The publication of the European Journal of Geography (EIG) is based on the European Association of Geographers' goal to make European Geography a worldwide reference and standard. Thus, the scope of the EIG is to publish original and innovative papers that will substantially improve, in a theoretical, conceptual, or empirical way the quality of research, learning, teaching, and applying geography, as well as in promoting the significance of geography as a discipline. Submissions are encouraged to have a European dimension. The European Journal of Geography is a peer-reviewed open access journal and is published quarterly.

Received: 17/09/2024
Revised: 22/11/2024
Accepted: 06/12/2024
Published: 07/12/2024

#### Academic Editor:

Dr. Alexandros Bartzokas-Tsiompras

**DOI:** 10.48088/ejg.a.fak.15.4.271.280

ISSN: 1792-1341



Copyright: © 2024 by the authors. Licensee European Association of Geographers (EUROGEO). This article is an open access article distributed under the terms and conditions of the Creative Commons Attribution (CC BY) license.



#### Research Article

# Exploring Spatiotemporal Patterns of Cardiovascular Disease in Greece: Insights from the ATTICA Study (2002-2022)

- <sup>1</sup> Department of Geography, School of Environment, Geography and Applied Economics, Harokopio University, Athens, Greece;
- <sup>2</sup> Department of Nutrition and Dietetics, School of Health Science and Education, Harokopio University, Athens, Greece;
- <sup>3</sup> First Cardiology Clinic, Medical School, National and Kapodistrian University of Athens, Hippokration Hospital, Athens, Greece;
- <sup>4</sup> Department of Internal Medicine, Medical School, University of Joannina, Joannina, Greece:
- <sup>5</sup> First Department of Propaedeutic Internal Medicine, Medical School, Laiko General Hospital, National and Kapodistrian University of Athens, Athens, Greece;

☑ Correspondence: afaka@hua.gr

**Abstract:** The objective of this study was to investigate spatiotemporal variability of cardiovascular disease (CVD) occurrence and identify spatial clusters on Attica region (Greece), over a 20-year period (2002-2022). The 10- and 20-year occurrence of fatal and non-fatal cardiovascular disease was obtained from the ATTICA study, which was conducted between 2002 and 2022. The sample used in this analysis included 1,935 (49,8% males) and 1,902 participants (49.5% males), respectively. CVD occurrence rate at the municipality level were mapped, and spatial autocorrelation analysis was performed to identify statistically significant clusters and outliers in the Attica region. The mapping of CVD occurrence rates revealed an observable increase in most municipalities during the observation period. In addition, a statistically significant clustering of high CVD occurrence rates was found in the most urbanized municipalities of the study area over the period under study. These findings underscore the need for targeted interventions, focusing on urban populations, to effectively address this trend.

Keywords: cardiovascular disease; spatial epidemiology; spatial autocorrelation; spatial clustering; Attica; Greece

#### Highlights:

- This study addresses the research gap on CVD trends in Attica, Greece, over 20 years.
- CVD rates rose notably in the most urbanized municipalities of central Athens, while suburban areas maintained lower levels.
- ullet Positive spatial autocorrelation analysis was revealed for both the 10-year and 20-year CVD occurrence rates.

#### 1. Introduction

Recent international reports show that cardiovascular disease (CVD) is the leading cause of morbidity and mortality worldwide. It is responsible for about 30% of all deaths, with large spatial and local variations (Timmis et al., 2022). This figure underlines the urgent need for a deeper understanding of the causes of cardiovascular disease and the implementation of more effective preventive measures. Furthermore, the epidemiology of cardiovascular disease is not fully explained, as a significant proportion of cases occur in the absence of identifiable risk factors (Roth et al., 2020). Many studies have reported that the prevalence of CVD varies across geographical regions and living environments (Ferrari et al., 2015; Zhang et al., 2020). This variability highlights the impact of socio-environmental factors on CVD prevalence. Geographic disparities in CVD prevalence may be attributed to lifestyle habits, dietary pattern, and access to healthcare resources. The impact of living environments, including urban versus rural settings, such as air pollution and green areas coverage, further contributes to the heterogeneous distribution of CVD burden worldwide (Dehbi et al., 2016; Liu et al., 2022).

Spatial analysis contributes to the investigation of the spatial variability of diseases, offering useful information for their distribution patterns (Doukissas et al., 2018; Ferreira & Ferreira, 2019; Smallman-Raynor et al., 2022a; Smallman-Raynor et al., 2022b; Wieland, 2020). Geographic Information Systems (GIS) and spatial statistical methods, facilitate the identification of spatial patterns of diseases across geographical areas (Gavalas, 2018; Mena et al., 2018; Wieland, 2022). These methods allow the identification of high-risk areas and the exploration of potential environmental or socioeconomic factors contributing to disease incidence (Weimann et al., 2016; Yeh et al., 2020). Several studies worldwide have explored the geographical distribution of various communicable and non-communicable diseases in order to identify spatial patterns (Faka



et al., 2023; Frings et al., 2018; Jaber et al., 2022; Yang et al., 2018; Zhang et al., 2019), as such findings are acknowledged for their utility in effective disease management, prevention, treatment, and improving health outcomes.

