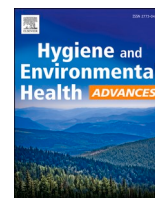


Contents lists available at [ScienceDirect](https://www.sciencedirect.com)

Hygiene and Environmental Health Advances

journal homepage: www.elsevier.com/locate/heha

From human cohorts to plant cohorts: The potential of plants in epidemiological studies

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ARTICLE INFO

Keywords:

Plants
Cohort studies
Environment
Epidemiology
Health

ABSTRACT

Cohort studies are traditionally focused on human participants. The emergence of the “Planetary Health” and “One Health” paradigms has expanded the scope of cohort studies to include animal participants. Despite this, plants remain largely overlooked in traditional biomedical research. This gap prompts the introduction of the concept of a “plant cohort,” which involves treating plants as participants in cohort studies. By collecting comprehensive data on plant characteristics and biosamples, plant cohorts may assist in enhancing our understanding of the interactions between plants, ecosystems, and human health. However, establishing plant cohorts presents unique challenges, including interdisciplinary collaboration and data collection methods. Nonetheless, the potential contribution of plant cohorts to environmental health and human well-being may warrant further exploration and research.

1. What is a plant cohort?

“A cohort is a group of subjects who share a defining characteristic.” Epidemiologically, cohort studies engage in the recruitment and tracking of participants, allowing the collection of evidence pertaining to suspected associations between exposures or causes and their outcomes or effects. In traditional biomedical studies, participants in cohorts are predominantly human beings. Meanwhile, with the emergence of the “Planetary Health” and “One Health” concepts, animal participants or cohorts have found their place in some large consortiums. The SHIP (Study of Health in Pomerania, <https://www2.medizin.uni-greifswald.de/cm/fv/ship/>) project, for instance, started to include pets and livestock in 2021, aiming to better understand zoonosis and the human-animal interaction by gathering meta-information and biosamples, such as blood and stools, from animal participants (<https://www2.medizin.uni-greifswald.de/cm/fv/ship/ship-next-one-health/>). Nonetheless, animals involved in epidemiological studies are not uncommon (Schäfer et al., 2008; Waser et al., 2005).

While the “Planetary Health” approach conceptually encompasses plants, they are relatively overlooked in traditional biomedical research. However, epidemiological studies have introduced several metrics that treat plants as aggregates, e.g., normalized difference vegetation index

(NDVI), and current findings of epidemiological studies generally support the beneficial effects of exposure to greenspace (Xie et al., 2024; Yang et al., 2021).

Nevertheless, NDVI quantifies the presence of green vegetation in a specific area based on satellite images but cannot capture the roles of different types of greenspace or plants. Thus, it is not a surprise that some inconsistent results were reported while these metrics were adopted; for example, studies found that increased NDVI was associated with faster lung function decline (Markevych et al., 2023). Interestingly, using NDVI data together with a tree registry, Markevych et al. (Markevych et al., 2020) observed that childhood exposure to trees, specifically allergenic trees, may increase the prevalence of allergic rhinitis later in adulthood. This may highlight the potential role of specific plants, like the allergenic trees.

Apart from NDVI, alternative metrics, such as percent of greenspace of different types, distance to discrete green spaces, or perceived greenspace exposure, are equally rough and do not reflect the specific role of plants in relation to human health and well-being. In contrast, metrics digging into a finer level of the “greenspace,” be they tree height or canopy size (Fig. 1) (Astell-Burt et al., 2020), may provide more information and deeper insights (Astell-Burt et al., 2020; Markevych et al., 2020). In addition, similar examples can be observed as well: a few

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<https://doi.org/10.1016/j.heha.2024.100105>

Received 3 May 2024; Received in revised form 31 August 2024; Accepted 2 September 2024

