Long-term exposure to residential green and blue spaces and anxiety and depression in adults: a cross-sectional study

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Abstract

Background: Although exposure to natural outdoor environments has been consistently associated with improved perceived general health, available evidence on a protective association between this exposure and specific mental health disorders such as depression and anxiety is still limited.

Objective: The aim of this study was to evaluate the effects of long-term exposure to residential green and blue spaces on anxiety and depression and intake of related medication. Additionally, we aimed to explore potential mediators and effect modifiers of this association.

Methods: The study was based on an existing adult cohort (ALFA – Alzheimer and Families) and includes 958 adult participants from Barcelona recruited in 2013-2014. For each participant residential green and blue exposure indicators [surrounding greenness (NDVI), amount of green (land-cover) and access to major green spaces and blue spaces] were generated for different buffers (100m, 300m and 500m). Participants reported their history of doctor-diagnosed anxiety and depressive disorders and intake of related medication. Logistic regression models were applied to assess the corresponding associations.

Results: Increasing surrounding greenness was associated with reduced odds of self-reported history of benzodiazepines [e.g. Odds ratio - OR (95%CI)=0.62 (0.43, 0.89) for 1-interquartile range (IQR) increase in NDVI in a 300m buffer] and access to major green spaces was associated with self-reported history of depression [OR (95%CI)=0.18 (0.06, 0.58)]. No statistically significant associations were observed with blue spaces. Air pollution (between 0.8% and 29.6%) and noise (between 2.2% and 5.3%) mediated a proportion of the associations observed, whereas physical activity and social support played a minor role.

Conclusion: Our findings suggest a potential protective role of green spaces on mental health (depression and anxiety) in adults, but further studies, especially longitudinal studies, are needed to provide further evidence of these benefits and of the mediation role of exposures like air pollution and noise.

Keywords: green spaces, blue spaces, air pollution, physical activity, social support, depression, anxiety, mental health

1. Introduction

Over the last decade a growing body of literature has provided evidence of the links between natural outdoor environments and improved health and well-being (WHO Regional Office for Europe, 2016). Proposed mechanisms of these health benefits are diverse: a main hypothesis is that the direct contact or viewing of these environments increases stress recovery and attention (restoring capacities). However, previous research also suggests that the presence of green and/or blue spaces reduces exposure to harmful environmental exposures (e.g. air pollution, noise, extreme temperatures) and may contribute to building capacities (e.g. encouraging physical activity and facilitating social cohesion) thereby providing the health benefits observed in many studies (Burkart et al., 2016; Grellier et al., 2017; Hartig et al., 2014; Markevych et al., 2017; Shanahan et al., 2015; Wolf and Robbins, 2015).

One of the main health outcomes evaluated in relation to these natural outdoor environments has been mental health, partly because of the burden that mental disorders represent in our society, particularly depression and anxiety (Alonso et al., 2004; Bloom et al., 2011; WHO, 2013), but also because of the potential of these environments to promote health, including mental health, through the different mechanisms described above. Two recent systematic reviews evaluated the existing evidence of the association between exposure to green (e.g. trees, grass, forests, parks) (Gascon et al., 2015) and blue spaces (e.g. lakes, rivers, coastal water, springs) (Gascon et al., 2017) and mental health. The first systematic review concluded that there was limited evidence for a causal relationship between residential surrounding greenness and mental health in adults, whereas the evidence was inadequate for children and the other exposure indicators evaluated (access to green spaces, quality of green spaces, and blue spaces)

(Gascon et al., 2015). The second systematic review, focusing on any blue space exposure (not only residential), also observed limited evidence of the mental health benefits of exposure to blue spaces among adults (Gascon et al., 2017). However, both systematic reviews highlighted the limited number of studies available - most of them of cross-sectional design -, the high heterogeneity in the methodologies used in each study and the few studies exploring the potential mechanisms explaining the associations (Gascon et al., 2017, 2015). Additionally, few studies specifically focused on anxiety and depression and there is a high heterogeneity among them in terms of exposure assessment to green (Araya et al., 2007; Beyer et al., 2014; de Vries et al., 2016; Duncan et al., 2013; Maas et al., 2009b; Melis et al., 2015; Mukherjee et al., 2017; Nutsford et al., 2013; Reklaitiene et al., 2014; Triguero-Mas et al., 2015; Weich et al., 2002) and blue spaces (de Vries et al., 2016; Triguero-Mas et al., 2015).

Using information from an already existing cohort, the aim of the present study was to evaluate the association between long-term exposure to residential green and blue spaces and mental health, particularly anxiety and depression and its related medication, in an adult population residing in Barcelona (Spain). Additionally, we aimed to evaluate the mediation of these associations by air pollution, noise, physical activity and social support and the effect modification by gender and education attainment.

2. Materials and methods

2.1. Study design and population

The study population used for the present cross-sectional analysis and the details of the recruitment of the original cohort, conducted between 2013 and 2014, have been described in details elsewhere (Molinuevo et al., 2016; Vert et al., 2017). Briefly,

participants come from the ALFA (ALzheimer and FAmilies) cohort, which aims to understand the natural history of the Alzheimer disease (AD) and to identify risk factors and biological indicators that could contribute to its development. Participant's inclusion criteria were (1) having normal cognition according to study definition, (2) being Spanish and/or Catalan-speaker, (3) aged between 45 and 74 years (4) agreeing with the study procedures and tests, and with the involvement of a close relative who would be implicated in the participant's functional evaluation. Exclusion criteria included (1) cognitive performance falling outside the established cut-offs, (2) having serious health conditions that could interfere with cognition, (3) severe auditory and/or visual disorder, neurodevelopment and/or psychomotor disorder, (4) brain injury, (5) suspected pattern of family history of autosomal dominant AD, (6) major active psychiatric disorders according to the Diagnostic and Statistical Manual of Mental Disorders (DSM-IV-TR) criteria (American Psychiatric Association, 2000), including schizophrenia, dementia, bipolar disorder, current general anxiety disorder or major depression. The reason to exclude subjects with active major psychiatric disorders from the baseline recruitment was because those could affect cognition and mask results regarding the development of AD, which was the main objective of the ALFA parent cohort study (Molinuevo et al., 2016). As described in Molinuevo et al. (2016), from the 3102 volunteers assessed, 2743 subjects met the selection criteria or decided to remain in the study. Out of these, 958 resided in the city of Barcelona and had reliable geocoded data to allow allocating an exposure to them based on the address of residence and were therefore included in this study (Vert et al., 2017). The local Ethics Committee approved the ALFA study, and all subjects and their accompanying close relative signed an informed consent form (Molinuevo et al., 2016).