Spatial analysis and spatial statistics methods have been employed to examine the burden of CVD. For instance, Rajabi et al. (2018), explored the spatial patterns of CVD in Sweden by implementing spatial autocorrelation analysis. Their aim was to identify spatial clusters of high and low CVD occurrence rates across the entire country. Similarly, Jordan et al. (2024) employed spatial autocorrelation indexes to detect hot and cold spots of CVD occurrence using data from a Swiss population-based cohort in the city of Lausanne. CVD spatial patterns have been investigated using similar spatial analysis methodologies worldwide, including studies in Turkey (Sener & Türk, 2021), Mexico (Baptista, 2024), China (Ren et al., 2019), and studies on a global scale (Baptista & Queiroz, 2022). These studies highlight the utility of spatial analysis in understanding the geographic distribution and clustering of CVD.

CVDs continue to be the leading cause of mortality and morbidity in Greece, despite the advancements made over the past decades in primary prevention, but even more consistently in secondary prevention (Michas et al., 2019). Many epidemiologic researches have explored the prevalence of CVD and its associated risk factors in Greece. However, few studies have examined the spatial variability of CVD rates (Tsiampalis et al., 2023), and only one brief report has investigated the spatial patterns of CVD (Faka et al., 2023).

To address this research gap, the aim of this study was to investigate the geographical distribution and spatiotemporal trends of CVD occurrence in the Attica region of Greece over a 20-year surveillance period from 2002 to 2022. By analyzing the spatial distribution of CVD burden over the years, regions with increased risk should be identified.

#### 2. Materials & Methods

#### 2.1. Data

The data used in this study were from the ATTICA cohort study, a health and nutrition prospective study. Initiated in 2001–2002, the study employed an age-sex representative population-based sampling scheme covering 58 municipalities in Attica region of Greece, including the metropolitan area of Athens (Pitsavos et al., 2003). The sampling was random and stratified according to the age-, sex-distribution of the referent population (census 2001), which represents the 35% of the total Greek population (and the 76% of the total urban population in Greece) (Fig. 1). Over a period of 20 years (2002-2022), the study conducted three follow-up examination surveys of the participants, in 2006, 2012, and 2022, respectively (Damigou et al., 2023; Panagiotakos et al., 2008; Panagiotakos et al., 2015). Specifically, a sample of 3,042 individuals without cardiovascular disease or other chronic diseases (as ascertained by the physicians of the study), out of the 4,056 individuals that were initially invited to participate, agreed to participate at baseline examination (75% participation rate). Of them, 1,514 (49.8%) were male [mean age=46 (SD=13) years old] and 1,528 (50.2%) were female [mean age = 45 (SD = 14) years old]. This sample was monitored throughout the follow-up examinations in 2006, 2012, and 2022, with some participants lost to follow-up. In particular, over the course of the 10-year follow-up (2002-2012), 2,020 of the participants were found in 2012 (49.9% males, 50.1% females; 66% participation rate), and during the 20-year follow-up (2002-2022), 1,988 of the participants were found (49.5% males, 50.5% females; 65% participation rate). Among the individuals lost to follow-up, the vast majority could not be contacted due to changes or errors in their contact details, while approximately 7% chose not to participate in the screening without providing specific reasons for their decision. The development of a first, fatal or non-fatal CVD event during the follow-up examinations was defined as the self-reported emergence of myocardial infarction, angina pectoris, or other identified forms of ischemia, heart failure of various types, chronic arrhythmias, or the onset of a stroke, according to the 10th WHO International Coding of Disease classification (ICD-10). Participants with complete data on geographic location and development of CVD events were used for this study. Therefore, a sample of 1,935 (49,8% males) and 1,902 participants (49.5% males) - from the 10- and 20-year follow-ups, respectively - were included in the current analysis (Faka et al., 2023). Based on the ATTICA study sample for each municipality population, the municipality-level data were used for both the 10-year and 20-year periods in the spatial analysis. Further details about the ATTICA study can be found in (Damigou et al., 2023).

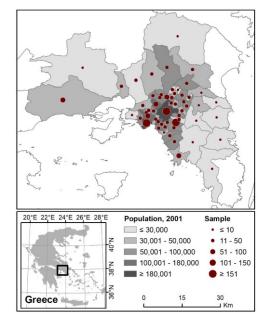


Figure 1. Population and sample size per municipality.



#### 2.1.1. Bioethics statement

The study was carried out in accordance with the Declaration of Helsinki (1989) of the World Medical Association and was approved by the Institutional Ethics Committee of Athens Medical School (#017/1.5.2001) and the Ethics Committee of the Harokopio University (#38/29.03.2022). All participants were informed about the study aims and provided written consent to participate in the study.

#### 2.2. Mapping CVD occurrence rates

GIS-based functions were implemented to map CVD occurrence rates across Attica municipalities. The epidemiological data were geocoded based on participants' residential municipality, ensuring each observation was assigned to the corresponding municipality code. Subsequently, the data were aggregated by municipality, allowing for the calculation of CVD occurrence rates (%) for the entire population, for both time periods. This study did not incorporate adjustments for sociodemographic variability, such as gender proportion, age distribution, or economic status, across regions. Therefore, any observed regional differences in CVD event rates are based on the aggregate outcomes without accounting for these potential covariates. CVD occurrence rates for both 10- and 20-year data were divided into five comparable classes. Geocoding and mapping were performed using ArcGIS 10.8 software package (ESRI Inc., Redlands, California, USA). A detailed workflow summarizing the methodological framework, from data acquisition to spatial analysis, is illustrated in Figure 2.

