

PEER REVIEW HISTORY

BMJ Open publishes all reviews undertaken for accepted manuscripts. Reviewers are asked to complete a checklist review form (<http://bmjopen.bmj.com/site/about/resources/checklist.pdf>) and are provided with free text boxes to elaborate on their assessment. These free text comments are reproduced below.

ARTICLE DETAILS

TITLE (PROVISIONAL)	Urban Environment and Health: a cross-sectional multiregional project based on Population Health Surveys in Spain (DAS-EP project), study protocol.
AUTHORS	Bereziartua, Ainhoa; Cabrera-León, Andrés; Subiza-Pérez, Mikel; García-Baquero, Gonzalo; Delís Gomez, Salvador; Ballester, Ferran; Estarlich, Marisa; Merelles, Antonio; Esplugues, Ana; Irlés, Maria Angeles; Barona, Carmen; Mas, Rosa; Font-Ribera, Laia; Bartoll, X; Pérez, Katherine; Oliveras, Laura; Binter, Anne-Claire; Daponte, Antonio; García Mochon, Leticia; García Cortés, Helena; Sánchez-Cantalejo Garrido, María del Carmen; Lacasaña, Marina; Cáceres, Rocío; Rueda, María; Saez, Marc; Lertxundi, Aitana

VERSION 1 – REVIEW

REVIEWER	Geir Aamodt Norwegian University of Life Sciences, Department of Public Health
REVIEW RETURNED	19-May-2023

GENERAL COMMENTS	<p>This protocol is really interesting and I hope for a successful implementation of the project.</p> <p>Please find some comments I had when I read your protocol.</p> <p>1) Activity space more important than buffers. Major roads and other built environment facilities might restrict individual's activity space. Buffers are therefore not always optimal.</p> <p>2) Do you have any information about where the inhabitants spend their outdoor time? Have you conducted any public participation GIS study to get information about places the inhabitants prefer or not prefer.</p> <p>3) How will you include socio-demographic and socioeconomic differences in your analyses?</p>
-------------------------	---

REVIEWER	Howard Frumkin University of Washington
REVIEW RETURNED	05-Jun-2023

GENERAL COMMENTS	<p>Thank you for the opportunity to review this very interesting study protocol. The key questions for this review, of a study protocol, are whether it is "scientifically credible and ... presented in an appropriate context" ... ethically and procedurally sound." On these points my assessment is generally "yes." The introduction provides ample context for the study. The study is scientifically credible; the data bases to be used are solid, the numbers of subjects appear ample, the measurement methods are well established, and the shortcomings of a cross-sectional study are acknowledged in the</p>
-------------------------	---

discussion. Relevant ethical and procedural issues are well addressed, with an exception raised below.

That said, I offer several points for the authors' consideration. First, the protocol might be strengthened by discussing several contextual issues in the introduction. Three relevant urban "exposures" are omitted: substandard housing, crowding, and economic inequality (as measured by, for example, the Gini index). While I understand that it is probably impossible to modify the study protocol at this point, it would be helpful to discuss the omission of these factors. Moreover, the protocol is silent on emerging issues relevant to urban health, in particular climate change (posing hazards such as heat and flooding) and climate resilience (a positive urban exposure), and in-migration from areas that will need to decant their populations due to climate change. Indeed, it can be argued that any contemporary study of urban health should consider not only the present, but the future, as climate change is rapidly transforming the realities of life in cities. I believe readers would appreciate a discussion in the introduction of how the investigators considered these various issues.

Data collection:

The discussion of exposure variables is thorough and rigorous. However, I would also raise several points for the authors' consideration:

With regard to walkability, the authors propose an index consisting of seven factors (lines 355-57). However, these factors do not include pedestrian infrastructure--the quality and completeness of sidewalks, the quality of street crossings, the presence or absence of shade over sidewalks, and so on. Here are a few recent references that explore these issues:

- Tsiompras AB, Photis YN. What matters when it comes to "Walk and the city"? Defining a weighted GIS-based walkability index. *Transportation Research Procedia*. 2017;24:523-30. doi: <https://doi.org/10.1016/j.trpro.2017.06.001>.
- Knapskog M, Hagen OH, Tennøy A, Rynning MK. Exploring ways of measuring walkability. *Transportation Research Procedia*. 2019;41:264-82. doi: <https://doi.org/10.1016/j.trpro.2019.09.047>.
- Arellana J, Saltarin M, Larrañaga AM, Alvarez V, Henao CA. Urban walkability considering pedestrians' perceptions of the built environment: a 10-year review and a case study in a medium-sized city in Latin America. *Transport Reviews*. 2020;40(2):183-203. doi: 10.1080/01441647.2019.1703842.
- Bartzokas-Tsiompras A, Photis YN, Tsagkis P, Panagiotopoulos G. Microscale walkability indicators for fifty-nine European central urban areas: An open-access tabular dataset and a geospatial web-based platform. *Data in Brief*. 2021;36:107048. doi: <https://doi.org/10.1016/j.dib.2021.107048>.
- Fonseca F, Ribeiro PJG, Conticelli E, Jabbari M, Papageorgiou G, Tondelli S, et al. Built environment attributes and their influence on walkability. *International Journal of Sustainable Transportation*. 2022;16(7):660-79. doi: 10.1080/15568318.2021.1914793.
- Guzman LA, Arellana J, Castro WF. Desirable streets for pedestrians: Using a street-level index to assess walkability. *Transportation Research Part D: Transport and Environment*. 2022;111:103462. doi: <https://doi.org/10.1016/j.trd.2022.103462>
- Metro Vancouver Walkability Index. <http://www.metrovancouver.org/metro2040/complete->

