MINDMAP: establishing an integrated database infrastructure for research in ageing, mental well-being, and the urban environment

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Abstract

Background: Urbanization and ageing have important implications for public mental health and well-being. Cities pose major challenges for older citizens, but also offer opportunities to develop, test, and implement policies, services, infrastructure, and interventions that promote mental well-being. The MINDMAP project aims to identify the opportunities and challenges posed by urban environmental characteristics for the promotion and management of mental well-being and cognitive function of older individuals.

Methods: MINDMAP aims to achieve its research objectives by bringing together longitudinal studies from 11 countries covering over 35 cities linked to databases of area-level environmental exposures and social and urban policy indicators. The infrastructure supporting integration of this data will allow multiple MINDMAP investigators to safely and remotely co-analyse individual-level and area-level data. Individual-level data is derived from baseline and follow-up measurements of ten participating cohort studies and provides information on mental well-being outcomes, sociodemographic variables, health behaviour characteristics, social factors, measures of frailty, physical function indicators, and chronic conditions, as well as blood derived clinical biochemistry-based biomarkers and genetic biomarkers. Area-level information on physical environment characteristics (e.g. green spaces, transportation), socioeconomic and sociodemographic characteristics (e.g. neighbourhood income, residential segregation, residential density), and social environment characteristics (e.g. social cohesion, criminality) and national and urban social policies is derived from publically available sources such as geoportals and administrative databases. The linkage, harmonization, and analysis of data from different sources are being carried out using piloted tools to optimize the validity of the research results and transparency of the methodology.

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Background
From 1990 to 2010, the burden of mental ill-health increased by 38%, an increase mostly attributable to population ageing [1]. Mental disorders in old age lead to impairments in the ability to function socially, decreased quality of life, and increased risk of health problems and comorbidities. Poor mental well-being in later life carries significant social and economic impacts on families and societies, imposing a substantial burden on health and social care services [1]. Mental disorders associated with ageing, therefore, have become a key priority for public health policy and prevention.

Today, over 70% of Europeans and over 80% of North Americans reside in cities [2]. While urbanization is expected to increase in these regions over the coming decades, there is limited understanding of the critical contribution of the urban environment to mental well-being in ageing societies. Cities pose major challenges for older citizens, but also offer opportunities to develop, test, and implement policies, services, infrastructure, and interventions that promote mental well-being. The MINDMAP project, building on a novel database infrastructure, aims to identify the opportunities and challenges posed by urban environmental characteristics for the promotion and management of mental well-being and cognitive function of older individuals.

Funded from 2016 to 2020 by the Horizon2020 programme of the European Commission, MINDMAP aims to achieve its research objectives by bringing together ten longitudinal studies from eight European countries, the United States (US), Canada and Russia (in total over 35 cities of different sizes) linked to databases of area-level environmental exposures and social and urban policy indicators. Linking micro- (i.e. individual), meso- (i.e. neighbourhood), and macro- (i.e. city or national) level data enables MINDMAP to investigate the causal pathways and multi-level interactions between characteristics of the urban environment and the behavioural, social, and biological determinants of mental well-being and cognitive function in older adults.

Compared to studies based on a single country or city, integrating data from cohort studies in multiple cities offers many advantages for research exploring the impact of the urban environment on mental well-being. Harmonizing information across international cohort studies and combining them with data from different sources (physical, social and socioeconomic environmental characteristics, policy indicators) allows examining contextual determinants of variation in mental well-being across different populations and exploring the impact of neighbourhood, urban, and national policies for the prevention of mental disorders in older people. Furthermore, integrating data increases sample sizes and statistical power necessary to identify high-risk population subgroups, study relatively rare health conditions, unravel causal pathways and explore interactions between risk factors. Finally, and potentially most relevant for studies investigating environmental influences on health, integrating data from different geographical locations increases the variation in environmental characteristics and policies that influence mental well-being and cognitive function both within and between cities.

The MINDMAP database infrastructure will support these research objectives by integrating data from multiple sources and providing investigators with a platform to analyse it. The infrastructure will allow multiple MINDMAP investigators to safely and remotely co-analyse data from multiple sources and across different populations. Integration of different data sources will facilitate analyses exploring the importance of individual- and area-level determinants of mental well-being and cognitive function.

Methods/design
Participating institutions and cohort studies
Research centres and longitudinal cohort studies from across Europe and North America are involved in the MINDMAP consortium.