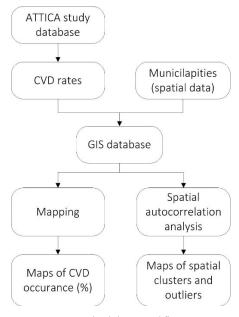


Figure 2. Methodology workflow.

#### 2.3. Spatial autocorrelation analysis

Spatial autocorrelation is a statistical method describing how a variable is autocorrelated through space. It assesses whether nearby locations tend to have similar values for the variable being studied, or whether there is a pattern of spatial dependence.

This analysis calculates measures of spatial autocorrelation, such as Moran's I index (global and local index) used in the current study, which quantifies the degree of spatial clustering or dispersion of the variable across the study area. Global Moran's I range from -1 to 1, where positive values indicate positive spatial autocorrelation (observations nearby have similar values), negative values indicate negative spatial autocorrelation (observations nearby have different values), and values near zero suggest spatial randomness (Moran, 1950). The global Moran's I is given as:

$$I = \frac{n\sum_{i}\sum_{j}w_{ij}\left(X_{i} - \bar{X}\right)\left(X_{j} - \bar{X}\right)}{\left(\sum_{i\neq j}w_{ij}\right)\sum_{i}\left(X_{i} - \bar{X}\right)^{2}} \tag{1}$$

where n is the number of spatial units, Xi is the variable's value for spatial unit i, Xj is the variable's value for spatial unit j, X is the mean of the variable's values, and wij is the spatial weight between features i and j. Spatial weights quantify the strength of the relationship between each pair of neighboring units. In spatial autocorrelation analysis, neighboring spatial units can be defined by either distance or contiguity criteria.

Global measures summarize the overall spatial autocorrelation of the study area in one single value, indicating the spatial autocorrelation existence. On the other hand, Local Indicators of Spatial Association (LISA), including local Moran's I, calculate spatial autocorrelation at the local level for each individual spatial unit, identifying local clusters (similar values cluster together) or spatial outliers (dissimilar values cluster together) (Anselin, 1995). The local Moran's I statistic of spatial association is given as:

$$I_{i} = \frac{n(X_{i} - \overline{X})}{\sum_{i} (X_{i} - \overline{X})^{2}} \sum_{j} w_{ij} (X_{i} - \overline{X})$$
(2)



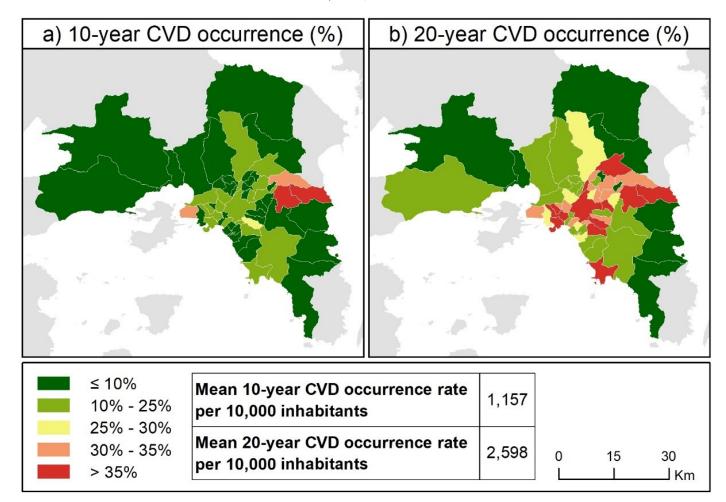
Local Moran's I values are assessed for statistical significance computing z-scores under the null hypothesis of spatial randomness. Spatial units are classified into four categories based on their values and the values of their neighboring units; (a) spatial units with high values neighboring units with also high values, indicating clusters of high values (High-High), (b) spatial units with low values neighboring units with also low values, indicating clusters of low values (Low-Low), (c) spatial units with low values neighboring units with high values, indicating Low-High spatial outliers, and (d) spatial units with high values neighboring units with low values, indicating High-Low spatial outliers.

While other local indicators of spatial autocorrelation primarily focus on identifying hot spots and cold spots—areas with significant clustering of high or low values—local Moran's I provides a broader view of spatial autocorrelation, identifying clusters and outliers, useful for understanding the spatial relationships between areas.

In the current analysis, spatial clusters and outliers were identified using contiguity-based spatial weights, chosen to account for the uneven structure and distribution of spatial units within the study area. According to this method spatial units are considered as neighbors if polygons share common sides or vertices. Spatial autocorrelation analysis was performed for CVD occurrence rates for each time period, with the significance level set at 0.05. The analysis resulted in a set of Moran scatter plots, providing a visual representation of spatial associations in the neighborhood around each observation, and a set of thematic maps demonstrating the statistically significant clusters and outliers. Local Moran's I was computed using software GeoDa version 1.16.0.12.

