



POSITIVE HEALTH EFFECTS OF THE NATURAL OUTDOOR ENVIRONMENT IN TYPICAL POPULATIONS IN DIFFERENT REGIONS IN EUROPE (PHENOTYPE)

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3 **POSITIVE HEALTH EFFECTS OF THE NATURAL OUTDOOR ENVIRONMENT**
4 **IN TYPICAL POPULATIONS IN DIFFERENT REGIONS IN EUROPE**
5 **(PHENOTYPE)**
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Abstract

Introduction: Growing evidence suggests that close contact with nature brings benefits to human health and well-being, but the proposed mechanisms are still not well understood and the associations with health effects remain uncertain. The PHENOTYPE project investigates the interconnections between natural outdoor environments, in both rural and urban settings, and better human health and well-being in the North West, South and East of Europe. Here we provide a description of the proposed work.

Aims and methods: The PHENOTYPE project explores the proposed underlying mechanisms at work (stress reduction/restorative function, physical activity, social interaction, exposure to environmental hazards) and examines the health effects (e.g. general health and wellbeing, mental health/neural development, stress, cardiovascular, cancer and respiratory mortality and morbidity, birth outcomes and obesity) for different population groups (e.g. pregnant women and/or foetus, different age groups, socioeconomic status, ethnic groups, and patients). It implements conventional and new innovative high tech methods to characterize the natural environment in terms of quality and quantity. Preventive as well as therapeutic effects of contact with the natural environment are being covered. PHENOTYPE further addresses implications for land-use planning and green space management.

Result: The main innovative part of the study is the evaluation of possible short and long term effect of green space and the possible underlying mechanisms in 4 different countries (with quite different type of green space and use of green space) using the same methods and methodology in one research program. This type of holistic approach has not been undertaken before. Furthermore there are technological innovations such as the use of remote sensing and smartphones in the assessment of green space.

Conclusion: The project will produce a more robust evidence base on links between exposure to natural outdoor environment and human health and well-being, in addition to a better integration of human health needs into land use planning and green space management in rural as well as urban areas.

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6 **Keywords:** green space, blue space, health, well being, physical activity, social
7 contacts, restoration, stress, air pollution, remote sensing, GIS, audit, questionnaire
8 survey, smartphones
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Article summary

Strengths

The PHENOTYPE project is the largest European project on green space and health

The PHENOTYPE project examines simultaneously the possible underlying mechanisms (stress reduction/restorative function, physical activity, social interaction, exposure to environmental hazards) for the relationship between green space and health in 4 different countries in Europe

The PHENOTYPE project examines a range of possible health effects of green space using 16 different cohorts and/registries in 4 different European countries

The PHENOTYPE project uses a range of novel tools and methods to assess access and use of green space including remote sensing, smartphones, audits and interviews.

The PHENOTYPE project works closely with stakeholders and produces new information for stakeholders.

Weakness

The limited funding may not lead to the full exploitation by the wealth of data generated within the life time of the project

Introduction

Positive health effects have been observed between green space and mortality longevity (Takano et al. 2002; Mitchell and Popham 2008, Villeneuve et al. 2012), cardiovascular disease (Pereira et al. 2012), people's self reported general health (de Vries et al. 2003; Maas et al. 2006), mental health (Grahn & Stigsdotter, 2003; Hartig et al. 2003; Maas, et al. 2009b; Ottosson & Grahn, 2005, Richardson et al. 2013), sleep patterns (Astell-Burt et al. 2013a), recovery from illness (Ulrich 1994), social health aspects (Kim & Kaplan, 2004; Sullivan et al. 2004; Kweon et al 1998; Maas et al. 2009a; de Vries 2010) and birth outcomes (Donavan et al. 2012; Dadvand et al. 2012a, Dadvand et al. 2012b). Some of the associations were shown to be modified by social economic status and level of urbanity, with greater benefits for populations with lower socioeconomic class (Mitchell & Popham, 2008, Dadvand et al. 2012a) and those in more urban areas (Maas et al. 2006; Mitchell et al. 2007). Furthermore gender has been shown to modify the relationship (Richardson and Mitchell 2010b).

Increased physical activity and social contacts, psychological restoration/stress reduction, and a reduction in pollutants such as noise and air pollution, and temperature have been proposed as possible mechanisms for the health benefits of green space. Access to and/or use of green space has been associated with higher levels of physical activity (Cohen et al. 2006; Cohen et al. 2007; Coombes et al. 2010; Lachowycz and Jones 2011; Toftager et al. 2011; Rodriguez et al. 2012; Mytton et al. 2012; Annerstedt et al. 2012; Almanza et al. 2012; Astell-Burt et al. 2013b; Richardson et al. 2013) and lower levels of obesity within communities (Coombes et al. 2010; Ellaway et al. 2005; Wolch et al. 2011; Toftager et al. 2011; Pereira et al. 2013; Astell-Burt et al. 2013c; Lovasi et al 2013). Studies even suggested that 'green exercise' can have even more positive mental health benefits than other kinds of exercise (Bodin et al. 2003; Pretty et al. 2005; Bowler et al. 2010; Thompson Coon et al. 2011).

Psychological restoration (Kaplan & Kaplan, 1989; van den Berg et al. 2003; van den Berg & Custers, 2011;) and reduced stress and anxiety (Ulrich et al., 1991, Grahn & Stigsdotter, 2003; Hartig et al. 2003; Maas et al. 2009; Stigsdotter et al 2010) have all been associated with access to and/or use of green and natural space. An inner city study in a deprived estate in Chicago showed the benefits of green space both to cognitive

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3 restoration (Faber Taylor 2002; Kuo & Sullivan, 2001a), self-discipline (Faber Taylor
4 et al. 2002), reduced aggression (Kuo & Sullivan, 2001a) and reduced crime (Kuo &
5 Sullivan, 2001b), with the latter also observed elsewhere recently (Wolfe and Mennis
6 2013)
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11 Furthermore a few studies have suggested that green space is associated with more
12 social contacts and cohesion (Kuo et al. 1998; Kweon et al. 1998; Maas et al 2009).
13 And finally reduction of personal exposure to air pollution has been observed in areas
14 with more green space (Dadvand et al. 2012c), while vegetation has been suggested to
15 reduce air pollution levels, and temperature (Baldauf et al. 2009; Su et al. 2011; Park et
16 al. 2012a, 2012b), with some suggestion that the benefits are greater for socially
17 disadvantaged groups (Su et al. 2011). It has also been suggested that vegetation (trees,
18 plants) and soil may have an impact on the sound level (Aylor, 1972; Fan et al. 2010;
19 Fang & Ling, 2003, 2005; Samara & Tsitsoni, 2007; Zhang & Kang, 2007). Part of the
20 appeal of green spaces may be related to pleasant acoustic environments (Brown, 2006
21 in: Health Council of the Netherlands, 2006). This may have its own, direct beneficial
22 health effect (Health Council of the Netherlands, 2006).
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33 While this growing evidence exists that close contact with nature brings benefits to
34 human health and well-being, the proposed mechanisms are still not well understood
35 and the associations with health effects remain uncertain. Furthermore, it is unclear if
36 the possible mechanisms act in isolation or together, since with some exceptions (de
37 Vries et al. 2013) they have been studied in isolation. A coherent conceptual framework
38 on the proposed mechanisms is currently lacking. Also, most of the research has been
39 conducted in the North West of Europe and USA leaving questions about the
40 generalisability to other regions. Inconsistency and variation in indicators (eg type, size
41 and quality) for green space have often made it difficult to compare results from
42 different studies, and a better characterisation including that of quantity and quality of
43 green and blue spaces is needed, not only for research but also for policymakers and
44 spatial planners. Studies have often focused on access to green space without taking into
45 account actual use of green space. While blue space may also have a positive effect on
46 health, probably in combination with green space, there are only a few epidemiological
47 studies investigating this (Völker and Kistemann 2011, Völker and Kistemann 2013,
48 White et al. 2013)
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4 PHENOTYPE, a collaborative research project and explores the proposed underlying
5 mechanisms at work (stress reduction/restorative function, physical activity, social
6 interaction, exposure to environmental hazards). PHENOTYPE is the first study
7 designed to examine these mechanisms simultaneously in a large sample (N=4000
8 subjects) in various European countries using the same methodology. This allows the
9 study of specific factors while adjusting for others, and thereby strengthening the
10 interpretation of the results. It further examines both the long term and short term health
11 effects (eg general health and wellbeing, mental health/neural development, stress,
12 cardiovascular, cancer and respiratory mortality and morbidity, birth outcomes and
13 obesity) for different population groups (e.g. pregnant women and/or foetus, different
14 age groups, socioeconomic status, ethnic groups, and patients), through analyses of
15 existing cohort studies, observational studies and experiments. Preventive as well as
16 therapeutic effects of contact with the natural environment are being evaluated. A
17 coherent conceptual framework on the association between the natural environment and
18 its effects on health and well-being is being developed, and it addresses implications for
19 land-use planning and green space management.
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33 The study includes both rural and urban settings, but the main focus is on the urban
34 environment, for a number of reasons. Most of the population lives in urban areas
35 (75%) in Europe, making these of greater relevance to public health, and rapid
36 urbanization continues to reduce accessible natural environments for urban residents.
37 Most people make more frequent use of the green spaces in their nearby living
38 environment instead of travelling greater distances to rural areas, in particular people
39 with lower socio-economic status, elderly people and children (Schwanen et al. 2002;
40 Maas 2008). Furthermore, rural dwellers tend to have constant contact with the natural
41 environment and it may therefore also be more difficult to assess its effects.
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49 Lastly, the project uses an interdisciplinary and integrated approach, applying the best
50 and most efficient methods to understand the relation between exposure to the natural
51 environment and health. It implements conventional and new innovative high tech
52 methods to characterize the natural environment in terms of quality and quantity. This
53 paper provides a general overview of the research methodology of PHENOTYPE.
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Methods and results

Figure 1 summarizes the different parts of the study and the interdependencies between the different parts, namely the characterisation of the natural environment and the way it is used, examination of the underlying mechanisms in daily life settings, short and long term effects of the natural environment, and the implications for management and policy of the natural environment (see overview Figures 1 and web figure 1). In this section we will elaborate on each of these parts. A summary of the mechanisms, outcomes, populations and areas selected for investigation are given in Table 1.

Characterising the natural environment and the way it is used.

The research includes evaluation of the natural environment, which includes for the purposes of the project:

- Green spaces (e.g. roof gardens, city parks, court yards) and “greenery”; forests, nature reserves/parks, mountains, farmland, trees, landscaping
- Blue spaces; water such as canals, ponds, creeks, rivers, beaches etc.

Although many of these may actually not be “natural” since they have been man-made, for the purpose of the project we classify them as such.

One of the main aims of PHENOTYPE is to examine the importance of both quantitative (e.g. amount, type, access, use) and qualitative characteristics (e.g. acoustic quality, identity, variety, safety, rubbish) of the natural environment by collecting detailed data on these characteristics using a combination of methods. The focus lies on natural environments at different scales and distances from the home (city/town, neighbourhood, street level) and where possible also at other places where people stay (work, school, on their way to home/school, recreational). In addition, actual use of the natural environment is taken into consideration. To achieve the aim, a detailed assessment will be conducted in 4 case cities (Barcelona, Spain; Doetinchem, the Netherlands; Kaunas, Lithuania; and Stoke-on-Trent, United Kingdom), with less detailed assessment in other study areas.

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3 PHENOTYPE uses conventional land use maps, remote sensing data from satellites and
4 aerial photography, complemented by detailed discussions with volunteers and other
5 stakeholder living and working in the studied areas to derive comparable classifications
6 of the natural environment in different countries. Collected data will contribute to the
7 characterisation of the natural environment (both quantitative and qualitative e.g.
8 accessibility, acoustical quality, recreational activities, walkability etc). For the
9 quantitative characterisation, PHENOTYPE makes use of available land use maps such
10 as COordination and INformation on the Environmental programme, initiated by the
11 European Commission (CORINE)(EAA 2005) and Urban Atlas (EAA 2010), and
12 remote sensing and aerial photography to obtain comparable indices such as NDVI
13 (Weier and Herring, 2011) of the natural outdoor environment in different countries.
14 Landsat Enhanced Thematic Mapper Plus (ETM+) data are applied to a classification
15 and regression tree (CART) model to categorise land cover types for the urban areas of
16 interest (Su et al 2010). Early application of the NDVI in Barcelona, Spain showed
17 good results (Web Figure 2, Dadvand et al. 2012a)
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30 To collect additional qualitative information on the natural environment and on other
31 physical and social features, systematic observations (audits) are conducted by trained
32 researchers in selected neighbourhoods in the 4 case cities. The researchers walk
33 through the neighbourhood, systematically coding characteristics such as the
34 architectural character, maintenance of the landscape, and perceptions on how a place
35 looks and feels. To collect comparable information in the 4 case cities, two standardized
36 forms are used. One form is used for evaluating the streetscape, using indicators derived
37 from the Street Typology developed by Leijdelmeijer et al. (2002), a list of evaluating
38 the quality of green by Van Dillen (2012) and the audit tool developed by Van Lenthe et
39 al. (2006). A second form is used for evaluating the natural spaces in the study areas of
40 at least 1 ha. It is an adapted form of the Neighbourhood Green Space Tool developed
41 by Gidlow et al. (2012).
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51 To gain insight into the way people use the natural environment, a face to face
52 questionnaire survey is conducted to collect data on 1000 people in the 30 selected
53 neighbourhoods in each of the 4 case cities, and an in-depth study using “Calfit”, a
54 smartphone-based monitor of time-location patterns and momentary states, on a
55 subsample (n=100) of the participants of the questionnaire survey. The Calfit software
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3 runs on a Google Android operating system and as currently configured can collect data
4 on physical activity using the motion sensor and geographic location through a global
5 positioning system (GPS), to obtain information on minutes spent and physical activity
6 levels in different natural environments (Web Figure 3). The instrument has been
7 validated against the Actigraph accelerometer (Donaire et al. 2013), combined with
8 other pollution measurements to assess likely inhalation (de Nazelle et al. 2013), and
9 lab-validated using the Cosmed metabolic monitoring system.
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16 The work will produce different indicators of natural space that can be used in the
17 studies described below. The aim is to make a hierarchy of indicators with on the
18 bottom simple measures such as NDVI that can be easily obtained for all the study areas
19 and on the top detailed measures of for example green space with actually information
20 on the quantity, quality and use that can only be obtained for only some areas after in-
21 depth study. As part of the work, we will examine the relationship between the simple
22 and detailed measures to better understand how detailed information on small scale can
23 help the interpretation of health studies conducted in larger areas with only simple
24 measures available using existing epidemiological studies and registries (see below).
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32 33 *Examining the underlying mechanism in the daily life setting*

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36 New data will be collected to explore in detail and simultaneously the proposed
37 mechanisms underlying the relationship between the natural environment and health
38 and well-being, in the four case cities. In each of these cities 30 neighbourhoods varying
39 in socio-economic status and in their distance to green space are selected. In these
40 neighbourhoods the natural environment will be characterised, and a selection of 1000
41 randomly selected residents (4000 in total, 18-75 years) will participate in a
42 questionnaire survey, a smartphone study, and in in-depth interviews (Web Figure 4).
43 The choice of items was based on the proposed mechanisms and was achieved via an
44 interactive process of experts within the PHENOTYPE team and others in the
45 institutions involved. As much as possible questions were derived from existing and
46 validated indices. The questionnaire was piloted by the four centers separately with
47 specific attention for comprehensibility, clarity and duration and was adapted based on
48 these pilots. The questionnaire is structured along several main clusters of questions: i)
49 residential situation: ii) dwelling iii) wellbeing and health, and iv) personal
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3 characteristics. It includes questions on perceived quality and use of green and blue
4 space in the residential area and in the immediate living environment, perceived
5 environmental and social quality including aspects as noise, amenities and social
6 cohesion, lifestyle, subjective health and questions related to personal background. The
7 questionnaire was developed in English and translated and back translated in Dutch,
8 Spanish and Lithuanian. More details on the frameworks and questionnaire will be
9 described in a forthcoming paper by Van Kamp et al. (In prep). Also we will assessment
10 cognitive fatigue in each subject as measured by CTT.
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18 From the 1,000 volunteers in each of the 4 case cities who complete the questionnaire,
19 100 people are approached to take part in a smartphone study (400 in total). During 7
20 subsequential days the emotional state of the subject, the local environment (e.g.,
21 different quantities or qualities of natural space) and the social setting are assessed with
22 the smartphone and the innovative Calfit technology. Besides objective geolocation and
23 physical activity, subjective data on stress reduction/restoration and social contacts are
24 collected simultaneously. The latter data are collected through interactive diaries
25 capable of eliciting ecological momentary assessment (EMA). EMA is a novel approach
26 to elicit responses to electronic surveys throughout the course of daily life (Shiffman et
27 al. 2008). The participant receives prompts at random intervals to complete small
28 surveys on the phone, which then have time and location stamp.
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38 From the people who participate in both the questionnaire survey and the CALFIT study
39 and who indicate they wanted to volunteer, 80 people (20 in each case city) are
40 approached for semi structured interviews. These interviews are conducted to gain more
41 detailed information on specific topics included in the questionnaire survey and
42 CALFIT/EMA. Topics addressed include the motivation for travel routes, the effect of
43 natural environment on mood, behaviour and well-being, the attitude towards and
44 importance of (experiences with) natural environment, and reasons for using or not
45 using the natural environment.
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52 ***Epidemiological studies to examine long term effects of the natural environment***

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56 By using existing epidemiological studies and registries and linking these to the natural
57 space indicators described earlier, the association between natural environment and a
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3 range of different long term health effects will be examined in an efficient and cost
4 effective manner. PHENOTYPE makes use of 16 existing cohorts and registries with
5 good health outcome data in Spain, the Netherland, Lithuania, and United Kingdom
6 (Web Table 1), linking these to newly created natural environment indicators.
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9 Comparable estimates are produced for various regions in Europe for the effects on
10 pregnancy outcomes, foetus development, children's health and adult population
11 morbidity and mortality. We specifically focus on:
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- 13 • the natural outdoor environment and ethnicity, socio-economic status, women's
14 health and pregnancy outcomes;
- 15 • the natural outdoor environment and foetus development, birth weight, and
16 gestational age;
- 17 • the natural outdoor environment and general development, neurodevelopment,
18 cognitive function and respiratory health in children;
- 19 • the natural outdoor environment and respiratory health in various European cities;
- 20 • the natural outdoor environment and general health, physical activity, specific
21 morbidity and mortality.
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31 The assessment of natural environment indicators will be mainly based on satellite data
32 and land use maps as CORINE and Urban atlas, and sometimes local data. This will
33 restrict to some extent the evaluation of the effect of the natural environment, but this is
34 the only realistic and achievable approach. All studies examine the role of socio-
35 economic status, which has been suggested as an effect modifier for the relationship
36 between exposure to the natural environment and health benefits. The European
37 Community Respiratory Health study (ECRHS) (Burney et al 1994) further allows for
38 examination of exposure to the natural outdoor environment and health effects in a
39 range of different European cities. Some cohorts such as the Born in Bradford study
40 (Wright et al. 2012) offers a unique opportunity to investigate the role of ethnicity in the
41 relationship between exposure to the natural outdoor environment and health benefits,
42 in Bradford study half of the participants are from Pakistani background, with
43 information on both the mother and baby from pregnancy to early years in life.
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54 ***Experiments to examine short term effects of the natural environment***

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3 To examine short term effects of the natural environment on health and well-being, one
4 or more experimental studies are conducted in each country in which individuals are
5 exposed to different types of natural and urban environments (i.e., environmental
6 conditions). The majority of data collection is field-based to maximise the ecological (as
7 well as internal) validity of any observed effects.
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11 Using a range of psychological and physiological indicators relevant to the various
12 possible mechanisms, and inclusion of healthy and patient population groups (with
13 mental and physical morbidities) collectively explore:
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- 15 - preventive and therapeutic effects of natural environments.
- 16 - immediate and sustained changes in affective, cognitive and physiological
17 responses indicative of well-being while engaged in a natural environment, and
18 after leaving a natural environment
- 19 - neurobiological responses to viewing natural or urban scenes before/after
20 experiencing stress.
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28 Through variation in experimental design, each partner makes a novel contribution(s) to
29 the area as (details in Web Table 2):
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- 31 • UK: In healthy individuals, Study 1 compares immediate and post-exposure psycho-
32 physiological effects of urban versus natural environments to explore whether any
33 beneficial effects are sustained following single exposures; Study 2 uses longer-term
34 follow-up and repeated exposure to natural environments to explore whether any
35 effects are accumulated, sustained or attenuated.
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- 38 • Netherlands: an experimental functional Magnetic Resonance Imaging (fMRI) study
39 is conducted in healthy individuals to investigate neurobiological responses to
40 viewing natural or urban scenes before/after experiencing stress; i.e., whether
41 viewing natural compared to urban scenery can prevent or buffer against stress
42 responses, and how this is represented in brain activation patterns.
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- 45 • Spain: in individuals with elevated stress levels, group-based exposure and
46 Ecological Momentary Assessment (EMA, using CALFIT technology) are used to
47 explore the role of social interaction and the nature of physical activity, in
48 immediate and longer term responses. Ecological validity will be enhanced through
49 ‘free-living’ activities within environments, rather than controlling activities, again,
50 using EMA, GPS and accelerometry to monitor the nature (and perceptions) of this
51 activity.
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- Lithuania: a clinical population with established coronary artery disease (CAD) are recruited to evaluate the therapeutic effect of the natural environment. The outcomes of this experiment may have direct clinical applications for the use of urban and different types of natural environment in cardiac rehabilitation.

Implications, policy and guidelines and involvement of stakeholders

Guidelines

PHENOTYPE will provide recommendations for policymakers and guidelines for professional practitioners involved with spatial planning and health to create natural environments that promote health and well being. For this, we focus on a human ecological perspective which allows for a better integration of human health needs into land use planning and green space management in both rural and urban areas (Lawrence 2001). Currently legal standards that have been developed with economic, technological and political priorities in mind, are leading in urban design, whereas the lifestyle, sense of community, identity, and health and well being of local populations have been largely undervalued. The guidelines will reflect the importance to consider environmental, social, economic and other components of the natural and built environments in ways that also take into account and result from the point of view of citizens. PHENOTYPE will complement the common quantitative approach by valorising the social/human functions of these environments, especially their contribution to promoting health and quality of life.