2.2. Residential exposure to green and blue spaces assessment

We used different indicators of exposure to residential green and blue spaces.

Surrounding greenness: we used the normalized difference vegetation index (NDVI) to define surrounding greenness. The NDVI is an indicator of greenness and is based on land surface reflectance of visible (red) and near-infrared parts of the spectrum (Weier and Herring, 2000). Its values range from −1 to 1, with higher positive numbers indicating more greenness (i.e. photosynthetically active vegetation). The index was derived from the Landsat 4-5 TM data at 30 m×30 m resolution. The Landsat 5 imagery data atmospherically corrected was acquired for 26/07/2009 covering Barcelona city area. As we wanted to treat separately the effect of green and blue spaces, and as water bodies are characterized for having NDVI values below 0, we excluded water bodies from the NDVI assessment for surrounding greenness. Since we have observed that other artificial surfaces may also have negative values, we used a land use layer (Urban Atlas) to remove water bodies from the NDVI imagery by means of a "mask". Afterwards, surrounding greenness was defined based on the NDVI average within 100m, 300m, and 500m buffers around participant's residences.

Amount of green and access to green and blue spaces: we used "Map of Land Covers of Catalonia (2009)" (Centre de Recerca Ecològica i Aplicacions Forestals (CREAF), 2013), which is based on orthophotos with a minimum map unit of 500m^2 (0.5 ha). The map contains a total of 241 simple covers, which can be hierarchically grouped into different levels. To conduct this study, three green spaces categories were created: *agricultural green*, which included arboreal and herbaceous crops, *forest green*, which included sclerophyllous, deciduous and conifer forests, and *urban green*, which included artificial green areas and urban woodland. *Blue spaces* included continental

waters (natural course, lakes, natural and artificial ponds, rivers, reservoir, coastal lagoons) and beaches. Using residential address of the participants, which was reported by them at recruitment (2013-2014), we calculated the hectares of green and blue spaces using buffers typically used in previous studies (Gascon et al., 2015). Based on this information we created the following exposure variables: 1) *amount of green*, which included all the hectares of any green space type within specific buffers (buffers 100m, 300m and 500m), 2) *access to major green spaces,* defined in previous literature as having access to green spaces of at least 0.5 ha in a buffer of 300m (WHO Regional Office for Europe, 2016) – all three categories of green spaces were included - , 3) *access to blue spaces*, defined as the presence of blue spaces of any type and size represented in the map around the residential address (buffers of 100, 300m and 500m). We also created the exposure variables of amount of green and access to major green spaces by type of green space (agricultural, forest and urban green).

2.3. Outcome assessment

Self-reported personal history of anxiety and depressive disorders and history of medication use of benzodiazepines and antidepressants were recorded between 2013 and 2014 by a trained neuropsychologist using personal interviews (Molinuevo et al., 2016). Particularly, participants were asked if they, whenever in the past, 1) have had depression or anxiety diagnosed by a medical doctor and/or 2) have used medication for these disorders (benzodiazepines and antidepressants). Since exposure assessment (i.e. exposure to green and blue spaces) was assessed in 2009, we used this year as cut-off for outcome occurrence and excluded participants reporting the outcomes occurrence before 2009. We then categorized these outcome variables into two categories taking into account the temporality; 1) subjects that never reported the outcomes occurrence, 2)

subjects whose outcome started in 2009 onwards (until 2014, when personal interviews were developed). This was an approach also applied by Vert et al. in a study on air pollution – an exposure also considered in this study - and mental health that used the same study population (Vert et al., 2017). This procedure resulted in the exclusion of 52 subjects for anxiety (we had one original missing), 82 subjects for depression (we had two original missings) and 42 and 32 subjects for the intake of benzodiazepines and antidepressants, respectively. Additionally, findings from previous studies support the stability of the NDVI spatial contrast over seasons and years (Dadvand et al., 2012a, 2012b) as well as for land-cover categories (Centre de Recerca Ecològica i Aplicacions Forestals (CREAF), 2013), when considering few years of difference. As exposure was estimated in 2009, and given the small variability between few years of difference, we considered exposure to green and blue spaces measured in 2009 as long-term exposure until the time of outcome assessment (2013-2014). Figure 1 summarizes the years of assessment of each variable and the stages of the analyses.

2.4. Other variables

Socio-demographic and other covariables were collected either during the clinical interview or through on-line self-administered questionnaires answered by the participants at recruitment: age, gender, education attainment (based on years of education), marital status, living alone, work category, physical activity, smoking, sleep quality, social support, perceived social support, meditation, information on whether they were caregivers of people with AD or other chronic disease, and family history of AD or any other dementia (Table 1). Further details on the covariables and how this information was collected can be found in Table S1 of the Supplemental material. Body mass index (BMI) was obtained from the height and weight of the participants at the

time of the interview (measured by a nurse) (Molinuevo et al., 2016). Additionally, using a Land Use Regression (LUR) model we estimated individual levels of air pollution - annual average levels of nitrogen oxides (NO_2 and NO_x) and particulate matter ($PM_{2.5}$, $PM_{2.5}$ absorbance (abs), PM_{10}, and PM coarse) measured in 2009 - at the residential addresses reported by the participants (see Vert et al. (2017) and Table S2 for further details). We also used the Noise Strategic Map of Barcelona I of 2007 (Generalitat de Catalunya. Direcció General Ambiental de Qualitat, 2007) to assign to each participant the noise levels within the street they lived in. We only included the annual average day-evening-night noise level (EU indicator, Lden) indicator in the mediation analyses because it was highly correlated to other noise indicators [e.g. a 0.99 correlation with annual average noise level at night (Lnight)].

2.5. Statistical Analysis

For some of the covariables there were missing values (between the 13% and the 19.5% of the study population – see Table 1 for further details). In order to avoid loss of participants, we imputed missing values by using multiple imputation methods (Royston, 2005). The procedure of the imputation process and the variables considered are detailed in Table S3 of the Supplemental material. Briefly, we conducted multiple imputations by chained equations carrying out 100 imputations with 10 cycles for each imputation that generated 100 complete datasets. We analyzed these 100 datasets following the standard combination rules for multiple imputations.