	<p>communities/connected-communities/walkability-index/Pages/default.aspx</p> <p>These references all refer to objectively measured pedestrian infrastructure. Do the available survey data permit characterization of *perceived* pedestrian infrastructure? This may be an even more important measure.</p> <p>Similarly, bicycle infrastructure is not addressed. This is an increasingly important determinant of travel behavior, especially in European cities.</p> <p>Under environmental stressors, while ambient air pollution and noise are included, indoor air pollution is not. While this may be a difficult variable to measure on the scale of this study, it is clearly an important determinant of health in the urban environment. Would information on the cooking fuel used be a useful proxy? If not possible to incorporate this exposure, perhaps include a discussion acknowledging it as an omitted exposure?</p> <p>The measurement of mental health outcomes (lines 413-15) is unclear. Three outcomes are mentioned (anxiety, depression, and sleep disorders). Then comes the confusing sentence “These dichotomized indicators were based on the physician diagnosis or self-diagnosis...” Does that mean that either a physician diagnosis or a self-diagnosis would establish a “yes” for each of those three outcomes? If so could this be clarified? Do physician diagnosis and self-diagnosis perform similarly as indicators? Should they be considered distinct measures?</p> <p>The measurement of loneliness (line 437) is unclear. The text includes only a sentence fragment that says “perceived loneliness is collected with a single item.” Is it possible to say what this item is and comment on its validity?</p> <p>The measurement of social cohesion seems to depend on the Duke-UNC and Oslo-3 scales, which are measures of social support. Is it possible to measure perceived sense of community or related indicators of social capital? These may have considerable importance in determining urban health and quality of life.</p> <p>Data analysis:</p> <p>The protocol does not state any hypotheses to be tested. This raises the concern that the data analysis might be a “fishing expedition,” simply looking for any associations that might emerge from the data. I defer to statisticians on this point but would the protocol be strengthened by the inclusion of some primary hypotheses that could drive the analysis? And by statistical techniques to account for multiple hypothesis testing?</p> <p>The protocol mentions the importance of equity at several points (lines 262, 498). Yet there is no discussion, in the data analysis section or elsewhere, of how equity will be incorporated into the protocol. What analyses will be done relative to equity? What subgroups will be studied? What indicators of equity will be used?</p> <p>Patient and public involvement</p> <p>This section indicates that the public will not be involved in</p>
--	--

	<p>dissemination plans. This raises some ethical concerns. If this research will utilize data from people in certain communities, should not these communities be informed of the research, invited to provide input as to key questions for study, and engaged in the research as appropriate, including in plans for dissemination of results?</p> <p>Minor comment:</p> <p>While the English in the manuscript is generally excellent, there are numerous small errors of usage, sentence structure, and grammar. I suggest a careful edit before finalizing the paper.</p>
--	--

REVIEWER	J Wu Peking University, Institute of Population Research, Peking University
REVIEW RETURNED	26-Nov-2023

GENERAL COMMENTS	<p>This study is a cross-sectional survey and try to compare multi-regional health results and urban environment exposures. The authors had clearly defined the environmental variables related to health results. However, as there were no baselines of population health status, such as the prevalence of chronic mental disorders, health-related quality of people's life and self-perceived general and mental health, the environmental stressors to population health may distorted by the demographic structure of the cities. For example, self-perceived general and mental health status related to the age and health status of the respondents. Are those surveyed cities have the same structure of population and without migration of the people? In short, the authors should clarify the standards of sample selection and health measures. For example, is standard mortality rates of health among the cities needed for compare the UrbEE? More, as self-perceived health and prevalence of chronic mental disorders and health-related quality of life measured different aspects of people's health, their relationships to UrbEE also have different mechanisms or pathologies. The authors should pay more epidemiological designing for this study, such as the population health measure and biases control, otherwise, the surveyed results may only show the differences of UrbEE and different prevalence of health status of people in each city, and could not explained the dose-response relationship or etiological study of environmental exposure risks to people's health.</p>
-------------------------	--

VERSION 1 – AUTHOR RESPONSE

Reviewer 1: Dr. Geir Aamodt, Norwegian University of Life Sciences

Comments to the Author:

R: This protocol is really interesting, and I hope for a successful implementation of the project. Please find some comments I had when I read your protocol.

A: We thank the Reviewer for the encouraging comments.

R: 1) Activity space more important than buffers. Major roads and other built environment facilities might restrict individual's activity space. Buffers are therefore not always optimal.

A: We appreciate the reviewer's insightful observation regarding the potential relevance of activity space over buffers for a comprehensive assessment of the impact of environmental exposures on health. We agree on the fact that buffers may not truly represent individuals' exposure environments due to the complexity of individual movements (Perchoux et al., 2013). Advanced methodologies such as GPS tracking, web mapping apps and massive mobile phone data have the potential to analyze the spatial-temporal distribution of residents' activities and their correlation with built environment

factors and other environmental exposures (Chaix et al., 2013; Gong et al., 2020). However, despite our agreement, we are afraid we cannot incorporate activity space metrics due to financial constraints. We run out of budget with the estimation of the GIS metrics already included in the study (and shown in the manuscript).

With the aim of reflecting on this limitation and encourage the use of activity spaces in future studies, we have incorporated these notions in the section (please see lines 369-373 of the current version of the manuscript):

The use of buffer zones may not be appropriate to evaluate contextual effects on health because they fail to analyze the spatial-temporal distribution of residents' activities and their relationship with built environment factors. Using activity space measures would be preferable to comprehensively assess of environmental exposures by capturing the complexity of individual movements [108–110].