Thirteen research teams with a wide range of expertise are contributing to the MINDMAP project (see Additional file 1). MINDMAP also brings together ten ongoing longitudinal ageing cohort studies from eight European countries, the US, Canada, and Russia (Table 1). The European cohort studies appropriately
cover urban areas in all regions including North, Central, Southern, and Eastern Europe (Fig. 1). Several cohort studies additionally include more rural areas, which will be useful for comparative purposes.

**Variables and data sources**

MINDMAP is integrating data from numerous sources for different observational units. Individual-level data collected by longitudinal ageing studies will be combined with area-level urban characteristics and local and national policy indicators.

Additional file 2 provides a visual representation of the structure of the MINDMAP project, including all work-packages and their relation to the different data presented below. A detailed overview of data used in the MINDMAP project is provided in Additional file 3. The selection of variables was based on scientific literature and a draft conceptual model on the influence of environmental factors on mental well-being and cognitive function that is being developed by MINDMAP investigators.

### Table 1 Overview of MINDMAP participating cohort studies

<table>
<thead>
<tr>
<th>Name</th>
<th>Type of study</th>
<th>Number of Participants</th>
<th>Country</th>
<th>Main study locations</th>
<th>Baseline</th>
<th>Last follow-up</th>
</tr>
</thead>
<tbody>
<tr>
<td>Canadian Longitudinal Study on Aging (CLSA) [34]</td>
<td>Cohort</td>
<td>50,000</td>
<td>Canada</td>
<td>Victoria, Vancouver, Surrey, Calgary, Winnipeg, Hamilton, Ottawa, Montréal, Sherbrooke, Halifax, St. John’s</td>
<td>2008</td>
<td>Ongoing (until 2018)</td>
</tr>
<tr>
<td>The Health, Alcohol and Psychosocial Factors in Eastern Europe Study (HAPIEE) [36]</td>
<td>Cohort</td>
<td>36,106</td>
<td>Russia, Poland, Lithuania, Czech Republic</td>
<td>Novosibirsk, Krakow, Kaunas, Hradec Kralove, Jihlava, Karvina, Kromeriz, Liberec, Usti nad Labem</td>
<td>2002</td>
<td>2015</td>
</tr>
<tr>
<td>Nord-Trøndelag Health Study (HUNT) [37]</td>
<td>Cohort</td>
<td>125,000</td>
<td>Norway</td>
<td>Nord-Trøndelag county</td>
<td>1984</td>
<td>2008</td>
</tr>
<tr>
<td>Longitudinal Aging Study Amsterdam (LASA) [38]</td>
<td>Cohort</td>
<td>5132</td>
<td>Netherlands</td>
<td>West (including Amsterdam) East (including Zwolle) South (including Oss)</td>
<td>1992</td>
<td>2014</td>
</tr>
<tr>
<td>Longitudinal Urban Cohort Ageing Study (LUCAS) [39]</td>
<td>Cohort</td>
<td>3326</td>
<td>Germany</td>
<td>Hamburg</td>
<td>2000</td>
<td>2017</td>
</tr>
<tr>
<td>Multi-Ethnic Study of Atherosclerosis – Neighbourhood (MESA Neighbourhood) [7]</td>
<td>Cohort</td>
<td>6191</td>
<td>United States of America</td>
<td>Forsyth County (NC), Northern Manhattan &amp; the Bronx (NY), Baltimore City &amp; Baltimore County (MD), St. Paul (MN), Chicago (IL), Los Angeles County (CA)</td>
<td>2000</td>
<td>2012</td>
</tr>
<tr>
<td>Residential Environment and CORonary Heart Disease Study (RECORD) [40]</td>
<td>Cohort</td>
<td>7290</td>
<td>France</td>
<td>Paris</td>
<td>2007</td>
<td>2015</td>
</tr>
<tr>
<td>Rotterdam Study (RS) [41]</td>
<td>Cohort</td>
<td>14,926</td>
<td>Netherlands</td>
<td>Rotterdam (Ommoord)</td>
<td>1989</td>
<td>Ongoing (until 2020)</td>
</tr>
<tr>
<td>Turin Longitudinal Study (TLS) [42]</td>
<td>Registry based cohort</td>
<td>2,391,833</td>
<td>Italy</td>
<td>Turin</td>
<td>1971</td>
<td>2015</td>
</tr>
</tbody>
</table>

The MINDMAP consortium makes use of baseline and follow-up data collected by 10 participating studies.

