0009-5

WHO. (2018). WHO | Types of Healthy Settings. Retrieved July 19, 2018, from http://www.who.int/healthy_settings/types/cities/en/

WHO, & Europe, W. R. O. for. (2016). *Urban green spaces and health: a review of the evidence*. *World Heal. Organ.* Copenhagen.

World Health Organization. (1986). *World Health Organization. "The Ottawa charter for health promotion: first international conference on health promotion, Ottawa, 21 November 1986*. Geneva.

World Health Organization, & Convention on Biological Diversity. (2015). *Connecting global priorities: biodiversity and human health. A state of knowledge review*. (C. Romanelli, D. Cooper, D. Campbell-Lendrum, M. Maiero, W. B. Karesh, D. Hunter, & C. D. Golden, Eds.). Geneva, Switzerland: WHO Press.

Yan, D., Mills, J. G., Gellie, N. J. C., Bissett, A., Lowe, A. J., & Breed, M. F. (2018). High-throughput eDNA monitoring of fungi to track functional recovery in ecological restoration. *Biological Conservation*, *217*, 113–120. https://doi.org/10.1016/j.biocon.2017.10.035

Solutions Box: We provide two examples of components of HUMIs in action: a policy-led, ‘top-down’ initiative in England, and a research, ‘bottom-up’ initiative in Australia.

England: Policy to Practice

England is the home of the Hygiene Hypothesis and more recently, the Old Friends Hypothesis, both of which emphasise the negative impact that separation from nature has on the physical health of humans. In 2012, the *Health and Social Care Act* transferred local public health resources back to local government from the National Health Service (NHS) and came into force along with a statutory requirement for local government to reduce health inequalities. This policy has driven a focus on the ‘wider determinants’ of health through local statutory fora such as health and wellbeing boards. Links of the environment to human activity and non-communicable diseases have been a particular focus of many of these boards.

More recently, the NHS has started to reshape the national health program to better align with local efforts in order to reduce the gaps in health and wellbeing, and improve quality of care and financial sustainability (NHS 2014). The outcomes of this policy initiative have been the ‘Sustainability and Transformation’ plans for each of 44 areas of England and the formation of Integrated Care Systems. This signals a shift beyond the typical focus on organisational and medical services to a lifecourse and systems approach.

These are early days in what will, for England, be a radical transformation, but already the issue of urban green space has been prominent in local discussions. Collaboration between Public Health Dorset and HUMI (see below) is an illustration of the potential for environmental and health co-benefits. However, those co-benefits can only be achieved if the mechanistic evidence can overcome the various international logistic and political challenges (Flies et al 2017).

Australia: the HUMI research

There are daily revelations connecting microbiomes to human health outcomes. The human microbiome has been linked to obesity, depression, and cancer. However, our understanding of how the surrounding environment impacts the human microbiome is in its infancy.

The Healthy Urban Microbiomes Initiative (HUMI, based at the University of Adelaide, Australia) was developed to fill that gap. HUMI integrates microbiome science with ecology, public health and urban development to elucidate what influences urban microbiomes, how they can be manipulated, and how urban microbiomes impact human health. To this end, HUMI works with partners in Australia, the UK, India and China to collect soil, vegetation and aerial samples from local green spaces. With metagenomics and quantitative spatial models, the factors influencing urban microbial communities are being elucidated. With partners in the public health sector, these environmental microbiomes are being connected to human health outcomes. This knowledge can then feed back to inform local governments and the education sector looking to develop healthy, prosperous cities.

Major green space biome	Sample type	Relevance for human health	Key references
Substrate	Surface soil, sub-surface soils, pebbles and gravel	During direct interaction with substrates (e.g. digging in garden), major source of aerial microbiome	(Bissett et al., 2016; Ramirez et al., 2014; Roesch et al., 2007)
Water	Streams, lakes, ponds, sea water	During direct interaction, also a major source of aerial microbiome	(McLellan, Fisher, & Newton, 2015; Vaz-Moreira, Nunes, & Manaia, 2014)
Vegetation	Whole leaf/bark/root or swabs/washings of plant surface	Direct contact with plants, consumption of plants (e.g. garden), major source of aerial microbiome	(Bulgarelli et al., 2012; Vacher et al., 2016)
Air	Settlement traps, petri dishes, filtered vacuum samples	Most direct route of human (e.g. respiratory, oral and skin) exposure	(Bowers et al., 2011; Brodie et al., 2007; Burrows, Elbert, Lawrence, & Pöschl, 2009; Mhuireach et al., 2016)

Table 1: Main sources of environmental microbiomes, sampling techniques and health relevance for each. Key citations/references are also provided.

Figure 1: Connections between green spaces and various components of health and wellbeing

Figure 2: San Mateo Park (California, USA) provides opportunities for exercise (walking, bike riding), relaxation, recreation and interaction with humans, plants and environmental microorganisms.

Figure 3: Does a diversity of substrates (mulch, sand, grass, pavement, fertilized soil) provide greater diversity of habitats, a greater microbial biodiversity and greater potential health benefits?

Figure 4: Humans are exposed to microbes from a variety of environmental sources including the soil, water (standing water and rainfall), air and plants.