Following this broad and innovative approach, PHENOTYPE will formulate, test and validate a set of recommendations and guidelines concerning the desired characteristics of different types of natural environments in urban and rural areas, specifically their characteristic features, accessibility to them for different population groups, as well as their facilities, maintenance and services. By doing so, the work will overcome the existing applicability gap between information and knowledge accumulated by much research and policy definition and implementation.

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3 The guidelines for professional practitioners involved with spatial planning and health
4 will consider three core topics in relation to each of the natural environment being
5 considered:
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- 7 1. Qualitative characteristics of natural environments; recommendations concerning
8 surface area, vegetation, water sources, ambient noise levels, views and
9 microclimate;
10
- 11 2. Facilities, Maintenance and Services; recommendations about the kinds of
12 communal facilities and services provided in each type of natural environment, as
13 well as suggested levels of maintenance;
14
- 15 3. Accessibility Guidelines to Natural Environments; including requirements about
16 access to different types of natural environments such as allotments,
17 neighbourhood parks, children's playgrounds and nature reserves.
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19 The baseline for the work is firstly the compilation and analysis of currently available
20 information from existing databases and literature, and later new data collected by the
21 project as described above. This will be complemented by the engagement with the
22 appropriate stakeholders to assess scope for development. These insights will be
23 combined into a conceptual framework on the underlying mechanisms of the effects of
24 the natural environment on health and well-being.
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34 *Stakeholders and dissemination*

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37 The participation provides a forum for project assurance and benefits for PHENOTYPE
38 are summarised as follows:
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- 42 - A more robust evidence base on links between exposure to natural outdoor
43 environment and human health/well-being for various regions in Europe. Hereby
44 we expect to develop a better understanding of the potential mechanisms.
45
- 46 - A better integration of human needs into land use planning and green space
47 management in rural as well as urban areas. Furthermore, the application of
48 these needs in practical guidelines.
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54 Stakeholder involvement is critical for bringing outside (policy) ideas into the research
55 planning, to increase the usefulness of the research, and to assure a better
56 implementation of the results of the project (Web Figure 5). In a research project, this is
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3 often limited because the lack of interest of stakeholders and the limited resources and
4 efforts of consortia.
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8 From the start of PHENOTYPE actively sought to establish and maintain relations and
9 dialogues with and between key stakeholders from local, regional and national health
10 and environment authorities, institutions and the international research community.
11 These include policy makers, architects, urban planners, natural space managers, health
12 professionals, and the international research community. This group is highly diverse,
13 as we are looking at a range of professions within the subject areas of environment and
14 health, from volunteers to scientists, community workers and policy developers.
15 PHENOTYPE has thus far been successful in its engagement activities, providing
16 continuous opportunities for information exchange and collaborations. These contribute
17 to strengthening networking between researchers, policy-makers and stakeholders in
18 order to facilitate the transfer of scientific knowledge to policy development, to
19 exchange ideas about best practice and to help identify emerging issues on the natural
20 outdoor environment and its mechanisms to improve health.
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31 The PHENOTYPE website www.phenotype.eu provides an overview of the project,
32 progress, actualities, surveys and publications. The site has a sign up form for periodic
33 newsletters through which all stakeholders are regularly informed. It guarantees
34 continuous visibility, and provides a means for interested parties to respond to activities,
35 or to contact us with invitations to attend workshops, etc. PHENOTYPE is also found
36 on social media twitter (@greenhealth4eu) and LinkedIn. The PHENOTYPE databases
37 and overall results will be exploitable by policy makers at national and international
38 level in areas including urban planning and health.
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48 **Conclusion**

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51 The PHENOTYPE project is an FP7 collaborative action, funded by the EC to explore
52 the mechanisms underlying positive short term and long term health effects for different
53 population groups. PHENOTYPE applies conventional and new innovative high tech
54 methods to characterize the natural environment in terms of quality and quantity.
55 Preventive as well as therapeutic effects of contact with the natural environment will be
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3 covered. The proposed work aims to address the limitations of some of the studies that
4 have been published so far (Table 2). Furthermore it addresses implications for land-
5 use planning and green space management. The project will produce a more robust
6 evidence base on links between exposure to natural outdoor environment and human
7 health and well-being. This in turn will contribute to improved integration of human
8 health needs into land use planning and green space management in rural and urban
9 areas.
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Author statement

Mark J Nieuwenhuijsen, Hanneke Kruize, Christopher Gidlow, Michael Jerrett, Jolanda Maas, Edmund Seto, Peter Jan van den Hazel, Roderick Lawrence, and Regina Grazuleviciene and wrote the original grant proposal on which the study design and paper is based. Mark J Nieuwenhuijsen drafted the version of the paper and received input from all the authors. All authors read and commented on the paper and agree with the final version.

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Ethics approval was obtained for all aspects of the study by the local ethics committees in the countries where the work was conducted, and sent to the European Commission before advancement of the study.

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39 in urban open spaces. *Environ Plann B*, 2007. 34: p. 68-86.
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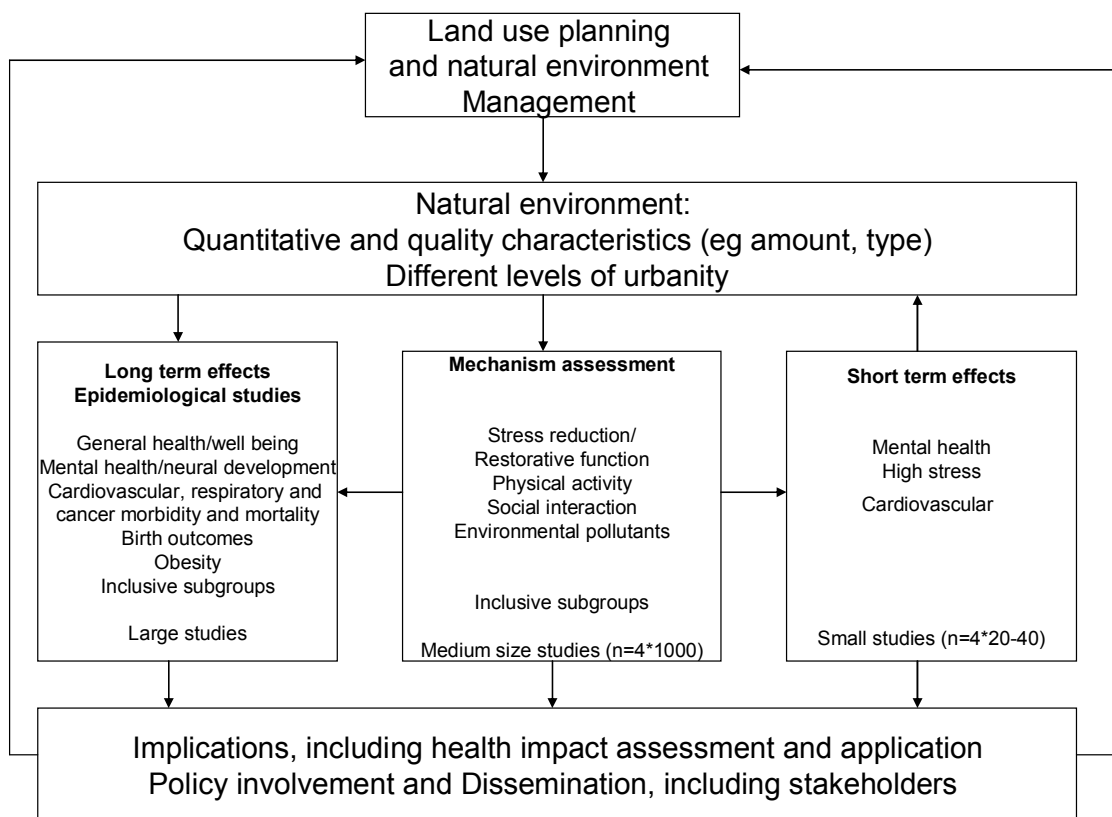


Figure 1: Interdependencies of different parts of the PHENOTYPE project

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3 Table 1 PHENOTYPE study mechanisms, outcomes, populations and regions
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6 It will explore underlying mechanisms related to:

- 7 ▪ stress reduction/restorative function
- 8 ▪ physical activity
- 9 ▪ social interaction/social cohesion
- 10 exposure to environmental hazards (e.g. noise/acoustic quality, air pollution)
- 11

12 Both preventative and therapeutic effects (patients) will be considered. Outcomes of
13 interest that are evaluated are:

- 14 ▪ general health and well-being (including medically unexplained symptoms
- 15 ▪ (MUPS))
- 16 ▪ mental health/neural development
- 17 ▪ stress
- 18 ▪ cardiovascular, cancer and respiratory mortality and morbidity
- 19 ▪ birth outcomes
- 20 ▪ obesity
- 21
- 22
- 23

24 It will examine the effects for different population groups, including more vulnerable
25 populations:

- 26 ▪ pregnant women and/or foetus
- 27 ▪ age groups (children, elderly)
- 28 ▪ (lower) socio-economic status
- 29 ▪ ethnic minorities
- 30 ▪ patients/people with specific health complaints
- 31

32 It will conduct comparative studies in different regions of Europe to examine any
33 underlying regional, social and/or cultural differences related to the meanings, uses,
34 mechanisms and health effects of the natural environment and we will include the:

- 35 ▪ North west (Netherlands, England)
- 36 ▪ South (Spain)
- 37 ▪ East (Lithuania)
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Table 2 Limitations of current green space work and work undertaken by PHENOTYPE to address these

| Limitations of current available work | What PHENOTYPE will do |
|--|--|
| <ul style="list-style-type: none"> ▪ Inconsistency and variation in indicators for green or natural space have often made it difficult to compare results from different studies. | <ul style="list-style-type: none"> ▪ Minimize the potential differences due to classification of natural space, by combining the use of conventional maps and data sources with remote sensing data and aerial photography, gather individual-level data through detailed discussions with subjects living in the areas, and use considerable stakeholder engagement to develop comparable classifications of the natural environment in different countries. ▪ Produce a more robust and comparable evidence base on links between exposure to natural outdoor environment and human health and well-being. |
| <ul style="list-style-type: none"> ▪ A number of disease outcomes have been studied, but besides the routinely collected data (which use ICD coding), not always in a standardized and comparable manner in different countries | <ul style="list-style-type: none"> ▪ Produce a more robust and comparable evidence base on links between exposure to natural outdoor environment and human health and well-being, using well studied and new outcomes with standardization between countries. |
| <ul style="list-style-type: none"> ▪ Potentially very sensitive groups such as pregnant women/fetus have not been studied at all. | <ul style="list-style-type: none"> ▪ Extend the evidence base to new outcomes and vulnerable populations e.g. pregnant women and their foetus, chronic respiratory and cardiovascular patients, ethnic minorities and |

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| | low social economic class. |
| <ul style="list-style-type: none"> Most studies focused on green space; the evidence base for the effects of blue space is very limited. | <ul style="list-style-type: none"> Not only examine the effects of green space, but also of blue space. |
| <ul style="list-style-type: none"> Most of the green space studies have been conducted in the US or the North West of Europe. | <ul style="list-style-type: none"> Conduct comparable studies across Europe and produce evidence for North Western, Eastern and Southern Europe. This will deliver insights into regional, social and/or cultural differences in relation to natural space. |
| <ul style="list-style-type: none"> Most studies do not include actual use of the natural environment. | <ul style="list-style-type: none"> Consider actual use of the natural environment, an often neglected but fundamental indicator in relation to exposure to natural environments. |
| <ul style="list-style-type: none"> There appeared to be differences by social group, with some apparently benefiting more than others from natural space, but the evidence is sparse. | <ul style="list-style-type: none"> Produce a more robust and comparable evidence base on links between exposure to natural outdoor environment and human health and well-being, with special attention for effect modification by social groups |
| <ul style="list-style-type: none"> A number of potential mechanisms have been suggested, including increased physical activity and social contacts for those living near natural space, natural environments exerting | <ul style="list-style-type: none"> Examine the proposed mechanisms (physical activity, stress, social contacts, and environmental risk factors) simultaneously in a large sample in various countries (WP2). This will enable |

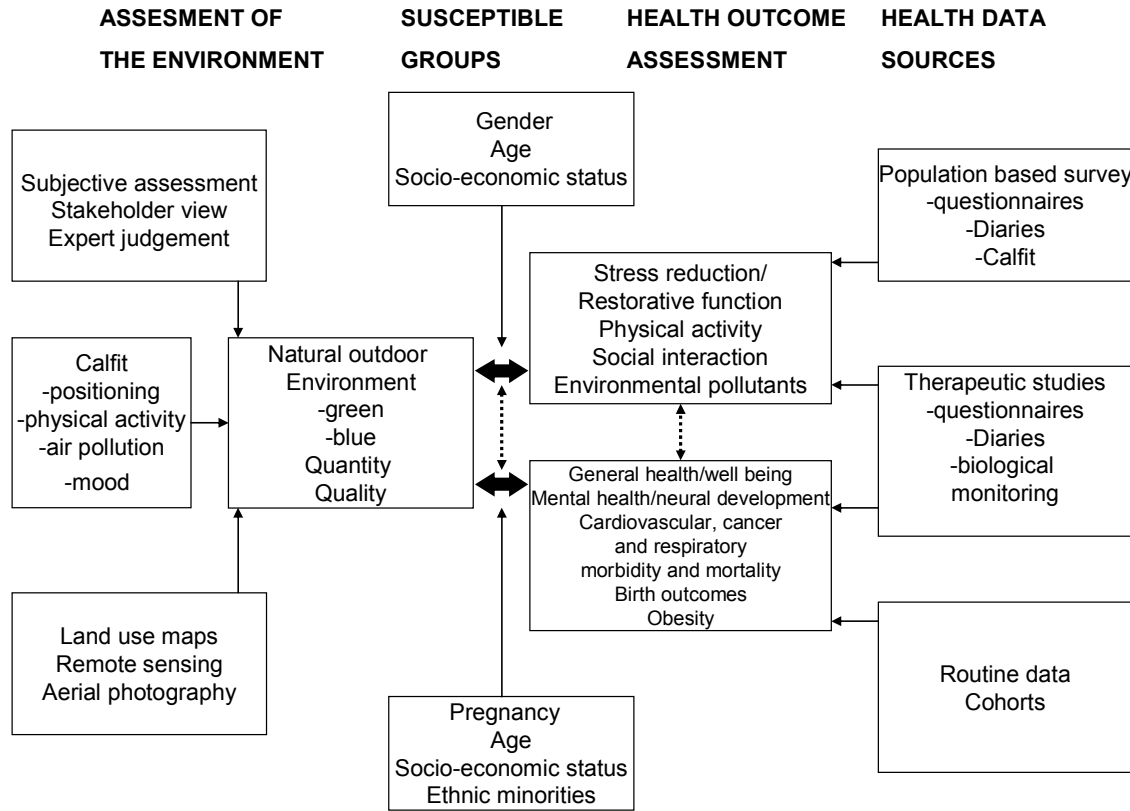
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| <p>stress lowering or attention restoring effects, and reducing environmental hazards (e.g. air pollution, high temperatures). However, the studies of potential mechanisms have often been limited to assessing one mechanism at the time, which increases the likelihood of unmeasured confounding effects and misses the opportunity to study these potentially interrelated mechanisms in coherence.</p> <ul style="list-style-type: none"> ▪ to study the mechanisms in coherence even though they may be interrelated | <p>us to study specific factors while adjusting for others, and thereby strengthening the interpretation of the results</p> |
| <ul style="list-style-type: none"> ▪ Unable to answer what specific quantitative and qualitative characteristics of the natural environment have a positive effect on health and well-being, through what pathways is still largely unknown. | <ul style="list-style-type: none"> ▪ Make classifications for the type and level of the indicators, which is important for policy makers. ▪ Examine the importance of both quantitative (amount, type, access, use) and qualitative characteristics (acoustic quality, identity, variety, safety) of the natural environment |
| <ul style="list-style-type: none"> ▪ Limited research exploring the sustained affective, cognitive and physiological responses to a single exposure and the effects of a repeated exposure to the same natural environment ▪ Unable to explain how policymakers and planners can design a natural environment to maximise health benefits | <ul style="list-style-type: none"> ▪ Explore longer-term changes in affect, cognitive function and physiological indicators that have to date only been studied during, or immediately after, engagement with the natural environment. ▪ Explore the immediate, maintained and long-term effects of repeated engagement with the same natural environment on |

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| | affect, cognitive function, and physiological indicators of well-being . |
| <ul style="list-style-type: none"> ▪ Guidelines of lifestyle, health and well being have largely undervalued local populations | <ul style="list-style-type: none"> ▪ Include lifestyle, health and well being factors of the local populations. |

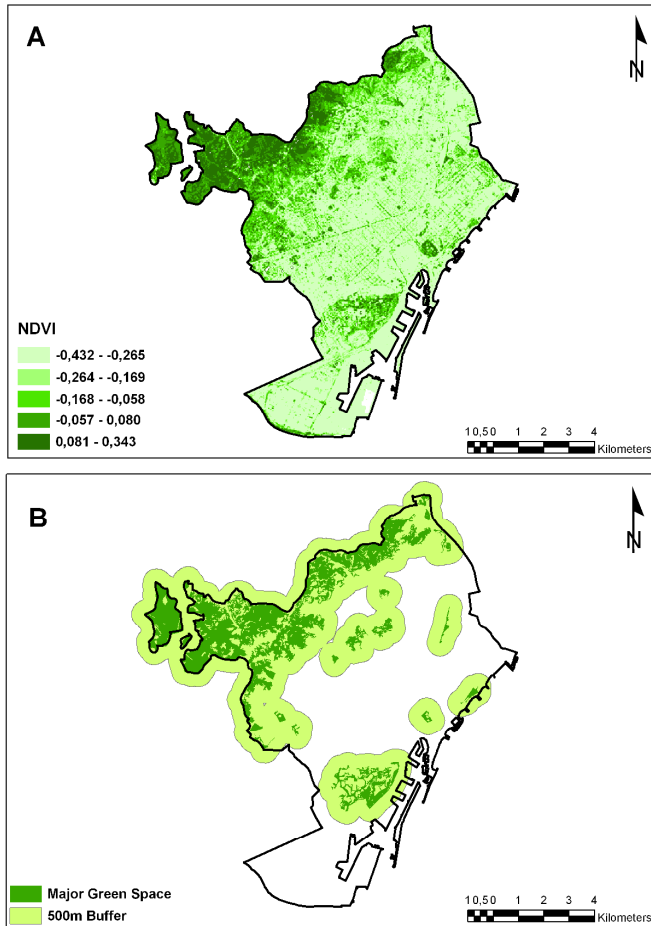
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Annex-websfigures



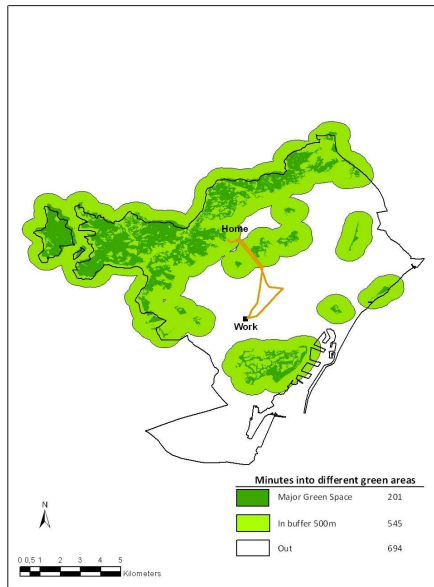
Web Figure 1 Natural outdoor environment, mechanisms and health data input in PHENOTYPE

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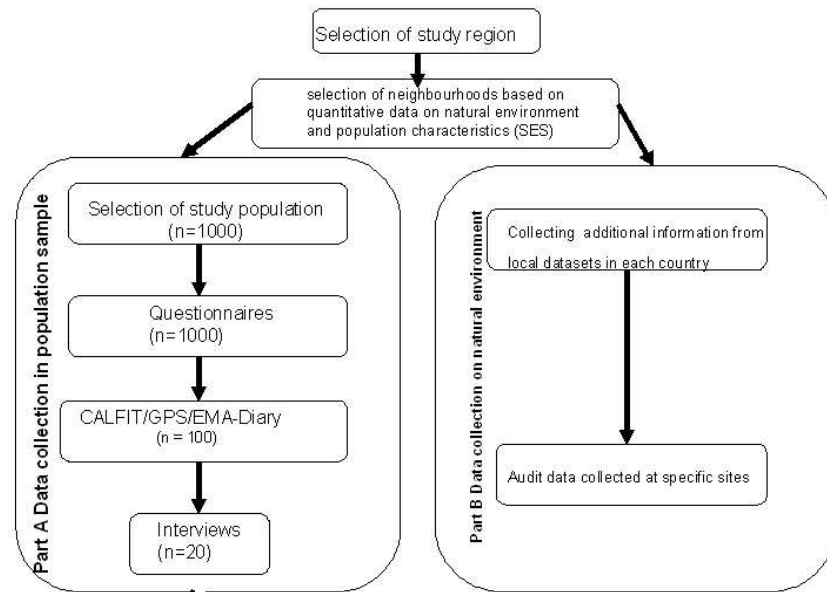
Web Figure 2 NDVI map of Barcelona and buffers around major green space areas



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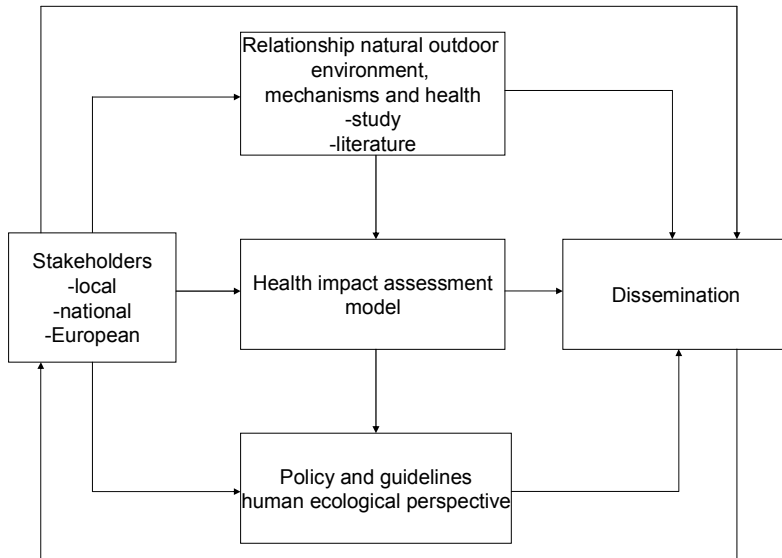
Web Figure 3 Mobility pattern for a subject in Barcelona obtained with the Calfit tool