**Individual-level data**

The main outcomes of interest within the MINDMAP project are indicators of mental health, mental well-being, and cognitive function. These indicators are measured in the cohort studies at multiple times through questionnaires, interviews, and cognitive tests and include variables covering life satisfaction, quality of life, depression and depressive symptoms, cognitive functioning, anxiety, and loneliness.

**Mental health, mental well-being and cognitive function**

Individual-level determinants, mediators and confounders MINDMAP-participating cohort studies have also collected detailed measures of sociodemographic variables, health behaviour characteristics, social factors, as well as measures of frailty and physical function indicators, and chronic conditions (multi-morbidities). An
important feature of the MINDMAP studies is the collection of repeated measurement of determinants of mental well-being and cognitive function in cohort studies of urban residents. Several studies also have information available on blood derived clinical biochemistry-based biomarkers and genetic biomarkers.

**Area-level data**

Area-level information on physical environment characteristics (e.g. green spaces, transportation), socioeconomic and sociodemographic characteristics (e.g. neighbourhood income, residential segregation, residential density), and social environment characteristics (e.g. social cohesion, criminality) and national and urban social policies is derived from publicly available resources.

**Physical environmental characteristics**

Geospatial data is being collected from existing data portals, and city-specific contacts across the MINDMAP study sites. In the European Union, publicly available spatial information has drastically improved thanks to INSPIRE [3], a 2007 European Directive that establishes a data infrastructure for the collection and distribution of spatial information in the European Union. The European Data Portal [4] was systematically reviewed for all files containing items relevant to mental well-being or intermediate factors for all countries and cities of the participating European cohort studies. In addition, using the European Data Portal, relevant national, regional, and local data portals were identified and are systematically searched for relevant data that is not yet catalogued on the European Data Portal.

Harmonized high-resolution land use data, road infrastructure files, and residential address databases of the general population over the study territory were obtained for all European MINDMAP cities. For its land use data, MINDMAP extracted data from the European Urban Atlas [5]. This data is derived from satellite imagery and consists of 21 distinct categories, which capture a city’s land use (including public green areas). This data is being used to calculate individual ‘greenness’ exposure. In combination with the infrastructure information, measures such as nearest road network distance to urban green spaces are also being calculated. Point data of all residential addresses is used to determine population density. Information on facilities, transportation, and pollution
have been obtained for a subset of cities from local and national data portals and are used to derive measures such as exposure to pollutants, access to public transport and availability of facilities.

The CLSA is part of the Canadian Urban Environmental Health Research Consortium (CANUE), a pan-Canadian initiative which is gathering and developing measures of environmental characteristics such as greenness, walkability, air pollution, and socioeconomic conditions for every neighbourhood across Canada [6]. As they become available, environmental characteristics developed within CANUE will be linked to CLSA cohort data. For our US cohort study, we will use the area-level geospatial data collected within the MESA neighbourhood study, which was specifically designed to study environmental influences on health [7].

**Socioeconomic, sociodemographic and social environmental characteristics** Area level variables on neighbourhood socioeconomic measures (e.g. average income, proportion of rental housing), sociodemographic composition (e.g. proportion of older people, residential segregation), and social interaction indicators (e.g. proxies of social cohesion, criminality) are also being derived from publicly available sources such as the local and national statistics agencies and local governments.

**National and local policies** Data on national and subnational policies that range from proximal to more distal influences on the mental well-being of older people in an urban environment has been collected within the MINDMAP project to evaluate the effects of public policies on mental well-being outcomes. Existing, cross-city and cross-national databases such as the Social Insurance Entitlements Dataset (SIED) [8], the Labour Market Reforms (LABREF) database [9], the Eurostat databases [10], and the OECD Long Term Care database [11] were the principal sources for social policies such as old age pensions and social care. Urban policy indicators, such as transportation affordability and accessibility indicators, were collected for each MINDMAP city from the Eurostat Urban Audit database [12] and the OECD Metropolitan Indicators database [13]. Mental health policy indicators, such as mental health system governance, resources and services were collected at the national level for European countries from the Eurostat Health Indicators database and the European Health for All database [14], and for all countries from the WHO Mental Health Atlas Country Profiles [15] and from two OECD data sources [16, 17]. MINDMAP aims to collate such policy data for the past 30 years, and earlier, when applicable. When longitudinal data was not available, we collected the latest available cross-sectional data. In addition, data has been collected on local mental health promotion and prevention policies through interviews with experts in MINDMAP cities [18].