Chaix, B., Méline, J., Duncan, S., Merrien, C., Karusisi, N., Perchoux, C., Lewin, A., Labadi, K., & Kestens, Y. (2013). GPS tracking in neighborhood and health studies: A step forward for environmental exposure assessment, a step backward for causal inference? *Health & Place*, 21, 46–51. <https://doi.org/10.1016/j.healthplace.2013.01.003>

Gong, L., Jin, M., Liu, Q., Gong, Y., & Liu, Y. (2020). Identifying Urban Residents' Activity Space at Multiple Geographic Scales Using Mobile Phone Data. *ISPRS International Journal of Geo-Information*, 9(4), Article 4. <https://doi.org/10.3390/ijgi9040241>

Perchoux, C., Chaix, B., Cummins, S., & Kestens, Y. (2013). Conceptualization and measurement of environmental exposure in epidemiology: Accounting for activity space related to daily mobility. *Health & Place*, 21, 86–93. <https://doi.org/10.1016/j.healthplace.2013.01.005>

R: 2) Do you have any information about where the inhabitants spend their outdoor time? Have you conducted any public participation GIS study to get information about places the inhabitants prefer or not prefer.

A: We appreciate reviewer's suggestion and acknowledge the importance of understanding where inhabitants spend their outdoor time which is indeed a pertinent consideration for gaining deeper insights into residents' daily routines and their exposure to relevant environmental factors. However, our current study relies on secondary data coming from regional population health surveys which neither took into consideration nor gathered such an information. Therefore, we are restricted to the already collected survey data, which, unfortunately, lacked information on where inhabitants specifically spend their outdoor time. Nevertheless, we recognize the value of employing PPGIS approach in gaining insights into the preferences and choices of residents regarding outdoor spaces. We will bear this aspect in mind for future research endeavours.

R: 3) How will you include socio-demographic and socioeconomic differences in your analyses?

A: We appreciate the attention to the crucial aspect of socio-demographic and socioeconomic differences in our analyses. For this study we have the following individual and area-level variables to describe socio-demographic and socioeconomic characteristics of the participants:

- Individual level variables: country of birth, marital status, household size, level of education, employment status, and occupational status, reported household income, and economic difficulty of the household (data collected through population health surveys)
- Neighbourhood-level variables: census tract income and income distribution P80/P20 (data source INE, based on data from 2021), and MEDEA deprivation index (by census tract, based on data from 2021) (Domínguez-Berjón et al., 2008).

We plan to address these differences by using Directed Acyclic Graphs (DAGs). These graphical models will depict the relationships between all these variables, the relevant environmental exposures and mental health outcomes for each individual study conducted within this research project. They will also guide the selection of the socio-demographic and socioeconomic variables for the adjustment sets of variables for each specific statistical model, allowing us to account for potential confounding factors and illuminate causal relationships. Recognizing the nuanced nature of individual-level versus area-level socioeconomic variables, we are know that their associations may vary across different outcomes. For instance, lifestyle factors and mental health outcomes might exhibit a stronger connection with individual-level socioeconomic status, reflecting personal circumstances and

resources (San Sebastián et al., 2018), while environmental outcomes could be more influenced by area-level socioeconomic factors, capturing broader community characteristics. To consider these distinctions, we will analyse the correlation between individual-level and area-level socioeconomic status. In cases where incongruencies arise, we will include these variables as strata to discern and appropriately address variations in the associations between socio-demographic factors and health outcomes.

We believe that having access to various variables describing both individual and area-level socioeconomic and sociodemographic and adhering to the principles of DAGs-based statistical analyses, we will be able to conduct a comprehensive analysis that appropriately addresses the intricate interplay between socio-demographic factors and health outcomes in our study.

Domínguez-Berjón, M. F., Borrell, C., Cano-Serral, G., Esnaola, S., Nolasco, A., Pasarín, M. I., Ramis, R., Saurina, C., & Escolar-Pujolar, A. (2008). Construcción de un índice de privación a partir de datos censales en grandes ciudades españolas: (Proyecto MEDEA). *Gaceta Sanitaria*, 22(3), 179–187.

INEbase / Standard of living and living conditions (CPI) /Living conditions /Household income distribution map / Results. (n.d.). INE. Retrieved 19 December 2023, from https://www.ine.es/dyngs/INEbase/en/operacion.htm?c=Estadistica_C&cid=1254736177088&menu=esultados&idp=1254735976608

San Sebastián, M., Mosquera, P. A., & Gustafsson, P. E. (2018). Whose income is more important: Mine, yours or ours? Income inequality and mental health in northern Sweden. *European Journal of Public Health*, 28(6), 1056–1061. <https://doi.org/10.1093/eurpub/cky110>

We added a new sub-section in the manuscript to describe in more detail the area-level SES variables (please see lines 195-201 of the current version of the manuscript):

2.3.2. Contextual socioeconomic variables

Neighbourhood-level socioeconomic status (SES) via three variables, namely, mean income, income distribution P80/P20, and the MEDEA deprivation index (composed by percentage of the population with manual labour, percentage of the population with casual labour, percentage of the population unemployed, percentage of the population with insufficient education, percentage of the population of young people with insufficient education) [72]. All these metrics will be obtained from the publicly available data developed by the Spanish National Institute for Statistics (INE) and expressed at the census tract level.

Domínguez-Berjón, M. F., Borrell, C., Cano-Serral, G., Esnaola, S., Nolasco, A., Pasarín, M. I., Ramis, R., Saurina, C., & Escolar-Pujolar, A. (2008). Construcción de un índice de privación a partir de datos censales en grandes ciudades españolas: (Proyecto MEDEA). *Gaceta Sanitaria*, 22(3), 179–187.

INEbase / Standard of living and living conditions (CPI) /Living conditions /Household income distribution map / Results. (n.d.). INE. Retrieved 19 December 2023, from https://www.ine.es/dyngs/INEbase/en/operacion.htm?c=Estadistica_C&cid=1254736177088&menu=esultados&idp=1254735976608

We also adjusted the information on individual-level SES variables provided in the 2.3.3 section (please see lines 203-205 of the current version of the manuscript):

To describe respondents' individual-level SES, eight variables will be selected: country of birth, marital status, household size, level of education, employment and occupational status, reported household income, and economic difficulty of the household.