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36 Web Figure 4 Design of data collection in 4 European case cities to study the underlying mechanism

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Web Figure 5 Stakeholder input and dissemination

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Web Table 1 Currently available databases and cohorts for inclusion in PHENOTYPE

| Study | n | Population | Collected outcomes | Relevant covariate and mechanism data |
|-------------|------|--|---|--|
| CREAL Spain | | | | |
| PISCINA | 3000 | Children 6-9, 2006, Sabadell, Catalonia | Respiratory health BMI | Social economic status Physical activity Air pollution |
| INMA | 3000 | Children, 2-10, ongoing around Spain | Birth weight and gestation, respiratory health, neural development | Social economic status Physical activity Stress Air pollution |
| PAC-COPD | 342 | Patients with chronic obstructive pulmonary disease (PAC-CODP) | Hospital admissions All cause and specific mortality Functional data (lung function, cardiovascular function) Symptoms and co-morbidities Quality of life Mental status Body weight and composition | Social economic status Physical activity Air pollution |

| | | | | |
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| ECRHS | 8500 | Adult population in many cities around Europe | Respiratory health Short form SF36 | Social economic status Physical activity Air pollution |
| Routine data Catalonia | Pop 7M 0.5 million deaths | All, 1999-2006, Catalonia | All cause and specific mortality | Social economic status |
| Hospital clinic database | 16000 | Births, 2000-2005 Barcelona | Birth weight and gestation | Social economic status Air pollution |
| Netherlands | | | | |
| Cohort of Dutch inhabitants Netherlands | Pop 16M | All, 2000-2008 | All cause and specific mortality and morbidity | Social economic status |
| Doetinchem cohort | Approximately 5000 over a period of 5 years | See: Verschuren WMM, Blokstra A, Picavet HSJ, Smit HA. The Doetinchem cohort study (cohort profile) Int J Epidemiol 2008; 37(6):1236-1241 | Body weight, serum cholesterol, mortality, morbidity, health- related quality of life (RAND-36) | Social economic status, physical activity |
| Health survey Utrecht | 3475 | Adults 3475 (19-99 years) | lifestyle, perceived health, chronic diseases | Socioeconomic status, physical activity |
| United Kingdom | | | | |
| Born in Bradford | 12000 | Babies, ongoing, England (large ethnic population) and their parents for a subgroup | Birth weight and gestation General and mental health parents in a | Social economic status Air pollution Detailed |

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| | | | subset of 1500 | ethnicity |
| Routine hospital emissions/disease incidence | | Small area-level data for Stoke-on-Trent/Staffordshire | Rates and nature of hospital episodes (e.g., respiratory, CVD), morbidity and mortality | Social economic status Air pollution |
| National health data | | Small area-level health data for UK | Nature and rates of morbidity and mortality | Social economic status Air pollution |
| Lithuania | | | | |
| Routine morbidity data Lithuania | 0.5 million | Lithuania population, all age groups. Classification of all registered cases causes according to ICD-10 revision codes | Urban-rural area, age, sex, cardiovascular, respiratory, cancer, and other morbidity by districts | Social and demographic status |
| Routine mortality data Lithuania | 0.5 million | Lithuania population, all age groups. Classification of all registered cases causes according to ICD-10 revision codes | Urban-rural area, age, sex, cardiovascular, respiratory, cancer, and other morbidity by districts | Social and demographic status |
| Detailed Health survey | 7000 | Representative sample adults of Kaunas citizens, Lithuania | General health including Blood pressure, high cholesterol and diabetes, Depression Physical functioning Cognitive function Psychosocial factors | Social economic status Air pollution Physical activities Stress |
| Kaunas birth | 4,260 | Kaunas babies and their parents for a subgroup | Birth weight and | Social, |

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| 6 | cohort | | http://www.birthcohorts.net/Cohort.Show.asp?cohortid=87 | gestational age |
| 7 | | | | demographic, economic status |
| 8 | | | | Air pollution |
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Web Table 2. Summary of proposed experimental design in each partner country in PHENOTYPE

| | Country | Sample | Summary design | Measures | | | | |
|-------------|----------------------|--|---|----------|--------------------|--|---|---|
| | | | | Affect | Cognition | Physiological | Environment | Other |
| Preventive | UK: study 1 | Healthy adults (n=40) | - Field-based - Within-subjects - 30-minute exposure to natural green, natural green/blue, and urban environment - Measures at baseline (pre-exposure), 30 and 60-minutes post exposure | Mood | Cognitive function | - Salivary cortisol - HR - HRV - BP | Perceived restoration | RPE Walking speed |
| | UK: study 2 | Healthy adults (n=40) | - Field-based - Between groups - 30-minute exposure to natural <i>or</i> urban environment on three consecutive days - Measures at baseline (day 1), 0, 30 and 60-minutes on exposure days (days 2-4) and final follow-up on day 5 | Mood | Cognitive function | - Salivary cortisol - HR - HRV - BP | Perceived restoration | RPE Walking speed Hedonic and eudemonic life satisfaction |
| | Netherlands: study 1 | Healthy adults (n=50) | - Laboratory-base - Within subjects - Shown images of natural and urban environment before a stressor (model 1) and after a stressor (model 2) stressor (to explore buffering and restorative effects, respectively) | Mood | Cognitive function | - Salivary cortisol - HR - HRV - BP | Perceived restoration | |
| | Netherlands: study 2 | Healthy adults (n=25) | - Laboratory-based - Within subjects - Shown images of natural and urban environment before a stressor (model 1) and after a stressor (model 2) stressor (to explore buffering and restorative effects, respectively) | Mood | Cognitive function | - Neurological response (fMRI) - Salivary cortisol - HR - HRV - BP | Perceived restoration | |
| Therapeutic | Spain | Adults with elevated stress levels (n=20-40) | - Field-based - Exposure to natural green, natural green/blue, and urban environment over several hours - Measures at baseline (pre-exposure), 30 and | Mood | Cognitive function | - Salivary cortisol - HR - HRV - BP | - Perceived restoration - Air pollution - Noise | RPE Walking speed Social interaction |

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| | | | 60-minutes post exposure - Participants given CALFIT phones for some days for longer term monitoring (mood, social interaction, physical activity) | | | | pollution | and physical activity (CALFIT) |
| | Lithuania | Adults with CAD (n=20) | - Field-based - Between-subjects - 30-minute exposure to natural green <i>or</i> urban environment on two consecutive days (days 2 and 3) - Measures at baseline (pre-exposure), 30 and 60-minutes post exposure - Walking treadmill test at baseline (day 1) and follow-up (day 2) | Mood | Cognitive function | - Exercise capacity (treadmill test) - Salivary cortisol - HR - HRV - BP | Perceived restoration | RPE Walking speed |

CAD, coronary artery disease; HR, heart rate; HRV, heart rate variability; BP, blood pressure, RPE, rate of perceived exertion; fMRI, functional magnetic resonance imaging

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POSITIVE HEALTH EFFECTS OF THE NATURAL OUTDOOR ENVIRONMENT IN TYPICAL POPULATIONS IN DIFFERENT REGIONS IN EUROPE (PHENOTYPE)-A STUDY PROGRAMME PROTOCOL

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|-------------------------------|---|
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| Primary Subject Heading: | Public health |
| Secondary Subject Heading: | Epidemiology, Public health, Occupational and environmental medicine |
| Keywords: | Green space, Blue space, Health, Well being, Physical activity |

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3 **POSITIVE HEALTH EFFECTS OF THE NATURAL OUTDOOR ENVIRONMENT**
4 **IN TYPICAL POPULATIONS IN DIFFERENT REGIONS IN EUROPE**
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6 **(PHENOTYPE)-A STUDY PROGRAMME PROTOCOL**
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Abstract

Introduction: Growing evidence suggests that close contact with nature brings benefits to human health and well-being, but the proposed mechanisms are still not well understood and the associations with health remain uncertain. The **Positive Health Effects of the Natural Outdoor environment in Typical Populations** in different regions in Europe (PHENOTYPE) project investigates the interconnections between natural outdoor environments and better human health and well-being..

Aims and methods: The PHENOTYPE project explores the proposed underlying mechanisms at work (stress reduction/restorative function, physical activity, social interaction, exposure to environmental hazards) and examines the associations with health outcomes for different population groups. It implements conventional and new innovative high tech methods to characterize the natural environment in terms of quality and quantity. Preventive as well as therapeutic effects of contact with the natural environment are being covered. PHENOTYPE further addresses implications for land-use planning and green space management.

The main innovative part of the study is the evaluation of possible short and long term associations of green space and health and the possible underlying mechanisms in 4 different countries (with quite different type of green space and use of green space) using the same methods and methodology in one research program. This type of holistic approach has not been undertaken before. Furthermore there are technological innovations such as the use of remote sensing and smartphones in the assessment of green space.

Conclusion: The project will produce a more robust evidence base on links between exposure to natural outdoor environment and human health and well-being, in addition to a better integration of human health needs into land use planning and green space management in rural as well as urban areas.

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3 **Keywords:** green space, blue space, health, well being, physical activity, social
4 contacts, restoration, stress, air pollution, remote sensing, GIS, audit, questionnaire
5 survey, smartphones
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Article summary

Strengths

The PHENOTYPE project is the largest European project on green space and health

The PHENOTYPE project examines simultaneously the possible underlying mechanisms (stress reduction/restorative function, physical activity, social interaction, exposure to environmental hazards) for the relationship between green space and health in 4 different countries in Europe

The PHENOTYPE project examines a range of possible associations of the natural outdoor environment and health using 16 different cohorts and/registries in 4 different European countries

The PHENOTYPE project uses a range of novel tools and methods to assess access and use of green space including remote sensing, smartphones, audits and interviews.

The PHENOTYPE project works closely with stakeholders and produces new information for stakeholders.

Introduction

Positive health effects have been observed between green space and mortality longevity[1-3], cardiovascular disease[4], people's self reported general health[5,6], mental health[7-11], sleep patterns[12], recovery from illness[13], social health aspects[14-18] and birth outcomes[19-21]. Some of the associations were shown to be modified by social economic status and level of urbanity, with greater benefits for populations with lower socioeconomic class[20,22] and those in more urban areas[6,22]. Furthermore gender has been shown to modify the relationship[11].

Increased physical activity and social contacts, psychological restoration/stress reduction, and a reduction in pollutants such as noise and air pollution, and temperature have been proposed as possible mechanisms for the health benefits of green space. Access to and/or use of green space has been associated with higher levels of physical activity[23-33] and lower levels of obesity within communities[25,27,34-38]. Studies even suggested that 'green exercise' can have even more positive mental health benefits than other kinds of exercise[39-42].

Psychological restoration[43-45] and reduced stress and anxiety[7,8,17,46,47] have all been associated with access to and/or use of green and natural space. An inner city study in a deprived estate in Chicago showed the benefits of green space both to cognitive restoration[48,49], self-discipline[48], reduced aggression[49] and reduced crime[50], with the latter also observed elsewhere recently[51]

Furthermore a few studies have suggested that green space is associated with more social contacts and cohesion[16,17,52]. And finally reduction of personal exposure to air pollution has been observed in areas with more green space[53], while vegetation has been suggested to reduce air pollution levels, and temperature[54-57], with some suggestion that the benefits are greater for socially disadvantaged groups[55]. It has also been suggested that vegetation (trees, plants) and soil may have an impact on the sound level[58-63]. Part of the appeal of green spaces may be related to pleasant acoustic environments. This may have its own, direct beneficial health effect (Health Council of the Netherlands, 2006).

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3 While this growing evidence exists that close contact with nature brings benefits to
4 human health and well-being, the proposed mechanisms are still not well understood
5 and the associations with health remain uncertain. Furthermore, it is unclear if the
6 possible mechanisms act in isolation or together, since with some exceptions[18] they
7 have been studied in isolation. A coherent conceptual framework on the proposed
8 mechanisms is currently lacking. Also, most of the research has been conducted in the
9 North West of Europe and USA leaving questions about the generalisability to other
10 regions. Inconsistency and variation in indicators (eg type, size and quality) for green
11 space have often made it difficult to compare results from different studies, and a better
12 characterisation including that of quantity and quality of green and blue spaces is
13 needed, not only for research but also for policymakers and spatial planners. Studies
14 have often focused on access to green space without taking into account actual use of
15 green space. While blue space may also have a positive effect on health, probably in
16 combination with green space, there are only a few epidemiological studies
17 investigating this[64-66]
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29 PHENOTYPE, a collaborative research project and explores the proposed underlying
30 mechanisms at work (stress reduction/restorative function, physical activity, social
31 interaction, exposure to environmental hazards). PHENOTYPE is the first study
32 designed to examine these mechanisms simultaneously in a large sample (N=4000
33 subjects) in various European countries using the same methodology. This allows the
34 study of specific factors while adjusting for others, and thereby strengthening the
35 interpretation of the results. It further examines both the long term and short term
36 associations with health (eg general health and wellbeing, mental health/neural
37 development, stress, cardiovascular, cancer and respiratory mortality and morbidity,
38 birth outcomes and obesity) for different population groups (e.g. pregnant women
39 and/or foetus, different age groups, socioeconomic status, ethnic groups, and patients),
40 through analyses of existing cohort studies, observational studies and experiments.
41 Preventive as well as therapeutic effects of contact with the natural environment are
42 being evaluated. A coherent conceptual framework on the association between the
43 natural environment and its effects on health and well-being is being developed, and it
44 addresses implications for land-use planning and green space management.
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3 The study includes both rural and urban settings, but the main focus is on the urban
4 environment, for a number of reasons. Most of the population lives in urban areas
5 (75%) in Europe, making these of greater relevance to public health, and rapid
6 urbanization continues to reduce accessible natural environments for urban residents.
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8 Most people make more frequent use of the green spaces in their nearby living
9 environment instead of travelling greater distances to rural areas, in particular people
10 with lower socio-economic status, elderly people and children[67,68]. Furthermore,
11 rural dwellers tend to have constant contact with the natural environment and it may
12 therefore also be more difficult to assess its effects.
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19 Lastly, the project uses an interdisciplinary and integrated approach, applying the best
20 and most efficient methods to understand the relation between exposure to the natural
21 environment and health. It implements conventional and innovative high tech methods
22 to characterize the natural environment in terms of quality and quantity. This paper
23 provides a general overview of the research methodology of PHENOTYPE.
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30 31 **Methods**

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34 Figure 1 summarizes the different parts of the study and the interdependencies between
35 the different parts, namely the characterisation of the natural environment and the way it
36 is used, examination of the underlying mechanisms in daily life settings, short and long
37 term effects of the natural environment, and the implications for management and
38 policy of the natural environment (see overview Figures 1 and web figure 1). In this
39 section we will elaborate on each of these parts. A summary of the mechanisms,
40 outcomes, populations and areas selected for investigation are given in Table 1.
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50 ***Characterising the natural environment and the way it is used.***

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53 The research includes evaluation of the natural environment, which includes for the
54 purposes of the project:

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56 - Green spaces (e.g. roof gardens, city parks, court yards) and “greenery”; forests, nature
57 reserves/parks, mountains, farmland, trees, landscaping
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3 - Blue spaces; water such as canals, ponds, creeks, rivers, beaches etc.

4 Although many of these may actually not be "natural" since they have been man-made,
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6 for the purpose of the project we classify them as such.
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10 One of the main aims of PHENOTYPE is to examine the importance of both
11 quantitative (e.g. amount, type, access, use) and qualitative characteristics (e.g. acoustic
12 quality, identity, variety, safety, rubbish) of the natural environment by collecting
13 detailed data on these characteristics using a combination of methods. The focus lies on
14 natural environments at different scales and distances from the home (city/town,
15 neighbourhood, street level) and where possible also at other places where people stay
16 (work, school, on their way to home/school, recreational). In addition, actual use of the
17 natural environment is taken into consideration. To achieve the aim, a detailed
18 assessment will be conducted in 4 case cities (Barcelona, Spain; Doetinchem, the
19 Netherlands; Kaunas, Lithuania; and Stoke-on-Trent, United Kingdom), with less
20 detailed assessment in other study areas.
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30 PHENOTYPE uses conventional land use maps, remote sensing data from satellites and
31 aerial photography, complemented by detailed discussions with volunteers and other
32 stakeholder living and working in the studied areas to derive comparable classifications
33 of the natural environment in different countries. Collected data will contribute to the
34 characterisation of the natural environment (both quantitative and qualitative e.g.
35 accessibility, acoustical quality, recreational activities, walkability etc). For the
36 quantitative characterisation, PHENOTYPE makes use of available land use maps such
37 as COordination and INformation on the Environmental programme, initiated by the
38 European Commission (CORINE)[69] and Urban Atlas[70], and remote sensing and
39 aerial photography to obtain comparable indices such as NDVI[71] of the natural
40 outdoor environment in different countries. Landsat Enhanced Thematic Mapper Plus
41 (ETM+) data are applied to a classification and regression tree (CART) model to
42 categorise land cover types for the urban areas of interest[55]. Early application of the
43 NDVI in Barcelona, Spain showed good results[20] (Web Figure 2)
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54 To collect additional qualitative information on the natural environment and on other
55 physical and social features, systematic observations (audits) are conducted by trained
56 researchers in selected neighbourhoods in the 4 case cities using the same methods.
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3 Since it is not feasible and not necessary to audit every street in a selected
4 neighbourhood, a purposeful sample of streets is drawn, ensuring that important
5 neighbourhood features are included. The selected neighbourhoods are divided into
6 more or less homogeneous sub-areas by means of data/maps on land use/function of
7 areas in combination with local knowledge of the area. Subsequently, trained auditors
8 are asked to visit the sub-areas and observe them in a systematic way (auditing) using a
9 paper form containing several close-ended questions. Every sub-area is visited by two
10 auditors. For the first 1-2 areas, the auditors fill in the list together, discussing
11 completion to reach consensus. In subsequent areas, where possible, the two auditors
12 complete the audit independently and simultaneously. Furthermore, up to two natural
13 environments of more than one hectare in size are selected per neighbourhood using
14 GIS. Again following training in completion of the audit, two auditors visit the
15 environments. For the first five areas, auditors undertake the interview together,
16 discussing completion to reach consensus, thus maximizing consistency. In subsequent
17 areas, where possible, two assessors complete the audit independently and
18 simultaneously. In the absence of existing measures that could meet our requirements,
19 the streetscape audit was developed for this project and the natural environment tool
20 was adapted from an existing measures. This kind of bespoke tool development is seen
21 in similar studies e.g. by Van Dillen[72]. One form is used for evaluating the
22 streetscape, using indicators derived from the Street Typology developed by
23 Leijdelmeijer et al. (2002)[73], a list of evaluating the quality of green by Van Dillen
24 (2012)[72] and the audit tool developed by Van Lenthe et al. (2006)[74]. The natural
25 environment audit is adapted from that developed by Gidlow et al (2012)[75] through
26 addition of items and domains to reflect the greater diversity in natural environments to
27 be included (i.e., different types of natural environment across four European cities).
28 The tools were piloted and adjusted prior to use. They have not been 'validated', but
29 there is no gold standard quality measure for natural environments against which to
30 compare. Inter-rater reliability will be estimated through derivation of Inter-rater
31 Correlation Coefficients (ICC) and PCA will be used to ensure that any redundant items
32 are removed and included items are grouped sensibly into domains, before overall
33 quality scores will be derived.

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56 To gain insight into the way people use the natural environment, a face to face
57 questionnaire survey is conducted to collect data on 1000 people in the 30 selected
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3 neighbourhoods in each of the 4 case cities, and an in-depth study using “Calfit”, a
4 smartphone-based monitor of time-location patterns and momentary states, on a
5 subsample (n=100) of the participants of the questionnaire survey (for further detailed
6 information, see next section on underlying mechanisms). The Calfit software[76,77]
7 runs on a Google Android operating system and as currently configured can collect data
8 on physical activity using the motion sensor and geographic location through a global
9 positioning system (GPS), to obtain information on minutes spent and physical activity
10 levels in different natural environments (Web Figure 3). The instrument has been
11 validated against the Actigraph accelerometer[76], combined with other pollution
12 measurements to assess likely inhalation[77], and lab-validated using the Cosmed
13 metabolic monitoring system.
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23 The work will produce different indicators of natural space that can be used in the
24 studies described below. The aim is to make a hierarchy of indicators with on the
25 bottom simple measures such as NDVI that can be easily obtained for all the study areas
26 and on the top detailed measures of for example green space with actually information
27 on the quantity, quality and use that can only be obtained for only some areas after in-
28 depth study. As part of the work, we will examine the relationship between the simple
29 and detailed measures to better understand how detailed information on small scale can
30 help the interpretation of health studies conducted in larger areas with only simple
31 measures available using existing epidemiological studies and registries (see below).
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40 ***Examining the underlying mechanism in the daily life setting***

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43 New data will be collected to explore in detail and simultaneously the proposed
44 mechanisms (physical activity, social contacts/cohesion, psychological restoration/stress
45 reduction) underlying the relationship between the natural environment and health and
46 well-being, in the four case cities. In each of these cities neighbourhoods varying in
47 socio-economic status and in their distance to green space are selected. In these
48 neighbourhoods the natural environment will be characterised, and (as mentioned above
49 already) a selection of 1000 randomly selected residents (4000 in total, 18-75 years)
50 will participate in a questionnaire survey, 100 in a smartphone study, and 20 in in-depth
51 interviews (Web Figure 4).
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3 To optimally investigate what types of natural environments and different levels of
4 accessibility are relevant in relation with the mechanisms that we investigate (physical
5 activity, stress and restoration, social interactions and environmental pollution), and to
6 investigate potential differences in this mechanism among the population, we use a
7 multiple level approach and select neighbourhoods with different socio-economic status
8 (SES) and access to the natural environment. We use existing statistical or
9 administrative units with Existing statistical or administrative units that were as similar
10 as possible with regard to variation in population size; in Stoke-on-Trent Lower Layer
11 Super Output Areas (LSOAs), in Barcelona census areas, in Kaunas voting districts and
12 in Doetinchem neighborhoods. Natural space and SES measures are assigned to all the
13 units, using existing data. For natural space, Urban Atlas is used for Stoke-on-Trent,
14 Barcelona and Kaunas. Since Urban Atlas is not available for Doetinchem, data of
15 another Dutch database ('Top10 nl') is used. For SES no comparable data existed for
16 the 4 cities. Therefore partners use their own local data. Then the units are ranked by
17 each natural space and SES. Subsequently a selection of two neighbourhoods from each
18 combination of top, middle and bottom tertiles of SES and quintiles of the natural space
19 is made (approx. $2 \times 3 \times 5 = 30$ units). A few extra units are added to optimize contrast
20 and reach a sufficient number of units to be able to recruit a 1000 subjects in each city
21 (30 subjects per units). Since there are no common person registries in these countries,
22 subjects (aged between 18 and 75) are selected using different approaches. In
23 Doetinchem and Stoke-on-Trent, addresses are sampled randomly from the BAG
24 Registry ('Buildings and Adresses') 2012 and a local address registry respectively and
25 the person with the closest birthday to the interview data is selected at each address, in
26 Barcelona subjects are randomly selected from the person registry (empadronamiento)
27 and in Kaunas subjects are sampled randomly from a 2006-2009 survey of randomly
28 sampled people of the city of Kaunas. In each case there is an over selection of
29 potential addresses or subjects to be able to interview at least a 1000 subjects (and 30
30 per unit) in each city. The target of a 1000 subjects per city was mostly based on the
31 available budget. To enable multi-level analysis, we estimated that a minimum of 30
32 participants per group (or neighbourhood) were required, with a minimum of 30 groups.