**The MINDMAP process**

To support cross-national research on ageing, mental well-being and the urban environment, the MINDMAP consortium adopted harmonization guidelines and software applications developed by Maelstrom Research [19, 20]. These tools have been employed under similar collaborative health research projects such as BioSHARE [21], InterConnect [22], and the Canadian Partnership for Tomorrow Project [23]. Seven consecutive actions are being undertaken to establish an integrated database infrastructure allowing analyses of individual- and area-level data for research in ageing, mental well-being, and the urban environment (Fig. 2).

**Define research questions**

As a first step, MINDMAP consortium investigators identified a number of research questions addressing the variation in mental well-being and disorders in old age, both within cities as well as between cities and exploring how environments and policies at different levels might influence mental well-being in later life. Table 2 shows main research questions to be answered with the integrated database infrastructure. In addition, more detailed domain-specific research questions were defined, to be explored by each work package (Additional file 2).

**Document metadata**

The design of participating studies and the data they collect were documented on a web-based platform [24]. This platform includes a search and query interface allowing MINDMAP investigators to quickly and easily identify studies collecting data items required to answer specific research questions. Questionnaires, standard operating procedures, and data dictionaries were also documented within the platform so that heterogeneity of data collection instruments could be properly assessed. Area-level urban characteristics as well as local and national policies of interest are also being documented.

**Develop data sharing and publication guidelines**

In order to establish basic governing principles for the consortium, MINDMAP principal investigators drafted guidelines covering access and usage of cohort study data and publication of results. First, each cohort study's regular data access procedures will be respected, including the submission of access applications and obtaining of all required approvals from ethical review boards. Second, only data relevant to answer MINDMAP research questions is being requested. Third, after receiving all necessary approvals, these subsets of cohort study data will be hosted on firewall-protected servers. Participating studies
were given the option of transferring a subset of their data to the coordinating centre’s (Erasmus MC) server or installing a local server at their home institution. Fourth, the MINDMAP coordinating team and cohort representatives will review each manuscript proposal. At this point, cohort representatives will need to confirm that they agree to the use of their data for a given manuscript, and will be able to opt-out if they wish. Lastly, a publication agreement was adopted to describe the authorship and acknowledgement guidelines relevant to work generated in connection with MINDMAP.

**Put in place IT infrastructure**

Given potential restrictions related to sharing of individual-level data, a distributed database infrastructure was put in place to support data harmonization and cross-study analyses (Fig. 3). As such, a primary data server was installed at Erasmus Medical Centre in Rotterdam (the MINDMAP coordinating centre) to host datasets from studies whose policies allow the physical transfer of data to a third party. Cohort studies with more restrictive data sharing rules were given the option of installing secondary data servers in their own institution, which would be remotely accessible via encrypted connections (using HTTPS). Finally, a central analysis server running RStudio [25] was set up and allows authenticated MINDMAP staff and investigators to securely access firewall-protected data on the primary and secondary data servers (see step 7 below).

**Harmonize cohort data**

MINDMAP research teams were assigned specific domains of information to harmonize across all MINDMAP cohort studies. Assignment of data harmonization work was based on the expertise of the investigators at participating institutions. University College London is responsible for mental well-being and cognitive outcomes harmonization, Vrije Universiteit Amsterdam (VU) University Medical Centre was assigned social factors and perceived environment variables harmonization, Erasmus Medical Centre, in collaboration with McGill University Health Centre, is harmonizing socioeconomic variables, multi-morbidities and health behaviours variables. Finally, biomarker data is harmonized by McMaster University (for details on the domains of information, see Additional file 3).