Reviewer 2: Dr. Howard Frumkin, University of Washington
Comments to the Author:

R: Thank you for the opportunity to review this very interesting study protocol. The key questions for this review, of a study protocol, are whether it is “scientifically credible and ... presented in an appropriate context” ... ethically and procedurally sound.” On these points my assessment is generally “yes.” The introduction provides ample context for the study. The study is scientifically credible; the data bases to be used are solid, the numbers of subjects appear ample, the measurement methods are well established, and the shortcomings of a cross-sectional study are acknowledged in the discussion. Relevant ethical and procedural issues are well addressed, with an exception raised below.

A: We thank the reviewer for the encouraging comments.

R: That said, I offer several points for the authors’ consideration. First, the protocol might be strengthened by discussing several contextual issues in the introduction. Three relevant urban “exposures” are omitted: substandard housing, crowding, and economic inequality (as measured by, for example, the Gini index). While I understand that it is probably impossible to modify the study protocol at this point, it would be helpful to discuss the omission of these factors. Moreover, the protocol is silent on emerging issues relevant to urban health, in particular climate change (posing hazards such as heat and flooding) and climate resilience (a positive urban exposure), and in-migration from areas that will need to decant their populations due to climate change. Indeed, it can be argued that any contemporary study of urban health should consider not only the present, but the future, as climate change is rapidly transforming the realities of life in cities. I believe readers would appreciate a discussion in the introduction of how the investigators considered these various issues.

A: We sincerely appreciate and thank the reviewer for providing these thoughtful considerations for our study protocol. We fully agree with him on the relevance of contextual issues such as substandard housing, crowding, and economic inequality and we acknowledge that this aligns with the importance of a comprehensive understanding of urban exposures. However, our study relies on secondary data obtained from four independent population health surveys, where specific information on substandard housing and crowding was not collected. Unfortunately, this limitation constrains our ability to incorporate these factors into the analysis we plan to do.

As for the economic inequality, as indicated in the section 2.3.2 of the manuscript (please see lines 195 - 201 of the current version of the manuscript), our dataset includes the MEDEA index (Domínguez-Berjón et al., 2008) which effectively captures the economic inequality of neighbourhoods. The components of the MEDEA index are: percentage of the population with manual labor, percentage of the population with casual labor, percentage of the population unemployed, percentage of the population with insufficient education, percentage of the population of young people with insufficient education. Furthermore, although initially we did not include the Gini index in our analyses, following the recommendation of the reviewer and after discussing with the GIS group, we opted to include additional variables to describe the potential neighbourhood-level economic inequalities: census tract Gini index and income distribution P80/P20. This latter variable is the coefficient that results from dividing the average income value of the 80th percentile by the one of the 20th, and is an indicator of economic inequalities.

Domínguez-Berjón, M. F., Borrell, C., Cano-Serral, G., Esnaola, S., Nolasco, A., Pasarín, M. I., Ramis, R., Saurina, C., & Escolar-Pujolar, A. (2008). Construcción de un índice de privación a partir de datos censales en grandes ciudades españolas: (Proyecto MEDEA). *Gaceta Sanitaria*, 22(3), 179–187.

INEbase / Standard of living and living conditions (CPI) /Living conditions /Household income distribution map / Results. (n.d.). INE. Retrieved 19 December 2023, from https://www.ine.es/dyngs/INEbase/en/operacion.htm?c=Estadistica_C&cid=1254736177088&menu=resultados&idp=1254735976608

To reflect these new additions, we extended the description of the area-based SES indicators (please see lines 195-201 of the current version of the manuscript):

Neighbourhood-level socioeconomic status (SES) via three variables, namely, mean income, income distribution P80/P20, and the MEDEA deprivation index (composed by percentage of the population with manual labour, percentage of the population with casual labour, percentage of the population

unemployed, percentage of the population with insufficient education, percentage of the population of young people with insufficient education) [72]. All these metrics will be obtained from the publicly available data developed by the Spanish National Institute for Statistics (INE) and expressed at the census tract level.

We also see the relevance of emerging issues related to urban health, especially those related to climate change. The reviewer highlights the importance of assessing cities' resilience to climate change, including indicators such as energy efficiency in houses. We acknowledge the significance of these aspects, and we believe it is a matter that deserves further scientific inquiry. However, as mentioned before, due to the nature of our study, we lack specific information on variables related to climate change, including indicators of resilience and adaptability because they were not initially included in the Population Health Surveys we are using. Moreover, we do not have access to GIS data with the spatial resolution and quality required to comprehensively assess climate adaptation strategies in all the cities included in the study. Addressing these complex issues would require alternative study designs and data sources specifically tailored to capture the multifaceted aspects of climate change, resilience, and adaptability in urban settings.

Despite our inability to include these variables in our study, we consider that discussing its relevance is a valuable conceptual addition to our manuscript and have added some lines to the introduction (please see lines 19-25 of the current version of the manuscript) with the hope of help to delineate potential avenues for future research:

A comprehensive approach is crucial for understanding the interplay of various environmental determinants with health and well-being within urban settings. A holistic multi-exposure framework should be adopted, as outlined by Hammersen et al. [16], that extends beyond traditional considerations and incorporates critical urban contextual issues such as substandard housing, crowding, economic inequality, and the evolving challenges posed by climate change, as well as individual psychosocial factors [17,18].