As the outcomes were binary variables, logistic regression models were applied to study the association between indicators of green and blue spaces (one at a time) and the mental health outcomes of interest. For surrounding greenness and amount of green the

variables were introduced in the models as a 1-interquartile range (IQR) increase of NDVI and land-cover green spaces (hectares), respectively, whereas for access to green and blue spaces the variables were binary (yes/no). Variables of adjustment included were selected based on previous literature (Gascon et al., 2015): gender, age, education attainment, living alone, BMI, smoking status, sleep difficulties, and caregivers' burden.

We used the mediation analyses described by Imai et al. (medeff STATA command, with bootstrapping) to separately establish the mediation roles of air pollution, noise, perceived social support and physical activity in the association between exposure to green and blue spaces and mental health outcomes (Imai et al., 2010). For air pollution we used fixed increments for each pollutant (20 μg/m^3 for NO_x, 10 μg/m^3 for PM_{10} and NO_2, 5 μg/m^3 for $PM_{2.5}$ and PM coarse, 10^{-5}/m for $PM_{2.5}$ abs), following the same methodology as previous studies (Vert et al., 2017). Besides, we also explored whether gender and education attainment were effect modifiers of the associations observed.

Finally, we conducted several sensitivity analyses. First, covariates were reported in 2013-2014 and therefore represented the situation at that specific time (e.g. working-category). However, information collected in 2013-2014 might not represent the situation between 2009 and 2014, period in which outcomes occurred. Also, we had missing values for some of the covariates. To ensure that results were not biased due to the imputation process or because of changes in the status for some of the covariates during the study period, we conducted sensitivity analysis by using non-imputed data and also by including only gender and age in the models (crude models), two variables without missing values. Third, in order to consider changes in exposure along the period of study, we conducted another sensitivity analyses by excluding those participants that

reported moving to the residence reported in 2013-2014 after 2009. Finally, we also conducted additional analyses by including green and blue space exposure variables into one single model. Statistical analyses were performed using the statistical software STATA version 12.

3. Results

3.1. Study population characteristics

Table 1 shows the main characteristics of the study population. Briefly, participants' mean age was 56.5 years, with a higher proportion of women (63.9%) and highly educated (54.3%). Few participants were living alone (16.3%) and reported or perceived having low social support (7.7 and 12.2%, respectively). A high percentage reported to be former or current smokers (55.7% and 28.3% respectively) and 62.8% reported to be physically active. Compared to the participants excluded from this analysis, there were no major differences except on air pollution exposure levels, which were higher for those participants living in Barcelona than in other regions of Catalonia (data not shown).

One of the objectives of the present study was to evaluate the potential associations with mental health outcomes by types of green spaces (agricultural, forest and urban green). However, urban green spaces had an important weight as compared to agricultural or forest green spaces: 74.5% of the study population had access to major green spaces (any type), 74.3% had access to major urban green spaces, but only 10.8% had access to major forest green spaces and 0% to major agricultural green spaces. The pattern was similar when considering presence of any hectare of green spaces (i.e. without considering major green spaces) or amount of green (land-cover).

Participants reported less anxiety (2.3%) and depression (1.3%) than medication use of benzodiazepines (5.3%) or antidepressants (5.8%). When considering all outcomes together, the cumulative-incidence of any disorder or medication use since 2009 was of 11.7%. No major differences were observed between women and men (data not shown).

3.2. Surrounding greenness (NDVI)

We observed inverse associations between surrounding greenness and self-reported history of anxiety and depression. However, none of the associations reached statistical significance (Table 2) [e.g. 1-IQR of surrounding greenness in a 300m buffer OR (95%CI)=0.61 (0.36, 1.05) for anxiety and 0.59 (0.30, 1.20) for depression]. Besides, while increasing surrounding greenness (all buffers) was statistically significantly associated with less use of benzodiazepines [e.g. 1-IQR of surrounding greenness in a 300m buffer OR (95%CI)=0.62 (0.43, 0.89)], no associations were observed regarding antidepressants use [e.g. 1-IQR of surrounding greenness in a 300m buffer OR (95%CI)=1.06 (0.83, 1.34)] (Table 2). Finally, when combining any of the self-reported outcomes into one single combined variable, we observed an almost statistically significant reduction for each 1-IQR of surrounding greenness for all buffers evaluated [e.g. in a 300m buffer OR (95%CI)=0.82 (0.67, 1.01)] (Table 2).

3.3. Amount of green (land-cover)

Increasing amount of green in a 300m [OR (95%CI)=0.83 (0.67, 1.03)] and a 500m buffer [OR (95%CI)=0.84 (0.69, 1.04)] was almost statistically significant associated with a reduction of the odds of suffering any self-reported disorder or medication use

(Table 2). However, when evaluating each outcome separately, the confidence interval became wider (Table 2).

3.4. Access to green and blue spaces

Access to green spaces was associated with a reduction of the odds of self-reported history of depression [OR (95%CI)=0.18 (0.06, 0.58)], whereas the association almost reached statistical significance with any self-reported disorder or medication use [OR (95%CI)=0.66 (0.43, 1.03)] (Table 3). For the other outcomes the estimates were below 1 but the associations were not statistically significant. None of the indicators of access to blue spaces were statistically significantly associated with any of the outcomes assessed (Table 3). However, most estimates were below 1 in all the associations evaluated [e.g. OR (95%CI)=0.53 (0.28, 1.03) for blue spaces within a buffer of 500m and the use of benzodiazepines or OR (95%CI)=0.70 (0.46, 1.08) for any self-reported disorder or medication] (Table 3).

3.5. Mediation analyses

We evaluated whether air pollutants, noise, physical activity or social support mediated the effects observed in the main analyses. Results, presented in Table 4, showed that NO_2 mediated a 4.1% (95%CI=1.7, 31.8) of the total effect between surrounding greenness (300m buffer) and self-reported history of benzodiazepines intake, whereas $PM_{2.5}$ mediated only a 0.8% (0.3, 6.0). Noise (Lden) mediated a 2.2% (0.9, 16.8) of the total effect, but physical activity and social support only mediated a 0.6% (0.3, 5.2) and a 0.3% (0.1, 2.3) of the total effect, respectively (Table 4). Results for buffers 100m and 500m were practically the same and therefore results are not shown. Regarding the association between access to major green spaces and self-reported history of

depression, we observed that NO_2 mediated a 29.6% (12.9, 94.0) of the total effect, whereas $PM_{2.5}$ mediated a 14.0 % (6.4, 40.7). Noise (Lden) mediated a 5.3% (2.3, 17.0) of the total effect and social support only mediated a 0.6% (0.2, 2.0). The mediation analysis showed a mediation of -3.0% (-10.1, -1.3) for physical activity, results explained by the negative correlation between access to green spaces and physical activity in our study population (Table S4).