Research teams began by reviewing the variables collected by each cohort study and related documentation (e.g. questionnaire(s), standard operating procedures, data dictionaries) for their assigned domain, and identifying missing information or highlighting unclear variable definitions, codes, or values. Targeted variables for harmonization are then defined (e.g. current cigarette consumption - categorical: yes (coded as 1) or no (coded as 0); pack-years of smoking - continuous variable) and documented in a central MINDMAP GitHub repository. The choice and specific definitions of targeted variables is determined by the research questions that they will help to address and the actual data collected by each cohort. Once defined, the potential for each cohort to generate target variables is assessed. Next, data harmonizers develop data transformation scripts to generate common-format variables in RStudio [25] on the password protected central analysis server. Decisions made and harmonization scripts applied for each study-specific dataset are documented using cohort-specific RMarkdown documents [26] in the publicly-accessible MINDMAP GitHub repository, thereby making data transformation decisions open and transparent. Lastly, quality control checks are conducted on harmonized variables by comparing the distribution and counts of harmonized datasets to the data originally collected by each study.
Link area-level data
Addresses and postal codes of cohort participants will be used to link urban environmental characteristics and policy data (i.e. area-level data) to harmonized cohort data (Fig. 4). Given that the utilization of residential locations in research projects compromises study participants’ privacy, the georeferenced information will be blinded in a step-by-step process. Firstly, the cohort data manager will generate new unique identifiers (UID2) for all individuals in cohort studies along with dummy (i.e. random) identifiers (DUID) and residential locations (home address or postal code) for approximately 5% of the total cohort
study's sample (more if preferred). Second, a Link file containing UID2 and residential locations (RL) as well as DUID and dummy RLs will be sent to the MINDMAP data manager. Third, MINDMAP will prepare a clearly documented Urban characteristics file to be merged with the Link file. Fourth, the Link file and Environmental exposures file will be merged into the Merged file using residential locations and dates of assessment. The resulting dataset is then sent back to the data manager of the cohort study who deletes all addresses. Lastly, the merged data is made available through the data infrastructure (either on the primary data server or a secondary data server).

**Co-analyse integrated data**

Using a web browser and secure internet connection, authenticated MINDMAP researchers can login to the central analysis server outlined in step four and conduct on-demand statistical analyses on geographically distributed firewall-protected databases using the RStudio web interface. While some studies have given permission for individual-level data to be analysed by MINDMAP investigators, others have restricted data access to aggregate-level information. For all analyses that include cohort studies prohibiting the use of individual-level data, the DataSHIELD approach is used [27, 28]. Under DataSHIELD, analysis requests are sent from the central analysis computer to the harmonized data held on the data servers. Computation is done simultaneously but in parallel on each data server linked by non-disclosive summary statistics. Individual-level cohort data thereby stay on their respective data server described in step four above.

Unlike experimental data, in our observational design, exposure to environmental and individual risk factors cannot be assumed to be randomly assigned [29, 30]. This is a challenge for research on the impact of the urban environment on health. To minimize risks of bias as much as possible with the available data, MINDMAP will capitalise on recent advances in causal inference and causal mediation methods, particularly derived from econometric and policy evaluation [29]. Because of the impossibility to randomize many of the key environmental determinants of mental well-being, quasi-experimental approaches applied to longitudinal data will provide the basis for the identification of causal effects. These techniques will include instrumental variables, regression discontinuity, and difference-in-differences approaches [31], which exploit naturally occurring changes in the environment, including policy reforms, to identify their causal effect on mental well-being. For example, the introduction of the free bus pass in England in 2006, a transportation policy, has been linked to increased physical activity and reduced obesity [32, 33]. Similar evaluations could be carried for the impact of policy reforms in the domains of housing, which affect the living arrangements of older people; pension policies, which influence the financial well-being of urban older dwellers; mental health promotion programmes that target the mental health of older people in cities; and environmental policies that affect access to outdoor and meeting spaces, lightening and walkability. MINDMAP will aim to implement policy evaluation studies to examine how some of these policies affecting older people living in MINDMAP cities may influence their mental health, with the aim of identifying transferrable lessons.

**Discussion**

The MINDMAP project aims to identify the opportunities and challenges posed by the urban environment for the promotion of mental well-being and cognitive function in later life. MINDMAP aims to achieve its research objectives by bringing together longitudinal studies from 11 countries covering over 35 cities linked to databases of area-level environmental exposures and social and urban policy indicators. The infrastructure supporting integration of this data will allow multiple MINDMAP investigators to safely and remotely co-analyse individual-level and area-level data through a single platform.

The MINDMAP project has several important strengths. Integrating data from cohort studies in multiple cities and across various exposure or policy databases allows examining the role of contextual determinants on variations in mental well-being across different populations. It also increases variations across these contextual determinants and it raises sample sizes and statistical power and, because the data is pooled from different regions and jurisdictions, allows exploring the effect of policy on mental well-being. The harmonization approach and tools that are employed by the project have been methodically developed by Maelstrom Research [19, 20] and put to use in similar research collaborations [21–23]. These tools and approaches have been adapted to accommodate the specific needs of the MINDMAP project and ensure that all aspects of the harmonization project are carried out in a uniform, open, and methodical way to optimize the validity of the research results and transparency of the methodology. Moreover, the research teams contributing to the project bring a wide range of experiences and expertise that complement each other.