Hambling, T., Weinstein, P., & Slaney, D. (2011). A Review of Frameworks for Developing Environmental Health Indicators for Climate Change and Health. *International Journal of Environmental Research and Public Health*, 8(7), 2854–2875. <https://doi.org/10.3390/ijerph8072854>

Hammersen, F., Niemann, H., & Hoebel, J. (2016). Environmental Noise Annoyance and Mental Health in Adults: Findings from the Cross-Sectional German Health Update (GEDA) Study 2012. *International Journal of Environmental Research and Public Health*, 13(10), Article 10. <https://doi.org/10.3390/ijerph13100954>

Pagani, A., Christie, D., Bourdon, V., Gago, C. W., Joost, S., Licina, D., Lerch, M., Rozenblat, C., Guessous, I., & Viganò, P. (2023). Housing, street and health: A new systemic research framework (1). *Buildings and Cities*, 4(1). <https://doi.org/10.5334/bc.298>

With a similar objective, we added the following extract to the discussion (please see lines 376-378 of the current version of the manuscript):

Moreover, future studies should not only include more variables reflecting the social capital (e.g., perceived sense of community) but also analyse the health implications of other relevant urban exposures like substandard housing, crowding, and indoor air pollution.

R: Data collection R: The discussion of exposure variables is thorough and rigorous. However, I would also raise several points for the authors' consideration:

With regard to walkability, the authors propose an index consisting of seven factors (lines 355-57). However, these factors do not include pedestrian infrastructure--the quality and completeness of sidewalks, the quality of street crossings, the presence or absence of shade over sidewalks, and so on. Here are a few recent references that explore these issues:

- Tsiompras AB, Photis YN. What matters when it comes to “Walk and the city”? Defining a weighted GIS-based walkability index. *Transportation Research Procedia*. 2017;24:523-30. doi: <https://doi.org/10.1016/j.trpro.2017.06.001>.

- Knapskog M, Hagen OH, Tennøy A, Rynning MK. Exploring ways of measuring walkability. *Transportation Research Procedia*. 2019;41:264-82. doi: <https://doi.org/10.1016/j.trpro.2019.09.047>.

- Arellana J, Saltaín M, Larrañaga AM, Alvarez V, Henao CA. Urban walkability considering pedestrians' perceptions of the built environment: a 10-year review and a case study in a medium-sized city in Latin America. *Transport Reviews*. 2020;40(2):183-203. doi: 10.1080/01441647.2019.1703842.
 - Bartzokas-Tsiompras A, Photis YN, Tsagkis P, Panagiotopoulos G. Microscale walkability indicators for fifty-nine European central urban areas: An open-access tabular dataset and a geospatial web-based platform. *Data in Brief*. 2021;36:107048. doi: <https://doi.org/10.1016/j.dib.2021.107048>.
 - Fonseca F, Ribeiro PJG, Conticelli E, Jabbari M, Papageorgiou G, Tondelli S, et al. Built environment attributes and their influence on walkability. *International Journal of Sustainable Transportation*. 2022;16(7):660-79. doi: 10.1080/15568318.2021.1914793.
 - Guzman LA, Arellana J, Castro WF. Desirable streets for pedestrians: Using a street-level index to assess walkability. *Transportation Research Part D: Transport and Environment*. 2022;111:103462. doi: <https://doi.org/10.1016/j.trd.2022.103462>
 - Metro Vancouver Walkability Index. <http://www.metrovancouver.org/metro2040/complete-communities/connected-communities/walkability-index/Pages/default.aspx>
- These references all refer to objectively measured pedestrian infrastructure. Do the available survey data permit characterization of *perceived* pedestrian infrastructure? This may be an even more important measure.

A: We appreciate the reviewer's insightful suggestion regarding the characterization of the walkability, and we would like to provide a detailed response. Regarding the construction of the objective walkability variable, we have relied on publicly available sources of information for 17 cities included in our study. While acknowledging the significance of incorporating additional significant factors in the formula (the Reviewer proposes several factors of striking importance like pedestrian infrastructure-- the quality and completeness of sidewalks, the quality of street crossings, the presence or absence of shade over sidewalks), implementing such approaches would face scalability challenges within our current project due to financial constraints and resource limitations. Our project marks a pioneering effort in utilizing data from population health surveys across diverse communities in Spain. In this initial phase, our primary focus has been on creating a large and inclusive sample, encompassing subjects from various territories. This approach, while valuable for the broad inclusivity of our study, has come with trade-offs, particularly in terms of limitations in GIS estimations. We are mindful that one limitation of our study lies in the necessity of using GIS variables available and adaptable to all urban areas included in the study, with some requiring more precise specifications than others. Therefore, these initial steps are foundational, with the expectation that, in the future, each study area can refine GIS variables to achieve more accurate estimations.

As for the perceived pedestrian infrastructure, due to the nature of our study, we cannot incorporate variables related to the perceived quality of pedestrian infrastructure. This is, as explained before, due to the fact that we are working with secondary data and the health surveys did not incorporate any measure of perceived walkability. However, given that the responsible parties of the surveys are integral members of our research project, we will share with them the need of incorporating such a variable in future population surveys.

We provided further details and made some amendments on the walkability index in the methodology section (please see lines 166-170 of the current version of the manuscript):

An overall walkability index in 100, 300 and 500 m buffers around the participants' home addresses will be calculated. This index will include of the following subindices: 1) population density (at the census tract level), 2) street density, 3) street connectivity, 4) land use Shannon Evenness Index, 5) facility richness, 6) facility density, 7) average slope, and 8) transport density [67,68].

We added the limitations discussed above in the discussion of the manuscript (please see lines 373-376 of the current version of the manuscript):

The reliance on publicly available data applicable to all study areas together with scalability challenges were major barriers to estimate street-level (or microscale) variables like bicycle and pedestrian infrastructure [111–113].

Fonseca, F., Ribeiro, P. J. G., Conticelli, E., Jabbari, M., Papageorgiou, G., Tondelli, S., & Ramos, R. A. R. (2022). Built environment attributes and their influence on walkability. *International Journal of Sustainable Transportation*, 16(7), 660–679. <https://doi.org/10.1080/15568318.2021.1914793>

Knapskog, M., Hagen, O. H., Tennøy, A., & Rynning, M. K. (2019). Exploring ways of measuring walkability. *Transportation Research Procedia*, 41, 264–282.