3.6. Gender and education as effect modifiers

We tested whether the association between green and blue space indicators and mental health outcomes differed by gender or by education attainment. Considering interactions with $p<0.10$, we observed that the association between access to major green spaces (300m) and depression differed by gender [males: OR (95%CI)=1.94 (0.10, 37.02), females: OR (95%CI)=0.07 (0.01, 0.37)], p-value for interaction=0.06] and the association between access to blue spaces in a 500m buffer and self-reported depression differed by education attainment [low and medium education: OR (95%CI)=3.39 (0.55, 21.00), high education: OR (95%CI)=0.23 (0.03, 2.09)], p-value for interaction=0.07].

3.7. Sensitivity analyses

None of the sensitivity analyses conducted showed significant changes of the estimates as compared to the results obtained in the main analyses. For example, the association between surrounding greenness in a 300 m buffer and use of benzodiazepines when using non-imputed data was OR (95%)=0.62 (0.43, 0.89), and when excluding participants that change their residency after 2009 it was OR (95%)=0.66 (0.42, 1.07), whereas the associations between access to major green spaces and depression were, respectively, OR (95%)=0.18 (0.05, 0.64) and OR (95%)=0.15 (0.03, 0.92) (data not

shown). Finally, including variables of green space and blue space exposure within one single model did not modify the results obtained in the main analyses (data not shown).

4. Discussion

In our study we observed associations between surrounding greenness and self-reported history of benzodiazepines, and between access to major green spaces and self-reported history of depression. Although results of the mediation analyses varied between exposures and outcomes, we observed that air pollution played a major role compared to noise, and that physical activity and perceived social support were less relevant mediators. No associations between access to blue spaces and mental health outcomes were observed.

4.1 Greenness and access to green spaces

Previous studies have reported mental health benefits of residential greenness, however, fewer have specifically focused on anxiety and depression or related medication (Gascon et al., 2015). Araya et al. reported a reduced risk of depression, but not anxiety, with increasing presence of public green areas near the residence of the participants (Araya et al., 2007). Other studies, most of them cross-sectional, observed reduced risk of depression and anxiety or treatment of these diseases with increasing greenness (Beyer et al., 2014; de Vries et al., 2016; Maas et al., 2009b; Nutsford et al., 2013; Triguero-Mas et al., 2015). However, these results were obtained for different units (Census Area Units) and buffers which mostly ranged from 1km to 3 km, except the study of Triguero-Mas et al., in which four different buffers were evaluated (100m, 300m, 500m and 1km). Other studies used other indicators, such as the percentage of canopy coverage (Beyer et al., 2014), or the number of trees and the amount of houses

with private garden in the housing area (Weich et al., 2002) – no associations were observed in this study -. Finally, a study conducted in India did find an association between increasing size of the nearest park and major depression, but not with total area of all parks in a 1 km buffer (Mukherjee et al., 2017). Although, overall, previous studies suggest beneficial effects of surrounding greenness on depression and anxiety, most of these studies evaluated much larger buffers (from 1km to 3km) than the ones used in the present study, which focused in shorter distances from the residential area (from 100m to 500m), and for which we observed similar results among them. With the current evidence it is hard to conclude which is the buffer that should be considered, both in future studies and in policies to increase greenness, and whether the effects observed for each buffer are due to different mechanisms. These are aspects that require further research.

Besides, in our study we used the definition suggested by international organizations (WHO Regional Office for Europe, 2016) to define access to major green spaces. Triguero et al. reported a reduced risk of perceived depression and/or anxiety with access to green spaces using the same definition as in the present study. However, no associations were observed with medication intake related to these health problems (Triguero-Mas et al., 2015). Another study that used a similar indicator observed a decreased risk of depression symptoms among Asians with access to recreational open spaces and parks in a 400m buffer, but an increased risk among Black people in a 800m buffer (Duncan et al., 2013). Two other studies used distance from these spaces and observed increased risk of anxiety or mood disorder treatment (Nutsford et al., 2013) and depressions symptoms (Reklaitiene et al., 2014) with increasing distance, whereas Mukherjee et al. did not observe any association between distance to the nearest park

and depression (Mukherjee et al., 2017). However, the associations observed by Reklaitiene et al. were only among park users (≥4h/week) and females. Finally, a study conducted in the city of Turin did not find evidence of an association between accessibility to green and pedestrian areas and antidepressant prescriptions (Melis et al., 2015). Although there are a few more studies on access to green spaces and general mental health, the evidence is still inadequate, mainly due to the limited number of studies and the heterogeneity in the methodology (Gascon et al., 2015). Future studies should use the definition of the WHO to facilitate comparability among studies, regardless of whether other indicators of access to green spaces are used in the respective studies.

Our results show that both indicators of exposure to green spaces - i.e. surrounding greenness and access to major green spaces - are associated with some of the outcomes evaluated. The results, though, were not consistent between both indicators; whereas surrounding greenness was associated with the use of benzodiazepines (anxiolytic), access to major green spaces was associated with self-reported history of depression. However, overall the estimates were mostly below 1 for all exposure indicators and outcomes (except for surrounding greenness and intake of antidepressants), whereas the lack of statistical significance might be, in part, due to the limited number of cases of self-reported history of depression, anxiety and use of related medication. Further studies are necessary to elucidate the weight of each green spaces indicator and their role in the urban space for the promotion of mental health, including not only the amount of green or the access (Euclidian distance) but also other aspects such as the real accessibility to these spaces, their attractiveness, perception (e.g. of safety) and actual use (Dzhambov et al., 2018; Pope et al., 2015; van den Bosch et al., 2015; Zhang et al.,

2015). Furthermore, even other characteristics of the built environment such as walkability or access to services might be also relevant for the occurrence of such mental health problems and should therefore be considered as well (Melis et al., 2015).

4.2 Blue spaces

In the present study access to blue spaces was not associated with anxiety and depression or related medication, although some associations were borderline significant. A recent review concluded that there was limited evidence of the mental health benefits of (residential and non-residential) blue spaces (Gascon et al., 2017). However, while most of the studies evaluated general mental health, only two specifically assessed anxiety and depression or intake of related medication (de Vries et al., 2016; Triguero-Mas et al., 2015). The study of Triguero-Mas et al. failed to show a significant association between residential access to blue spaces in 100 m and 300 m buffers and perceived depression or anxiety [OR (95%CI)=1.13 (0.90, 1.41)] or intake of tranquilizers and sedatives [0.85 (0.61, 1.17)] and antidepressants [0.84 (0.59, 1.19)] (Triguero-Mas et al., 2015). However, de Vries et al. reported associations between amount (%) of blue spaces within a 1km buffer and anxiety, mood disorders (which includes depression) and substance use disorder in a study including more than 6600 study subjects [e.g. association with any common mental disorder, which included the previously mentioned outcomes was OR (95%CI)=0.984 (0.974, 0.994)](de Vries et al., 2016). The limited number of studies highlights the need of more research, particularly longitudinal studies, evaluating not only the distance but also other aspects already discussed for green spaces like real accessibility, quality, or the actual use of these spaces (Gascon et al., 2017; Grellier et al., 2017).