#### 3. Results

The mean CVD occurrence rate across the entire study area increased notably from 1,157 per 10,000 inhabitants over the 10-year period to 2,598 per 10,000 inhabitants over the 20-year period (Fig. 2). This rise, however, was not uniformly distributed, with certain municipalities experiencing more pronounced increases than others. The mapping of CVD occurrence in the area under investigation revealed higher rates for most municipalities over the 20-year period compared to the 10-year period (Fig. 3a, 3b). Urban municipalities in the central Athens metropolitan area showed a notable increase in CVD occurrence over the two periods, while rates in the suburbs remained lower.



**Figure 3.** Spatial variability of the fatal or non-fatal CVD occurrence rates across Attica municipalities: (a) 10-year CVD occurrence rates, 2012; (b) 20-year CVD occurrence rates, 2022.

The Moran scatter plots produced by spatial autocorrelation analysis, combined with Moran's I statistic, illustrate the presence and strength of spatial clustering or dispersion of CVD occurrence rates over time (Fig. 4). The Moran scatter plot demonstrates the variable's values (X-axis) against its spatially lagged values (Y-axis). Spatial lag represents the average value of the variable for a spatial entity's neighboring entities. Depending on the distribution of the values in the quadrants of a Moran scatter plot the spatial clusters and outliers are defined.

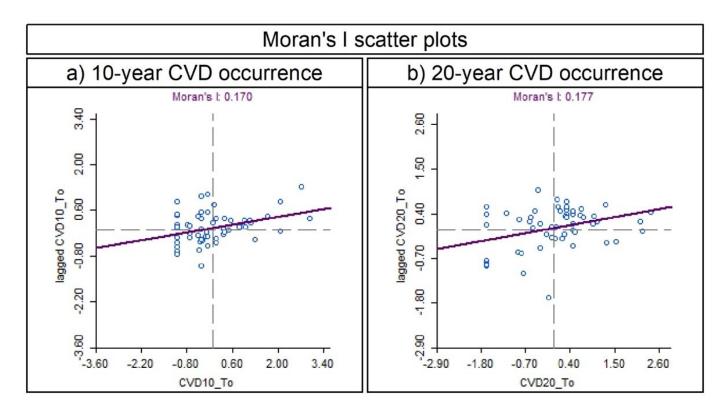


Figure 4. Moran I scatter plots of the fatal or non-fatal CVD occurrence rates in Attica municipalities: (a) 10-year CVD occurrence rates, 2012; (b) 20-year CVD occurrence rates, 2022.

Positive spatial autocorrelation analysis was revealed for both the 10-year and 20-year CVD occurrence rates. The Moran's I index was 0.170 (z-score = 2.230, p-value = 0.02) after the 10-year time period (Fig. 4a), and increased slightly to 0.177 (z-score = 2.300, p-value = 0.02) after the 20-year period (Fig. 4b), suggesting a slightly stronger spatially correlation over the longer time span. Both results underscore the presence of positive spatial autocorrelation, indicating that areas with similar CVD occurrence rates tend to cluster together spatially.

Spatial clusters and outliers for both time periods are presented in Fig. 5. After the 10-year time period, statistically significant High-High clusters were revealed in the eastern suburban municipalities of the study area (Figu. 5a), whereas a Low-Low cluster was identified at the western boundaries of the study area, where municipalities had limited neighbours. Similarly, after the 20-year time period, Low-Low clusters were observed at the boundaries of the study area, while a statistically significant High-High spatial cluster was located in the central municipalities of the study area (Fig. 5b). Municipalities with low rates neighboring municipalities with high rates (Low-High outliers) were identified in both time periods, primarily adjacent to High-High clusters.

### 4. Discussion

The aim of this study was to investigate the geographical distribution and spatio-temporal patterns of the occurrence of fatal and non-fatal CVD in the Attica region of Greece over the last two decades. This study makes an important contribution to the field by addressing a non-communicable disease, which is a critical area of public health research often overshadowed by the predominant focus on infectious diseases. While infectious diseases typically receive significant attention due to their potential for rapid transmission and immediate public health impact, non-communicable diseases such as CVD present unique challenges. They contribute to a substantial burden of illness, disability, and mortality globally, affecting individuals over extended periods and often requiring complex, long-term management strategies. Spatial analysis of non-communicable diseases like CVD is especially crucial, as it allows for the identification of geographical patterns and high-risk areas, providing insights that are essential for targeted public health interventions. By focusing on the spatial distribution of CVD in our study, we highlight the importance of understanding the geographical dimensions of non-communicable diseases, which can ultimately help address the rising global impact of these leading causes of death and disability.

The results revealed a considerable increase in 10-year cardiovascular disease occurrence rates in only a few municipalities. However, a notable increase was observed in most municipalities in the 20-year follow-up, especially in urban areas. This escalation in urban areas also showed statistically significant spatial clusters of high rates. The origins of CVD epidemiology in Greece can be traced back to the Seven Countries Study (Keys et al., 1966). Initiated in the late 1950s, the research included 7 studies and 16 cohorts investigated by 10 and 25 years follow-up examinations. The study concluded that the Greek cohort, enrolled around 1,300 men aged 40-59 years, exhibited the lowest CVD occurrence rates of all cohorts for both follow-up examinations. On the other hand, the Athens Study, conducted in Athens city about 30 years later and assessing the CVD risk factors in a sample of 4,097 individuals (Moulopoulos et al., 1987), resulted in same or greater prevalence rates of CVD risk factors compared to those in countries with advanced economies.