The integration of different data sources from different countries also present several challenges. Firstly, different questions and scales have been used within the participating cohort studies to measure similar underlying concepts. For some measures, harmonizing across the cohort studies is relatively straightforward (e.g. simple algorithmic transformations or calibrations). However, for measures such as mental well-being outcomes, this process is more complex, requiring the application of
statistical modelling (e.g. standardization, latent variable or multiple imputation) [11]. Further, in many instances not all variables can be harmonized and constructed for all participating studies, because this might compromise the quality of the constructed variables. Secondly, all environmental data needs to be methodically checked for accuracy, completeness (e.g. missing roads), and geocoding or projection errors (e.g. a road is projected next to the real location of the road) to ensure the validity of the data. Furthermore, there is often a lack of historical data due to rapid changes in geographical information system (GIS) techniques and the tendency to only publish the most recent data by many of the sources publishing geospatial data. Extensive efforts are therefore needed to obtain high quality historical measures of environmental exposures. Thirdly, linking environmental data to cohort data can lead to privacy concerns when not dealt with properly. To prevent this, we developed a process to link the environmental data to cohort data that protects participant privacy by isolating residential addresses from privacy sensitive health data. Finally, integrating data from 10 longitudinal studies requires extensive coordination. Streamlining this process while respecting each study’s guidelines and regulations necessitates considerable time investments and meticulous planning.

MINDMAP is a novel research collaboration which is combining population-based cohort data with publicly available datasets not typically used for ageing and mental well-being research. Integration of various data sources and observational units into a single platform will facilitate multilevel analyses exploring the influence of individual- and area-level determinants of mental well-being. In the end, this infrastructure will help to explain the differences in ageing-related mental and cognitive disorders both within as well as between cities around the world and assess the causal pathways and interactions between the urban environment and the individual determinants of mental well-being and cognitive ageing in older adults.

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Availability of data and materials
The datasets generated in the context of the MINDMAP project are not publicly available due to study participant privacy considerations. However, data access can be requested from the individual cohort studies via the respective data access procedures in place.

Authors’ contributions
MAR and DD coordinate the construction of the MINDMAP integrated database infrastructure. Together they drafted and critically reviewed the full manuscript. FjvL and IA coordinate the MINDMAP project and IF coordinated the development of the Maelstrom Research tools and guidelines that are used for the harmonisation and analysis of the data. MBN, JPN, ENH and EC contributed to the area-level data collection. FjvL, MB, BC, GC, UID, AVDR, MH, EG, SK, PM and PR were involved in the design of the study and contributed to the data collection of the included cohort studies. All authors have critically reviewed the manuscript. All authors read and approved the final manuscript.

Ethics approval and consent to participate
MINDMAP will do secondary analyses on the data collected within the participating cohort studies. All participating cohort studies have originally received consent of the participants and ethical approval from their respective institutions: LASA received ethical approval by the Medical Ethical Committee of the Vrije Universiteit medisch centrum, HUNT received ethical approval from the Regional Committee for Medical Research Ethics, Mid-Norway. In addition, MINDMAP specific approval was received from the same committee. RECORD received ethical approval from the Commission Nationale de l’Informatique et des Libertés. LUCAS received ethical approval from the Ethik-Kommission der Ärztekammer Hamburg. Additional MINDMAP specific ethical approval has been received from the same committee. Furthermore, MINDMAP specific consent is requested from the participants in the latest wave of LUCAS. HAPIEE received ethical approval from the Joint UCL/UCLH Committees on the Ethics of Human Research. Furthermore, all local institutes also provided ethical approval (the Jagiellonian University’s Committee on the Ethics of Clinical Research, the Kaunas Regional Biomedical Research Ethical Committee, and the Institution Ethical Commission of the Czech Republic – National Institute of Public Health). The Rotterdam study has received ethical approval from the Medical Ethical Committee of Erasmus MC. The GLOBE study has received a declaration of no objection from the same committee. CLSA has received ethical approval from the Hamilton Integrated Research Ethics Board. MESA was approved by the institutional review boards of all participating institutions (Johns Hopkins University, Northwestern University, Wake Forest University, University of California at Los Angeles, Columbia University, University of Minnesota) as well as the National Heart, Lung and Blood Institute.

Consent for publication
Not applicable.

Competing interests
The authors declare that they have no competing interests.

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