4.3 Mediators

In the present analysis we explored the role of potential mediators of the associations observed between indicators of green spaces exposure and the mental health outcomes evaluated. We found that air pollution mediated an important proportion of the observed effects, however, this proportion varied a lot between indicators of exposure to green spaces and also between air pollutants (NO_2 and $PM_{2.5}$, from 0.8% to 29.4%). Noise (Lden) mediated a less relevant part of the total effect, between a 2.2% and a 5.3%, whereas physical activity and social support seemed to play a minor role. Results for physical activity were surprising as we observed a negative correlation between access to green spaces and physical activity, something unexpected as the hypothesis is that greater access to green spaces increases physical activity. This negative correlation, which did not occur between surrounding greenness and physical activity, explains the results obtained in the mediation analysis (-3%). In fact, previous research has observed inconsistent results about the association between green spaces availability and physical activity (Calogiuri and Chroni, 2014; Mytton et al., 2012); in this sense future studies should consider not only the availability of green spaces but other factors related to personal characteristics and environmental barriers (Calogiuri and Chroni, 2014). Besides, in the present study we decided to stick to single mediation models for each mediator, acknowledging that these mediators can be interrelated and that the effects might not be independent among them (see correlations between predictors, mediators and outcomes in Table S4). However, we think that conducting parallel or serial models (Dzhambov et al., 2018) would difficult the interpretation of the results and, secondly, we consider that we do not have enough statistical power to conduct these models and trust the results. Furthermore, we consider that the results of the mediation analyses in our study should be taken with caution given the few number of cases, particularly for

the association between access to green spaces and history of depression (only 5 cases among exposed). In this sense, studies evaluating the health effects of green spaces on mental health and general health are still inconclusive, as some report a certain mediation role of air pollution, physical activity and/or social support while others do not (Dadvand et al., 2016; de Vries et al., 2013; Maas et al., 2009a; Mukherjee et al., 2017; Sugiyama et al., 2008; Triguero-Mas et al., 2015). However, the number of studies is still limited to conclude whether the associations observed are mediated by just the viewing or the direct contact with green and/or blue spaces or whether other factors mediate the associations. Understanding the underlying mechanisms is important particularly for policy makers, as then the implementation and the promotion of these natural spaces can be better fit to the needs of the population regarding health promotion while considering other characteristics of the urban environment.

4.4 Effect modifiers

Evidence so far has not clarified whether exposure to green and blue spaces benefits certain population subgroups more than others (e.g. females, low-income groups, etc) (Gascon et al., 2015; Ruijsbroek et al., 2017). In the present study one statistically significant interaction was observed regarding gender differences; the association between access to major green spaces and self-reported history of depression was statistically significant for women but not for men. Regarding education attainment, we only observed a statistically significant interaction for the associations between access to blue spaces in a 500m buffer and self-reported depression. However, associations were not statistically significant in any of the subgroups evaluated. Although some studies suggest that natural outdoor environments may benefit women more than men (Gascon et al., 2015), results of the present analysis are inconclusive, probably due to

limitations of statistical power. Thus, further research is needed to explore potential differences between subgroups of the population.

4.3 Strengths and limitations

One of the strengths of the present study is that we evaluated different green and blue space indicators as well as buffers. Unfortunately, we could not distinguish the effects of different green space types because urban green space had a significant weight in the total amount of green space exposure and practically all participants with access to major green spaces had access to urban major green spaces as well.

Our study population was well characterized and several co-variables of adjustment were considered, as well as for the conduction of sensitivity analysis. However, the limited number of cases may have resulted in many non-statistically significant associations, although the direction of the associations was consistent between buffers and green and blue space indicators. The fact that results were statistically significant for surrounding greenness (NDVI) and not for amount of green (land-cover) might be related to the fact that NDVI has a better resolution than land-cover maps and therefore captures better the total quantity of greenness. Additionally, we feel relevant to debate whether small buffers, such as the 100m buffer, should be assessed given the resolution and the minimum mapping unit used for NDVI. However, from our experience, using 100m buffer together with a 0.5ha resolution map is still acceptable since the buffer area represents six times the resolution units from the map. Additionally, in our study the results obtained for the 100m buffer are similar to those obtained for the other two buffers used.

The restrictive inclusion and exclusion criteria also led to a study population that was not necessarily representative of the general population of Barcelona: age ranged between 44 and 74 years, more than half were highly educated, and 88% were among the qualified non-manual, professional or managerial work categories. The selection of such a population would also explain the low cumulative-incidence of anxiety and depression and related treatment among our study population as compared to the general population, since lower socioeconomic status is associated with a higher risk of suffering mental health problems (Delgadillo et al., 2015). Therefore, the results of the present study might not be representative of the general population, but we do not think that the selection criterion has an effect on the internal validity of this study, in which we considered education and work category as potential confounders. In this sense, studies trying to include more representative populations are needed in order to explore in more detail which segments of the population benefit the most of being exposed to these natural environments.

An innovative aspect of our work is that we conducted the present analysis using cumulative-incidence based on retrospective information. This approach, though, has two limitations. First, since data was collected retrospectively, there might be non-differential outcome misclassification, which might attenuate risk estimates towards the null. Second, potential exposure misclassification, as some of the participants might have moved after 2009 and therefore the exposure assigned based on the residential address in 2009 was not correct. To address this, we conducted a sensitivity analysis excluding movers after 2009, and the results showed that the direction of the associations was the same as in the main analysis. Similarly, results did not significantly change when we conducted analyses with crude models (only age and gender included)

and when using non-imputed data, which provides robustness of our results. Moreover, although we used exposures assessed in 2007 (noise) and 2009 (air pollution and green and blue spaces), these did not significantly vary throughout 2013-2014, when participants were recruited and information on the address of residence obtained (e.g. correlation for noise (Lden) was of 0.95 between 2007 and 2012). However, for physical activity and social support temporal evolution from 2009 until 2013-2014 (time of assessment of these variables) is more problematic as we do not have information on this. A final limitation is the cross-sectional character of the study, something common with most of the previous studies published so far (Gascon et al., 2015). In this sense, we plan to conduct future longitudinal studies with the follow-up data collected from this particular cohort.