The ATTICA study was initiated in the early 2000s to assess the prevalence of CVD risk factors and associated cardio-metabolic disorders such as hypertension, obesity, dyslipidemia and diabetes, as well as the long-term occurrence of CVD. The 5-year follow-up of the study showed that 8.5% of participants experienced a CVD event during this period. After 10 years, this rate increased to 15.7% and rose to 36.1% within 20



years (Damigou et al., 2023; Panagiotakos et al., 2008; Panagiotakos et al., 2015). The spatial analysis highlighted the heterogeneity of CVD occurrence rates among the municipalities of Attica region. A notable finding was the marked increased rates after the 20-year period, particularly in urban municipalities within the metropolitan area of Athens. This finding is in line with those of other studies (Deng et al., 2024; Huang et al., 2024), aligning with broader global patterns of urbanization and lifestyle changes, where urban populations tend to experience higher rates of CVD due to factors such as sedentary lifestyle, unhealthy diet, and pollution (Cerin et al., 2024; Gouveia et al., 2024; Henning, 2024).

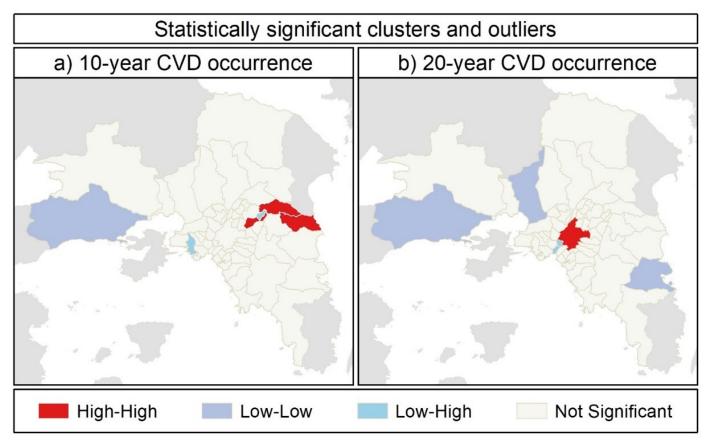


Figure 5. Statistically significant (p=<0.05) spatial clusters and outliers of the fatal or non-fatal CVD occurrence rates in Attica municipalities: (a) 10-year CVD occurrence rates, 2012; (b) 20-year CVD occurrence rates, 2022.

In this study, we utilized Moran's I to examine spatial autocorrelation and identify both clusters and outliers. A key finding from the current analysis was the identification of low-high outliers, which represent regions with lower CVD occurrence rates surrounded by areas with higher rates. During the 10-year period, two low-high outliers were identified. However, these specific low-high outliers disappeared in the 20-year analysis, suggesting that the spatial disparity in CVD rates in these regions may have diminished over time. This change could be attributed to a relative increase in CVD rates in the previously identified low-high regions, bringing them closer to the levels observed in their higher-rate neighbors and thus reducing their outlier status. Such a shift might reflect potential spillover effects, where neighboring high-risk areas influence or reflect evolving health trends in adjacent regions. The 20-year analysis revealed a new low-high outlier in a different region. While these municipalities may not currently exhibit the highest CVD rates, their proximity to areas with significantly elevated rates warrants closer monitoring. Early interventions in such areas could help address emerging trends before they escalate into broader public health challenges. This temporal shift in outlier locations underscores the dynamic nature of spatial patterns in CVD occurrence over time. It also highlights the importance of continuous spatial monitoring to identify evolving trends and prioritize areas for targeted public health actions.

The spatial autocorrelation also revealed significant clusters of high and low values for both time periods. The clusters of low values were found in the bordering municipalities of the Attica region. These clusters are likely influenced by the characteristics of their neighboring municipalities, which also exhibited relatively low CVD rates. Moreover, these bordering municipalities are predominantly suburban, though they encompass extensive rural regions as well, a factor that likely contributes to the observed clustering. Suburban and rural areas often characterized by lower population density, differing lifestyle factors, and potentially reduced stress levels compared to urban areas. These factors may collectively contribute to lower CVD occurrence rates (Hartig et I., 2014). The analysis also revealed a rise in low-low clusters over time, particularly in the suburban areas. Specifically, while only one low-low cluster was observed during the 10-year period, this increased to three clusters in the 20-year analysis. This rise suggests that the suburban and rural nature of these municipalities may have fostered greater cohesion over time, with an increasing number of municipalities forming spatial clusters characterized by uniformly low CVD rates. This trend could reflect the strengthening of shared protective factors or the broader dissemination of health-promoting behaviors and resources within these regions.

The geographic context of these municipalities, with fewer neighbors, may also play a role in the observed clustering patterns. Regions with fewer neighbors tend to show more distinct spatial effects in autocorrelation analysis, as their spatial relationships are determined by a smaller pool of surrounding values. This highlights the importance of considering the geographic and demographic context when interpreting spatial clusters, particularly in areas where administrative boundaries limit the number of neighboring municipalities.



