Ecological Determinants of Antidepressants Prescriptions in England: Using Machine Learning for Causal Discovery

Shan Zhao[1] Sanja Šćepanović[2] Gergő Baranyi[3] Zhitong Xiong[1] Daniele Quercia,[4] Xiao Xiang Zhu[1,5]

[1] Data Science in Earth Observation, Technical University of Munich, Ottobrunn, 85521, Germany
[2] Nokia Bell Labs, Cambridge, CB3 0FA, United Kingdom
[3] Centre for Longitudinal Studies, UCL Institute of Education, University College London, WC1H 0AL, London, United Kingdom
[4] King's College London, WC2R 1LA London, United Kingdom
[5] Munich Centre for Machine Learning, 80333 Munich, Germany

Abstract

Ecological studies on depression have explored the complex associations between environmental, social, and economic factors and mental health outcomes, but they often fall short of answering causal questions, which can limit the effectiveness of the interventions. To demonstrate the potential of machine learning in uncovering the causal mechanisms behind antidepressant prescriptions, which are overwhelmingly used to treat depressive disorders, we systematically examined 28,640 small geographical areas in England, each labeled with 27 socio-demographic and environmental indicators, as well as with the total annual per capita antidepressant prescriptions. Specifically, we employed a novel approach that integrates statistical analysis, machine learning, and domain expertise. Our results highlight the pivotal roles of ethnicity, green spaces, and dense urban structure as indirect causal links shaping antidepressant prescriptions, potentially mediated by hidden variables such as cultural attitudes and the likelihood of experiencing depressive symptoms. To validate our findings, we compared them with previous research, statistical modeling of ecological data, and results obtained through querying Large Language Models about causal links. Our causal inference approach showed efficacy in determining information flow directions and unveiling subtle relationships by considering a web of causation. Specifically, the results aligned for the most part with existing research, such as the complex associations with employment and economic conditions. Moreover, the findings also brought up some connections that warrant further research with individual-level data, including different effects from tree cover versus NDVI greenery. The code is available at .

Code — https://github.com/zhu-xlab/Causal_health

1 Introduction

Mental health is defined as "a state of wellbeing in which the individual realizes his or her own abilities, can cope with the normal stresses of life, can work productively and fruitfully, and is able to make a contribution to his or her community" (World Health Organization 2004). The prevalence of mental disorders is increasing (Twenge et al. 2019; Newson, Sukhoi, and Thiagarajan 2023); it especially went up by more than 25% in the first year of the coronavirus disease (COVID-19) pandemic (World Health Organization 2022). Depressive disorders contribute significantly to the global burden of disease, with an associated economic impact estimated at 5 trillion USD (Arias, Saxena, and Verguet 2022). The causes of depression can be complex and multi-faceted, encompassing a plethora of factors relating to biological, psychological, and social determinants (Remes, Mendes, and Templeton 2021). Deepening our understanding of the disease mechanism is essential to develop effective strategies to improve population mental health. To treat depression, antidepressants are frequently prescribed. However, there is a notable disparity in the use of these medications, influenced by factors such as access to healthcare, individual and healthcare provider preferences, and the effectiveness of alternative treatments like psychotherapy (Donoghue and Tylee 1996; Mars et al. 2017). Despite these limitations, antidepressant prescribing remains indicative of the prevalence and severity of psychological conditions (Gidlow et al. 2016; Marselle et al. 2020; Baranyi et al. 2020).

Previous studies on antidepressant prescriptions in England have shown an increasing temporal trend (Heald et al. 2020) and a correlation with socioeconomic deprivation (Lalji, McGrogan, and Bailey 2021). On average, 11% of people took more than one antidepressant on any given day in England in 2018 (Heald et al. 2020). Research on the determinants of antidepressant use suggested that environmental factors can play a role, as they can contribute to or diminish psychological distress and depression. These studies have considered a wide range of exposures, including green space (Yañez et al. 2023), air pollutants (Zhang et al. 2024), and water contamination (Manczak, Miller, and Gotlib 2020). On the other hand, numerous studies and surveys reported that demographic factors and socioeconomic status play a significant role in affecting mental health (Backhouse et al. 2018; Bone, Lewis, and Lewis 2020). These studies differ in terms of the number of participants and their geographic origins. However, many of these cohort and cross-sectional studies rely on individual-level data, which is expensive to collect and may present ethical challenges.

Commonly used methods to investigate the associations between determinants and the outcome are based on statistical analysis, such as Logistic Regression (Turunen et al. 2023), Generalized Linear Model (Astell-Burt et al. 2022), and Poisson Regression (Gidlow et al. 2016). Nevertheless, their suggested associations cannot answer causal questions from the data, and these methods are limited in capturing the complex interplay among determinants. To better understand disease mechanisms and facilitate effective interventions, causal inference has come to the fore. A family of causal inference methods (Tsonis et al. 2018; Spirtes, Glymour, and Scheines 2001; Spirtes, Meek, and Richardson 2013) combining statistical and machine learning (ML) basis has been developed. Case studies in various domains such as ecosystem (Sugihara et al. 2012), geoscience (Pérez-Suay and Camps-Valls 2018), biology (Lee et al. 2023), and healthcare (Wu et al. 2022) manifest the efficacy of these methods in uncovering the causal structures among high-level semantic variables. VanderWeele, Jackson, and Li (2016) applied Marginal Structural Models to estimate the potential effects of religious service attendance on depression.

Besides, Large Language Models (LLMs), which are pretrained on extensive datasets, have gained prominence for their versatility, proving effective in applications ranging from mental health support (Sharma et al. 2023) to outperforming humans in tasks like text annotation (Gilardi, Alizadeh, and Kubli 2023), and even surpassing traditional approaches in causal reasoning (Kıcıman et al. 2023; Takayama et al. 2024; Khatibi et al. 2024). Despite these methodological advancements, the use of observational causal inference to understand the environmental effects on health (Han et al. 2025) in general and antidepressant consumption, in particular, remains largely underexplored.

This study aims to deepen our understanding of how an advanced causal method can help disentangle the diverse, interconnected factors influencing antidepressant prescriptions through a web of causation. It also seeks to compare this method with more traditional statistical methods and recently proposed LLMs for this task. Specifically, we used high-quality aggregated data in England, including 27 socio-demographic and environmental indicators. We proposed a workflow based on observational causal inference, wherein strong domain expertise knowledge is integrated to ensure the relevance and comprehensiveness of findings, followed by higher-level graph analyses. Several key findings about ethnicity, green space, and urban structures were revealed through our methods. In addition, we compared and discussed how causal questions can be addressed using different methods.

The main contributions of this work are:

- We prepared a comprehensive dataset of environmental and socio-demographic variables suitable for discovering causal relationships in public health using ML.
- We designed a causal analysis framework for public health that integrates ML, domain knowledge, and graph analysis.
- We explored the potential of LLMs as an emerging tool for causal and correlational analysis in this context.
- We uncovered several key findings related to ethnicity, green space, and urban structure, which can inform future investigations using individual-level data.

The overall structure of this paper is as follows. Section 2 introduces our causal analysis framework, including the construction of the causal graph and the subsequent graphical analysis. Section 3 describes the study data and baseline methods. Section 4 presents the main results, and Section 5 provides an in-depth discussion of the findings.