Conclusions

The present study suggests a potential protective role of green spaces on mental health (depression and anxiety) in adults. Results also indicate that these associations are partly mediated by air pollution and in a lesser extent noise, whereas physical activity and social support seem to play a minor role. Also, we did not find consistent evidences that the observed benefits are particular for certain subgroups of the society. Further studies are needed to address some of the remaining questions and limitations of the research so far, including the underlying mechanisms, the potentiality of blue spaces, the inclusion of other built environment indicators, and the conduction of longitudinal studies.

Conflicts of interest

The authors declare no conflicts of interest.

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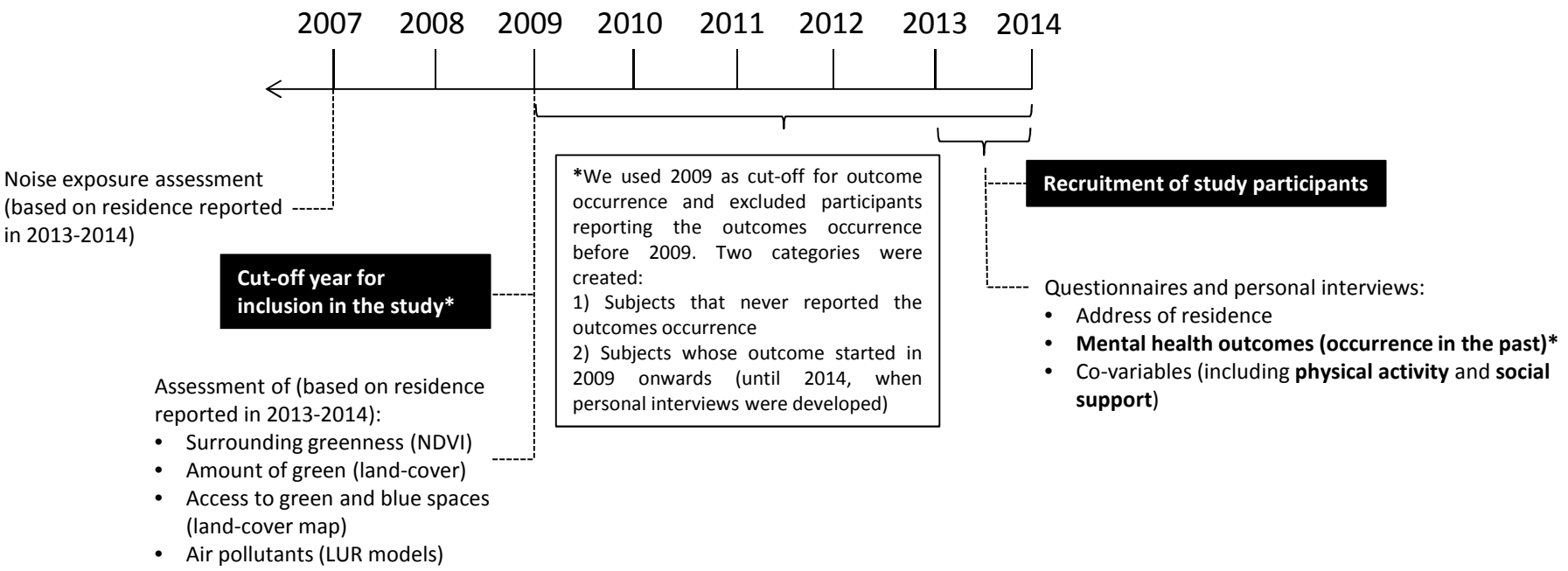
2007
2008
2009
2010
2011
2012
2013
2014
Noise exposure assessment (based on residence reported in 2013-2014)
Cut-off year for inclusion in the study*
Assessment of (based on residence reported in 2013-2014):
• Surrounding greenness (NDVI)
• Amount of green (land-cover)
• Access to green and blue spaces (land-cover map)
• Air pollutants (LUR models)
*We used 2009 as cut-off for outcome occurrence and excluded participants reporting the outcomes occurrence before 2009. Two categories were created:
1) Subjects that never reported the outcomes occurrence
2) Subjects whose outcome started in 2009 onwards (until 2014, when personal interviews were developed)
Recruitment of study participants
Questionnaires and personal interviews:
• Address of residence
• Mental health outcomes (occurrence in the past)*
• Co-variables (including physical activity and social support)

Table 1. Main characteristics of the study population (N=958)

Age [mean (min-max)]	56.5 (44-74)
Gender (%)	
Female	63.9
Male	36.1
Education attainment[a] (%)	
Low	26.2
Medium	19.5
High	54.3
Marital status (%)	
Married/Civil partnership	73.7
Single	10.4
Divorced/Separated	12.0
Widow	3.7
Others	0.2
Living alone (%)	
Yes	16.3
No	83.7
Work category (%)	
Non-qualified	3.9
Qualified manual	7.9
Qualified non-manual	35.5
Professional	42.1
Head / Boss	10.7
BMI [mean (min-max)]	26.6 (17.8-49.6)
Physical activity[b] (%)	
Active	62.8
Inactive	37.2
Smoke[b](%)	
No	16.0
Former smoker	55.7
Current smoker	28.3
Sleep difficulties[b] (%)	
No	61.4
Yes	38.6
Social support[b] (%)	
High	92.3
Low	7.7
Perceived social support[b] (%)	
High	87.8
Low	12.2
Practice meditation[b] (%)	
No	83.5
Yes	16.5
Being caregiver[b] (%)	
No	82.8
Yes	17.2
Parents with Alzheimer (%)	
No	5.2
Yes	83.1
Dementia other than AD	11.7

[a]Based on years of education

[b]These variables had missing values between the 13% and the 19.5% of the population

Table 2. Association between surrounding greenness (NDVI) and amount of green (land-cover) and self-reported history of anxiety and depression disorders and of medication use