Available online 2 September 2024

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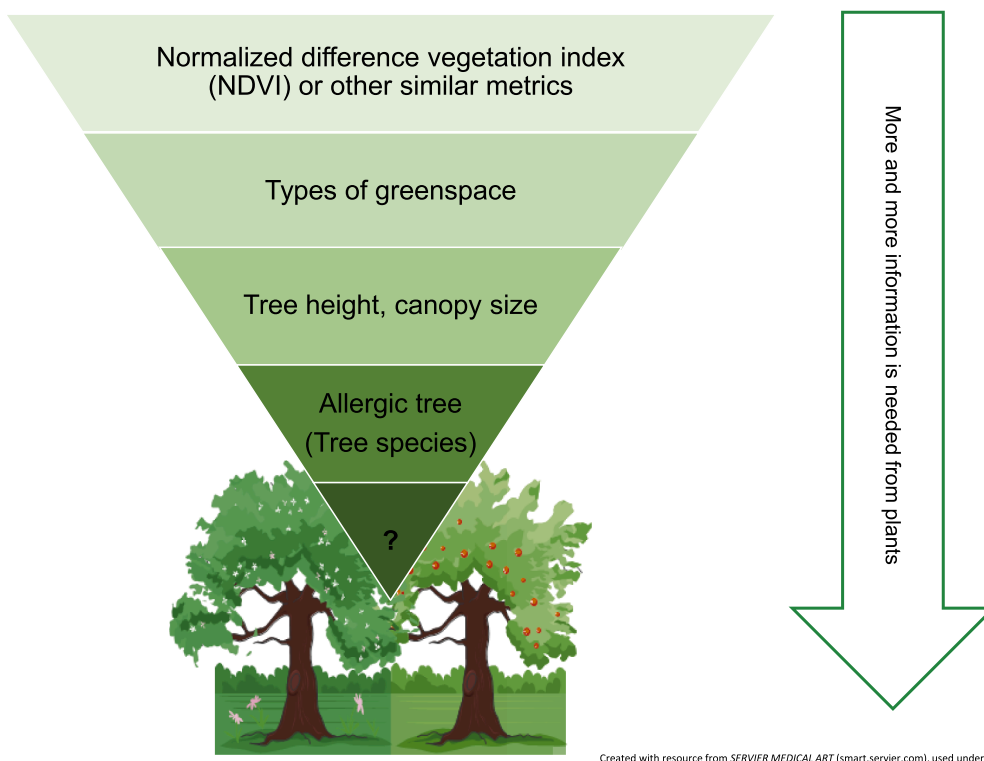


Fig. 1. A “zoom-in” of the greenspace metrics used in epidemiological studies. Finer exposures require more information from plants.

natural experiment studies have shown associations between tree loss, plus tree age and growth, and certain diseases or mortality of humans (Donovan, 2013, 2022).

Therefore, a novel dimension may become accessible if researchers try to collect more data from greenspace or plants. This may involve the comprehensive collection of plant data, including meta-information, such as species, age, size, and physiological status, along with bio-samples, like biogenic volatile organic compounds (BVOCs, Fitzky et al., 2019) or tissues of the plant, as well as follow-ups of the plants via a human cohort-like approach. The abundant data gathered can be combined with existing human cohorts, thereby paving the way for more sophisticated analyses in traditional biomedical research, particularly in exploring the associations between the environment and human health. Taken together, the term “plant cohorts” could be a reasonable term to summarize these research activities.

2. What could a plant cohort do?

Despite receiving minimal attention in traditional biomedical studies, environmental science has performed biomonitoring with plants since the 19th century (Abas, 2021). Plants, considered as individuals, play a crucial role in monitoring specific environmental impacts, including air pollution and heavy metals (Abas, 2021). As communities, the density and specific diversity of plant populations contribute significantly to assessing long-term effects within ecosystems (Tiwari and Agrawal, 2022). More data derived from a plant cohort would thus undoubtedly enhance our knowledge and understanding of plants themselves, the interactions between plants, ecosystems, and the environment, and the complex interplay between human behavior and plants.

Apart from the botanical or agricultural perspectives, a plant cohort holds significant potential for advancing research in human health. Firstly, such a cohort can offer invaluable insights into the bio-monitoring function of plants. This not only supplements physico-chemical monitoring techniques but also allows plants to monitor long-term and difficult-to-measure factors like climate change (Eglin et al.,

2008). These data can assist in the assessment of exposures in epidemiological studies. Secondly, plants or their characteristics per se can be treated as exposures, as straightforwardly exemplified in the study above on allergic trees (Markevych et al., 2020). With more comprehensive data on plants, researchers can better explore how and what kinds or characteristics of plants can be associated with various health effects.