2 Methods

In causal graph theory, each node x_i represents a high-level semantic concept, while the edges delineate the presence and direction of causal relationships. Our goal is to construct a causal graph that captures how socio-demographic and environmental factors are causally linked to antidepressant prescriptions and to uncover higher-level patterns within this web of causation (Fig. 1).

2.1 Causal graph construction

In our study, we treat 27 indicators (17 socio-demographic and 10 environmental) and one outcome variable (per capita antidepressant prescriptions) (Table 1) as nodes in the causal graph. Edges are placed between nodes when a causal relationship is inferred to exist between them. One prominent method in this field is Fast Causal Inference (FCI) (Spirtes, Meek, and Richardson 2013), which is a constraint-based causal discovery approach.

However, a limitation of FCI is that it can only identify a causal graph up to its Markov equivalence class. In other words, while FCI uncovers potential causal structures, it cannot distinguish between different graphs that encode the same conditional independencies. As a result, directly applying FCI in the domain science may produce conclusions that conflict with established knowledge. To address this, we introduce a workflow to resolve the ambiguities in causal models, aiming to refine the causal inference process and gain the causal relationships that align with both empirical evidence and theoretical understanding. The steps are as follows:

1. **Skeleton detection.** Initially, each pair of nodes is presumed to be connected. We used Fisher's Z conditional independence test at the significance level of 0.05. If the test fails to reject the hypothesis of independence, the connection between those nodes is removed.
2. **Causal structure detection.** Causal graphs comprise several fundamental structures, such as chains, forks, and colliders, each exhibiting distinct behaviors in response to conditional independence tests.

   In a chain ($x_1 \to x_2 \to x_3$) or a fork ($x_2 \to x_1$, $x_2 \to x_3$), conditioning on the intermediate variable blocks the association between the other two variables; this is formalized in Eq. (1). In contrast, in an immorality structure ($x_1 \to x_2 \leftarrow x_3$), conditioning on the collider

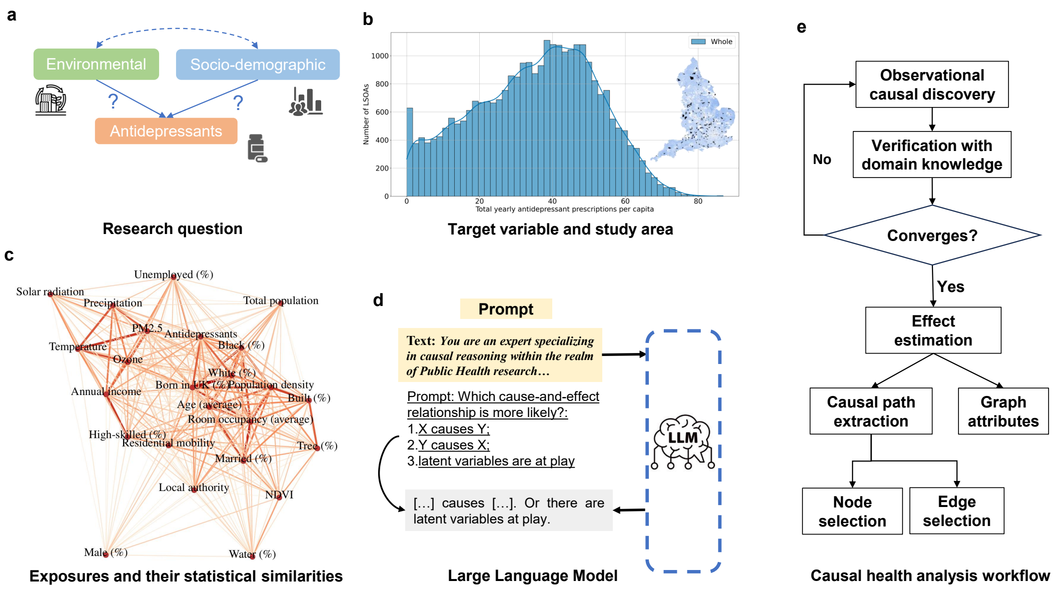

Figure 1: Graphical abstract. (a) Research question: Which socio-demographic or environmental factors are causally linked with antidepressant prescriptions? We demonstrated how causal discovery methods can answer this question. (b) Study data: We used high-quality aggregated dataset over England comprising 28,640 areas to study causal links. (c-d) Baselines: We used Spatial Lag Model and queried a Large Language Model to check the relationships among variables. (e) Method: We designed a causal discovery framework to explore the causal relationships among our variables.

variable introduces a dependence, as shown in Eq. (2). Latent (unobserved) confounders can be inferred using the “Y”-shaped primitive: both x_1 and x_3 point to x_2, which in turn points to x_4. In this configuration, x_1 and x_3 are independent of x_4 conditional on x_2, allowing us to rule out an unmeasured confounder between x_2 and x_4. More generally, potentially unobserved confounders are represented by bidirectional (“$\longleftrightarrow$”) edges between two nodes.

$$\begin{aligned} P(x_1, x_3|x_2) &= \frac{P(x_1)P(x_2|x_1)P(x_3|x_2)}{P(x_2)} \\ &= \frac{P(x_1, x_2)}{P(x_2)} P(x_3|x_2) = P(x_1|x_2)P(x_3|x_2) \\ &\iff x_1 \perp x_3 \mid x_2. \end{aligned} \tag{1}$$

$$\begin{aligned} P(x_1, x_3) &= \sum_{x_2} P(x_1, x_2, x_3) = \sum_{x_2} P(x_1)P(x_3)P(x_2|x_1, x_3) \\ &= P(x_1)P(x_3) \sum_{x_2} P(x_2|x_1, x_3) = P(x_1)P(x_3) \\ &\iff x_1 \not\perp x_3 \mid x_2. \end{aligned} \tag{2}$$

The conditional test isolates the influence of a set of variables, thereby yielding more accurate insights into how changes in one variable affect another.

3. **Orient the rest of edges.** Undirected edges are assigned with a direction without introducing any new colliders and “Y”-shaped causal structures.
4. **Prior knowledge orientation.** We refine the directionality of certain edges in our causal graph by integrating insights from well-established relationships grounded in scientific evidence. For example, the established principle from physics suggested direction from “Temperature” $\rightarrow$ “Pressure”.
5. **Inspection and Convergence.** After correcting, we repeat the process 2–4, until the graph convergence.
6. **Effect inspection.** Causal inference focuses on identifying the underlying causal structure and does not allow for direct inspection of effects. Therefore, Pearson correlations between variable pairs with identified links are additionally estimated to reflect the effect (positive or negative).

The iterative process ensures that our causal model not only aligns with empirical data but also resonates with scientifically validated principles, thereby enhancing the trustworthiness of our findings.

2.2 Graph analysis

Graph or network analysis has emerged as a rapidly evolving field, offering insights into the properties of the systems. Much of graph analysis in this domain has been based on correlation-based networks. However, they fall short in providing causal interpretations. Grounding network theory in causal networks allows us to better interpret network measures, such as understanding the direction of information flow within the system (Runge et al. 2019).