	Surrounding greenness (NDVI)			Amount of green (land-cover map)		
	100 m (IQR=0.052)	300 m (IQR=0.044)	500 m (IQR=0.039)	100 m (IQR=2873)	300 m (IQR=24028)	500 m (IQR=64054)
Outcomes (Ncases/Ntotal study population)	**OR (95%CI)**	**OR (95%CI)**	**OR (95%CI)**	**OR (95%CI)**	**OR (95%CI)**	**OR (95%CI)**
Self-reported history of:						
Anxiety (21/905)	0.56 (0.29, 1.06)	0.61 (0.36, 1.05)	0.64 (0.40, 1.05)	0.98 (0.66, 1.46)	0.70 (0.40, 1.23)	0.79 (0.48, 1.28)
Depression (13/874)	0.54 (0.23, 1.24)	0.59 (0.30, 1.20)	0.63 (0.33, 1.18)	0.95 (0.55, 1.63)	0.47 (0.18, 1.25)	0.60 (0.27, 1.34)
Self-reported history of medication with:						
Benzodiazepines (49/916)	0.58 (0.37, 0.87)	0.62 (0.43, 0.89)	0.65 (0.47, 0.90)	0.86 (0.62, 1.18)	0.83 (0.61, 1.15)	0.88 (0.66, 1.18)
Antidepressants (54/926)	1.07 (0.81, 1.42)	1.06 (0.83, 1.34)	1.05 (0.85, 1.30)	1.13 (0.90, 1.43)	0.93 (0.72, 1.21)	0.88 (0.67, 1.16)
Any self-reported disorder or medication (112/958)	0.79 (0.62, 1.01)	0.82 (0.67, 1.01)	0.84 (0.70, 1.01)	0.96 (0.79, 1.17)	0.83 (0.67, 1.03)	0.84 (0.69, 1.04)

Models adjusted for gender, age, education, living alone, BMI, smoking status, sleep difficulties, and caregivers' burden
NDVI: normalized difference vegetation index

Table 3. Association between access to major green and blue spaces and self-reported history of anxiety and depression disorders and medication use

Outcomes (Ncases/Ntotal study population)	Access to major green spaces 300m		Access to blue spaces 300m		Access to blue spaces 500m	
	N (%) of cases among exposed[a]	OR (95%CI)	N (%) of cases among exposed[b]	OR (95%CI)	N (%) of cases among exposed[c]	OR (95%CI)
Self-reported history of:						
Anxiety (21/905)	15 (2.2)	0.95 (0.35, 2.55)	2 (1.2)	0.45 (0.10, 1.98)	6 (1.7)	0.65 (0.25, 1.73)
Depression (13/874)	5 (0.8)	0.18 (0.06, 0.58)	3 (1.8)	1.28 (0.34, 4.83)	5 (1.5)	0.99 (0.32, 3.12)
Self-reported history of medication with:						
Benzodiazepines (49/916)	35 (5.1)	0.80 (0.41, 1.53)	8 (4.7)	0.82 (0.37, 1.82)	13 (3.7)	0.53 (0.28, 1.03)
Antidepressants (54/926)	38 (5.5)	0.73 (0.39, 1.36)	10 (5.7)	0.87 (0.42, 1.80)	18 (4.9)	0.68 (0.37, 1.23)
Any self-reported disorder or medication (112/958)	76 (10.6)	0.66 (0.43, 1.03)	20 (11.2)	0.92 (0.54, 1.55)	36 (9.7)	0.70 (0.46, 1.08)

Models adjusted for gender, age, education, living alone, BMI, smoking status, sleep difficulties, and caregivers' burden

[a]828 (86.4%) study participants had access to major green spaces within a buffer of 300m

[b]178 (18.6%) study participants had access to blue spaces within a buffer of 300m

[c]370 (38.6%) study participants had access to blue spaces within a buffer of 500m

Table 4. Percentage of the total effect mediated by air pollutants, noise indicators, physical activity and social support[a].

	Surrounding greenness (NDVI) 300m[b]	Access to major green spaces 300m
	% of the total effect (95% CI)	**% of the total effect (95% CI)**
Self-reported history of depression		
Air pollutants		
NO_2	-	29.6 (12.9, 94.0)
$PM_{2.5}$	-	14.0 (6.4, 40.7)
Noise (Lden)		5.3 (2.3, 17.0)
Physical activity	-	- 3.0 (-10.2, -1.3)
Social support	-	0.6 (0.2, 2.0)
Self-reported history of medication with benzodiazepines		
Air pollutants		
NO_2	4.1 (1.7, 31.8)	-
$PM_{2.5}$	0.8 (0.3, 6.0)	-
Noise (Lden)	2.2 (0.9, 16.8)	
Physical activity	0.6 (0.3, 5.2)	-
Social support	0.3 (0.1, 2.3)	-

Lden: annual average day-evening-night noise level (EU indicator)
[a]The mediation analysis was only conducted for those statistically significant associations observed in the main analyses.
[b]Results for the other two buffers (100m and 500m) were very similar to those obtained for the 300m buffer.

Figure 1. Summary of the years of assessment of each variable and the stages of the analyses.

SUPPLEMENTARY MATERIAL

Long-term exposure to residential green and blue spaces and anxiety and depression in adults: a cross-sectional study

Contents

Table S1. Characteristics of socio-demographic and epidemiological covariates.

Variables	Categories	Observations	Reference questionnaires
Age	(continuous variable)		Ad-hoc
Gender	Male, Female		Ad-hoc
Years of education	Low (≤11 years), medium (12-14 years), or high (≥15 years).	According to the number of years of formal education attained.	Ad-hoc
Marital status	Single, married/civil partnership, divorced/separated, widow, or others.		Ad-hoc
Living alone	Yes, no.		Ad-hoc
Work category	Non-qualified, qualified manual, qualified non-manual, professional, or manager.		Ad-hoc
BMI	(continuous variable)		Ad-hoc
Physical activity	Active (if participants reported to perform >150 minutes of moderate exercise - e.g. cycling, swimming -, or >75 minutes of vigorous exercise per week - e.g. ball sports, cardio training-) or inactive (if they did not perform the abovementioned).	According to the American Heart Association.	(Elousa et al., 2000)
Smoking	Current smoker, never smokers (if participants never smoked), former smoker (if they quitted smoking at least 1 year ago).		Ad-hoc
Sleep difficulties	Yes, no (if participants answered “no” to the four variables referring to sleep difficulties).	Created from a combination of four variables asking about sleeping problems (to fall asleep, to keep sleeping during the night, to wake up too early, or to be asleep during the day) in the last 12 months, and during at least 2 weeks.	Based on Haro et al. 2006 questionnaires
Social support	Low, high.	Frequency of social support, which includes contact’s frequency with family and friends.	Ad-hoc

Perceived social support	Low, high.	Referred to how people can count on their family or friends.	Ad-hoc
Meditation	Yes, no.	Whether the participant practised meditation or not at recruitment.	Ad-hoc
Caregivers	Yes, no.	Caregivers of AD patients or any other dependent person with chronic disease. The question that was used to ask about this variable is the 1st question of the Zarit Burden Interview.	(Martin et al., 1996)
Parents with AD	Yes, no, other dementia but not AD.	The 3rd category refers to the subjects whose parents have a dementia which is not AD or not confirmed AD.	Ad-hoc

Table S2. Description of LUR models applied to estimate air pollution exposure.