3. What should be considered for a plant cohort?

The participants of a plant cohort may come from three scenarios: outdoor nature plants, indoor plants, and biomonitoring or experimental plants. The latter contributes more to exposure assessment, e.g., biomonitoring, or specific research aims, while the former two, outdoor and indoor plants, are usually in closer contact with humans, thus holding greater relevance for biomedical research. However, the abundance and the complex presence of outdoor plants, including trees, bushes, grasses, and lichens, together with their interactions, might hinder the data collection process of these participants. Notwithstanding the assistance of some region-specific tree registry data, the lack of more detailed and up-to-date information on outdoor plants remains a major issue.

On the contrary, indoor plants, typically small-scale and home-based, offer promising possibilities for collecting detailed information from these participants. Our prior scoping review revealed that current epidemiological studies on indoor plants may often rely on simplistic questions such as “Do you have plants at home?” (Zhao et al., 2023). Consequently, these studies fall short of thoroughly investigating potential associations between indoor plants and health effects. It is presumed that enhancing epidemiological studies on indoor plants could be achieved by collecting more relevant information of the plants, e.g., number, species, size, and condition (physiological status). Nevertheless, while the idea of mimicking a human cohort using plants may seem intuitive, it is by no means a low-hanging fruit. Collecting data from plants poses exceptional challenges as it requires additional effort and expertise from diverse disciplines, including but not limited to biomedicine, epidemiology, botany and horticulture, city planning, as

Table 1
Potential framework to initiate a plant cohort.

Starting point of a plant cohort	Outdoor trees	Indoor plants
Data collection	Tree registry, modelling, fieldwork	Questionnaire, fieldwork
Data source	Specific buffers around participant's residential address	Participants with a certain number of indoor plants
Potential data of interest	Tree species, canopy size, height, etc.	Species, size, horticultural behaviors, and even biochemical indicators or microbiomes, etc.

well as design and architecture.

Before integrating plant participants into biomedical, especially epidemiological studies, researchers must define the necessary data to be collected. We are currently unaware of any ongoing projects focused on such a “plant cohort,” but our prior work proposes various metrics that could be considered in studies involving indoor plants (Zhao et al., 2023). These metrics span from quantitative measures like the “number of plants” or “frequency of viewing indoor plants” to qualitative metrics, including species, size, horticultural behaviors, and even biochemical indicators or microbiomes. Most of these metrics can be efficiently surveyed through questionnaires, with fieldwork primarily constrained to biosample collection for subsequent lab analysis. Conversely, for outdoor plants, data beyond the tree registry are typically lacking, thereby demanding extensive fieldwork on meta-information collection. However, this offers as well an opportunity to conveniently collect biosamples for further measurements. And focusing on one species, like trees, could be a potential starting point for outdoor plant cohort studies. We summarized potentially brief frameworks to initiate an outdoor tree cohort or indoor plant cohort in Table 1. It is also worth noting that outdoor and indoor plants interact with each other. While we have discussed these elements separately, we recommend a joint study of both outdoor and indoor plants if feasible.

Shifting the participants from humans to plants, a plant cohort has the potential to collect data and conduct follow-up surveys, thus enabling more comprehensive studies on the interaction between plants and human health and contributing to exposome research. All the mentioned work can be integrated into at least one follow-up of an existing cohort study. Whilst the idea holds promise, it is accompanied by several uncertainties. In addition to the requisite interdisciplinary expertise and challenges in data collection, there remains a vague understanding of how to statistically integrate the increasing volume of plant data and how to elucidate the mechanisms underpinning the association between plant characteristics and health outcomes. Additionally, plant ethical considerations (Kallhoff et al., 2018), with one possible case like “how often can we sample a plant”, might be taken into account before such studies gain momentum.

4. Conclusions

Overall, here we present a rough idea of a “plant cohort”. Integrating plants into biomedical and epidemiological studies through plant cohorts shows promise but comes with challenges. By presenting this idea,

we hope to spark interest among researchers and encourage further studies in relevant areas.

CRedit authorship contribution statement

Tianyu Zhao: Writing – review & editing, Writing – original draft, Methodology, Investigation, Conceptualization. **Joachim Heinrich:** Writing – review & editing, Conceptualization.

Declaration of competing interest

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

Acknowledgments

The work is supported by the National Natural Science Foundation of China (M-0420).

Dr. hab. Iana Markevych (Jagiellonian University, Poland) is sincerely thanked for the helpful discussions and insightful comments.

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