In contrast, significant clusters of high values were identified in the suburban central-eastern municipalities after the 10-year period, and in the metropolitan urban area of the Attica region after the 20-year period. Despite the persistence of high CVD occurrence rates in the central-eastern study area after the 20-year period, the high-value cluster bounded in the most urbanized area of the Attica region, which experienced a considerable rise in CVD occurrence rates between the two time periods. Such spatial clustering implies the presence of underlying factors, whether environmental, socioeconomic, or behavioral, that contribute to the observed distribution of CVD occurrence across the region.

One potential contributing factor to this spatial clustering could be the limited availability of sports facilities. Inadequate access to sports facilities such as public gyms, swimming pools, and sports fields may prevent individuals from engaging in regular physical activity, contributing to the higher occurrence of CVD in urban areas (Deng et al., 2024). Beyond sports facilities, the availability and accessibility of green spaces in urban areas, including parks and recreational areas, play an important role in urban populations physical activity (Seo et al., 2019). Urbanization often leads to the reduction of green spaces, which are crucial for promoting physical activity, reducing stress, and improving overall cardiovascular health. The association between green neighborhoods and CVD outcomes has been demonstrated in many studies worldwide (Bianconi et al., 2023; Hartig et al., 2014; Li & Siegrist, 2012; Seo et al., 2019), as living in greener neighborhoods and near parks tends to encourage physical activity, which in turn has a positive effect on cardiovascular health. With fewer opportunities for outdoor activities and exercise, city dwellers may be more prone to sedentary lifestyle, a known risk factor for CVD. However, it is not just the extent of green urban areas that matters; their functionality is crucial for promoting public exercise. Previous studies have reported that many of the green urban areas in these municipalities lack functionality and are not conducive to public recreation (Faka et al., 2019).

Furthermore, the age distribution across areas could significantly influence these patterns. Greece, like many other countries, experiences regional variations in age demographics, with some areas having a disproportionately higher elderly population. Older age is a well-known risk factor for CVD, as aging is associated with the accumulation of cardiovascular risk factors and comorbidities. These age-related disparities could partly explain the uneven distribution of CVD occurrence.

Athens metropolitan area also deals with significant spatial disparities, including socioeconomic inequalities and environmental degradation (Faka et al., 2021). The socioeconomic status of the residential area, often measured by factors such as educational and income levels, can have a substantial impact the prevalence and management of CVD. Areas characterized by lower socioeconomic status tend to have higher rates of CVD compared to more affluent areas (Wang et al., 2024). Communities with lower educational and income levels may lack access to information about healthy lifestyle choices and preventive measures, or may face barriers to accessing quality healthcare services, including preventive medications, and follow-up care for managing CVD risk factors (Backholer et al., 2017). This can result in poorer health outcomes related to CVD.

Addressing socioeconomic inequalities and environmental factors is essential for promoting cardiovascular health and reduce the disparities in CVD occurrence rates. Policies and interventions that aim to enhance education, healthcare resources, and economic opportunities can help mitigate the impact of socioeconomic factors on CVD risk. Additionally, implementing urban planning strategies that prioritize green space preservation and expansion, can create healthier environments and promote public physical activity.

Future research could focus on investigating the impact of neighborhood-level socioeconomic, demographic and environmental factors on CVD occurrence rates. Factors such as education level, income, availability of green spaces, accessibility to parks, access to sports facilities and other recreational areas that promote physical activity may be related to the occurrence of cardiovascular disease. Employing spatial regression models, such as Geographically Weighted Regression (GWR), could provide valuable insights into empirically analyzing the distribution patterns of CVD occurrence.

This study is the first investigating the spatiotemporal clustering of the CVD occurrence rates in Attica region, Greece, over a 20-year period. Mapping the dynamic distribution of CVD occurrence and measuring their correlation between neighboring spatial units enabled the identification of spatial patterns and hot spots of CVD occurrence. The longitudinal nature of the research provides valuable insights into temporal changes in disease prevalence, facilitating the identification of shifts in CVD burden over time. Furthermore, the study's findings offer significant public health implications, providing evidence-based insights for targeted interventions aimed at reducing CVD prevalence and improving population health outcomes in the Attica region.

#### Limitations

Although this study improves our understanding of the dynamics of cardiovascular disease occurrence in Attica region, in Greece, some limitations should be noted. The aggregation of data on cardiovascular disease outcomes at the municipal level was based on the assumption of uniform distribution. Nevertheless, it should be noted that the sample of the ATTICA study is representative of the population living in the study area, but not of other regions of Greece, especially the rural or insular areas. Furthermore, the reduced sample sizes in municipalities with smaller populations could impact the estimates in these areas. Smaller samples may result in wider confidence intervals, potentially reducing the accuracy of the findings. However, this approach ensures that each municipality is represented in proportion to its population, helping to mitigate biases related to the over- or under-representation of less populated areas. Nonetheless, the findings for these municipalities should be interpreted with caution, as they may be less robust due to the smaller sample size. In addition, the modifiable areal unit problem underscores that the outcomes of the spatial analysis may vary depending on the degree of spatial aggregation of the data, as CVD occurrence rates may differ across neighborhoods within municipalities. This exploratory analysis was based on Moren's I index; future analyses can be based on advanced modelling techniques such as Poisson conditional autoregressive models or Poisson convolution autoregressive models. Finally, the present analysis did not incorporate factors such as family medical history, differences in population aging between municipalities, and other socio-demographic variables, which could influence the occurrence of CVD. Their exclusion may potentially lead to an overestimation of the study's findings. Future research could stratify the sample of the analysis by such variables to provide a more detailed understanding of the factors contributing to cardiovascular disease in our sample pop