Graph measures A common network measure is the node degree, which quantifies the number of edges linked to a node. In a graph $G(N, L)$, the degree of a node i d_i is defined as the number of its neighboring nodes and $0 \leq d_i \leq N-1$.

$$d_i = \sum_j a_{i,j}, \tag{3}$$

where $a_{i,j}$ is the edge between node i and node j and the sum is over all nodes in the network. A node with larger degree typically is more influential and important, playing crucial role in the dynamics of the network and leads to potential information hub.

Graph density is a graph-level measure that quantifies the number of edges in the graph compared to a fully-connected graph. For an undirected graph, the density is computed by

$$D = \frac{2|E|}{|V|(|V|-1)}, \tag{4}$$

where $|E|$ is the number of edges and $|V|$ is the number of nodes in the graph. The graph density measures how connected the network is compared to a fully connected graph. Besides, it differentiates two networks with the same number of nodes and the same type of relationships. In the real world, a graph is usually sparse.

Community detection Community detection is a graph clustering technique used to cluster the nodes into different communities based on their connectivity and node attributes. Modularity, which measures the density of links inside communities as compared to links between communities, is used to assess the quality of graph partition. Blondel *et al.* (Blondel et al. 2008) directly used modularity as the optimization object. This method starts with assigning a graph of node N with N distinct communities, then partition the isolated node i into a community C which maximizes the gain in modularity. The gain in modularity can be computed by Eq.5

$$\Delta Q = \left[\frac{\sum_{in} + k_{i,in}}{2m} - \left(\frac{\sum_{tot} + k_i}{2m})\right)^2\right] - \left[\frac{\sum_{in}}{2m} - \left(\frac{\sum_{tot}}{2m}\right)^2 - \left(\frac{k_i}{2m}\right)^2\right], \tag{5}$$

where $\sum_{in}$ is the sum of the number of the links inside C, $\sum_{tot}$ is the sum of the number of the links incident to nodes in C, k_i is the sum of the number of the links incident to node i, $k_{i,in}$ is the sum of the number of the links from i to nodes in C and m is the sum of weights of all links in the network.

3 Experiments

3.1 Study data

We prepared a dataset with 28,640 LSOAs, each comprising 10 environmental and 17 socio-demographic variables, and one outcome variable. The outcome variable is the total annual quantity of the defined daily doses of antidepressant prescriptions per capita in 2019 (we use the terms "antidepressants" or "per capita antidepressant prescriptions" interchangeably). LSOAs are small geographic units in England (around 1,000–3,000 residents) that offer the highest available spatial detail for census data and most of the variables in this study. Their size captures neighborhood effects (Reades, De Souza, and Hubbard 2019) and allows subtle changes in population health to be detected (Zhang et al. 2022; Clarke et al. 2020). The mean ($\pm$SD) and median per capita antidepressant prescriptions across all LSOAs are 35.09$\pm$16.88 and 36.77, respectively. We started with the recently published high-quality dataset MedSat (Scepanovic et al. 2023), subsetting exposure variables pertinent to population health research and complementing it with additional sources. While aiming for a comprehensive understanding by considering as many variables as possible, it is essential to balance the computation cost. The variable selection was based on the following criteria: (1) strong impact on healthcare based on empirical evidence, (2) public health relevance, and (3) avoidance of collinearity with other factors. The detailed information on the selected variables is provided in Appendices Table 1. Categorical features were converted into a single numerical value by calculating the weighted average of all types, with each category's value serving as its weight.

3.2 Baselines

We compare our results with the following baselines:

- Correlation. The Pearson correlation coefficient r measures the linear relationship between two variables. We also performed a test of the null hypothesis that the distributions underlying the samples are uncorrelated and normally distributed. We used Fisher's transformation to compute the confidence interval of the correlation coefficient statistic for the given confidence level.
- Spatial lag model (SLM). SLM is a statistical technique used to analyze relationships between spatially distributed variables. Each observation of Y is regressed on the weighted average of neighboring observations of Y and other factors X. We used the Maximum Likelihood Estimation of SLM.
- Large Language Model. Drawing inspiration from Kıcıman et al. (2023)'s recent findings, our study aims to investigate the capability of an LLM model, agnostic in terms of our specific real-world data, to generate credible causal inferences. Additionally, we seek to evaluate how these generated inferences align with the results from our own causal modeling efforts. The detailed implementation is in Appendices 8.2.

4 Results

The complex interactions among 27 indicators were estimated using four methods, and we displayed their interactions through a graph representation. Each node in the graph corresponds to a factor. Graph links are placed between two nodes if the corresponding associations or causal relations are detected.

4.1 Causal inference among exposures and antidepressants

Our causal graph is in Fig.2, and the statistical and LLM based results are in Fig. 3. In our causal graph, many of the detected links are bidirectional, suggesting the presence of potential hidden variables. The 1-hop neighbors of antidepressants contain Black, population density, born in UK,

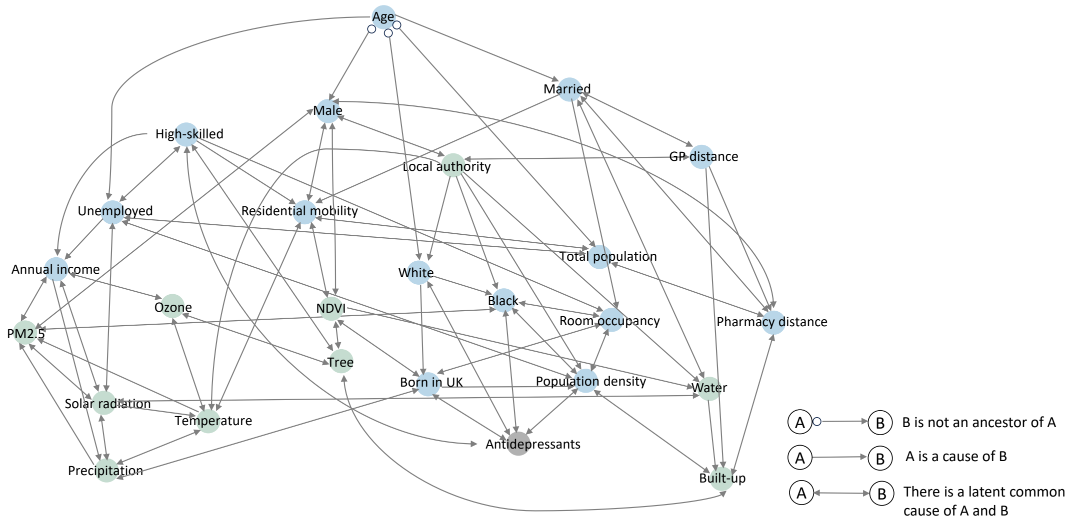

Figure 2: Causal graph discovered by our framework. Green nodes are environmental variables, blue nodes are socio-demographic variables, and grey node is the outcome. Directed edges connect causes (source nodes) to effects (destination nodes); and bi-directional edges suggest the presence of unobserved variables influencing changes on both sides. Considering ethnic variables are multi-correlated with each other, we dropped Mixed and Asian from the graph.