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The questionnaire survey was designed to investigate three potential mechanisms in
relation to natural environments and health: via physical activity, stress and restoration
and social interactions as described in. In addition questions are included about

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3 environmental worries and reactions to perceived exposures (air pollution, noise, etc).
4 The choice of indicators was based on these three mechanisms and was achieved via an
5 interactive process of experts within the PHENOTYPE team. As much as possible
6 questions were derived from existing and validated indices, some tailored to the specific
7 objectives of PHENOTYPE. The questionnaire was developed in English and was
8 translated (and back translated) into Dutch, Spanish, Catalan, and Lithuanian. The
9 questionnaire was developed to be applied in an oral interview of at maximum 60
10 minutes. In Kaunas it is not common to have face-to-face interviews; therefore a written
11 questionnaire is sent by post to the selected people. The questionnaire was piloted by all
12 partners, with specific attention for comprehensibility, clarity and duration and was
13 adapted at some points based on outcomes of these pilots.
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23 The final questionnaire is structured along four main clusters of questions: I. Green and
24 Blue Spaces; II Residential situation: Dwelling & Neighbourhood; III Wellbeing and
25 Health; IV Personal characteristics. Per mechanism questions are asked about
26 availability, use, importance, and satisfaction. In the sequencing of the questions we
27 strive for a coherent set of questions per cluster moving from general to specific and
28 from ‘easy’ to more intruding questions. Furthermore, most of the answer categories
29 moved from neutral negative towards positive items. For all answers showcards have
30 been developed by RIVM, to make it easier for both interviewers and respondents, and
31 to speed up the interview process. A separate instruction document was developed to
32 train the interviewers. The questionnaire ended with an optional a pencil paper attention
33 test (Color Trails Test (CTT-A)) add ref.
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43 Finally for the smartphone study at least 100 volunteers from each country are randomly
44 selected from the participants of the questionnaire survey who indicated that they were
45 willing to participate in the smartphone study. For these subjects, during 7 subsequential
46 days the emotional state of the subject, the local environment (e.g., different quantities
47 or qualities of natural space) and the social setting are assessed with the smartphone and
48 the innovative Calfit technology. Besides objective geolocation and physical activity
49 (see section Characterisation the natural environment), subjective data on stress
50 reduction/restoration and social contacts are collected simultaneously. The latter data
51 are collected through interactive diaries capable of eliciting ecological momentary
52 assessment (EMA). EMA is a novel approach to elicit responses to electronic surveys
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3 throughout the course of daily life[78]. The participant receives prompts at random
4 intervals to complete small surveys on the phone, which then have time and location
5 stamp.
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9 From the people who participate in both the questionnaire survey and the CALFIT study
10 and who indicate they wanted to volunteer, 80 people (20 in each case city) are
11 approached for semi structured interviews. These interviews are conducted to gain more
12 detailed information on specific topics included in the questionnaire survey and
13 CALFIT/EMA. Topics addressed include the motivation for travel routes, the
14 associations of natural environment with mood, behaviour and well-being, the attitude
15 towards and importance of (experiences with) natural environment, and reasons for
16 using or not using the natural environment.
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23 24 *Epidemiological studies to examine long term effects of the natural environment* 25

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27 By using existing epidemiological studies and registries and linking these to the natural
28 space indicators described earlier, the association between natural environment and a
29 range of different long term health outcomes will be examined in an efficient and cost
30 effective manner. PHENOTYPE makes use of 16 existing cohorts and registries with
31 good health outcome data in Spain, the Netherland, Lithuania, and United Kingdom
32 (Web Table 1), linking these to newly created natural environment indicators.
33 Comparable estimates are produced for various regions in Europe for the associations
34 with pregnancy outcomes, foetus development, children's health and adult population
35 morbidity and mortality. We specifically focus on:
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- 43 • the natural outdoor environment and ethnicity, socio-economic status, women's
44 health and pregnancy outcomes;
- 45 • the natural outdoor environment and foetus development, birth weight, and
46 gestational age;
- 47 • the natural outdoor environment and general development, neurodevelopment,
48 cognitive function and respiratory health in children;
- 49 • the natural outdoor environment and respiratory health in various European cities;
- 50 • the natural outdoor environment and general health, physical activity, specific
51 morbidity and mortality.
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4 The assessment of natural environment indicators will be mainly based on satellite data
5 and land use maps as CORINE and Urban atlas, and sometimes local data. This will
6 restrict to some extent the evaluation of the association with the natural environment,
7 but this is the only realistic and achievable approach. All studies examine the role of
8 socio-economic status, which has been suggested as an effect modifier for the
9 relationship between exposure to the natural environment and health benefits. The
10 European Community Respiratory Health study (ECRHS)[79] further allows for
11 examination of exposure to the natural outdoor environment and associations with
12 health in a range of different European cities. Some cohorts such as the Born in
13 Bradford study[80] offers a unique opportunity to investigate the role of ethnicity in the
14 relationship between exposure to the natural outdoor environment and health benefits,
15 in Bradford study half of the participants are from Pakistani background, with
16 information on both the mother and baby from pregnancy to early years in life.
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28 *Experiments to examine short term effects of the natural environment*

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31 To examine short term effects of the natural environment on health and well-being, one
32 or more experimental studies are conducted in each country in which individuals are
33 exposed to different types of natural and urban environments (i.e., environmental
34 conditions). The majority of data collection is field-based to maximise the ecological (as
35 well as internal) validity of any observed effects.
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39 Using a range of psychological and physiological indicators relevant to the various
40 possible mechanisms, and 2) healthy and patient population groups (with mental and/or
41 somatic morbidities) we will collectively explore::
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- 44 - preventive and therapeutic effects of natural environments.
- 45 - immediate and sustained changes in affective, cognitive and physiological
46 responses indicative of well-being while engaged in a natural environment, and
47 after leaving a natural environment
- 48 - neurobiological responses to viewing natural or urban scenes before/after
49 experiencing stress.
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56 Through variation in experimental design, each partner makes a novel contribution(s) to
57 the area as (details in Web Table 2):
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- UK: In healthy individuals, Study 1 compares immediate and post-exposure psychophysiological effects of urban versus natural environments to explore whether any beneficial effects are sustained following single exposures; Study 2 uses longer-term follow-up and repeated exposure to natural environments to explore whether any effects are accumulated, sustained or attenuated.
- Netherlands: an experimental functional Magnetic Resonance Imaging (fMRI) study is conducted in healthy individuals to investigate neurobiological responses to viewing natural or urban scenes before/after experiencing stress; i.e., whether viewing natural compared to urban scenery can prevent or buffer against stress responses, and how this is represented in brain activation patterns.
- Spain: in individuals with elevated stress levels, group-based exposure and Ecological Momentary Assessment (EMA, using CALFIT technology) are used to explore the role of social interaction and the nature of physical activity, in immediate and longer term responses. Ecological validity will be enhanced through ‘free-living’ activities within environments, rather than controlling activities, again, using EMA, GPS and accelerometry to monitor the nature (and perceptions) of this activity.
- Lithuania: a clinical population with established coronary artery disease (CAD) are recruited to evaluate the therapeutic effect of the natural environment. The outcomes of this experiment may have direct clinical applications for the use of urban and different types of natural environment in cardiac rehabilitation.

Implications, policy and guidelines and involvement of stakeholders

Guidelines

PHENOTYPE will provide recommendations for policymakers and guidelines for professional practitioners involved with spatial planning and health to create natural environments that promote health and well being. For this, we focus on a human ecological perspective which allows for a better integration of human health needs into land use planning and green space management in both rural and urban areas[81].

Currently legal standards that have been developed with economic, technological and

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3 political priorities in mind, are leading in urban design, whereas the lifestyle, sense of
4 community, identity, and health and well being of local populations have been largely
5 undervalued. The guidelines will reflect the importance to consider environmental,
6 social, economic and other components of the natural and built environments in ways
7 that also take into account and result from the point of view of citizens. PHENOTYPE
8 will complement the common quantitative approach by valorising the social/human
9 functions of these environments, especially their contribution to promoting health and
10 quality of life.
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18 Following this broad and innovative approach, PHENOTYPE will formulate, test and
19 validate a set of recommendations and guidelines concerning the desired characteristics
20 of different types of natural environments in urban and rural areas, specifically their
21 characteristic features, accessibility to them for different population groups, as well as
22 their facilities, maintenance and services. By doing so, the work will overcome the
23 existing applicability gap between information and knowledge accumulated by much
24 research and policy definition and implementation.
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31 The guidelines for professional practitioners involved with spatial planning and health
32 will consider three core topics in relation to each of the natural environment being
33 considered:
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- 36 1. Qualitative characteristics of natural environments; recommendations concerning
37 surface area, vegetation, water sources, ambient noise levels, views and
38 microclimate;
- 39 2. Facilities, Maintenance and Services; recommendations about the kinds of
40 communal facilities and services provided in each type of natural environment, as
41 well as suggested levels of maintenance;
- 42 3. Accessibility Guidelines to Natural Environments; including requirements about
43 access to different types of natural environments such as allotments,
44 neighbourhood parks, children's playgrounds and nature reserves.
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51 The baseline for the work is firstly the compilation and analysis of currently available
52 information from existing databases and literature, and later new data collected by the
53 project as described above. This will be complemented by the engagement with the
54 appropriate stakeholders to assess scope for development. These insights will be
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3 combined into a conceptual framework on the underlying mechanisms of the effects of
4 the natural environment on health and well-being.
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7 *Stakeholders and dissemination*

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11 The participation provides a forum for project assurance and benefits for PHENOTYPE
12 are summarised as follows:
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16 - A more robust evidence base on links between exposure to natural outdoor
17 environment and human health/well-being for various regions in Europe. Hereby
18 we expect to develop a better understanding of the potential mechanisms.
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21 - A better integration of human needs into land use planning and green space
22 management in rural as well as urban areas. Furthermore, the application of
23 these needs in practical guidelines.
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28 Stakeholder involvement is critical for bringing outside (policy) ideas into the research
29 planning, to increase the usefulness of the research, and to assure a better
30 implementation of the results of the project (Web Figure 5). In a research project, this is
31 often limited because the lack of interest of stakeholders and the limited resources and
32 efforts of consortia.
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38 From the start of PHENOTYPE actively sought to establish and maintain relations and
39 dialogues with and between key stakeholders from local, regional and national health
40 and environment authorities, institutions and the international research community.
41 These include policy makers, architects, urban planners, natural space managers, health
42 professionals, and the international research community. This group is highly diverse,
43 as we are looking at a range of professions within the subject areas of environment and
44 health, from volunteers to scientists, community workers and policy developers.
45 PHENOTYPE has thus far been successful in its engagement activities, providing
46 continuous opportunities for information exchange and collaborations. These contribute
47 to strengthening networking between researchers, policy-makers and stakeholders in
48 order to facilitate the transfer of scientific knowledge to policy development, to
49 exchange ideas about best practice and to help identify emerging issues on the natural
50 outdoor environment and its mechanisms to improve health.
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4 The PHENOTYPE website www.phenotype.eu provides an overview of the project,
5 progress, actualities, surveys and publications. The site has a sign up form for periodic
6 newsletters through which all stakeholders are regularly informed. It guarantees
7 continuous visibility, and provides a means for interested parties to respond to activities,
8 or to contact us with invitations to attend workshops, etc. PHENOTYPE is also found
9 on social media twitter (@greenhealth4eu) and LinkedIn. The PHENOTYPE databases
10 and overall results will be exploitable by policy makers at national and international
11 level in areas including urban planning and health.
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21 **Conclusion**

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24 The PHENOTYPE project is an FP7 collaborative action, funded by the EC to explore
25 the mechanisms underlying positive short term and long term health effects for different
26 population groups. PHENOTYPE applies conventional and new innovative high tech
27 methods to characterize the natural environment in terms of quality and quantity.
28 Preventive as well as therapeutic effects of contact with the natural environment will be
29 covered. The proposed work aims to address the limitations of some of the studies that
30 have been published so far (Table 2). Furthermore it addresses implications for land-
31 use planning and green space management. The project will produce a more robust
32 evidence base on links between exposure to natural outdoor environment and human
33 health and well-being. This in turn will contribute to improved integration of human
34 health needs into land use planning and green space management in rural and urban
35 areas.
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Ethics approval was obtained for all aspects of the study by the local ethics committees in the countries where the work was conducted, and sent to the European Commission before advancement of the study.

Author statement

Mark J Nieuwenhuijsen, Hanneke Kruize, Christopher Gidlow, Michael Jerrett, Jolanda Maas, Edmund Seto, Peter Jan van den Hazel, Roderick Lawrence, and Regina Grazuleviciene and wrote the original grant proposal on which the study design and paper is based. Mark J Nieuwenhuijsen drafted the version of the paper and received input from all the authors. All authors read and commented on the paper and agree with the final version.

Competing Interests

None

Data Sharing Statement

"No additional data available yet"

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Table 1 PHENOTYPE study mechanisms, outcomes, populations and regions

It will explore underlying mechanisms related to:

- stress reduction/restorative function
 - physical activity
 - social interaction/social cohesion
- exposure to environmental hazards (e.g. noise/acoustic quality, air pollution)

Both preventative and therapeutic effects (patients) will be considered. Outcomes of interest that are evaluated are:

- general health and well-being (including medically unexplained symptoms (MUPS))
- mental health/neural development
- stress
- cardiovascular, cancer and respiratory mortality and morbidity
- birth outcomes
- obesity

It will examine the effects for different population groups, including more vulnerable populations:

- pregnant women and/or foetus
- age groups (children, elderly)
- (lower) socio-economic status
- ethnic minorities
- patients/people with specific health complaints

It will conduct comparative studies in different regions of Europe to examine any underlying regional, social and/or cultural differences related to the meanings, uses, mechanisms and health effects of the natural environment and we will include the:

- North west (Netherlands, England)
- South (Spain)
- East (Lithuania)

Table 2 Limitations of current green space work and work undertaken by PHENOTYPE to address these

| Limitations of current available work | What PHENOTYPE will do |
|--|--|
| <ul style="list-style-type: none"> ▪ Inconsistency and variation in indicators for green or natural space have often made it difficult to compare results from different studies. | <ul style="list-style-type: none"> ▪ Minimize the potential differences due to classification of natural space, by combining the use of conventional maps and data sources with remote sensing data and aerial photography, gather individual-level data through detailed discussions with subjects living in the areas, and use considerable stakeholder engagement to develop comparable classifications of the natural environment in different countries. ▪ Produce a more robust and comparable evidence base on links between exposure to natural outdoor environment and human health and well-being. |
| <ul style="list-style-type: none"> ▪ A number of disease outcomes have been studied, but besides the routinely collected data (which use ICD coding), not always in a standardized and comparable manner in different countries | <ul style="list-style-type: none"> ▪ Produce a more robust and comparable evidence base on links between exposure to natural outdoor environment and human health and well-being, using well studied and new outcomes with standardization between countries. |
| <ul style="list-style-type: none"> ▪ Potentially very sensitive groups such as pregnant women/fetus have not been studied at all. | <ul style="list-style-type: none"> ▪ Extend the evidence base to new outcomes and vulnerable populations e.g. pregnant women and their foetus, chronic respiratory and cardiovascular patients, ethnic minorities and |

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| | low social economic class. |
| <ul style="list-style-type: none"> Most studies focused on green space; the evidence base for the effects of blue space is very limited. | <ul style="list-style-type: none"> Not only examine the effects of green space, but also of blue space. |
| <ul style="list-style-type: none"> Most of the green space studies have been conducted in the US or the North West of Europe. | <ul style="list-style-type: none"> Conduct comparable studies across Europe and produce evidence for North Western, Eastern and Southern Europe. This will deliver insights into regional, social and/or cultural differences in relation to natural space. |
| <ul style="list-style-type: none"> Most studies do not include actual use of the natural environment. | <ul style="list-style-type: none"> Consider actual use of the natural environment, an often neglected but fundamental indicator in relation to exposure to natural environments. |
| <ul style="list-style-type: none"> There appeared to be differences by social group, with some apparently benefiting more than others from natural space, but the evidence is sparse. | <ul style="list-style-type: none"> Produce a more robust and comparable evidence base on links between exposure to natural outdoor environment and human health and well-being, with special attention for effect modification by social groups |
| <ul style="list-style-type: none"> A number of potential mechanisms have been suggested, including increased physical activity and social contacts for those living near natural space, natural environments exerting | <ul style="list-style-type: none"> Examine the proposed mechanisms (physical activity, stress, social contacts, and environmental risk factors) simultaneously in a large sample in various countries (WP2). This will enable |

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| <p>stress lowering or attention restoring effects, and reducing environmental hazards (e.g. air pollution, high temperatures). However, the studies of potential mechanisms have often been limited to assessing one mechanism at the time, which increases the likelihood of unmeasured confounding effects and misses the opportunity to study these potentially interrelated mechanisms in coherence.</p> <ul style="list-style-type: none"> ▪ to study the mechanisms in coherence even though they may be interrelated | <p>us to study specific factors while adjusting for others, and thereby strengthening the interpretation of the results</p> |
| <ul style="list-style-type: none"> ▪ Unable to answer what specific quantitative and qualitative characteristics of the natural environment have a positive effect on health and well-being, through what pathways is still largely unknown. | <ul style="list-style-type: none"> ▪ Make classifications for the type and level of the indicators, which is important for policy makers. ▪ Examine the importance of both quantitative (amount, type, access, use) and qualitative characteristics (acoustic quality, identity, variety, safety) of the natural environment |
| <ul style="list-style-type: none"> ▪ Limited research exploring the sustained affective, cognitive and physiological responses to a single exposure and the effects of a repeated exposure to the same natural environment ▪ Unable to explain how policymakers and planners can design a natural environment to maximise health benefits | <ul style="list-style-type: none"> ▪ Explore longer-term changes in affect, cognitive function and physiological indicators that have to date only been studied during, or immediately after, engagement with the natural environment. ▪ Explore the immediate, maintained and long-term effects of repeated engagement with the same natural environment on |

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| | affect, cognitive function, and physiological indicators of well-being . |
| <ul style="list-style-type: none"> ▪ Guidelines of lifestyle, health and well being have largely undervalued local populations | <ul style="list-style-type: none"> ▪ Include lifestyle, health and well being factors of the local populations. |

For peer review only

Figure legend

Figure 1: Interdependencies of different parts of the PHENOTYPE project

Annex-web figures

Web Figure 1 Natural outdoor environment, mechanisms and health data input in PHENOTYPE

Web Figure 2 NDVI map of Barcelona and buffers around major green space areas

Web Figure 3 Mobility pattern for a subject in Barcelona obtained with the Calfit tool

Web Figure 4 Design of data collection in 4 European case cities to study the underlying mechanism

Web Figure 5 Stakeholder input and dissemination

(All attached separately)

POSITIVE HEALTH EFFECTS OF THE NATURAL OUTDOOR ENVIRONMENT IN TYPICAL POPULATIONS IN DIFFERENT REGIONS IN EUROPE (PHENOTYPE)-A STUDY PROGRAMME PROTOCOL

POSITIVE HEALTH EFFECTS OF THE NATURAL OUTDOOR ENVIRONMENT IN TYPICAL POPULATIONS IN DIFFERENT REGIONS IN EUROPE (PHENOTYPE)

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Abstract

Introduction: Growing evidence suggests that close contact with nature brings benefits to human health and well-being, but the proposed mechanisms are still not well understood and the associations with health ~~effects~~ remain uncertain. The Positive Health Effects of the Natural Outdoor environment in Typical Populations in different regions in Europe (PHENOTYPE) project investigates the interconnections between natural outdoor environments ~~, in both rural and urban settings,~~ and better human health and well-being ~~being in the North West, South and East of Europe. Here we provide a description of the proposed work.~~

Aims and methods: The PHENOTYPE project explores the proposed underlying mechanisms at work (stress reduction/restorative function, physical activity, social interaction, exposure to environmental hazards) and examines the associations with health effects-outcomes ~~(e.g. general health and wellbeing, mental health/neural development, stress, cardiovascular, cancer and respiratory mortality and morbidity, birth outcomes and obesity)~~ for different population groups ~~(e.g. pregnant women and/or foetus, different age groups, socioeconomic status, ethnic groups, and patients)~~. It implements conventional and new innovative high tech methods to characterize the natural environment in terms of quality and quantity. Preventive as well as therapeutic effects of contact with the natural environment are being covered. PHENOTYPE further addresses implications for land-use planning and green space management.

Result: The main innovative part of the study is the evaluation of possible short and long term effect associations of green space and health and the possible underlying mechanisms in 4 different countries (with quite different type of green space and use of green space) using the same methods and methodology in one research program. This type of holistic approach has not been undertaken before. Furthermore there are technological innovations such as the use of remote sensing and smartphones in the assessment of green space.

Conclusion: The project will produce a more robust evidence base on links between exposure to natural outdoor environment and human health and well-being, in addition

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6 to a better integration of human health needs into land use planning and green space
7 management in rural as well as urban areas.
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11 **Keywords:** green space, blue space, health, well being, physical activity, social
12 contacts, restoration, stress, air pollution, remote sensing, GIS, audit, questionnaire
13 survey, smartphones
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Article summary

Strengths

The PHENOTYPE project is the largest European project on green space and health

The PHENOTYPE project examines simultaneously the possible underlying mechanisms (stress reduction/restorative function, physical activity, social interaction, exposure to environmental hazards) for the relationship between green space and health in 4 different countries in Europe

The PHENOTYPE project examines a range of possible associations of the natural outdoor environment and health ~~health effects of green space~~ using 16 different cohorts and/registries in 4 different European countries

The PHENOTYPE project uses a range of novel tools and methods to assess access and use of green space including remote sensing, smartphones, audits and interviews.