#### 6. Conclusions

This study highlights the geographical heterogeneity of CVD occurrence in the region of Attica, Greece. This spatial variability could be indicative of variations in the municipalities' environmental attributes, as higher rates were found in the most urbanized municipalities of the Attica region. The results of this study contribute to our understanding of the spatial and temporal dynamics of CVD occurrence in urban populations. They provide policy makers and healthcare stakeholders with important insights to develop targeted interventions and allocate resources effectively to reduce the CVD burden. Furthermore, the findings of this research could serve as a basis for investigating further factors contributing to CVD in this region, such as socioeconomic status, environmental factors, healthcare accessibility etc.



**Funding:** The ATTICA Study received funding from the Hellenic Cardiology Society (#001/2002), and the Hellenic Atherosclerosis Society (#1/2007). E.D. has received scholarship from the Hellenic Atherosclerosis Society (2022-2025).

Acknowledgments: The authors would like to thank the ATTICA study group of investigators: E. Kravvariti, C. Vafia, E. Vlachopoulou, P.S. Adamidis, G. Anastasiou, A.D. Koutsogianni, A. Loukina, G. Mentzantonakis, E. Michelis, M. Kambaxis, K. Dimitriadis, I. Andrikou, A. Sofianidi, N. Sinou, A. Skandali, C. Sousouni, for their assistance on the 20-year follow-up, as well as E.N. Georgousopoulou, N. Katinioti, L. Papadimitriou, K. Masoura, S. Vellas, Y. Lentzas, M. Kambaxis, K. Palliou, V. Metaxa, A. Ntzouvani, D. Mpougatsas, N. Skourlis, C. Papanikolaou, G.-M. Kouli, A. Christou, A. Zana, M. Ntertimani, A. Kalogeropoulou, E. Pitaraki, A. Laskaris, M. Hatzigeorgiou and A. Grekas, E. Tsetsekou, C. Vassiliadou, G. Dedoussis, M. Toutouza-Giotsa, K. Tselika and S. Poulopoulou and M. Toutouza for their assistance in the initial and follow-up evaluations.