<https://doi.org/10.1016/j.trpro.2019.09.047>

Tsiompras, A. B., & Photis, Y. N. (2017). What matters when it comes to “Walk and the city”? Defining a weighted GIS-based walkability index. *Transportation Research Procedia*, 24, 523–530.

<https://doi.org/10.1016/j.trpro.2017.06.001>

R: Similarly, bicycle infrastructure is not addressed. This is an increasingly important determinant of travel behavior, especially in European cities.

A: Bicycle infrastructure is indeed a determinant factor of travel behaviour, particularly in European cities. Following reviewer’s suggestion we raised this issue to the GIS technicians working in the project. Once again, the absence of good quality and publicly available data for the 17 cities included in the study prevents us from calculating this variable.

We added this as a limitation in our discussion together with other micro-scale variables commented in relation to the walkability index (see the previous response) (please see lines 373-376 of the current version of the manuscript):

The reliance on publicly available data applicable to all study areas together with scalability challenges were major barriers to estimate street-level (or microscale) variables like bicycle and pedestrian infrastructure [111–113].

Fonseca, F., Ribeiro, P. J. G., Conticelli, E., Jabbari, M., Papageorgiou, G., Tondelli, S., & Ramos, R. A. R. (2022). Built environment attributes and their influence on walkability. *International Journal of Sustainable Transportation*, 16(7), 660–679. <https://doi.org/10.1080/15568318.2021.1914793>

Knapskog, M., Hagen, O. H., Tennøy, A., & Rynning, M. K. (2019). Exploring ways of measuring walkability. *Transportation Research Procedia*, 41, 264–282.

<https://doi.org/10.1016/j.trpro.2019.09.047>

Tsiompras, A. B., & Photis, Y. N. (2017). What matters when it comes to “Walk and the city”? Defining a weighted GIS-based walkability index. *Transportation Research Procedia*, 24, 523–530.

<https://doi.org/10.1016/j.trpro.2017.06.001>

R: Under environmental stressors, while ambient air pollution and noise are included, indoor air pollution is not. While this may be a difficult variable to measure on the scale of this study, it is clearly an important determinant of health in the urban environment. Would information on the cooking fuel used be a useful proxy? If not possible to incorporate this exposure, perhaps include a discussion acknowledging it as an omitted exposure?

A: We sincerely appreciate the reviewer’s insightful comment regarding the inclusion of indoor air pollution as an environmental stressor in our study as we fully acknowledge its importance. Nevertheless, we are constrained by the information available in the population health surveys that have already been conducted, and unfortunately, they did not collect any information on indoor air pollution.

We acknowledged the omission of indoor air pollution (together with other relevant urban exposures) as a limitation and emphasize its relevance for a comprehensive understanding of urban health in our discussion (please see lines 376-378 of the current version of the manuscript):

Moreover, future studies should not only include more variables reflecting the social capital (e.g., perceived sense of community) but also analyse the health implications of other relevant urban exposures like substandard housing, crowding, and indoor air pollution.

R: The measurement of mental health outcomes (lines 413-15) is unclear. Three outcomes are mentioned (anxiety, depression, and sleep disorders). Then comes the confusing sentence “These dichotomized indicators were based on the physician diagnosis or self-diagnosis...” Does that mean that either a physician diagnosis or a self-diagnosis would establish a “yes” for each of those three outcomes? If so could this be clarified? Do physician diagnosis and self-diagnosis perform similarly as indicators? Should they be considered distinct measures?

A: We recognize that in the previous version of the manuscript, the text on the common mental disorders diagnosis was equivocal and we want to express our gratitude to the reviewer for raising it up so we could amend the text. In this context, we would like to clarify that none of the questions in the health surveys gathered any information about “self-diagnosis” (i.e., meaning the person would indicate whether they consider they were suffering from certain conditions). The questions were indeed about diagnosis of mental health conditions by a health professional, the former formula was a slip.

In the revised manuscript, we have reworded the text to enhance the transparency and understandability of the measures (please see lines 237-239 of the current version of the manuscript): Participants had to indicate whether they had been diagnosed with depression, anxiety, and sleeping disorders at any time throughout the life. We then built a dichotomized (yes/no) variable for each condition.

R: The measurement of loneliness (line 437) is unclear. The text includes only a sentence fragment that says “perceived loneliness is collected with a single item.” Is it possible to say what this item is and comment on its validity?

A: The four population health surveys included in the study included a question which invited participants to report how often did they feel lonely. This variable was collected in a very similar in all of them, by means of a single item with a response scale of 1-4. In order to make this clearer to the reader, we added a sentence in the revised version of the manuscript (please see lines 259-261): Perceived loneliness is collected with a single item for participants to report about the frequency in which they feel loneliness. The variable is displayed in a 1 to 4 (1= always; 2= often; 3= sometimes; 4= never) response scale.

The inclusion of this variable in the study is interesting because it may work as a mediator of the effects of environmental exposures on mental health. However, it is true, that single items measures are less desirable than those composed by several items. The reliability of single-item measures is usually calculated with test-retest indexes that inform about their internal consistency (Allen et al., 2022). In this case, given the cross-sectional nature of the health surveys included in the study, we cannot run such analyses. In the case of validity, we will run convergent validity analyses by studying its association with the social support variable.

Allen, M.S., Iliescu, D., Greiff, S., 2022. Single Item Measures in Psychological Science: A Call to Action. *European Journal of Psychological Assessment* 38, 1–5. <https://doi.org/10.1027/1015-5759/a000699>

R: The measurement of social cohesion seems to depend on the Duke-UNC and Oslo-3 scales, which are measures of social support. Is it possible to measure perceived sense of community or related indicators of social capital? These may have considerable importance in determining urban health and quality of life.