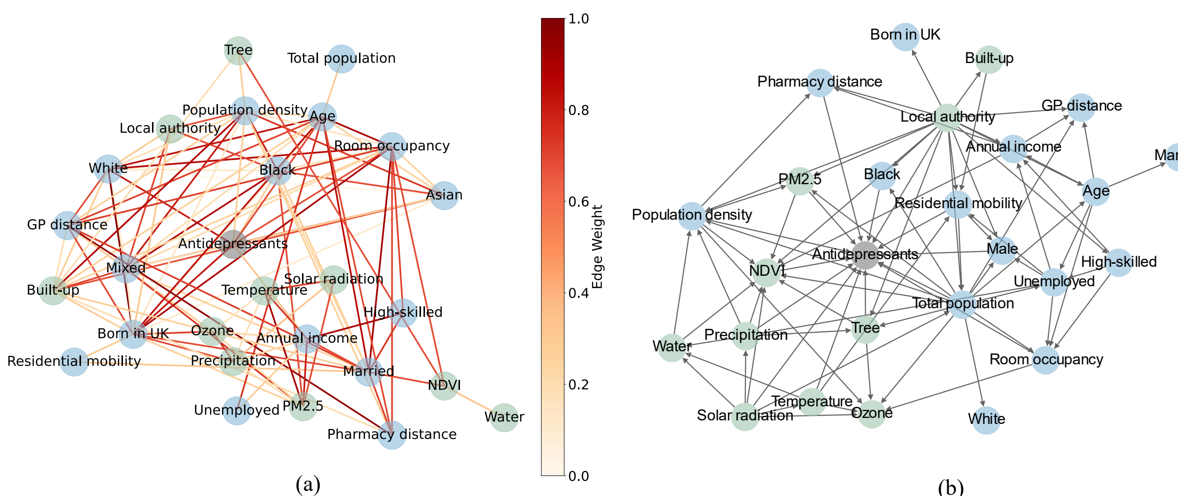

Figure 3: (a) The graph based on correlation coefficient between each pair of variables in Table 1. In total, there are 378 edges. We excluded links with very low correlation ($|r| \leq 0.3$). Edge colors indicate the strength of their correlation (normalized to [0,1]). The full correlation matrix is in Appendics Fig.6. (b) Causal links output by the LLM.

White, and high-skilled. The causal results for all these variables, except for high-skilled, align with those estimated by the LLM. While the SLM identified White, born in UK, and high-skilled to have a significant association with antidepressants, it does not include Black and population density. Nonetheless, all the 1-hop neighbors are socio-demographic factors and none of them are the direct cause of antidepressants.

In the correlation-based graph, among the 378 pairs of factors examined, 355 pairs exhibited statistically significant correlations ($P < 0.001$, Appendics Fig. 6). The SLM accounts for spatial correlations, with detailed results provided in Appendix 8.4. The LLM-based analysis identified 14 variables as potential causes of antidepressant prescriptions (e.g., pharmacy distance, residential mobility, NDVI, and population density), along with interpretative insights. The graph inferred by the LLM had a density of 0.846. Unlike the correlation-based graph and SLMs, which primarily highlighted socio-demographic factors, the LLM also suggested environmental contributions. For example, it noted that "changes in weather patterns, such as precipitation, could potentially influence mental health outcomes. Prolonged periods of rain can lead to Seasonal Affective Disorder (SAD), which in turn may increase antidepressant prescriptions.”. On the contrary, our causal graph density was 0.218, indicating sparser connectivity compared to others. This likely reflects its ability to remove spurious links (Rohrer 2018).

Given the complexity of the associations, we focused on some specific segments of the causal graph (Fig.4). These segments include antidepressants and at least one 1-hop neighboring node. We preserved the edges among the selected nodes to form causal paths, and we inferred their positive (or negative) effects based on the sign of their correlation. Local authority was identified as a cause influencing Black, White, and population density.

Antidepressants show a positive association (bidirectional) with the White and a negative association (bidirectional) with the Black (Fig. 4(a)). The Black and White populations are interdependent through both a direct link and a confounder (local authority).

NDVI was identified to be a cause of residential mobility. Specifically, there are increased relocation rates when transitioning from areas with high NDVI to those with lower NDVI (Fig. 4(b)). High-skilled was found to have a positive association with residential mobility. Different from NDVI, tree positively associates with high-skilled. Interestingly, NDVI and tree demonstrate contrasting effects on antidepressants: increased tree coverage leads to a decrease in antidepressants, while a higher NDVI results in an increase in antidepressants. While NDVI measures all types of vegetation as greenery, the tree variable specifically quantifies the extent of tree canopy. In contrast to the LLM findings, this causal graph suggests that GP distance is not a cause of antidepressants.

Both an increase in NDVI and a higher White are linked to an increase in born in UK. Additionally, both White and born in UK are positively associated (bidirectional links) with an increase in antidepressants (Fig. 4(c)). Population density exhibits a negative association with antidepressants (Fig. 4(d)).

4.2 Causal graph attributes

To understand which factors were linked causally with most other factors, we computed node degree in our causal graph. The highly influential nodes, such as population density, born in UK, and annual income, stand out (Fig.5). Most of these highly influential factors were found as directly linked with antidepressants. The average node degree of environmental factors is lower than that of socio-demographic factors.

After community detection, three classes were revealed. The computed modularity is 0.353 at the resolution of 1.5. The first class (brown) primarily comprises environmental variables, while the remaining classes are more about socio-demographic factors.

5 Discussion

For networks that are constructed from similarities, the statistical problem because of multiple comparisons can arise (Boers et al. 2019), resulting in the potential presence of spurious links. Besides, the thresholding of strong

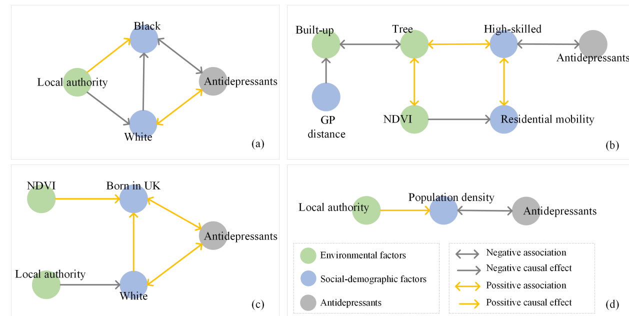

Figure 4: Four causal paths (a-d) that directly link to per capita antidepressant prescriptions in 2019. Yellow edges indicate positive effects (or associations) from the source node to the target node, whereas grey edges indicate negative effects (or associations). All 1-hop neighbors of antidepressants are socio-demographic variables, including those related to ethnicity, professions, and urban structure. Environmental variables are linked to per capita antidepressant prescriptions through socio-demographic factors.