	N of sampling sites	LUR models				Cross-validation	
		Model	Predictor variables	Adjusted R^2	RSME	R^2	RSME
NO_2	40	3.1646 + 0,0062563*__intinvdist1__ + 0,0001183*__hdres_300__ + 992,0893*__distinvmajor2__ + 0,0003512*__roadlenght_1000__	High density residential area within a 300m buffer, square of inverse distance to the nearest major road, inverse distance to the nearest road*traffic intensity in the nearest road, and length of roads within a 1000m buffer.	0.75	10.74	0.68	11.59
NO_x	40	32,851 + 0,0002545*__hdres_300__ + 2815,143*__distinvmajor2__ + 0,0000387*__trafload_25__	High density residential area within a 300m buffer, square of inverse distance to the nearest major road, and traffic intensity within a 25m buffer.	0.71	24.94	0.65	27.68
$PM_{2.5}$	20	16,2083 - 4,08e-06*__green_1000__ + 2,04e-07*__trafload_100__ + 0,0068219*__intinvdist2__	Green area within a 1000m buffer, traffic intensity within a 100m buffer, and square of inverse distance to the nearest road*traffic intensity in the nearest road.	0.80	1.71	0.71	2.10
$PM_{2.5-10}$	20	25,628 - 0,7276929*__sqralt__ + 4.74e-07*__trafmajorload_50__	Square root of altitude, and traffic intensity of major roads within a 50m buffer.	0.72	2.13	0.70	2.27
PM_{10}	20	38,51345 - 0,9074864*__sqralt__ + 0,0030629*__intinvdist1__ + 0,0424837*__roadlenght_25__	Square root of altitude, inverse distance to the nearest road*traffic intensity in the nearest road, and length of roads within a 25m buffer.	0.85	2.78	0.82	3.11
$PM_{2.5}$ absorbance	20	1,007372 + 7,46e-06*__hdres_300__ + 0,0026581*__intinvdist2__ + 1,11e-07*__trafload_50__	High density residential area within a 300m buffer, inverse distance to the nearest road*traffic intensity in the nearest road, and traffic intensity within a 50m buffer.	0.83	0.38	0.80	0.43

Table S3. Description of the imputation procedure.

Software used and key setting: STATA 12 software (Stata Corporation, College Station, Texas) – *ice* command (with 100 cycles)

Number of imputed datasets created: 100

- **Variables included in the imputation procedure:**
  - Exposure variables: access to green spaces (100m, 300m, 500m), area of major green spaces (100m, 300m, 500m), NDVI (100m, 300m, 500m), access to blue spaces (100m, 300m, 500m) air pollutants (NO_2, NO_x, $PM_{2.5}$, PM_{10}, PM_{25} abs, PM coarse), annual average day-evening-night noise level (Lden).
  - Other variables: age, gender, years of education, marital status, living alone, working category, BMI, smoking status, physical activity, sleep difficulties, social support, perceived social support, mediation, caregivers and parents with AD.
- **Treatment of binary/categorical variables:** logistic, ordinal, and multinomial models.

Table S4. Correlation matrix of predictors, mediators and outcomes.

	NDVI 100m	NDVI 300m	NDVI 500m	LC map 100m	LC map 300m	LC map 500m	Access GS 300m	Access BS 300m	Access BS 500m	Noise Lden	NO2	PM2.5	Physical activity	Social support	ANX	DEP	BZP	ANTI DEP	ANY OUTC
NDVI 100m	1																		
NDVI 300m	0.77	1																	
NDVI 500m	0.67	0.94	1																
LC map 100m	0.59	0.47	0.44	1															
LC map 300m	0.58	0.79	0.76	0.68	1														
LC map 500m	0.55	0.79	0.84	0.59	0.93	1													
Access GS 300m	0.48	0.77	0.75	0.60	0.97	0.93	1												
Access BS 300m	0.02	0.06	0.02	0.08	0.16	0.11	0.13	1											
Access BS 500m	0.04	0.01	-0.02	0.06	0.10	0.08	0.11	1	1										
Noise Lden	-0.18	-0.26	-0.29	-0.22	-0.33	-0.36	-0.09	-0.04	-0.07	1									
NO2	-0.37	-0.44	-0.44	-0.41	-0.55	-0.56	-0.35	-0.16	-0.18	0.58	1								
PM2.5	-0.28	-0.34	-0.38	-0.25	-0.42	-0.48	-0.16	-0.13	-0.16	0.52	0.66	1							
Physical activity	0.08	0.08	0.06	0.04	0.05	0.05	-0.07	0.15	0.00	-0.04	-0.08	-0.05	1						
Social support	0.07	0.12	0.13	-0.03	0.03	0.05	0.05	-0.04	0.00	-0.03	-0.01	-0.11	-0.13	1					
ANX	-0.21	-0.20	-0.06	-0.01	-0.12	-0.08	0.04	-0.28	-0.13	-0.02	0.08	0.04	-0.09	-0.15	1				
DEP	-0.23	-0.32	-0.29	-0.09	-0.29	-0.26	-0.42	0.08	0.03	0.12	0.32	0.28	-0.10	-0.10	0.57	1			
BZP	-0.31	-0.34	-0.29	-0.05	-0.15	-0.10	-0.11	-0.10	-0.15	0.06	0.07	0.03	-0.11	-0.15	0.41	0.30	1		
ANTIDEP	0.04	0.00	-0.02	0.09	0.00	-0.02	-0.11	0.05	0.02	0.12	-0.03	0.03	-0.14	-0.07	0.04	0.52	0.36	1	
ANY OUTC	-0.13	-0.18	-0.14	0.00	-0.10	-0.08	-0.14	-0.05	-0.07	0.08	0.05	0.05	-0.13	-0.17	1	1	1	1	1

LC map: land-cover map, GS: green spaces, BS: blue spaces, Lden: annual average day-evening-night noise level, ANX: anxiety, DEP: depression, BZP: benzodiazepines, ANTIDEP: antidepressants, ANY OUTC: any self-reported disorder or medication