The PHENOTYPE project works closely with stakeholders and produces new information for stakeholders.

Weakness

~~The limited funding may not lead to the full exploitation by the wealth of data generated within the life time of the project~~

Introduction

Positive health effects have been observed between green space and mortality longevity[1-3]([Takano et al. 2002](#); [Mitchell and Popham 2008](#), [Villeneuve et al. 2012](#)), cardiovascular disease[4]([Pereira et al. 2012](#)), people's self reported general health[5,6]([de Vries et al. 2003](#); [Maas et al. 2006](#)), mental health[7-11]([Grahn & Stigsdotter, 2003](#); [Hartig et al. 2003](#); [Maas, et al. 2009b](#); [Ottoosson & Grahn, 2005](#); [Richardson et al. 2013](#)), sleep patterns[12]([Astell-Burt et al. 2013a](#)), recovery from illness[13]([Ulrich 1994](#)), social health aspects[14-18]([Kim & Kaplan, 2004](#); [Sullivan et al. 2004](#); [Kweon et al 1998](#); [Maas et al. 2009a](#); [de Vries 2010](#)) and birth outcomes[19-21]([Donovan et al. 2012](#); [Dadvand et al. 2012a](#), [Dadvand et al. 2012b](#)). Some of the associations were shown to be modified by social economic status and level of urbanity, with greater benefits for populations with lower socioeconomic class[20,22]([Mitchell & Popham, 2008](#), [Dadvand et al. 2012a](#)) and those in more urban areas[6,22]([Maas et al. 2006](#); [Mitchell et al. 2007](#)). Furthermore gender has been shown to modify the relationship[11]([Richardson and Mitchell 2010b](#)).

Increased physical activity and social contacts, psychological restoration/stress reduction, and a reduction in pollutants such as noise and air pollution, and temperature have been proposed as possible mechanisms for the health benefits of green space. Access to and/or use of green space has been associated with higher levels of physical activity[23-33]([Cohen et al. 2006](#); [Cohen et al. 2007](#); [Coombes et al. 2010](#); [Lachowycz and Jones 2011](#); [Toftager et al. 2011](#); [Rodriguez et al. 2012](#); [Mytton et al. 2012](#); [Annerstedt et al. 2012](#); [Almanza et al. 2012](#); [Astell-Burt et al. 2013b](#); [Richardson et al. 2013](#)) and lower levels of obesity within communities[25,27,34-38]([Coombes et al. 2010](#); [Ellaway et al. 2005](#); [Wolch et al. 2011](#); [Toftager et al. 2011](#); [Pereira et al. 2013](#); [Astell-Burt et al. 2013c](#); [Lovasi et al 2013](#)). Studies even suggested that 'green exercise' can have even more positive mental health benefits than other kinds of exercise[39-42]([Bodin et al. 2003](#); [Pretty et al. 2005](#); [Bowler et al. 2010](#); [Thompson Coon et al. 2011](#)).

Psychological restoration[43-45]([Kaplan & Kaplan, 1989](#); [van den Berg et al. 2003](#); [van den Berg & Custers, 2011](#);) and reduced stress and anxiety[7,8,17,46,47]([Ulrich et al., 1991](#), [Grahn & Stigsdotter, 2003](#); [Hartig et al. 2003](#); [Maas et al. 2009](#); [Stigsdotter et al 2010](#)) have all been associated with access to and/or use of green and natural space.

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6 An inner city study in a deprived estate in Chicago showed the benefits of green space
7 both to cognitive restoration[48,49](Faber Taylor 2002; Kuo & Sullivan, 2001a), self-
8 discipline[48](Faber Taylor et al. 2002), reduced aggression[49](Kuo & Sullivan,
9 2001a) and reduced crime[50](Kuo & Sullivan, 2001b), with the latter also observed
10 elsewhere recently[51](Wolfe and Mennis 2013)
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15 Furthermore a few studies have suggested that green space is associated with more
16 social contacts and cohesion[16,17,52](Kuo et al. 1998; Kweon et al. 1998; Maas et al
17 2009).
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19 And finally reduction of personal exposure to air pollution has been observed in areas
20 with more green space[53](Dadvand et al. 2012e), while vegetation has been suggested
21 to reduce air pollution levels, and temperature[54-57](Baldauf et al. 2009; Su et al.
22 2011; Park et al. 2012a, 2012b), with some suggestion that the benefits are greater for
23 socially disadvantaged groups[55](Su et al. 2011). It has also been suggested that
24 vegetation (trees, plants) and soil may have an impact on the sound level[58-63](Aylor,
25 1972; Fan et al. 2010; Fang & Ling, 2003, 2005; Samara & Tsitsoni, 2007; Zhang &
26 Kang, 2007). Part of the appeal of green spaces may be related to pleasant acoustic
27 environments (Brown, 2006 in: Health Council of the Netherlands, 2006). This may
28 have its own, direct beneficial health effect (Health Council of the Netherlands, 2006).
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35 While this growing evidence exists that close contact with nature brings benefits to
36 human health and well-being, the proposed mechanisms are still not well understood
37 and the associations with health effects remain uncertain. Furthermore, it is unclear if
38 the possible mechanisms act in isolation or together, since with some exceptions[18](de
39 Vries et al. 2013) they have been studied in isolation. A coherent conceptual framework
40 on the proposed mechanisms is currently lacking. Also, most of the research has been
41 conducted in the North West of Europe and USA leaving questions about the
42 generalisability to other regions. Inconsistency and variation in indicators (eg type, size
43 and quality) for green space have often made it difficult to compare results from
44 different studies, and a better characterisation including that of quantity and quality of
45 green and blue spaces is needed, not only for research but also for policymakers and
46 spatial planners. Studies have often focused on access to green space without taking into
47 account actual use of green space. While blue space may also have a positive effect on
48 health, probably in combination with green space, there are only a few epidemiological
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6 studies investigating this [\[64-66\]](#) ([Völker and Kistemann 2011](#), [Völker and Kistemann](#)
7 [2013](#), [White et al. 2013](#))
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10 PHENOTYPE, a collaborative research project and explores the proposed underlying
11 mechanisms at work (stress reduction/restorative function, physical activity, social
12 interaction, exposure to environmental hazards). PHENOTYPE is the first study
13 designed to examine these mechanisms simultaneously in a large sample (N=4000
14 subjects) in various European countries using the same methodology. This allows the
15 study of specific factors while adjusting for others, and thereby strengthening the
16 interpretation of the results. It further examines both the long term and short term ~~health~~
17 ~~effects-associations with health~~ (eg general health and wellbeing, mental health/neural
18 development, stress, cardiovascular, cancer and respiratory mortality and morbidity,
19 birth outcomes and obesity) for different population groups (e.g. pregnant women
20 and/or foetus, different age groups, socioeconomic status, ethnic groups, and patients),
21 through analyses of existing cohort studies, observational studies and experiments.
22 Preventive as well as therapeutic effects of contact with the natural environment are
23 being evaluated. A coherent conceptual framework on the association between the
24 natural environment and its effects on health and well-being is being developed, and it
25 addresses implications for land-use planning and green space management.
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35 The study includes both rural and urban settings, but the main focus is on the urban
36 environment, for a number of reasons. Most of the population lives in urban areas
37 (75%) in Europe, making these of greater relevance to public health, and rapid
38 urbanization continues to reduce accessible natural environments for urban residents.
39 Most people make more frequent use of the green spaces in their nearby living
40 environment instead of travelling greater distances to rural areas, in particular people
41 with lower socio-economic status, elderly people and children [\[67,68\]](#) ([Schwanen et al.](#)
42 [2002](#); [Maas 2008](#)). Furthermore, rural dwellers tend to have constant contact with the
43 natural environment and it may therefore also be more difficult to assess its effects.
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50 Lastly, the project uses an interdisciplinary and integrated approach, applying the best
51 and most efficient methods to understand the relation between exposure to the natural
52 environment and health. It implements conventional and ~~new~~ innovative high tech
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6 methods to characterize the natural environment in terms of quality and quantity. This
7 paper provides a general overview of the research methodology of PHENOTYPE.
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10 11 12 **Methods and results** 13

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15 Figure 1 summarizes the different parts of the study and the interdependencies between
16 the different parts, namely the characterisation of the natural environment and the way it
17 is used, examination of the underlying mechanisms in daily life settings, short and long
18 term effects of the natural environment, and the implications for management and
19 policy of the natural environment (see overview Figures 1 and web figure 1). In this
20 section we will elaborate on each of these parts. A summary of the mechanisms,
21 outcomes, populations and areas selected for investigation are given in Table 1.
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28 *Characterising the natural environment and the way it is used.* 29

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31 The research includes evaluation of the natural environment, which includes for the
32 purposes of the project:

- 33 - Green spaces (e.g. roof gardens, city parks, court yards) and “greenery”; forests, nature
34 reserves/parks, mountains, farmland, trees, landscaping
- 35 - Blue spaces; water such as canals, ponds, creeks, rivers, beaches etc.

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37 Although many of these may actually not be “natural” since they have been man-made,
38 for the purpose of the project we classify them as such.
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43 One of the main aims of PHENOTYPE is to examine the importance of both
44 quantitative (e.g. amount, type, access, use) and qualitative characteristics (e.g. acoustic
45 quality, identity, variety, safety, rubbish) of the natural environment by collecting
46 detailed data on these characteristics using a combination of methods. The focus lies on
47 natural environments at different scales and distances from the home (city/town,
48 neighbourhood, street level) and where possible also at other places where people stay
49 (work, school, on their way to home/school, recreational). In addition, actual use of the
50 natural environment is taken into consideration. To achieve the aim, a detailed
51 assessment will be conducted in 4 case cities (Barcelona, Spain; Doetinchem, the
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6 Netherlands; Kaunas, Lithuania; and Stoke-on-Trent, United Kingdom), with less
7 detailed assessment in other study areas.
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10 PHENOTYPE uses conventional land use maps, remote sensing data from satellites and
11 aerial photography, complemented by detailed discussions with volunteers and other
12 stakeholder living and working in the studied areas to derive comparable classifications
13 of the natural environment in different countries. Collected data will contribute to the
14 characterisation of the natural environment (both quantitative and qualitative e.g.
15 accessibility, acoustical quality, recreational activities, walkability etc). For the
16 quantitative characterisation, PHENOTYPE makes use of available land use maps such
17 as COordination and INformation on the Environmental programme, initiated by the
18 European Commission (CORINE)[69](EAA-2005) and Urban Atlas[70](EAA-2010),
19 and remote sensing and aerial photography to obtain comparable indices such as
20 NDVI[71](Weier and Herring, 2011) of the natural outdoor environment in different
21 countries. Landsat Enhanced Thematic Mapper Plus (ETM+) data are applied to a
22 classification and regression tree (CART) model to categorise land cover types for the
23 urban areas of interest[55](Su et al 2010). Early application of the NDVI in Barcelona,
24 Spain showed good results[20] (Web Figure 2), Dadvand et al. 2012a)

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34 To collect additional qualitative information on the natural environment and on other
35 physical and social features, systematic observations (audits) are conducted by trained
36 researchers in selected neighbourhoods in the 4 -case cities using the same methods.

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38 Since it is not feasible and not necessary to audit every street in a selected
39 neighbourhood, a purposeful sample of streets is drawn, ensuring that important
40 neighbourhood features are included. The selected neighbourhoods are divided into
41 more or less homogeneous sub-areas by means of data/maps on land use/function of
42 areas in combination with local knowledge of the area. Subsequently, trained auditors
43 are asked to visit the sub-areas and observe them in a systematic way (auditing) using a
44 paper form containing several close-ended questions. Every sub-area is visited by two
45 auditors. For the first 1-2 areas, the auditors fill in the list together, discussing
46 completion to reach consensus. In subsequent areas, where possible, the two auditors
47 complete the audit independently and simultaneously. Furthermore, up to two natural
48 environments of more than one hectare in size are selected per neighbourhood using
49 GIS. Again following training in completion of the audit, two auditors visit the
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6 environments. For the first five areas, auditors undertake the interview together,
7 discussing completion to reach consensus, thus maximizing consistency. In subsequent
8 areas, where possible, two assessors complete the audit independently and
9 simultaneously. In the absence of existing measures that could meet our requirements,
10 the streetscape audit was developed for this project and the natural environment tool
11 was adapted from an existing measures. This kind of bespoke tool development is seen
12 in similar studies e.g.[72] (e.g., Van Dillen et al. 2012.). One form is used for evaluating
13 the streetscape, using indicators derived from the Street Typology developed by
14 Leijdelmeijer et al. (2002)[73], a list of evaluating the quality of green by Van Dillen
15 (2012)[72] and the audit tool developed by Van Lenthe et al. (2006)[74]. The natural
16 environment audit is adapted from that developed by Gidlow et al (2012)[75] through
17 addition of items and domains to reflect the greater diversity in natural environments to
18 be included (i.e., different types of natural environment across four European cities).
19 The tools were piloted and adjusted prior to use. They have not been ‘validated’, but
20 there is no gold standard quality measure for natural environments against which to
21 compare. Inter-rater reliability will be estimated through derivation of Inter-rater
22 Correlation Coefficients (ICC) and PCA will be used to ensure that any redundant items
23 are removed and included items are grouped sensibly into domains, before overall
24 quality scores will be derived.

25 The researchers walk through the neighbourhood, systematically coding characteristics
26 such as the architectural character, maintenance of the landscape, and perceptions on
27 how a place looks and feels. To collect comparable information in the 4 case cities, two
28 standardized forms are used. One form is used for evaluating the streetscape, using
29 indicators derived from the Street Typology developed by Leijdelmeijer et al. (2002), a
30 list of evaluating the quality of green by Van Dillen (2012) and the audit tool developed
31 by Van Lenthe et al. (2006). A second form is used for evaluating the natural spaces in
32 the study areas of at least 1 ha. It is an adapted form of the Neighbourhood Green Space
33 Tool developed by Gidlow et al. (2012).

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49 To gain insight into the way people use the natural environment, a face to face
50 questionnaire survey is conducted to collect data on 1000 people in the 30 selected
51 neighbourhoods in each of the 4 case cities, and an in-depth study using “Calfit”, a
52 smartphone-based monitor of time-location patterns and momentary states, on a
53 subsample (n=100) of the participants of the questionnaire survey (for further detailed
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6 information, see next section on underlying mechanisms). The Calfit software^[76,77]
7 (Donaire-Gonzales et al. 2013, de Nazelle et al. 2013) runs on a Google Android
8 operating system and as currently configured can collect data on physical activity using
9 the motion sensor and geographic location through a global positioning system (GPS), to
10 obtain information on minutes spent and physical activity levels in different natural
11 environments (Web Figure 3). The instrument has been validated against the Actigraph
12 accelerometer^[76] (Donaire-Gonzales et al. 2013), combined with other pollution
13 measurements to assess likely inhalation^[77] (de Nazelle et al. 2013), and lab-validated
14 using the Cosmed metabolic monitoring system.
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21 The work will produce different indicators of natural space that can be used in the
22 studies described below. The aim is to make a hierarchy of indicators with on the
23 bottom simple measures such as NDVI that can be easily obtained for all the study areas
24 and on the top detailed measures of for example green space with actually information
25 on the quantity, quality and use that can only be obtained for only some areas after in-
26 depth study. –As part of the work, we will examine the relationship between the simple
27 and detailed measures to better understand how detailed information on small scale can
28 help the interpretation of health studies conducted in larger areas with only simple
29 measures available using existing epidemiological studies and registries (see below).
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35 *Examining the underlying mechanism in the daily life setting*

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39 New data will be collected to explore in detail and simultaneously the proposed
40 mechanisms (physical activity, social contacts/cohesion, psychological restoration/stress
41 reduction) underlying the relationship between the natural environment and health and
42 well-being, in the four case cities. In each of these cities ~~30~~ neighbourhoods varying in
43 socio-economic status and in their distance to green space are selected. In these
44 neighbourhoods the natural environment will be characterised, and (as mentioned above
45 already) a selection of 1000 randomly selected residents (4000 in total, 18-75 years)
46 will participate in a questionnaire survey, 100 in a smartphone study, and 20 in in-depth
47 interviews (Web Figure 4).
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53 To optimally investigate what types of natural environments and different levels of
54 accessibility are relevant in relation with the mechanisms that we investigate (physical
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6 activity, stress and restoration, social interactions and environmental pollution), and to
7 investigate potential differences in this mechanism among the population, we use a
8 multiple level approach and select neighbourhoods with different socio-economic status
9 (SES) and access to the natural environment. We use existing statistical or
10 administrative units with Existing statistical or administrative units that were as similar
11 as possible with regard to variation in population size; in Stoke-on-Trent Lower Layer
12 Super Output Areas (LSOAs), in Barcelona census areas, in Kaunas voting districts and
13 in Doetinchem neighborhoods. Natural space and SES measures are assigned to all the
14 units, using existing data. For natural space, Urban Atlas is used for Stoke-on-Trent,
15 Barcelona and Kaunas. Since Urban Atlas is not available for Doetinchem, data of
16 another Dutch database ('Top10 nl') is used. For SES no comparable data existed for
17 the 4 cities. Therefore partners use their own local data. Then the units are ranked by
18 each natural space and SES. Subsequently a selection of two neighbourhoods from each
19 combination of top, middle and bottom tertiles of SES and quintiles of the natural space
20 is made (approx. 2*3*5= 30 units). A few extra units are added to optimize contrast
21 and reach a sufficient number units to be able to recruit a 1000 subjects in each city (30
22 subjects per units). Since there is no common person registries in these countries,
23 subjects (aged between 18 and 75) are selected using different approaches. In
24 Doetinchem and Stoke-on-Trent, addresses are sampled randomly from the BAG
25 Registry ('Buildings and Adresses') 2012 and a local address registry respectively and
26 the person with the closest birthday to the interview data is selected at each address, in
27 Barcelona subjects are randomly selected from the person registry (empadronamiento)
28 and in Kaunas subjects are sampled randomly from a 2006-2009 survey of randomly
29 sampled people of the city of Kaunas. In each case there is an over selection of
30 potential addresses or subjects to be able to interview at least a 1000 subjects (and 30
31 per unit) in each city. The target of a 1000 subjects per city was based on the available
32 budget. To enable multi-level analysis, we estimated that a minimum of 30 participants
33 per group (or neighbourhood) were required, with a minimum of 30 groups.
34 The choice of items was based on the proposed mechanisms and was achieved via an
35 interactive process of experts within the PHENOTYPE team and others in the
36 institutions involved. As much as possible questions were derived from existing and
37 validated indices. The questionnaire was piloted by the four centers separately with
38 specific attention for comprehensibility, clarity and duration and was adapted based on
39 these pilots. The questionnaire is structured along several main clusters of questions: i)
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6 residential situation: ii) dwelling iii) wellbeing and health, and iv) personal
7 characteristics. It includes questions on perceived quality and use of green and blue
8 space in the residential area and in the immediate living environment, perceived
9 environmental and social quality including aspects as noise, amenities and social
10 cohesion, lifestyle, subjective health and questions related to personal background. The
11 questionnaire was developed in English and translated and back translated in Dutch,
12 Spanish and Lithuanian. More details on the frameworks and questionnaire will be
13 described in a forthcoming paper by Van Kamp et al. (In prep). Also we will assessment
14 cognitive fatigue in each subject as measured by CTT.

15
16 The questionnaire survey was designed to investigate three potential mechanisms in
17 relation to natural environments and health: via physical activity, stress and restoration
18 and social interactions as described in. In addition questions are included about
19 environmental worries and reactions to perceived exposures (air pollution, noise, etc).
20 The choice of indicators was based on these three mechanisms and was achieved via an
21 interactive process of experts within the PHENOTYPE team. As much as possible
22 questions were derived from existing and validated indices, some tailored to the specific
23 objectives of PHENOTYPE. The questionnaire was developed in English and was
24 translated (and back translated?) into Dutch, Spanish, Catalan, and Lithuanian. The
25 questionnaire was developed to be applied in an oral interview of at maximum 60
26 minutes. In Kaunas it is not common to have face-to-face interviews; therefore a written
27 questionnaire is sent by post to the selected people. The questionnaire was piloted by all
28 partners, with specific attention for comprehensibility, clarity and duration and was
29 adapted at some points based on outcomes of these pilots.

30
31 The final questionnaire is structured along four main clusters of questions: I. Green and
32 Blue Spaces; II Residential situation: Dwelling & Neighbourhood; III Wellbeing and
33 Health; IV Personal characteristics. Per mechanism questions are asked about
34 availability, use, importance, and satisfaction. In the sequencing of the questions we
35 strive for a coherent set of questions per cluster moving from general to specific and
36 from “easy” to more intruding questions. Furthermore, most of the answer categories
37 moved from neutral negative towards positive items.

38
39 For all answers showcards have been developed by RIVM, to make it easier for both
40 interviewers and respondents, and to speed up the interview process. A separate
41 instruction document was developed to train the interviewers. The questionnaire ended
42 with an optional a pencil paper attention test (Color Trails Test (CTT-A)) add ref.
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8 Finally for the smartphone study at least 100 volunteers from each country are randomly
9 selected from the participants of the questionnaire survey who indicated that they were
10 willing to participate in the smartphone study. For these subjects,

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11 ~~From the 1,000 volunteers in each of the 4 case cities who complete the questionnaire,~~
12 ~~100 people are approached to take part in a smartphone study (100 in total).~~ During 7
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subsequential days the emotional state of the subject, the local environment (e.g.,
different quantities or qualities of natural space) and the social setting are assessed with
the smartphone and the innovative Calfit technology. Besides objective geolocation and
physical activity (see section [Characterisation the natural environment](#)), subjective data
on stress reduction/restoration and social contacts are collected simultaneously. The
latter data are collected through interactive diaries capable of eliciting ecological
momentary assessment (EMA). EMA is a novel approach to elicit responses to
electronic surveys throughout the course of daily life^[78] (Shiffman et al. 2008). The
participant receives prompts at random intervals to complete small surveys on the
phone, which then have time and location stamp.