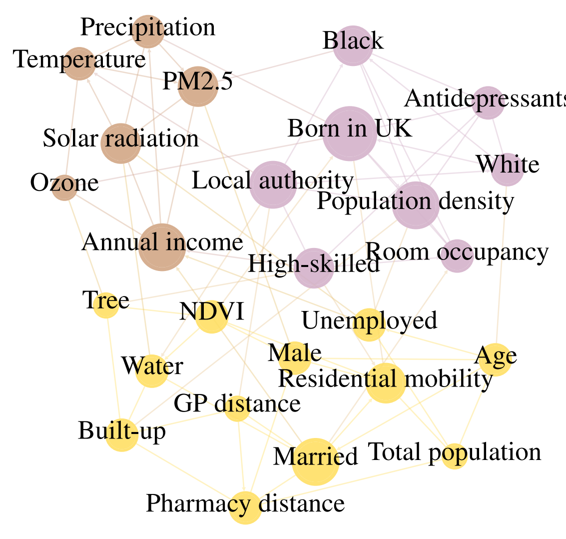

Figure 5: Analysis of the causal graph in Fig 2. Node size is proportional to its degree, indicating the level of connectivity. Node colors represent the detected communities. The top five highest-degree nodes includes born in UK, annual income, married, population density, and local authority.

or weak correlations often relies on arbitrary values. While SLM accounts for the spatial autocorrelation in geospatial data, it is limited to measuring only one dependent variable at a time and cannot capture the mutual interactions among the input variables. LLMs can estimate causal links and provide reasonable interpretations (Yu et al. 2024). Nevertheless, because it does not consider the real data, its ability to capture temporal and spatial dynamics of the specific context, i.e., England in 2019 is limited. In contrast, our causal discovery method 1) can return information flow direction (edge direction), and 2) uncovers inexplicit relationships by considering a web of causation among multiple variables. For example, from the immorality structure (Pearl and Mackenzie 2018) estimated from our method, we found that high-skilled professions and unemployment become dependent when conditioning on annual income.

Our analysis highlights several crucial factors influencing per capita antidepressant prescriptions. Firstly, we confirmed strong associations between socio-demographic factors and antidepressants, as discussed in the existing literature (Backhouse et al. 2018; Remes, Mendes, and Templeton 2021; Bone, Lewis, and Lewis 2020). The significant influence of socio-demographic factors is evident from their high node degree and presence as 1-hop neighbors of antidepressants in the causal graph. For example, employment and economic conditions are important. However, the intricate dynamics surrounding income levels and their impact on antidepressant prevalence remain complicated. Nevertheless, assuming no hidden variables, some interventions, such as enhancing local economic conditions, and providing skill-based training, could be exploited to mitigate the prevalence of antidepressants.

Besides, we uncovered that the discrepancy of antidepressant prescriptions among ethnic groups might exist. the Black population is the 1-hop neighbor of the outcome variable in both LLM and our causal graphs. Black is also found to have a negative association with antidepressant prescription quantities in the SLM. This finding aligns with the latest Adult Psychiatric Morbidity Survey in England, which reports that Black ethnic groups have particularly low mental health service use (McManus et al. 2016). However, given the bidirectional edges detected, it is unclear whether ethnicity is a direct cause of antidepressants. Unmeasured latent variables, such as cultural attitudes toward medication usage, structural discrimination (gen 2001), or the likelihood of experiencing depressive symptoms, may contribute to these associations. Recent research conducted in England during the COVID-19 pandemic suggests that individuals from ethnic minorities are not necessarily mentally healthier; rather, they are more likely to be referred to social prescribing services, which are not captured in conventional prescription data (Fu, Tang, and Yu 2024).

Other than that, environmental factors undoubtedly influence antidepressant usage, yet unraveling these associations proves challenging. For instance, we found the effect of tree cover on lower antidepressant prescriptions, and, on the contrary, of NDVI on higher prescriptions. Indeed, there is previous work finding similar beneficial associations for street trees (Marselle et al. 2020; Taylor et al. 2015), and nonintuitive detrimental associations for NDVI (Astell-Burt et al. 2022; Hyam 2020). However, the findings from previous literature are inconsistent, with some studies also linking NDVI with fewer prescriptions (Yañez et al. 2023) and others finding insignificant associations (Gidlow et al. 2016). Further study of these associations using individual-level data is necessary.

Overall, many of these findings suggest a potential link between dense urban structure and antidepressants. Areas characterized by high population density and high-skill professions, often located in large cities, tend to be associated with reduced antidepressant prescriptions. This could be attributed to the socio-cultural dynamics prevalent in urban environments. Higher population density may coincide with better access to social support (Robertson et al. 2004) and diverse treatments, potentially contributing to lower antidepressant prescriptions. Nonetheless, previous research has also shown some inconsistent findings, suggesting a positive association between urban stressful life and depressive symptoms (Kautz et al. 2020; Abela et al. 2011).

There are also several contradictory results returned by different methods, indicating the pitfalls of studying mental health using ML. For example, access to healthcare, identified by the LLM as a cause of antidepressant prescriptions, shows limited impacts in our causal graph. Instead, it is more closely related to built-up areas, which include both GP offices and pharmacies. This discrepancy likely stems from the LLM's failure to consider the specific context of our dataset, i.e., England in 2019. While in some contexts access to healthcare might be a key factor influencing prescriptions, especially in areas heavily lacking it, this is likely not the case in modern-day England. Furthermore, although the SLM identified significant positive interactions between age and antidepressant prescriptions, our causal graph does not support this finding. While old age is linked to an increased risk of depression (Lu and Peng 2019), some studies propose that human well-being follows a U-shaped trajectory throughout life (Blanchflower and Oswald 2016; Blanchflower and Bryson 2022). These nonlinear responses may result in divergent outcomes.

6 Conclusion

We linked socio-demographic and environmental factors to per capita antidepressant prescriptions using 28,640 LSOA-level areas in England for the year 2019. Given these high-quality aggregated data, we explored statistical methods (SLM and Pearson's r), ML method (LLM), and the combination of both (our framework) to uncover the complex interactions among the variables. Causal graph analyses further revealed higher-level structural properties. For each of these approaches, we analyzed their pros and cons and explored the potential causal findings they could reveal, while also discussing pitfalls in ecological public health research.

Generally, making causal inferences from a large set of potential exposures is challenging due to confounding factors, partially fulfilled assumptions, collinearity, and nonlinear interdependence. The observational causal discovery still requires verification with domain knowledge, wherein

LLM might serve as a potential resource. Our findings underscore ethnicity, green spaces, and urban density as indirect causal drivers of antidepressant prescriptions, likely mediated by latent factors such as cultural attitudes and depression risk.

Despite the findings, our approach faces some limitations. First, the current model cannot adequately handle non-linear relationships among variables. While kernel-based conditional independence tests offer a potential solution, their scalability to large datasets poses a significant challenge. Second, noisy measurements in the data can impact the accuracy of our outputs. Last, the use of aggregated data instead of individual-level data raises key concerns about ecological fallacy. Future work should incorporate individual-level data to mitigate ecological fallacy, and extend to temporal data to help address issues such as reverse causation.

7 Acknowledgements

The work is partly supported by the German Federal Ministry of Education and Research (BMBF) in the framework of the international future AI lab "AI4EO – Artificial Intelligence for Earth Observation: Reasoning, Uncertainties, Ethics and Beyond" (grant number: 01DD20001), by German Federal Ministry for Economic Affairs and Climate Action in the framework of the "national center of excellence ML4Earth" (grant number: 50EE2201C), by the Excellence Strategy of the Federal Government and the Länder through the TUM Innovation Network EarthCare and by Munich Center for Machine Learning.

References

2001. Mental health: Culture, race, and ethnicity. *A supplement to mental health: A report of the Surgeon General. Rockville, MD: US Department of Health and Human Services*.

Abela, J. R.; Stolow, D.; Mineka, S.; Yao, S.; Zhu, X. Z.; and Hankin, B. L. 2011. Cognitive vulnerability to depressive symptoms in adolescents in urban and rural Hunan, China: a multiwave longitudinal study. *Journal of Abnormal Psychology*, 120(4): 765.