A: We appreciate the insightful comment from the reviewer regarding the measurement of social cohesion in our study. We fully agree on the importance of including indicators related to perceived sense of community or social capital, as these factors can significantly contribute to our understanding of urban health and quality of life, and the mechanisms through which the effects of urban exposures may take place. Unfortunately, the surveys we utilized did not include specific questions related to perceived sense of community or other indicators of social capital. However, our dataset includes the variable of “perceived insecurity”, which, while conceptually different, provides valuable information on an essential aspect of neighbourhood perception. While this variable may not fully capture the nuances of social cohesion, it sheds light on an important facet of how residents perceive their neighbourhoods.

In the revised manuscript, we acknowledge the omission of variables reflecting social capital (together with other relevant urban exposures) as a limitation and emphasize its relevance for a comprehensive understanding of urban health in our discussion (please see lines 376-378 of the current version of the manuscript):

Moreover, future studies should not only include more variables reflecting the social capital (e.g., perceived sense of community) but also analyse the health implications of other relevant urban exposures like substandard housing, crowding, and indoor air pollution.

Data analysis R: The protocol does not state any hypotheses to be tested. This raises the concern that the data analysis might be a “fishing expedition,” simply looking for any associations that might emerge from the data. I defer to statisticians on this point but would the protocol be strengthened by the inclusion of some primary hypotheses that could drive the analysis? And by statistical techniques to account for multiple hypothesis testing?

A: In line with reviewer’s comment, we acknowledge the importance of clarifying our study’s guiding hypothesis. In that vein, we believe it is important to emphasise that our approach is grounded in the methodology of Directed Acyclic Graphs (DAGs). This robust methodology ensures that our analyses are not exploratory but rather hypothesis driven. DAGs provide a structured framework where, before each analysis, hypotheses are formulated based on existing literature for each exposure, outcome and potential confounders and covariates. These hypotheses are reflected in the presence (or absence) of arcs between the variables, which reflect whether we think that there is a link between variables (e.g., NO₂ -> mental health). This approach allows us to develop specific and targeted hypotheses for each analysis. With regard to the issue of multiple testing, we will resort to the use of statistical tools (e.g., Bonferroni correction) whenever needed.

In response to this suggestion, we have revised the introduction to include overarching hypotheses that guide our study (please see lines 77-90 of the current version of the manuscript):

The general hypothesis of this research project is that the urban environment directly or indirectly affects mental health and quality of life. In line with the first objective of the project, we expect significant differences in levels of exposure to urban environmental variables among the cities under study. Regarding the second objective, we expect participants with lower socio-economic status, lower educational levels, and less remunerated occupations to live in residential environments of poorer environmental quality. We expect them to live in areas with less availability of green and blue spaces, lower walkability scores, and higher levels of noise and air pollution. Finally, we expect the various environmental exposures reported in this study to be significantly associated with the various health and mental health variables studied in the project. Notably, we anticipate that air pollution and noise may have negative effects on mental health, while exposure to natural (green and blue), and more walkable spaces will show protective effects against bad mental health. Furthermore, in line with recent literature, we expect that part of these potential effects on mental health might be produced through increased physical activity and social cohesion.

R: The protocol mentions the importance of equity at several points (lines 262, 498). Yet there is no discussion, in the data analysis section or elsewhere, of how equity will be incorporated into the protocol. What analyses will be done relative to equity? What subgroups will be studied? What indicators of equity will be used?

A: We are grateful for the reviewer’s thoughtful comment, and we wholeheartedly agree on the necessity of addressing equity considerations more explicitly in our study. In response to this insightful feedback, we will augment the data analysis section to outline in detail how equity will be incorporated into our protocol. We want to emphasize that the population-based surveys we are drawing upon are designed with the primary goal of identifying vulnerable groups to ensure that public health interventions are inclusive and effective. Equity is, therefore, a central focus, and our approach aligns with this overarching objective. As part of our equity analysis, we will specifically investigate subgroups that may be disproportionately affected by urban health disparities. Examples of potential vulnerable groups that we aim to consider include but are not limited to lower-income populations, the elderly, women, and marginalized communities.

Added in methods (please see lines 300-302 of the current version of the manuscript):

Equity will be addressed performing subgroup analysis to investigate potential vulnerable groups such as lower-income populations, the elderly, women, and marginalized communities.

Patient and public involvement R: This section indicates that the public will not be involved in dissemination plans. This raises some ethical concerns. If this research will utilize data from people in

certain communities, should not these communities be informed of the research, invited to provide input as to key questions for study, and engaged in the research as appropriate, including in plans for dissemination of results?

A: We appreciate the thoughtful consideration and ethical concerns raised by the reviewer regarding public involvement in our dissemination plans. We agree on the fundamental importance of public participation in scientific research and the dissemination of results. Public engagement not only enhances the transparency of the research process but also ensures that the communities involved have a voice in shaping and benefiting from the outcomes.

Regrettably, our reliance on anonymized data from population health surveys precludes direct contact with the individuals, as privacy and ethical considerations are paramount. It is important to note that our study is constrained by the design of the population health surveys, which do not include any question about future contact with participants in the informed consent form. This means, the participants agreed to participate in the health surveys and their data used for scientific studies but not for further contact for other reasons. Despite these constraints, we want to emphasize that all project information will be made publicly available, and the results will be disseminated through articles, reports, seminars, and various outreach activities, some of them directly targeting the general population. While we regret the inability to engage with the communities directly, we remain committed to transparency and ensuring that the research findings are effectively communicated to the public. We appreciate the reviewer's ethical considerations, and we are dedicated to optimizing the dissemination process within the confines of our study's limitations.

Minor comment R: While the English in the manuscript is generally excellent, there are numerous small errors of usage, sentence structure, and grammar. I suggest a careful edit before finalizing the paper.