From the people who participate in both the questionnaire survey and the CALFIT study
and who indicate they wanted to volunteer, 80 people (20 in each case city) are
approached for semi structured interviews. These interviews are conducted to gain more
detailed information on specific topics included in the questionnaire survey and
CALFIT/EMA. Topics addressed include the motivation for travel routes, the **effect**
associations of natural environment ~~on-with~~ mood, behaviour and well-being, the
attitude towards and importance of (experiences with) natural environment, and reasons
for using or not using the natural environment.

Epidemiological studies to examine long term effects of the natural environment

By using existing epidemiological studies and registries and linking these to the natural
space indicators described earlier, the association between natural environment and a
range of different long term health **effects-outcomes** will be examined in an efficient and
cost effective manner. PHENOTYPE makes use of 16 existing cohorts and registries
with good health outcome data in Spain, the Netherland, Lithuania, and United
Kingdom (Web Table 1), linking these to newly created natural environment indicators.

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6 Comparable estimates are produced for various regions in Europe for the ~~effects~~
7 ~~on~~associations with pregnancy outcomes, foetus development, children's health and
8 adult population morbidity and mortality. We specifically focus on:
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- 10 • the natural outdoor environment and ethnicity, socio-economic status, women's
11 health and pregnancy outcomes;
- 12 • the natural outdoor environment and foetus development, birth weight, and
13 gestational age;
- 14 • the natural outdoor environment and general development, neurodevelopment,
15 cognitive function and respiratory health in children;
- 16 • the natural outdoor environment and respiratory health in various European cities;
- 17 • the natural outdoor environment and general health, physical activity, specific
18 morbidity and mortality.

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26 The assessment of natural environment indicators will be mainly based on satellite data
27 and land use maps as CORINE and Urban atlas, and sometimes local data. This will
28 restrict to some extent the evaluation of the ~~effect of~~association with the natural
29 environment, but this is the only realistic and achievable approach. All studies
30 examine the role of socio-economic status, which has been suggested as an effect
31 modifier for the relationship between exposure to the natural environment and health
32 benefits. The European Community Respiratory Health study (ECRHS)[\[79\]](#) ([Burney et](#)
33 [al-1994](#)) further allows for examination of exposure to the natural outdoor environment
34 and ~~health effects~~associations with health in a range of different European cities. Some
35 cohorts such as the Born in Bradford study[\[80\]](#) ([Wright et al. 2012](#)) offers a unique
36 opportunity to investigate the role of ethnicity in the relationship between exposure to
37 the natural outdoor environment and health benefits, in Bradford study half of the
38 participants are from Pakistani background, with information on both the mother and
39 baby from pregnancy to early years in life.
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46 47 ***Experiments to examine short term effects of the natural environment***

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50 To examine short term effects of the natural environment on health and well-being, one
51 or more experimental studies are conducted in each country in which individuals are
52 exposed to different types of natural and urban environments (i.e., environmental
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6 conditions). The majority of data collection is field-based to maximise the ecological (as
7 well as internal) validity of any observed effects.
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9 Using a range of psychological and physiological indicators relevant to the various
10 possible mechanisms, and 2) healthy and patient population groups (with mental and/or
11 somatic morbidities) we will collectively explore:~~Using a range of psychological and~~
12 ~~physiological indicators relevant to the various possible mechanisms, and inclusion of~~
13 ~~healthy and patient population groups (with mental and physical morbidities)~~
14 ~~collectively explore:~~
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18 - preventive and therapeutic effects of natural environments.
19 - immediate and sustained changes in affective, cognitive and physiological
20 responses indicative of well-being while engaged in a natural environment, and
21 after leaving a natural environment
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23 - neurobiological responses to viewing natural or urban scenes before/after
24 experiencing stress.
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28 Through variation in experimental design, each partner makes a novel contribution(s) to
29 the area as (details in Web Table 2):
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- 31 • UK: In healthy individuals, Study 1 compares immediate and post-exposure psycho-
32 physiological effects of urban versus natural environments to explore whether any
33 beneficial effects are sustained following single exposures; Study 2 uses longer-term
34 follow-up and repeated exposure to natural environments to explore whether any
35 effects are accumulated, sustained or attenuated.
36
37 • Netherlands: an experimental functional Magnetic Resonance Imaging (fMRI) study
38 is conducted in healthy individuals to investigate neurobiological responses to
39 viewing natural or urban scenes before/after experiencing stress; i.e., whether
40 viewing natural compared to urban scenery can prevent or buffer against stress
41 responses, and how this is represented in brain activation patterns.
42
43 • Spain: in individuals with elevated stress levels, group-based exposure and
44 Ecological Momentary Assessment (EMA, using CALFIT technology) are used to
45 explore the role of social interaction and the nature of physical activity, in
46 immediate and longer term responses. Ecological validity will be enhanced through
47 'free-living' activities within environments, rather than controlling activities, again,
48 using EMA, GPS and accelerometry to monitor the nature (and perceptions) of this
49 activity.
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- Lithuania: a clinical population with established coronary artery disease (CAD) are recruited to evaluate the therapeutic effect of the natural environment. The outcomes of this experiment may have direct clinical applications for the use of urban and different types of natural environment in cardiac rehabilitation.

Implications, policy and guidelines and involvement of stakeholders

Guidelines

PHENOTYPE will provide recommendations for policymakers and guidelines for professional practitioners involved with spatial planning and health to create natural environments that promote health and well being. For this, we focus on a human ecological perspective which allows for a better integration of human health needs into land use planning and green space management in both rural and urban areas^[81] (Lawrence 2004). Currently legal standards that have been developed with economic, technological and political priorities in mind, are leading in urban design, whereas the lifestyle, sense of community, identity, and health and well being of local populations have been largely undervalued. The guidelines will reflect the importance to consider environmental, social, economic and other components of the natural and built environments in ways that also take into account and result from the point of view of citizens. PHENOTYPE will complement the common quantitative approach by valorising the social/human functions of these environments, especially their contribution to promoting health and quality of life.

Following this broad and innovative approach, PHENOTYPE will formulate, test and validate a set of recommendations and guidelines concerning the desired characteristics of different types of natural environments in urban and rural areas, specifically their characteristic features, accessibility to them for different population groups, as well as their facilities, maintenance and services. By doing so, the work will overcome the existing applicability gap between information and knowledge accumulated by much research and policy definition and implementation.

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6 The guidelines for professional practitioners involved with spatial planning and health
7 will consider three core topics in relation to each of the natural environment being
8 considered:
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- 10 1. Qualitative characteristics of natural environments; recommendations concerning
11 surface area, vegetation, water sources, ambient noise levels, views and
12 microclimate;
- 13 2. Facilities, Maintenance and Services; recommendations about the kinds of
14 communal facilities and services provided in each type of natural environment, as
15 well as suggested levels of maintenance;
- 16 3. Accessibility Guidelines to Natural Environments; including requirements about
17 access to different types of natural environments such as allotments,
18 neighbourhood parks, children's playgrounds and nature reserves.

19 The baseline for the work is firstly the compilation and analysis of currently available
20 information from existing databases and literature, and later new data collected by the
21 project as described above. This will be complemented by the engagement with the
22 appropriate stakeholders to assess scope for development. These insights will be
23 combined into a conceptual framework on the underlying mechanisms of the effects of
24 the natural environment on health and well-being.
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34 *Stakeholders and dissemination*

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37 The participation provides a forum for project assurance and benefits for PHENOTYPE
38 are summarised as follows:
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- 40 - A more robust evidence base on links between exposure to natural outdoor
41 environment and human health/well-being for various regions in Europe. Hereby
42 we expect to develop a better understanding of the potential mechanisms.
- 43 - A better integration of human needs into land use planning and green space
44 management in rural as well as urban areas. Furthermore, the application of
45 these needs in practical guidelines.
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51 Stakeholder involvement is critical for bringing outside (policy) ideas into the research
52 planning, to increase the usefulness of the research, and to assure a better
53 implementation of the results of the project (Web Figure 5). In a research project, this is
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6 often limited because the lack of interest of stakeholders and the limited resources and
7 efforts of consortia.
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10 From the start of PHENOTYPE actively sought to establish and maintain relations and
11 dialogues with and between key stakeholders from local, regional and national health
12 and environment authorities, institutions and the international research community.

13 These include policy makers, architects, urban planners, natural space managers, health
14 professionals, and the international research community. This group is highly diverse,
15 as we are looking at a range of professions within the subject areas of environment and
16 health, from volunteers to scientists, community workers and policy developers.

17 PHENOTYPE has thus far been successful in its engagement activities, providing
18 continuous opportunities for information exchange and collaborations. These contribute
19 to strengthening networking between researchers, policy-makers and stakeholders in
20 order to facilitate the transfer of scientific knowledge to policy development, to
21 exchange ideas about best practice and to help identify emerging issues on the natural
22 outdoor environment and its mechanisms to improve health.
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25 The PHENOTYPE website www.phenotype.eu provides an overview of the project,
26 progress, actualities, surveys and publications. The site has a sign up form for periodic
27 newsletters through which all stakeholders are regularly informed. It guarantees
28 continuous visibility, and provides a means for interested parties to respond to activities,
29 or to contact us with invitations to attend workshops, etc. PHENOTYPE is also found
30 on social media twitter (@greenhealth4eu) and LinkedIn. The PHENOTYPE databases
31 and overall results will be exploitable by policy makers at national and international
32 level in areas including urban planning and health.
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43 44 45 **Conclusion**

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48 The PHENOTYPE project is an FP7 collaborative action, funded by the EC to explore
49 the mechanisms underlying positive short term and long term health effects for different
50 population groups. PHENOTYPE applies conventional and new innovative high tech
51 methods to characterize the natural environment in terms of quality and quantity.
52 Preventive as well as therapeutic effects of contact with the natural environment will be
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6 covered. The proposed work aims to address the limitations of some of the studies that
7 have been published so far (Table 2). Furthermore it addresses implications for land-
8 use planning and green space management. The project will produce a more robust
9 evidence base on links between exposure to natural outdoor environment and human
10 health and well-being. This in turn will contribute to improved integration of human
11 health needs into land use planning and green space management in rural and urban
12 areas.
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Author statement

Mark J Nieuwenhuijsen, Hanneke Kruize, Christopher Gidlow, Michael Jerrett, Jolanda Maas, Edmund Seto, Peter Jan van den Hazel, Roderick Lawrence, and Regina Grazuleviciene and wrote the original grant proposal on which the study design and paper is based. Mark J Nieuwenhuijsen drafted the version of the paper and received input from all the authors. All authors read and commented on the paper and agree with the final version.

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[ENV.2011.1.2.3-2] Positive effects of natural environment for human health and well-being] Duration 1 Jan 2012-31 Dec 2015

Ethics approval was obtained for all aspects of the study by the local ethics committees in the countries where the work was conducted, and sent to the European Commission before advancement of the study.

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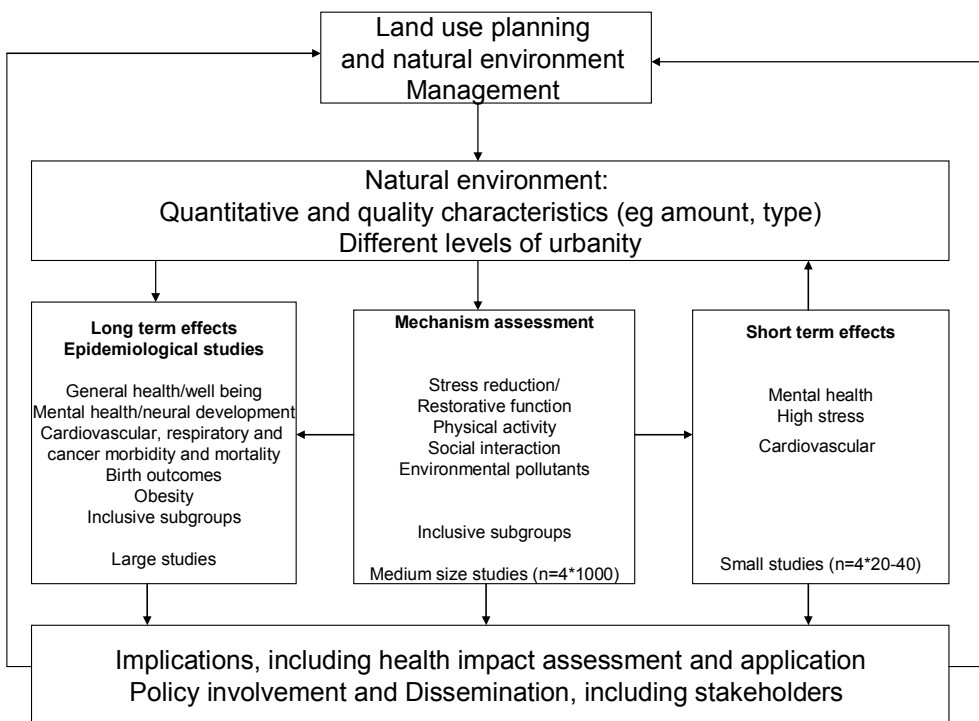


Figure 1: Interdependencies of different parts of the PHENOTYPE project

Table 1 PHENOTYPE study mechanisms, outcomes, populations and regions

It will explore underlying mechanisms related to:

- stress reduction/restorative function
 - physical activity
 - social interaction/social cohesion
- exposure to environmental hazards (e.g. noise/acoustic quality, air pollution)

Both preventative and therapeutic effects (patients) will be considered. Outcomes of interest that are evaluated are:

- general health and well-being (including medically unexplained symptoms (MUPS))
- mental health/neural development
- stress
- cardiovascular, cancer and respiratory mortality and morbidity
- birth outcomes
- obesity

It will examine the effects for different population groups, including more vulnerable populations:

- pregnant women and/or foetus
- age groups (children, elderly)
- (lower) socio-economic status
- ethnic minorities
- patients/people with specific health complaints

It will conduct comparative studies in different regions of Europe to examine any underlying regional, social and/or cultural differences related to the meanings, uses, mechanisms and health effects of the natural environment and we will include the:

- North west (Netherlands, England)
- South (Spain)
- East (Lithuania)

Table 2 Limitations of current green space work and work undertaken by PHENOTYPE to address these

| Limitations of current available work | What PHENOTYPE will do |
|--|--|
| <ul style="list-style-type: none"> ▪ Inconsistency and variation in indicators for green or natural space have often made it difficult to compare results from different studies. | <ul style="list-style-type: none"> ▪ Minimize the potential differences due to classification of natural space, by combining the use of conventional maps and data sources with remote sensing data and aerial photography, gather individual-level data through detailed discussions with subjects living in the areas, and use considerable stakeholder engagement to develop comparable classifications of the natural environment in different countries. ▪ Produce a more robust and comparable evidence base on links between exposure to natural outdoor environment and human health and well-being. |
| <ul style="list-style-type: none"> ▪ A number of disease outcomes have been studied, but besides the routinely collected data (which use ICD coding), not always in a standardized and comparable manner in different countries | <ul style="list-style-type: none"> ▪ Produce a more robust and comparable evidence base on links between exposure to natural outdoor environment and human health and well-being, using well studied and new outcomes with standardization between countries. |
| <ul style="list-style-type: none"> ▪ Potentially very sensitive groups such as pregnant women/fetus have not been studied at all. | <ul style="list-style-type: none"> ▪ Extend the evidence base to new outcomes and vulnerable populations e.g. pregnant women and their foetus, chronic respiratory and cardiovascular patients, ethnic minorities and |

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| | low social economic class. |
| <ul style="list-style-type: none"> Most studies focused on green space; the evidence base for the effects of blue space is very limited. | <ul style="list-style-type: none"> Not only examine the effects of green space, but also of blue space. |
| <ul style="list-style-type: none"> Most of the green space studies have been conducted in the US or the North West of Europe. | <ul style="list-style-type: none"> Conduct comparable studies across Europe and produce evidence for North Western, Eastern and Southern Europe. This will deliver insights into regional, social and/or cultural differences in relation to natural space. |
| <ul style="list-style-type: none"> Most studies do not include actual use of the natural environment. | <ul style="list-style-type: none"> Consider actual use of the natural environment, an often neglected but fundamental indicator in relation to exposure to natural environments. |
| <ul style="list-style-type: none"> There appeared to be differences by social group, with some apparently benefiting more than others from natural space, but the evidence is sparse. | <ul style="list-style-type: none"> Produce a more robust and comparable evidence base on links between exposure to natural outdoor environment and human health and well-being, with special attention for effect modification by social groups |
| <ul style="list-style-type: none"> A number of potential mechanisms have been suggested, including increased physical activity and social contacts for those living near natural space, natural environments exerting | <ul style="list-style-type: none"> Examine the proposed mechanisms (physical activity, stress, social contacts, and environmental risk factors) simultaneously in a large sample in various countries (WP2). This will enable |

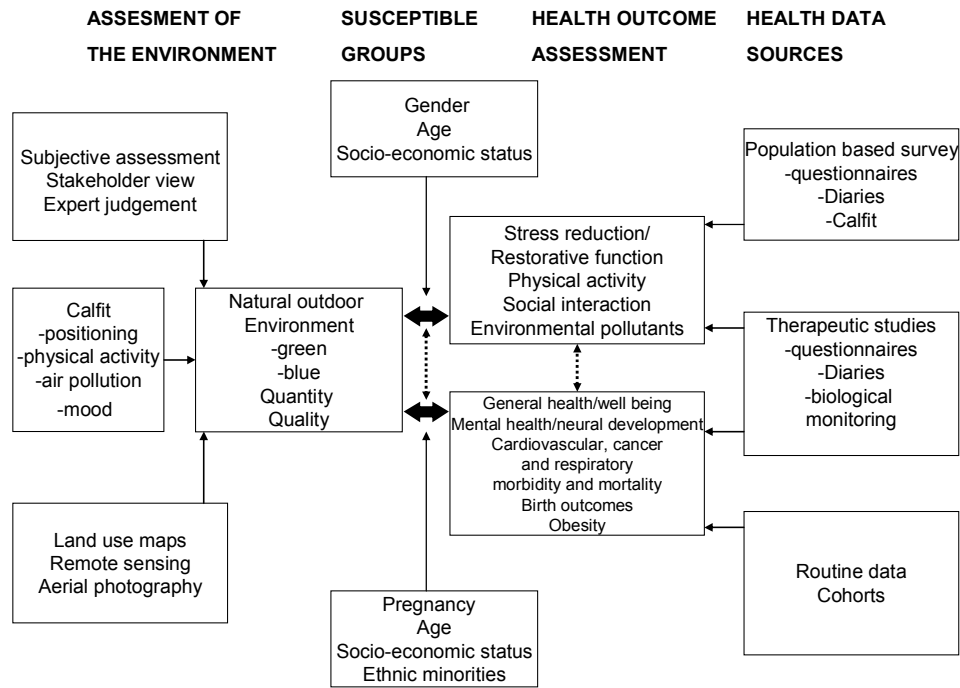
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| <p>stress lowering or attention restoring effects, and reducing environmental hazards (e.g. air pollution, high temperatures). However, the studies of potential mechanisms have often been limited to assessing one mechanism at the time, which increases the likelihood of unmeasured confounding effects and misses the opportunity to study these potentially interrelated mechanisms in coherence-</p> <ul style="list-style-type: none"> ▪ to study the mechanisms in coherence even though they may be interrelated | <p>us to study specific factors while adjusting for others, and thereby strengthening the interpretation of the results</p> |
| <ul style="list-style-type: none"> ▪ Unable to answer what specific quantitative and qualitative characteristics of the natural environment have a positive effect on health and well-being, through what pathways is still largely unknown. | <ul style="list-style-type: none"> ▪ Make classifications for the type and level of the indicators, which is important for policy makers. ▪ Examine the importance of both quantitative (amount, type, access, use) and qualitative characteristics (acoustic quality, identity, variety, safety) of the natural environment |
| <ul style="list-style-type: none"> ▪ Limited research exploring the sustained affective, cognitive and physiological responses to a single exposure and the effects of a repeated exposure to the same natural environment ▪ Unable to explain how policymakers and planners can design a natural environment to maximise health benefits | <ul style="list-style-type: none"> ▪ Explore longer-term changes in affect, cognitive function and physiological indicators that have to date only been studied during, or immediately after, engagement with the natural environment. ▪ Explore the immediate, maintained and long-term effects of repeated engagement with the same natural environment on |

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| | affect, cognitive function, and physiological indicators of well-being . |
| <ul style="list-style-type: none"> ▪ Guidelines of lifestyle, health and well being have largely undervalued local populations | <ul style="list-style-type: none"> ▪ Include lifestyle, health and well being factors of the local populations. |

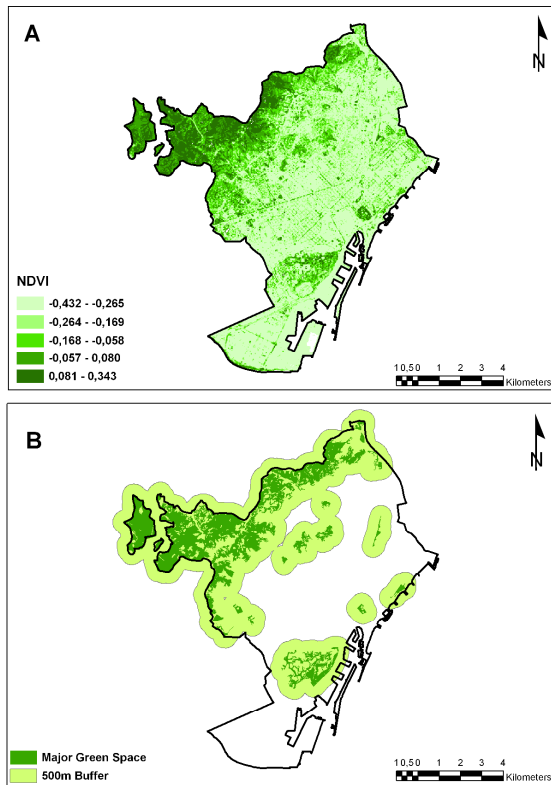
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Annex-websfigures