Arias, D.; Saxena, S.; and Verguet, S. 2022. Quantifying the global burden of mental disorders and their economic value. *EClinicalMedicine*, 54.

Astell-Burt, T.; Navakatikyan, M.; Eckermann, S.; Hackett, M.; and Feng, X. 2022. Is urban green space associated with lower mental healthcare expenditure? *Social Science & Medicine*, 292: 114503.

Backhouse, E. V.; McHutchison, C. A.; Cvoro, V.; Shenkin, S. D.; and Wardlaw, J. M. 2018. Cognitive ability, education and socioeconomic status in childhood and risk of post-stroke depression in later life: a systematic review and meta-analysis. *PloS one*, 13(7): e0200525.

Baranyi, G.; Cherrie, M.; Curtis, S.; Dibben, C.; and Pearce, J. R. 2020. Neighborhood crime and psychotropic medications: a longitudinal data linkage study of 130,000 Scottish adults. *American Journal of Preventive Medicine*, 58(5): 638–647.

Blanchflower, D. G.; and Bryson, A. 2022. Covid and mental health in America. *Plos one*, 17(7): e0269855.

Blanchflower, D. G.; and Oswald, A. J. 2016. Antidepressants and age: A new form of evidence for U-shaped well-being through life. *Journal of Economic Behavior & Organization*, 127: 46–58.

Blondel, V. D.; Guillaume, J.-L.; Lambiotte, R.; and Lefebvre, E. 2008. Fast unfolding of communities in large networks. *Journal of statistical mechanics: theory and experiment*, 2008(10): P10008.

Boers, N.; Goswami, B.; Rheinwalt, A.; Bookhagen, B.; Hoskins, B.; and Kurths, J. 2019. Complex networks reveal global pattern of extreme-rainfall teleconnections. *Nature*, 566(7744): 373–377.

Bone, J. K.; Lewis, G.; and Lewis, G. 2020. The role of gender inequalities in adolescent depression. *The Lancet Psychiatry*, 7(6): 471–472.

Clarke, J.; Beaney, T.; Majeed, A.; Darzi, A.; and Barahona, M. 2020. Identifying naturally occurring communities of primary care providers in the English National Health Service in London. *BMJ open*, 10(7): e036504.

Donoghue, J.; and Tylee, A. 1996. The treatment of depression: prescribing patterns of antidepressants in primary care in the UK. *The British Journal of Psychiatry*, 168(2): 164–168.

Fu, Y.; Tang, E.; and Yu, G. 2024. Impact of pandemics on primary care: changes in general practitioner antidepressant prescriptions and mental health referrals during lockdowns in England, UK. *Public Health*, 236: 60–69.

Ganaie, M.; Hu, M.; Malik, A.; Tanveer, M.; and Suganthan, P. 2022. Ensemble deep learning: A review. *Engineering Applications of Artificial Intelligence*, 115: 105151.

Gidlow, C. J.; Smith, G.; Martinez, D.; Wilson, R.; Trinder, P.; Gražulevičienė, R.; and Nieuwenhuijsen, M. J. 2016. Research note: Natural environments and prescribing in England. *Landscape and Urban Planning*, 151: 103–108.

Gilardi, F.; Alizadeh, M.; and Kubli, M. 2023. ChatGPT outperforms crowd-workers for text-annotation tasks. *Proceedings of the National Academy of Sciences 120 (30)*.

Han, X.; Hu, P.; Ding, J.-E.; Lu, C.; Liu, F.; and Ning, Y. 2025. No Black Boxes: Interpretable and Interactable Predictive Healthcare with Knowledge-Enhanced Agentic Causal Discovery. *arXiv preprint arXiv:2505.16288*.

Heald, A. H.; Stedman, M.; Davies, M.; Livingston, M.; Taylor, D.; and Gadsby, R. 2020. Antidepressant prescribing in England: patterns and costs. *The Primary Care Companion for CNS Disorders*, 22(2): 26631.

Hyam, R. 2020. Greenness, mortality and mental health prescription rates in urban Scotland-a population level, observational study. *Research Ideas and Outcomes*, 6: e53542.

Kautz, M. M.; Coe, C. L.; McArthur, B. A.; Mac Giollabhui, N.; Ellman, L. M.; Abramson, L. Y.; and Alloy, L. B. 2020. Longitudinal changes of inflammatory biomarkers moderate the relationship between recent stressful life events and prospective symptoms of depression in a diverse sample of urban adolescents. *Brain, Behavior, and Immunity*, 86: 43–52.

Khatibi, E.; Abbasian, M.; Yang, Z.; Azimi, I.; and Rahmani, A. M. 2024. Alcm: Autonomous llm-augmented causal discovery framework. *arXiv preprint arXiv:2405.01744*.

Kıcıman, E.; Ness, R.; Sharma, A.; and Tan, C. 2023. Causal reasoning and Large Language Models: Opening a new frontier for causality. *arXiv preprint arXiv:2305.00050*.

Lalji, H. M.; McGrogan, A.; and Bailey, S. J. 2021. An analysis of antidepressant prescribing trends in England 2015–2019. *Journal of affective disorders reports*, 6: 100205.

Lee, J.; Jukarainen, S.; Karvanen, A.; Dixon, P.; Davies, N. M.; Smith, G. D.; Natarajan, P.; and Ganna, A. 2023. Quantifying the causal impact of biological risk factors on healthcare costs. *Nature Communications*, 14(1): 5672.

Liu, X.; Zhang, F.; Hou, Z.; Mian, L.; Wang, Z.; Zhang, J.; and Tang, J. 2023. Self-Supervised Learning: Generative or Contrastive. *IEEE Transactions on Knowledge and Data Engineering*, 35(1): 857–876.

Lu, N.; and Peng, C. 2019. Community-based structural social capital and depressive symptoms of older urban Chinese adults: The mediating role of cognitive social capital. *Archives of gerontology and geriatrics*, 82: 74–80.

Manczak, E. M.; Miller, J. G.; and Gotlib, I. H. 2020. Water contaminant levels interact with parenting environment to predict development of depressive symptoms in adolescents. *Developmental Science*, 23(1): e12838.

Mars, B.; Heron, J.; Kessler, D.; Davies, N. M.; Martin, R. M.; Thomas, K. H.; and Gunnell, D. 2017. Influences on antidepressant prescribing trends in the UK: 1995–2011. *Social psychiatry and psychiatric epidemiology*, 52: 193–200.

Marselle, M. R.; Bowler, D. E.; Watzema, J.; Eichenberg, D.; Kirsten, T.; and Bonn, A. 2020. Urban street tree biodiversity and antidepressant prescriptions. *Scientific reports*, 10(1): 22445.

McManus, S.; Bebbington, P. E.; Jenkins, R.; and Brugha, T. 2016. *Mental health and wellbeing in England: the adult psychiatric morbidity survey 2014*. NHS digital.

Newson, J.; Sukhoi, O.; and Thiagarajan, T. 2023. MHQ: Constructing an aggregate metric of mental wellbeing.

Pearl, J.; and Mackenzie, D. 2018. *The book of why: the new science of cause and effect*. Basic books.

Pérez-Suay, A.; and Camps-Valls, G. 2018. Causal inference in geoscience and remote sensing from observational data. *IEEE Transactions on Geoscience and Remote Sensing*, 57(3): 1502–1513.