A: We appreciate the Reviewer's feedback. We have made a great effort to review and enhance the English in our text to ensure the manuscript reflects the necessary quality and clarity. We hope to have elevated the overall quality of English in this second version of the manuscript.

Reviewer 3: Dr. J Wu, Peking University

Comments to the Author R: This study is a cross-sectional survey and try to compare multi-regional health results and urban environment exposures. The authors had clearly defined the environmental variables related to health results. However, as there were no baselines of population health status, such as the prevalence of chronic mental disorders, health-related quality of people's life and self-perceived general and mental health, the environmental stressors to population health may distorted by the demographic structure of the cities. For example, self-perceived general and mental health status related to the age and health status of the respondents. Are those surveyed cities have the same structure of population and without migration of the people? In short, the authors should clarify the standards of sample selection and health measures. For example, is standard mortality rates of health among the cities needed for compare the UrbEE?

A: We are very thankful for reviewer's comments and suggestions that have given us the opportunity to improve our manuscript. We further discussed the standards of sample selection and clarified the baseline health measures across the study areas in section 3.A of the Supplementary file.

A recent report published by the Spanish National Health System (2020), based on a representative sample of users of said system, found that the overall prevalence of mental health problems in Spain is 27.4%. The most common general mental health issues were anxiety, depression, and sleep disorders, with a prevalence of 6.7%, 4.1%, and 5.4%, respectively. Higher prevalence of these disorders was observed in the female population, those born in Spain and with increasing age. The same report notes that in the case of anxiety and depression, a clear social gradient is observed, with both disorders being 3.4 and 2.5 times more prevalent in the population with lower income levels. In the case medication prescriptions, anxiolytics, antidepressants, and hypnotics were prescribed at rates of 34% for women and 17% for males over 40. The 2020 European Health Survey revealed no discernible territorial differences in the prevalence of chronic mental health conditions among individuals aged 15 and older in Spain. However perceived health status showed slight regional disparities, with Valencia reporting the highest percentage of "bad or very bad" health at 9.4%, followed by Andalucía (7.4%), the Basque Country (7%), and Catalonia (4.9%). However, given that the results presented in this report pertain to a timeframe predating the onset of the COVID-19 pandemic, it is anticipated that the prevalence of these conditions has risen universally among all age groups and regions (Henares et al., 2020). This increase can be attributed to escalated stress and health-related concerns stemming from the pandemic, exacerbated by associated constraints like lockdown measures and the resultant impact on mental health care services during the pandemic (Balluerka et al., 2020).

Sistema Nacional de Salud. (2020). Base de Datos Clínicos de Atención Primaria-BDCAP.

<https://cpage.mpr.gob.es/>

INEbase / Society /Health /European Survey of Health in Spain / Latest data. INE. Retrieved 20 December 2023, from

https://www.ine.es/dyns/INEbase/en/operacion.htm?c=Estadistica_C&cid=1254736176784&idp=1254735573175

Balluerka, N., Gómez, J., Hidalgo, M., Gorostiaga, A., Espada, P., Padilla, J., & Santed, M. (2020). LAS CONSECUENCIAS PSICOLÓGICAS DE LA COVID-19 Y EL CONFINAMIENTO INFORME DE INVESTIGACIÓN

In order to make this information available to readers, we have inserted a foot note in page 10:

For a summary of current prevalence of common mental disorders in Spain, please see section 3.A in the Supplementary file.

R: More, as self-perceived health and prevalence of chronic mental disorders and health-related quality of life measured different aspects of people's health, their relationships to UrbEE also have different mechanisms or pathologies. The authors should pay more epidemiological designing for this study, such as the population health measure and biases control, otherwise, the surveyed results may only show the differences of UrbEE and different prevalence of health status of people in each city, and could not explained the dose-response relationship or etiological study of environmental exposure risks to people's health.

A: We acknowledge the reviewers' insightful comments regarding the study design and the limitations inherent in a prevalence-based approach for establishing causality. We agree on the fact that our study primarily assesses relationships rather than causation. However, the questions related to chronic mental disorders span recent years, and efforts will be made to do sensitivity analysis with participants living in their residence for at least 5 years, thereby assuming a tentative temporal relationship between exposure and effect. Nevertheless, we recognize a key limitation in assuming a relatively constant urban environment exposure, without accounting for exposure variability outside the residential area.

While acknowledging the limitations inherent to cross-sectional nature of the study, we believe that our study is poised to test hypotheses that would be challenging to derive otherwise. Regarding the epidemiological design, our study relies on cross-sectional individual-level data, encompassing exposures, covariates, and outcomes. To address potential biases, we intend to employ tailored models for each exposure-outcome pair, guided by Directed Acyclic Graphs (DAGs). Sensitivity analyses will further enhance the robustness of our findings. Critical variables (e.g., individual and area-level SES, age, gender, country of origin, etc.) that have been reported to interact in the association between the exposure-outcome under study, will be used as stratifying variables to see whether the potential effects are stronger in certain populations.

We provided further details and extended on the data analysis procedure in the methodology 2.4 section (please see lines 296-302 of the current version of the manuscript):

These graphical models will guide the inclusion of relevant socio-demographic and socioeconomic variables, allowing us to account for potential confounding factors and illuminate causal relationships.

The length of time living in the same home/place will be taken into account by excluding individuals living at the same place of residence for less than one and less than five years in separate models.

Equity will be addressed performing subgroup analysis to investigate potential vulnerable groups such as lower-income populations, the elderly, women, and marginalized communities.

VERSION 2 – REVIEW

REVIEWER	J Wu Peking University, Institute of Population Research, Peking University
REVIEW RETURNED	14-Jan-2024
GENERAL COMMENTS	As this paper had discussed an important issue on environment and subject health, this topic is new and interesting to public and society development. The issues of first review on it had been well responded. There are no further issue about this paper and hope the survey could have abundant scientific research results.