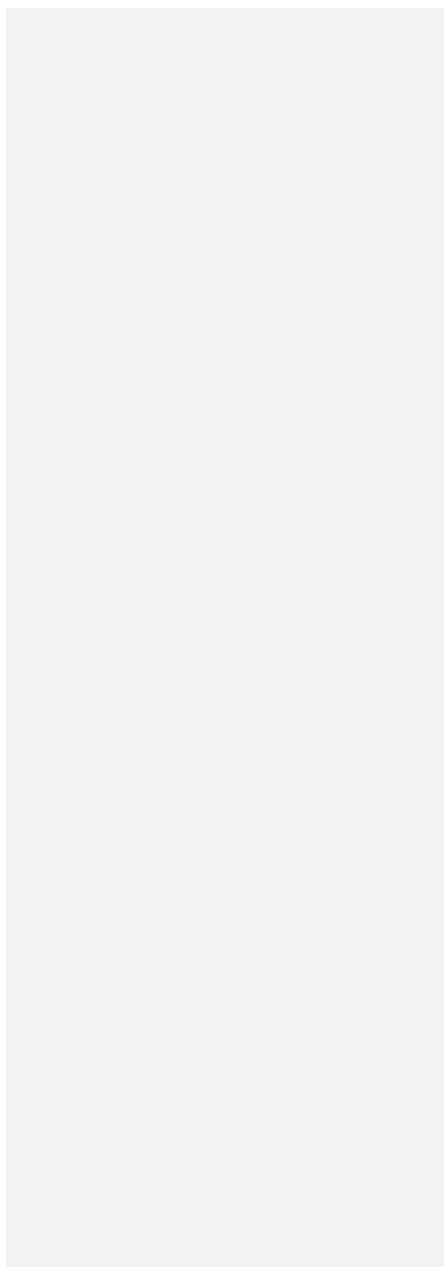


Web Figure 1 Natural outdoor environment, mechanisms and health data input in PHENOTYPE

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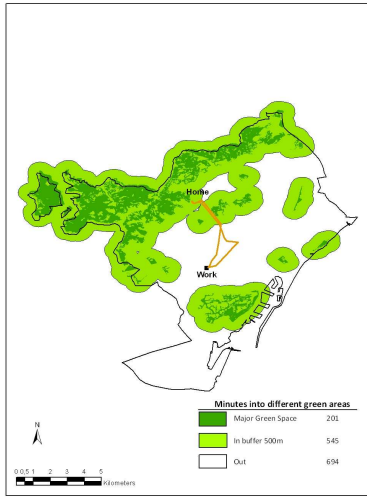


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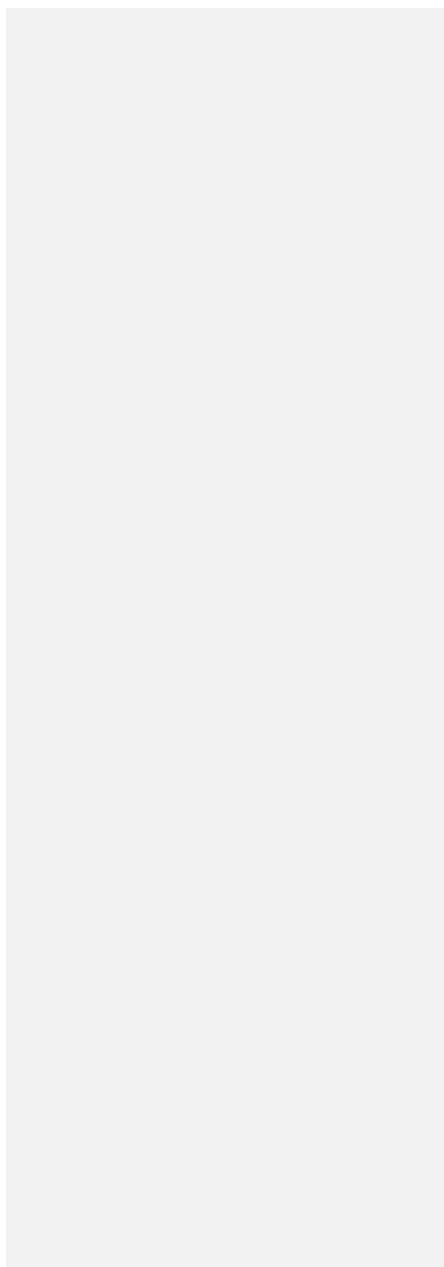


Web Figure 2 NDVI map of Barcelona and buffers around major green space areas

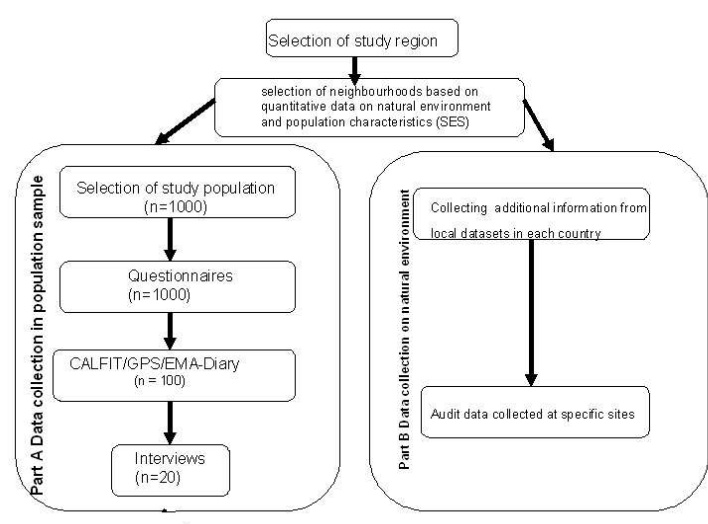
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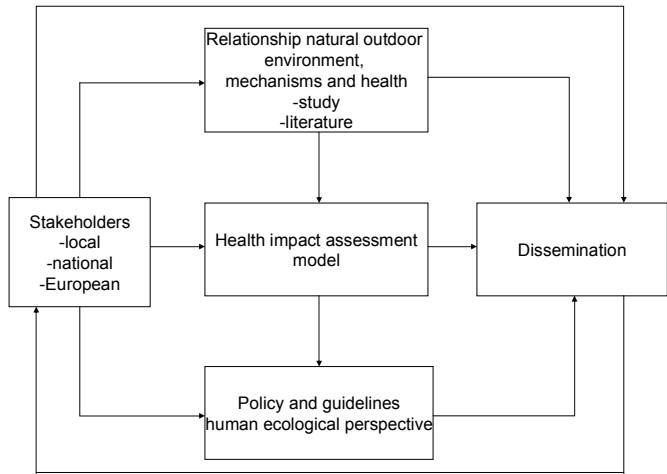
Web Figure 3 Mobility pattern for a subject in Barcelona obtained with the Calfit tool



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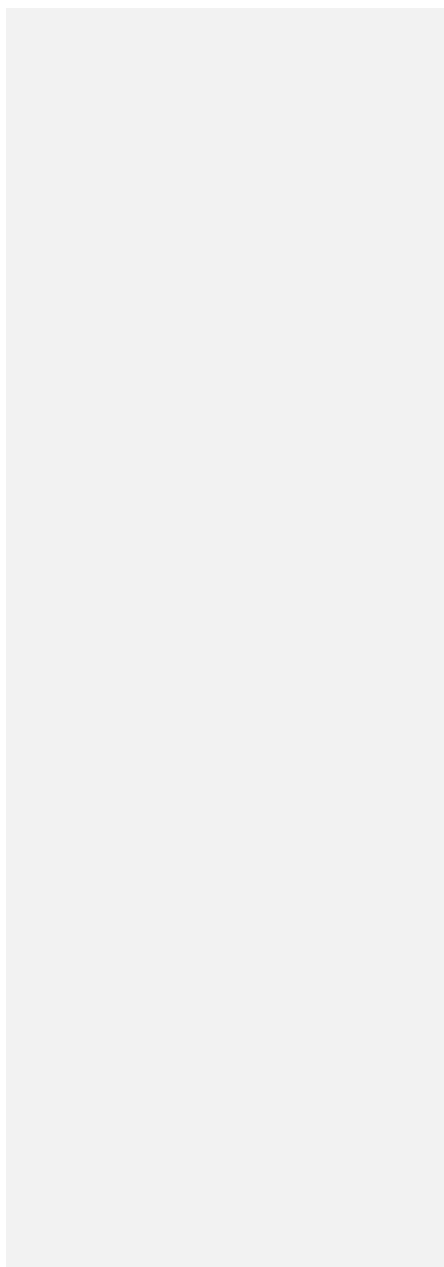
Web Figure 4 Design of data collection in 4 European case cities to study the underlying mechanism

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Web Figure 5 Stakeholder input and dissemination

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Web Table 1 Currently available databases and cohorts for inclusion in PHENOTYPE

| Study | n | Population | Collected outcomes | Relevant covariate and mechanism data |
|-------------|------|--|---|--|
| CREAL Spain | | | | |
| PISCINA | 3000 | Children 6-9, 2006, Sabadell, Catalonia | Respiratory health BMI | Social economic status Physical activity Air pollution |
| INMA | 3000 | Children, 2-10, ongoing around Spain | Birth weight and gestation, respiratory health, neural development | Social economic status Physical activity Stress Air pollution |
| PAC-COPD | 342 | Patients with chronic obstructive pulmonary disease (PAC-CODP) | Hospital admissions All cause and specific mortality Functional data (lung function, cardiovascular function) Symptoms and co-morbidities Quality of life Mental status Body weight and composition | Social economic status Physical activity Air pollution |

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| ECRHS | 8500 | Adult population in many cities around Europe | Respiratory health Short form SF36 | Social economic status Physical activity Air pollution |
| Routine data Catalonia | Pop 7M 0.5 million deaths | All, 1999-2006, Catalonia | All cause and specific mortality | Social economic status |
| Hospital clinic database | 16000 | Births, 2000-2005 Barcelona | Birth weight and gestation | Social economic status Air pollution |
| Netherlands | | | | |
| Cohort of Dutch inhabitants Netherlands | Pop 16M | All, 2000-2008 | All cause and specific mortality and morbidity | Social economic status |
| Doetinchem cohort | Approximately 5000 over a period of 5 years | See: Verschuren WMM, Blokstra A, Picavet HSJ, Smit HA. The Doetinchem cohort study (cohort profile) Int J Epidemiol 2008; 37(6):1236-1241 | Body weight, serum cholesterol, mortality, morbidity, health-related quality of life (RAND-36) | Social economic status, physical activity |
| Health survey Utrecht | 3475 | Adults 3475 (19-99 years) | lifestyle, perceived health, chronic diseases | Socioeconomic status, physical activity |
| United Kingdom | | | | |
| Born in Bradford | 12000 | Babies, ongoing, England (large ethnic population) and their parents for a subgroup | Birth weight and gestation General and mental health parents in a | Social economic status Air pollution Detailed |

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| | | | subset of 1500 | ethnicity |
| Routine hospital emissions/disease incidence | | Small area-level data for Stoke-on-Trent/Staffordshire | Rates and nature of hospital episodes (e.g., respiratory, CVD), morbidity and mortality | Social economic status Air pollution |
| National health data | | Small area-level health data for UK | Nature and rates of morbidity and mortality | Social economic status Air pollution |
| Lithuania | | | | |
| Routine morbidity data Lithuania | 0.5 million | Lithuania population, all age groups. Classification of all registered cases causes according to ICD-10 revision codes | Urban-rural area, age, sex, cardiovascular, respiratory, cancer, and other morbidity by districts | Social and demographic status |
| Routine mortality data Lithuania | 0.5 million | Lithuania population, all age groups. Classification of all registered cases causes according to ICD-10 revision codes | Urban-rural area, age, sex, cardiovascular, respiratory, cancer, and other morbidity by districts | Social and demographic status |
| Detailed Health survey | 7000 | Representative sample adults of Kaunas citizens, Lithuania | General health including Blood pressure, high cholesterol and diabetes, Depression Physical functioning Cognitive function Psychosocial factors | Social economic status Air pollution Physical activities Stress |
| Kaunas birth | 4,260 | Kaunas babies and their parents for a subgroup | Birth weight and | Social, |

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| cohort | | http://www.birthcohorts.net/Cohort.Show.asp?cohortid=87 | gestational age | demographic, economic status Air pollution |
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Web Table 2. Summary of proposed experimental design in each partner country in PHENOTYPE

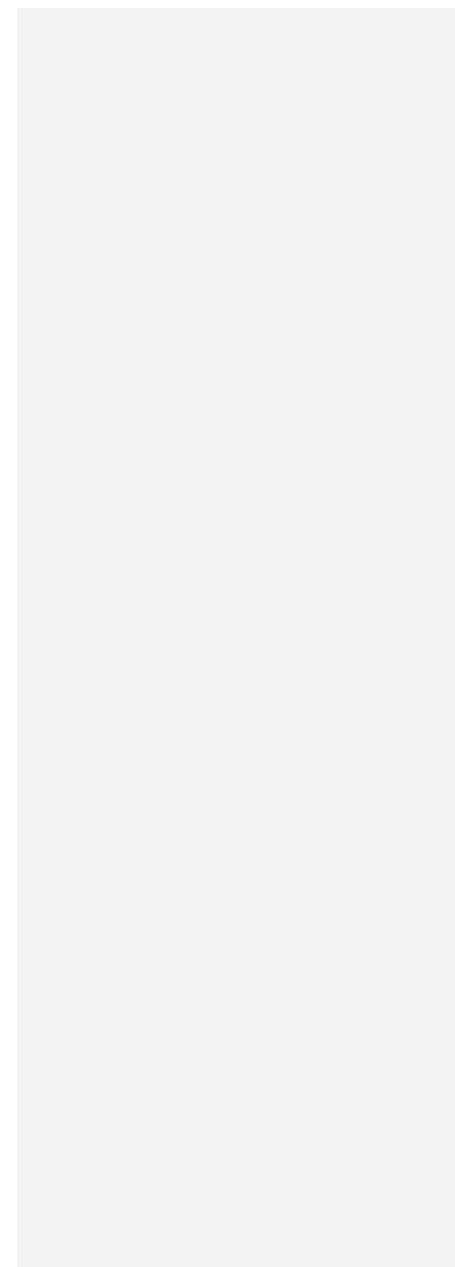
| | Country | Sample | Summary design | Measures | | | | |
|-------------|----------------------|--|---|----------|--------------------|--|---|---|
| | | | | Affect | Cognition | Physiological | Environment | Other |
| Preventive | UK: study 1 | Healthy adults (n=40) | - Field-based - Within-subjects - 30-minute exposure to natural green, natural green/blue, and urban environment - Measures at baseline (pre-exposure), 30 and 60-minutes post exposure | Mood | Cognitive function | - Salivary cortisol - HR - HRV - BP | Perceived restoration | RPE Walking speed |
| | UK: study 2 | Healthy adults (n=40) | - Field-based - Between groups - 30-minute exposure to natural <i>or</i> urban environment on three consecutive days - Measures at baseline (day 1), 0, 30 and 60-minutes on exposure days (days 2-4) and final follow-up on day 5 | Mood | Cognitive function | - Salivary cortisol - HR - HRV - BP | Perceived restoration | RPE Walking speed Hedonic and eudemonic life satisfaction |
| | Netherlands: study 1 | Healthy adults (n=50) | - Laboratory-base - Within subjects - Shown images of natural and urban environment before a stressor (model 1) and after a stressor (model 2) stressor (to explore buffering and restorative effects, respectively) | Mood | Cognitive function | - Salivary cortisol - HR - HRV - BP | Perceived restoration | |
| | Netherlands: study 2 | Healthy adults (n=25) | - Laboratory-based - Within subjects - Shown images of natural and urban environment before a stressor (model 1) and after a stressor (model 2) stressor (to explore buffering and restorative effects, respectively) | Mood | Cognitive function | - Neurological response (fMRI) - Salivary cortisol - HR - HRV - BP | Perceived restoration | |
| Therapeutic | Spain | Adults with elevated stress levels (n=20-40) | - Field-based - Exposure to natural green, natural green/blue, and urban environment over several hours - Measures at baseline (pre-exposure), 30 and | Mood | Cognitive function | - Salivary cortisol - HR - HRV - BP | - Perceived restoration - Air pollution - Noise | RPE Walking speed Social interaction |

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| | | | 60-minutes post exposure - Participants given CALFIT phones for some days for longer term monitoring (mood, social interaction, physical activity) | | | | pollution | and physical activity (CALFIT) |
| | Lithuania | Adults with CAD (n=20) | - Field-based - Between-subjects - 30-minute exposure to natural green <i>or</i> urban environment on two consecutive days (days 2 and 3) - Measures at baseline (pre-exposure), 30 and 60-minutes post exposure - Walking treadmill test at baseline (day 1) and follow-up (day 2) | Mood | Cognitive function | - Exercise capacity (treadmill test) - Salivary cortisol - HR - HRV - BP | Perceived restoration | RPE Walking speed |

CAD, coronary artery disease; HR, heart rate; HRV, heart rate variability; BP, blood pressure, RPE, rate of perceived exertion; fMRI, functional magnetic resonance imaging

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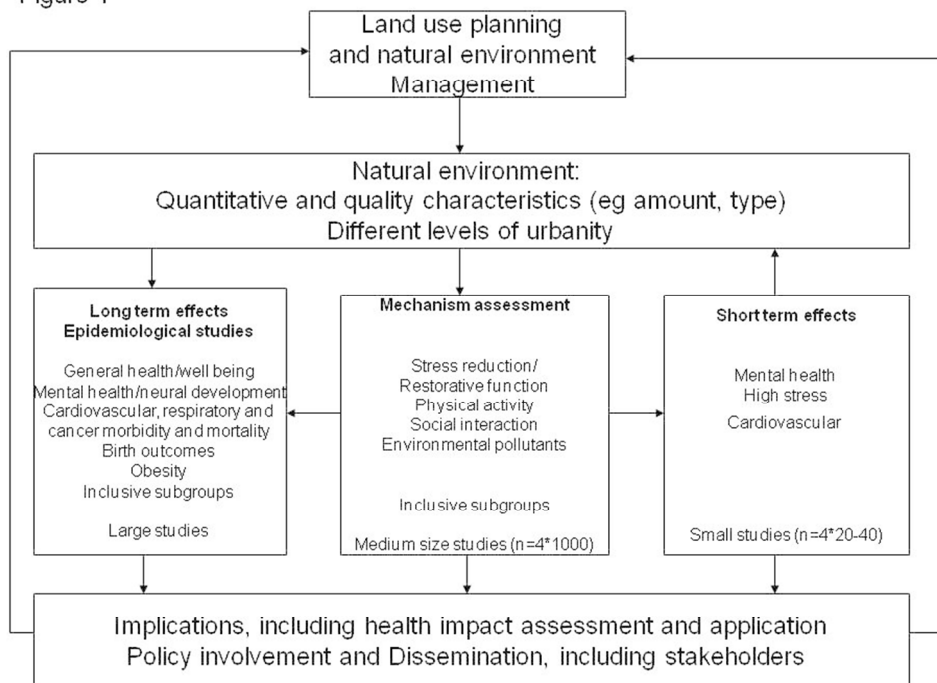
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For peer review only

Figure 1



254x190mm (96 x 96 DPI)

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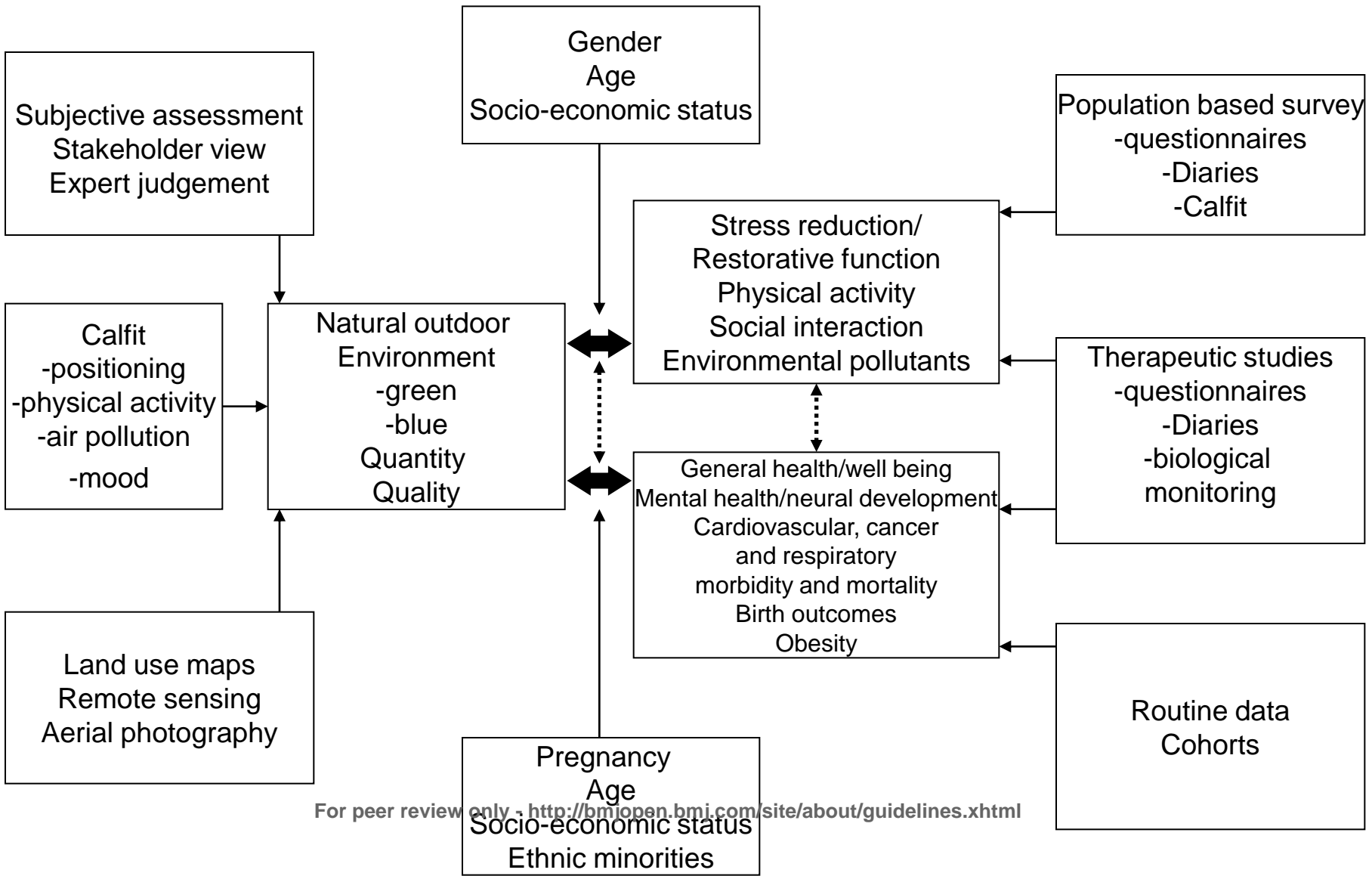
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ASSESSMENT OF THE ENVIRONMENT