Reades, J.; De Souza, J.; and Hubbard, P. 2019. Understanding urban gentrification through machine learning. *Urban Studies*, 56(5): 922–942.

Remes, O.; Mendes, J. F.; and Templeton, P. 2021. Biological, psychological, and social determinants of depression: a review of recent literature. *Brain sciences*, 11(12): 1633.

Robertson, E.; Grace, S.; Wallington, T.; and Stewart, D. E. 2004. Antenatal risk factors for postpartum depression: a synthesis of recent literature. *General hospital psychiatry*, 26(4): 289–295.

Rohrer, J. M. 2018. Thinking clearly about correlations and causation: Graphical causal models for observational data. *Advances in methods and practices in psychological science*, 1(1): 27–42.

Runge, J.; Bathiany, S.; Bollt, E.; Camps-Valls, G.; Coumou, D.; Deyle, E.; Glymour, C.; Kretschmer, M.; Mahecha, M. D.; Muñoz-Marí, J.; et al. 2019. Inferring causation from time series in Earth system sciences. *Nature communications*, 10(1): 2553.

Scepanovic, S.; Obadic, I.; Joglekar, S.; Giustarini, L.; Nattero, C.; Quercia, D.; and Zhu, X. X. 2023. MedSat: A Public Health Dataset for England Featuring Medical Prescriptions and Satellite Imagery. In *Thirty-seventh Conference on Neural Information Processing Systems Datasets and Benchmarks Track*.

Sharma, A.; Rushton, K.; Lin, I. W.; Wadden, D.; Lucas, K. G.; Miner, A. S.; Nguyen, T.; and Althoff, T. 2023. Cognitive reframing of negative thoughts through human-language model interaction. *arXiv preprint arXiv:2305.02466*.

Spirtes, P.; Glymour, C.; and Scheines, R. 2001. *Causation, Prediction, and Search*. Cambridge: MIT Press.

Spirtes, P. L.; Meek, C.; and Richardson, T. S. 2013. Causal inference in the presence of latent variables and selection bias. *arXiv preprint arXiv:1302.4983*.

Sugihara, G.; May, R.; Ye, H.; Hsieh, C.-h.; Deyle, E.; Fogarty, M.; and Munch, S. 2012. Detecting causality in complex ecosystems. *science*, 338(6106): 496–500.

Takayama, M.; Okuda, T.; Pham, T.; Ikenoue, T.; Fukuma, S.; Shimizu, S.; and Sannai, A. 2024. Integrating large language models in causal discovery: A statistical causal approach. *arXiv preprint arXiv:2402.01454*.

Taylor, M. S.; Wheeler, B. W.; White, M. P.; Economou, T.; and Osborne, N. J. 2015. Research note: Urban street tree density and antidepressant prescription rates—A cross-sectional study in London, UK. *Landscape and Urban Planning*, 136: 174–179.

Tsonis, A. A.; Deyle, E. R.; Ye, H.; and Sugihara, G. 2018. Convergent cross mapping: theory and an example. *Advances in nonlinear geosciences*, 587–600.

Turunen, A. W.; Halonen, J.; Korpela, K.; Ojala, A.; Pasanen, T.; Siponen, T.; Tiittanen, P.; Tyrväinen, L.; Yli-Tuomi, T.; and Lanki, T. 2023. Cross-sectional associations of different types of nature exposure with psychotropic, antihypertensive and asthma medication. *Occupational and environmental medicine*, 80(2): 111–118.

Twenge, J. M.; Cooper, A. B.; Joiner, T. E.; Duffy, M. E.; and Binau, S. G. 2019. Age, period, and cohort trends in mood disorder indicators and suicide-related outcomes in a nationally representative dataset, 2005–2017. *Journal of abnormal psychology*, 128(3): 185.

VanderWeele, T. J.; Jackson, J. W.; and Li, S. 2016. Causal inference and longitudinal data: a case study of religion and mental health. *Social psychiatry and psychiatric epidemiology*, 51: 1457–1466.

Wei, C.; Wang, Y. C.; Wang, B.; and Kuo, C.-C. J. 2023. An Overview on Language Models: Recent Developments and Outlook. *ArXiv*, abs/2303.05759.

World Health Organization. 2004. Promoting mental health : concepts, emerging evidence, practice : summary report / a report from the World Health Organization, Department of Mental Health and Substance Abuse in collaboration with the Victorian Health Promotion Foundation and the University of Melbourne. "An editorial summary of a report of the same title published by WHO".

World Health Organization. 2022. World mental health report: Transforming mental health for all. Executive Summary.

Wu, J. Q.; Horeweg, N.; de Bruyn, M.; Nout, R. A.; Jürgenliemk-Schulz, I. M.; Lutgens, L. C.; Jobsen, J. J.; Van der Steen-Banasik, E. M.; Nijman, H. W.; Smit, V. T.; et al. 2022. Automated causal inference in application to randomized controlled clinical trials. *Nature Machine Intelligence*, 4(5): 436–444.

Yañez, D. V.; Barboza, E. P.; Cirach, M.; Daher, C.; Nieuwenhuijsen, M.; and Mueller, N. 2023. An urban green space intervention with benefits for mental health: A health impact assessment of the Barcelona "Eixos Verds" Plan. *Environment International*, 174: 107880.

Yu, L.; Chen, D.; Xiong, S.; Wu, Q.; Liu, Q.; Li, D.; Chen, Z.; Liu, X.; and Pan, L. 2024. Improving causal reasoning in large language models: A survey. *arXiv preprint arXiv:2410.16676*.

Zhang, P.; Carleton, T.; Lin, L.; and Zhou, M. 2024. Estimating the role of air quality improvements in the decline of suicide rates in China. *Nature Sustainability*, 1–10.

Zhang, Y.; Cao, M.; Cheng, L.; Gao, X.; and De Vos, J. 2022. Exploring the temporal variations in accessibility to health services for older adults: A case study in Greater London. *Journal of Transport & Health*, 24: 101334.

8 Appendices

8.1 Socio- and environmental variables.

The data and variables used in this study are listed in Table 1.

8.2 LLM querying

Recent advances in Artificial Intelligence have given rise to LLMs, sophisticated systems built by analyzing vast datasets with trillions of textual elements through self-supervised (Liu et al. 2023) and semi-supervised learning approaches (Ganaie et al. 2022). These models create a probabilistic framework (Wei et al. 2023) capable of producing text that closely resembles human writing in both complexity and flow.

We have, specifically, adapted the prompt for the pairwise causal discovery from (Kıcıman et al. 2023) to our public health context by adding the appropriate system role. We include the statements
``[...] you are an advanced expert specializing in causal reasoning within the realm of Public Health research. [...] you are proficient in identifying, assessing, and interpreting the complex interactions among variables.'',
and describing carefully the type of variables that the system would get for our task. Specifically, we include the following explanations
``You will receive input featuring two variables pertinent to Public Health research, each representing attributes of geographically-defined areas within a country. Specifically: Socio-demographic Variables will be prefixed with "c", Environmental Variables prefixed with "e" [...], and Health Condition Variables prefixed with "o" [...]''.