SUSCEPTIBLE GROUPS

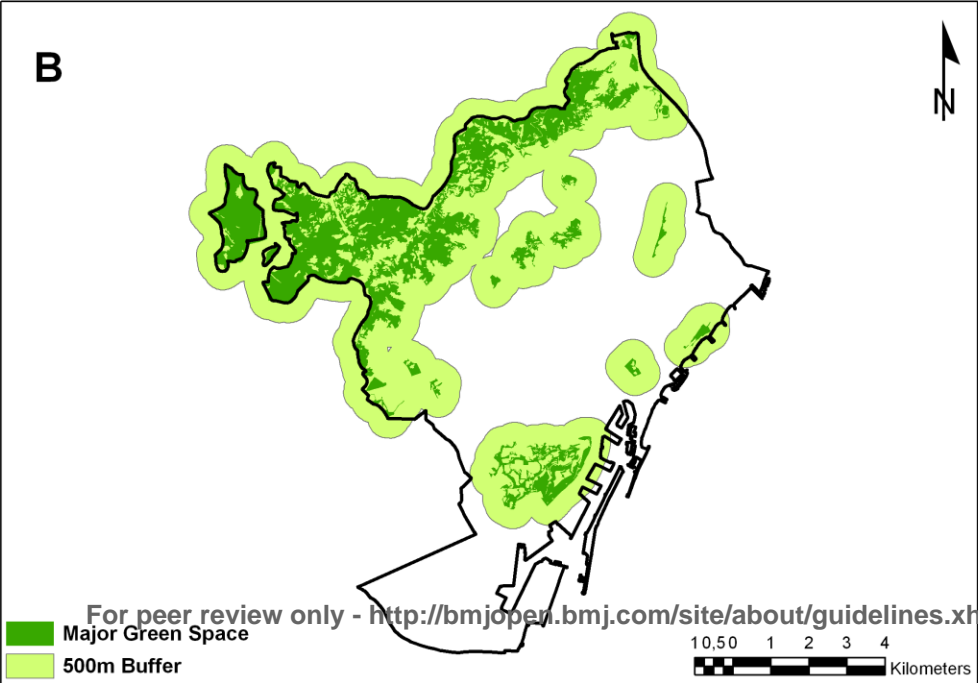
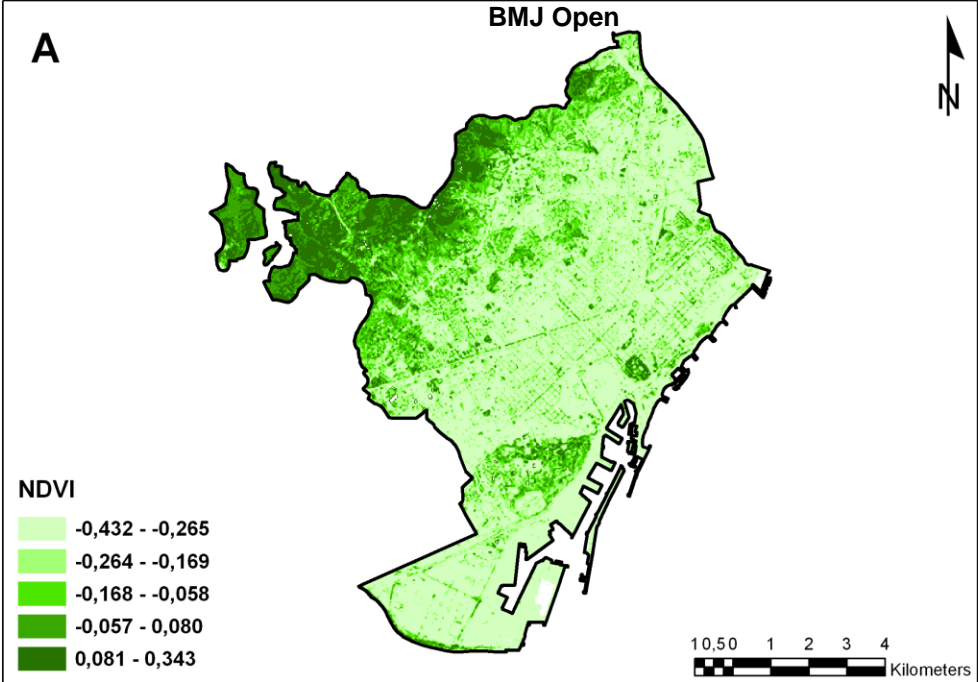
HEALTH OUTCOME ASSESSMENT

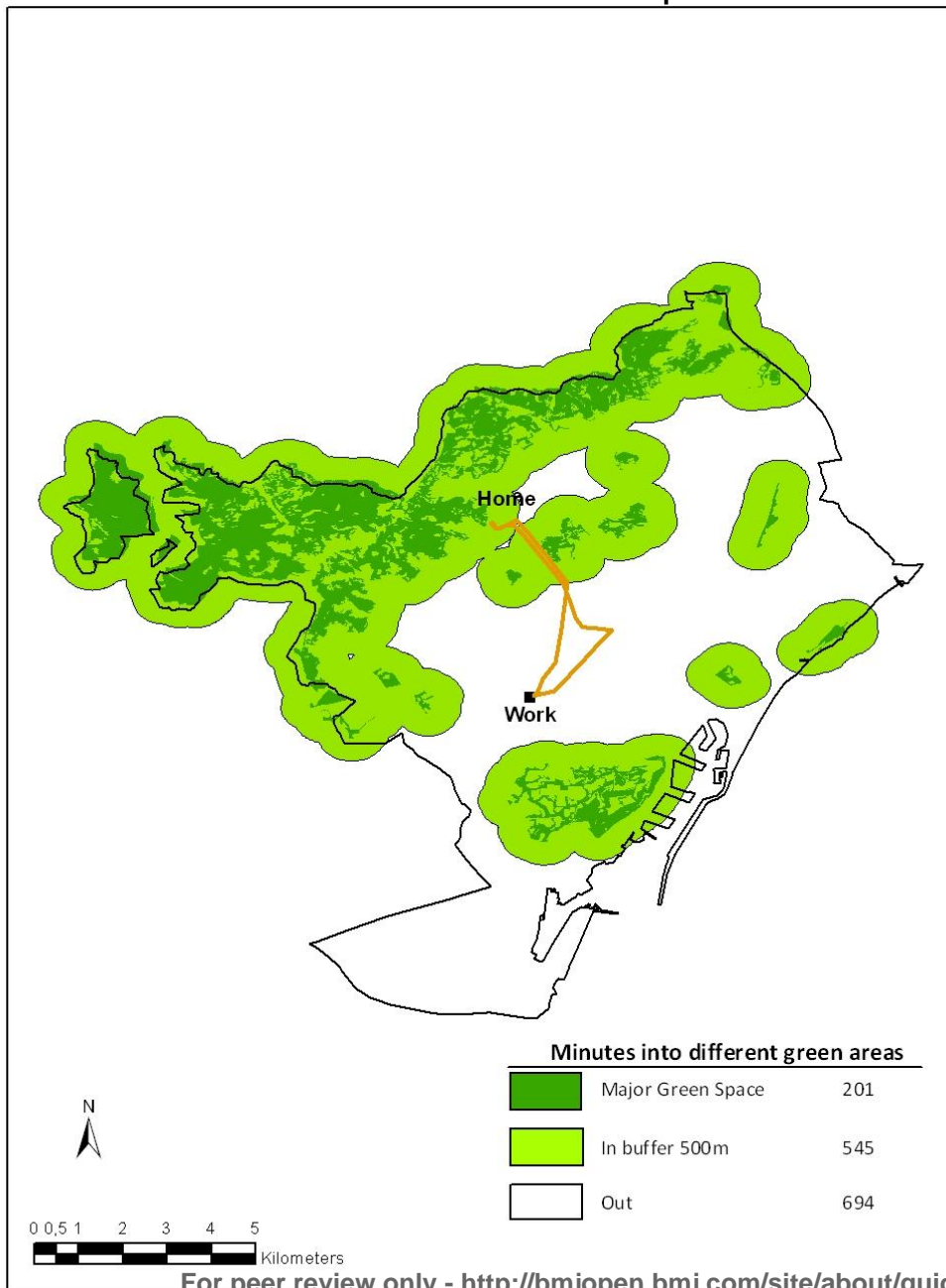
HEALTH DATA SOURCES



Web figure 2

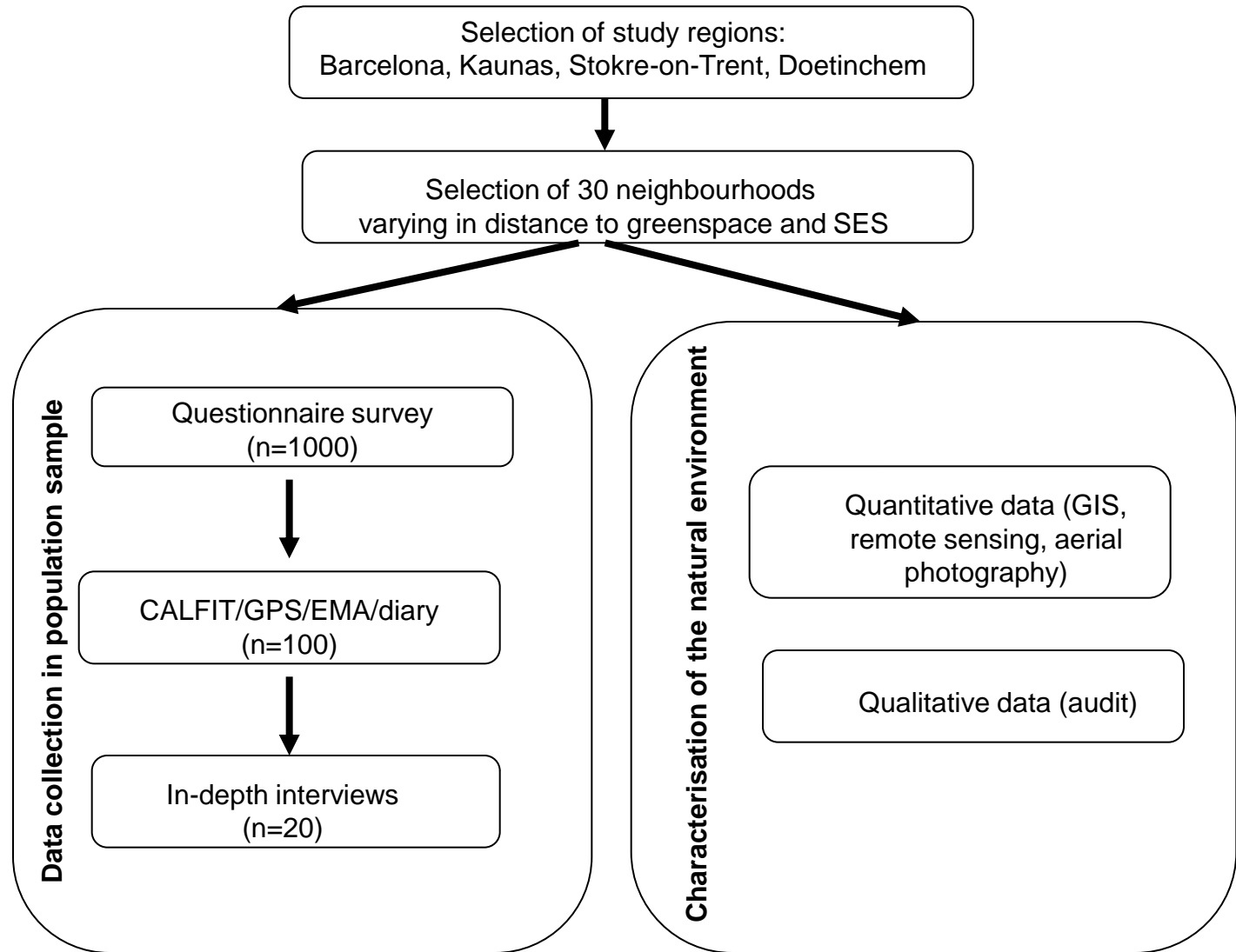
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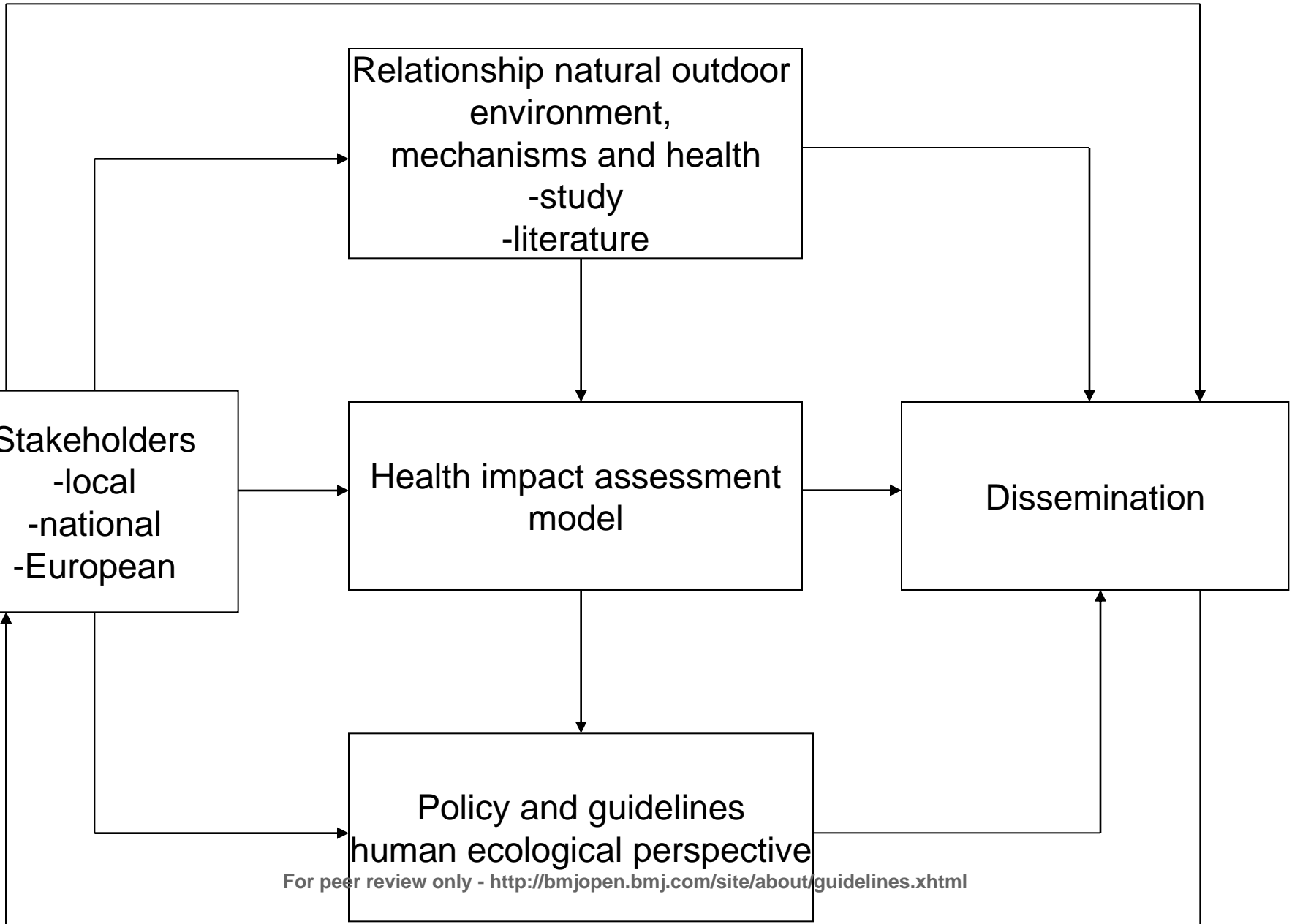


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Web figure 4



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Web Table 1 Currently available databases and cohorts for inclusion in PHENOTYPE

| Study | n | Population | Collected outcomes | Relevant covariate and mechanism data |
|-------------|------|--|---|--|
| CREAL Spain | | | | |
| PISCINA | 3000 | Children 6-9, 2006, Sabadell, Catalonia | Respiratory health BMI | Social economic status Physical activity Air pollution |
| INMA | 3000 | Children, 2-10, ongoing around Spain | Birth weight and gestation, respiratory health, neural development | Social economic status Physical activity Stress Air pollution |
| PAC-COPD | 342 | Patients with chronic obstructive pulmonary disease (PAC-CODP) | Hospital admissions All cause and specific mortality Functional data (lung function, cardiovascular function) Symptoms and co-morbidities Quality of life Mental status Body weight and composition | Social economic status Physical activity Air pollution |
| ECRHS | 8500 | Adult population in many cities around Europe | Respiratory health Short form SF36 | Social economic status Physical activity |

| | | | | |
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| | | | | Air pollution |
| Routine data Catalonia | Pop 7M 0.5 million deaths | All, 1999-2006, Catalonia | All cause and specific mortality | Social economic status |
| Hospital clinic database | 16000 | Births, 2000-2005 Barcelona | Birth weight and gestation | Social economic status Air pollution |
| Netherlands | | | | |
| Cohort of Dutch inhabitants Netherlands | Pop 16M | All, 2000-2008 | All cause and specific mortality and morbidity | Social economic status |
| Doetinchem cohort | Approximately 5000 over a period of 5 years | See: Verschuren WMM, Blokstra A, Picavet HSJ, Smit HA. The Doetinchem cohort study (cohort profile) Int J Epidemiol 2008; 37(6):1236-1241 | Body weight, serum cholesterol, mortality, morbidity, health- related quality of life (RAND-36) | Social economic status, physical activity |
| Health survey Utrecht | 3475 | Adults 3475 (19-99 years) | lifestyle, perceived health, chronic diseases | Socioeconomic status, physical activity |
| United Kingdom | | | | |
| Born in Bradford | 12000 | Babies, ongoing, England (large ethnic population) and their parents for a subgroup | Birth weight and gestation General and mental health parents in a subset of 1500 | Social economic status Air pollution Detailed ethnicity |
| Routine hospital | | Small area-level data for Stoke-on-Trent/Staffordshire | Rates and nature of hospital episodes (e.g., | Social economic status |

| | | | | |
|--|-------------|---|--|--|
| emissions/ disease incidence | | | respiratory, CVD), morbidity and mortality | Air pollution |
| National health data | | Small area-level health data for UK | Nature and rates of morbidity and mortality | Social economic status Air pollution |
| Lithuania | | | | |
| Routine morbidity data Lithuania | 0.5 million | Lithuania population, all age groups. Classification of all registered cases causes according to ICD-10 revision codes | Urban-rural area, age, sex, cardiovascular, respiratory, cancer, and other morbidity by districts | Social and demographic status |
| Routine mortality data Lithuania | 0.5 million | Lithuania population, all age groups. Classification of all registered cases causes according to ICD-10 revision codes | Urban-rural area, age, sex, cardiovascular, respiratory, cancer, and other morbidity by districts | Social and demographic status |
| Detailed Health survey | 7000 | Representative sample adults of Kaunas citizens, Lithuania | General health including Blood pressure, high cholesterol and diabetes, Depression Physical functioning Cognitive function Psychosocial factors | Social economic status Air pollution Physical activities Stress |
| Kaunas birth cohort | 4,260 | Kaunas babies and their parents for a subgroup http://www.birthcohorts.net/Cohort.Show.asp?cohortid=87 | Birth weight and gestational age | Social, demographic, economic status Air pollution |

Web Table 2. Summary of proposed experimental design in each partner country in PHENOTYPE

| | Country | Sample | Summary design | Measures | | | | |
|-------------|----------------------|--|---|----------|--------------------|--|---|---|
| | | | | Affect | Cognition | Physiological | Environment | Other |
| Preventive | UK: study 1 | Healthy adults (n=40) | - Field-based - Within-subjects - 30-minute exposure to natural green, natural green/blue, and urban environment - Measures at baseline (pre-exposure), 30 and 60-minutes post exposure | Mood | Cognitive function | - Salivary cortisol - HR - HRV - BP | Perceived restoration | RPE Walking speed |
| | UK: study 2 | Healthy adults (n=40) | - Field-based - Between groups - 30-minute exposure to natural <i>or</i> urban environment on three consecutive days - Measures at baseline (day 1), 0, 30 and 60-minutes on exposure days (days 2-4) and final follow-up on day 5 | Mood | Cognitive function | - Salivary cortisol - HR - HRV - BP | Perceived restoration | RPE Walking speed Hedonic and eudemonic life satisfaction |
| | Netherlands: study 1 | Healthy adults (n=50) | - Laboratory-base - Within subjects - Shown images of natural and urban environment before a stressor (model 1) and after a stressor (model 2) stressor (to explore buffering and restorative effects, respectively) | Mood | Cognitive function | - Salivary cortisol - HR - HRV - BP | Perceived restoration | |
| | Netherlands: study 2 | Healthy adults (n=25) | - Laboratory-based - Within subjects - Shown images of natural and urban environment before a stressor (model 1) and after a stressor (model 2) stressor (to explore buffering and restorative effects, respectively) | Mood | Cognitive function | - Neurological response (fMRI) - Salivary cortisol - HR - HRV - BP | Perceived restoration | |
| Therapeutic | Spain | Adults with elevated stress levels (n=20-40) | - Field-based - Exposure to natural green, natural green/blue, and urban environment over several hours - Measures at baseline (pre-exposure), 30 and | Mood | Cognitive function | - Salivary cortisol - HR - HRV - BP | - Perceived restoration - Air pollution - Noise | RPE Walking speed Social interaction |

| | | | | | | | | |
|--|-----------|------------------------|---|------|--------------------|--|-----------------------|--------------------------------|
| | | | 60-minutes post exposure - Participants given CALFIT phones for some days for longer term monitoring (mood, social interaction, physical activity) | | | | pollution | and physical activity (CALFIT) |
| | Lithuania | Adults with CAD (n=20) | - Field-based - Between-subjects - 30-minute exposure to natural green <i>or</i> urban environment on two consecutive days (days 2 and 3) - Measures at baseline (pre-exposure), 30 and 60-minutes post exposure - Walking treadmill test at baseline (day 1) and follow-up (day 2) | Mood | Cognitive function | - Exercise capacity (treadmill test) - Salivary cortisol - HR - HRV - BP | Perceived restoration | RPE Walking speed |

CAD, coronary artery disease; HR, heart rate; HRV, heart rate variability; BP, blood pressure, RPE, rate of perceived exertion; fMRI, functional magnetic resonance imaging

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