The prompt instruction for the LLM is then to answer
``Which cause-and-effect relationship is more likely? If none of the relationships is likely, output N. If they are both likely, output B.''.
By applying such a prompt to each pair of our variables, we were presented with the output in the form of

"<Answer>L/R/N/B<Answer>",

where L means "changing the first variable causes a change in the second", R means "changing the second variable causes a change in the first", B means "there is a latent variable affecting both", and N means "the variables are likely unrelated".

8.3 Correlation coefficient

The Correlation coefficient among exposures and antidepressants are in Fig. 6.

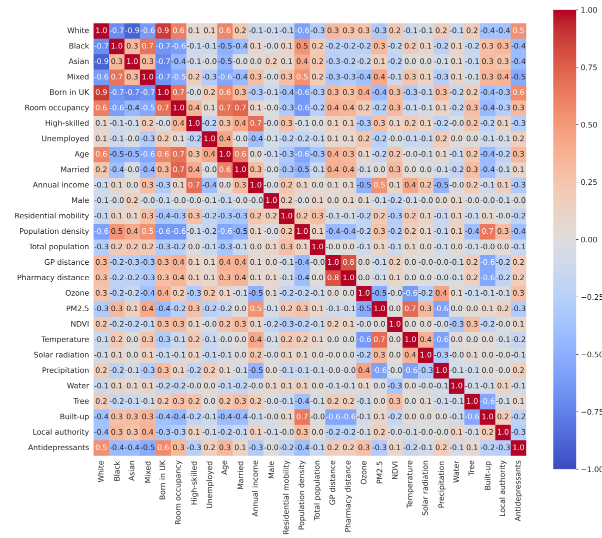

Figure 6: The correlation coefficient for each variable pair was computed using the dataset in 2019. This measure provides statistical insights between two variables. The values are in the range from -1 to +1, where ±1 indicates the strongest possible correlation and 0 indicates no correlation.

8.4 Spatial Lag Models

Considering the spatial autocorrelation present in our dataset, Pearson's correlation coefficient may overestimate the associations. Therefore, we performed the Spatial Lag Model (SLM) on antidepressants. SLM utilized all factors from Table 1 as independent variables. However, Asian and Mixed were excluded to mitigate multicollinearity among ethnic groups. The results suggest that four factors show statistically significant ($P < 0.01$) negative coefficients with antidepressants: high-skilled ($\beta = -0.4036, P = 0$), unemployed ($\beta = -0.3033, P = 0$), room occupancy ($\beta = -0.2219, P = 0.0001$), and pharmacy distance ($\beta = -0.1355, P = 0.0013$). Conversely, four factors show statistically significant ($P < 0.01$) positive coefficients with antidepressants: age ($\beta = 0.3816, P = 0$), White ($\beta = 0.3614, P = 0$), born in UK ($\beta = 0.3542, P = 0$), and local authority ($\beta = 0.0842, P = 0.0094$) (Appendices Table.2).

Type	Category	Variable[source]	Explanation
socio-demographic	Ethnicity	Asian[a]	Percentage of Asian ethnicity
		Black[a]	Percentage of Black ethnicity
		Mixed[a]	Percentage of Mixed ethnicity
		White[a]	Percentage of White ethnicity
	Migration indicator	Born in UK[a]	Percentage born in UK
		Residential mobility[b]	Percentage of people who relocated to this area
	Room occupancy	Room occupancy[a]	Average percentage of occupancy rating rooms. A higher value suggests that the rooms are over-occupied, while a lower value indicates that the rooms are under-occupied.
	Professions	High-skilled[a]	Percentage of high-skilled jobs (managers, directors, senior officials, professional and technical occupations)
	Unemployment	Unemployed[a]	Percentage of unemployed
	Age	Age[a]	Average age of residents in the designated area
	Marital status	Married[a]	Percentage of married
	Net income	Average income[a]	Average net annual income
	Gender	Male[a]	Percentage of male
	Population	Population density[a]	Population density
		Total population[a]	Total population
	Medical access	GP distance[c]	Distance to the nearest general practitioner (GP)
		Pharmacy distance[c]	Distance to the nearest pharmacy
Environmental	Climate	Solar radiation[a]	Surface solar radiation downwards is the amount of solar radiation (sunlight) that is incident on the Earth's surface.
		Precipitation[a]	Amount of precipitation that has fallen over a specified area during a given time period.
		Temperature[a]	Air temperature at a height of 2 meters above the ground
	Air quality	Ozone[a]	Ozone concentration
		$PM_{2.5}$[a]	Particulate matter with a diameter less than 2.5 micrometers
	Greenery	NDVI[a]	Normalized difference vegetation index
	Land cover	Water[a]	Percentage of water area
		Trees[a]	Percentage of tree area
		Built-up[a]	Percentage of urban areas that are characterized by a high concentration of buildings, infrastructure, and human-made features
	Geography	Local authority[d]	371 local government areas responsible for services such as education, transportation, planning applications, and waste collection and disposal
	Outcome	(per capita) antidepressants[a]	The total annual quantity of antidepressant prescriptions per capita

Table 1: Socio-demographic, environmental factors, and outcome variable used in this study. The environmental variable metrics represent average annual levels within the specified areas. The data are from multiple sources, including a. MedSat dataset, b. Access to Healthy Assets & Hazards (AHAH) dataset, c. CDRC Residential Mobility and Deprivation (RMD) Index (LSOA Geography) dataset, and d. Lower Tier Local Authorities to Inner and Outer London Lookup Table for England.

Variable	Coefficient	Std.Error	z-Statistic	Probability
Black	-0.0279	0.0402	-0.6945	0.4874
White	0.3614	0.0759	4.7582	**0.0000**
Born in UK	0.3542	0.0721	4.9111	**0.0000**
Residential mobility	-0.0458	0.0354	-1.2960	0.1950
Room occupancy	-0.2219	0.0570	-3.8912	**0.0001**
High-skilled	-0.4036	0.0449	-8.9878	**0.0000**
Unemployed	-0.3033	0.0367	-8.2622	**0.0000**
Age	0.3816	0.0554	6.8900	**0.0000**
Married	-0.0218	0.0579	-0.3774	0.7059
Average income	-0.0795	0.0453	-1.7567	0.0790
Male	0.0324	0.0269	1.2049	0.2282
Population density	0.0437	0.0432	1.0116	0.3117
Total population	-0.0679	0.0284	-2.3887	0.0169
GP distance	-0.0183	0.0428	-0.4278	0.6688
Pharmacy distance	-0.1355	0.0422	-3.2077	**0.0013**
Solar radiation	-0.0303	0.0273	-1.1115	0.2663
Precipitation	-0.0801	0.0344	-2.3289	0.0199
Temperature	0.0214	0.0437	0.4903	0.6239
Ozone	0.0029	0.0362	0.0791	0.9369
$PM_{2.5}$	0.0467	0.0419	1.1146	0.2650
NDVI	-0.0382	0.0297	-1.2861	0.1984
Water	-0.0177	0.0286	-0.6174	0.5370
Trees	0.0160	0.0335	0.4766	0.6336
Built-up	-0.0982	0.0452	2.1740	0.0297
Local authority	0.0842	0.0299	2.8148	**0.0049**
Antidepressants	0.9502	0.0016	592.8623	**0.0000**

Table 2: SLM results using the dataset in 2019. The dependent variable is antidepressants. Probability less than 0.01 is considered significant, as highlighted by the bold text.