**Conflicts of Interest:** The authors declare no conflict of interest.

#### References

- Anselin, L. (1995). Local Indicators of Spatial Association—LISA. *Geographical analysis*, 27(2), 93–115. <a href="https://doi.org/10.1111/j.1538-4632.1995.tb00338.x">https://doi.org/10.1111/j.1538-4632.1995.tb00338.x</a>
- Backholer, K., Peters, S. A. E., Bots, S. H., Peeters, A., Huxley, R. R., & Woodward, M. (2017). Sex differences in the relationship between socioeconomic status and cardiovascular disease: a systematic review and meta-analysis. *Journal of Epidemiology and Community Health*, 71(6), 550–7. https://doi.org/10.1136/jech-2016-207890
- Baptista, E. A., & Queiroz, B. L. (2022). Spatial analysis of cardiovascular mortality and associated factors around the world. *BMC Public Health*, 22(1), 1556. https://doi.org/10.1186/s12889-022-13955-7
- Baptista, E.A. (2024). Cardiovascular Diseases Mortality in Mexican Municipalities: A Spatio-Temporal Approach. *Applied Spatial Analysis and Policy*, 17(2), 637–650. https://doi.org/10.1007/s12061-023-09562-7
- Bianconi, A., Longo, G., Coa, A. A., Fiore, M., & Gori, D. (2023). Impacts of Urban Green on Cardiovascular and Cerebrovascular Diseases—A Systematic Review and Meta-Analysis. *International Journal of Environmental Research and Public Health*, 20(11), 5966. https://doi.org/10.3390/ijerph20115966
- Cerin, E., Chan, Y.-K., Symmons, M., Soloveva, M., Martino, E., Shaw, J. E., Knibbs, L. D., Jalaludin, B., & Barnett, A. (2024). Associations of the neighbourhood built and natural environment with cardiometabolic health indicators: A cross-sectional analysis of environmental moderators and behavioural mediators. *Environmental Research*, 240, 117524. https://doi.org/10.1016/j.envres.2023.117524
- Damigou, E., Kouvari, M., Chrysohoou, C., Barkas, F., Kravvariti, E., Pitsavos, C., Skoumas, J., Michelis, E., Liberopoulos, E., Tsioufis, C., Sfikakis, P. P., & Panagiotakos, D. B. (2023). Lifestyle Trajectories Are Associated with Incidence of Cardiovascular Disease: Highlights from the ATTICA Epidemiological Cohort Study (2002-2022). *Life (Basel)*, 13(5), 1142. <a href="https://doi.org/10.3390/life13051142">https://doi.org/10.3390/life13051142</a>
- Dehbi, H. M., Blangiardo, M., Gulliver, J., Fecht, D., De Hoogh, K., Al-Kanaani, Z., Tillin, T., Hardy, R., Chaturvedi, N., & Hansell, A. L. (2016). Air pollution and cardiovascular mortality with over 25years follow-up: A combined analysis of two British cohorts. *Environment International*, 99, 275–281. https://doi.org/10.1016/j.envint.2016.12.004
- Deng, S., Liang, J., Peng, Y., Liu, W., Su, J., & Zhu, S. (2024). Spatial analysis of the impact of urban built environment on cardiovascular diseases: a case study in Xixiangtang, China. *BMC. Public Health*, 24(1), 2368. <a href="https://doi.org/10.1186/s12889-024-19884-x">https://doi.org/10.1186/s12889-024-19884-x</a>
- Doukissas, L., Kalogirou, S., & Tsimbos, C. (2018). Spatial patterns of SMRs due to the virus A(H1N1)PDM09 during the pandemic in Greece in 2009 2010. European Journal of Geography, 9(2), 134–148.
- Faka, A., Chalkias, C., Georgousopoulou, E.N., Tripitsidis, A., Pitsavos, C., & Panagiotakos, D. B. (2019). Identifying determinants of obesity in Athens, Greece through global and local statistical models. *Spatial and Spatio-temporal Epidemiology*, *29*, 31–41. <a href="https://doi.org/10.1016/j.sste.2019.02.002">https://doi.org/10.1016/j.sste.2019.02.002</a>
- Faka, A., Kalogeropoulos, K., Maloutas, T., & Chalkias, C. (2021). Urban Quality of Life: Spatial Modeling and Indexing in Athens Metropolitan Area, Greece. ISPRS International Journal of Geo-Information, 10(5), 347. https://doi.org/10.3390/ijgi10050347
- Faka, A., Ntafla, L. M., Chalkias, C., & Panagiotakos, D. B. (2023). Geographical variation in diabetes mellitus prevalence rates in Greece. *The Review of Diabetic Studies*, 19(2), 62-70. https://doi.org/10.1900/RDS.2023.19.62
- Faka, A., Damigou, E., Chrysohoou, C., Barkas, F., Vlachopoulou, E., Dalmyras, D., Vafia, C., Michelis, E., Loukina, A., Mentzantonakis, G., Adamidis, P. S., Anastasiou, G., Koutsogianni, A. D., Chalkias, C., Pitsavos, C., Liberopoulos, E., Tsioufis, C., Sfikakis, P. P., & Panagiotakos, D. (2023). Twenty-year incidence rates of cardiovascular disease in Greece: A geospatial analysis in the Attica study context, 2002-2022. *Journal of Atherosclerosis Prevention and Treatment*, 14(3), 97–102. https://doi.org/10.53590/japt.02.1050
- Ferrari, R., Ford, I., Greenlaw, N., Tardif, J. C., Tendera, M., Abergel, H., Fox, K., Hu, D., Shalnova, S., & Steg, P. G. (2015). Geographical variations in the prevalence and management of cardiovascular risk factors in outpatients with CAD: Data from the contemporary CLARIFY registry. *European Journal of Preventive Cardiology*, 22(8), 1056–1065. https://doi.org/10.1177/2047487314547652
- Ferreira, M., & Ferreira, M. M. (2019). Using geospatial analysis techniques for evaluating the association between socioenvironmental factors and the geographical distribution of leptospirosis in Sao Paulo, Brazil. *European Journal of Geography*, 10(3), 137–153.
- Frings, M., Lakes, T., Müller, D., Khan, M. H., Epprecht, M., Kipruto, S., Galea, S., & Gruebner, O. (2018). Modeling and mapping the burden of disease in Kenya. *Scientific Reports*, 8(1), 9826. https://doi.org/10.1038/s41598-018-28266-4
- Gavalas, V. S. (2018). Long-term trends and recent upturns in regional mortality variations in Greece. European Journal of Geography, 9(1), 6–22. <a href="https://eurogeojournal.eu/articles/Long-term%20trends%20and%20recent%20upturns%20in%20regional%20mortality%20variations%20in%20Greece.pdf">https://eurogeojournal.eu/articles/Long-term%20trends%20and%20recent%20upturns%20in%20regional%20mortality%20variations%20in%20Greece.pdf</a>
- Gouveia, N., Rodriguez-Hernandez, J. L., Kephart, J. L., Ortigoza, A., Betancourt, R. M., Sangrador, J. L. T., Rodriguez, D. A., Diez Roux, A. V., Sanchez, B., Yamada, G., & The SALURBAL Group. (2024). Short-term associations between fine particulate air pollution and cardiovascular and respiratory mortality in 337 cities in Latin America. Science of the Total Environment, 920, 171073. <a href="https://doi.org/10.1016/j.scitotenv.2024.171073">https://doi.org/10.1016/j.scitotenv.2024.171073</a>
- Hartig, T., Mitchell, R., de Vries, S., & Frumkin, H. (2014). Nature and Health. *Annual Review of Public Health*, 35, 207–228. https://doi.org/10.1146/annurev-publhealth-032013-182443



- Henning, R. J. (2024). Particulate Matter Air Pollution is a Significant Risk Factor for Cardiovascular Disease. *Current Problems in Cardiology*, 49(1), 102094. https://doi.org/10.1016/j.cpcardiol.2023.102094
- Huang, X., Wang, Z., Lei, F., Liu, W., Lin, L., Sun, T., Cao, Y., Zhang, X., Cai, J., & Li, H. (2024). Association of urban environments with Atherosclerotic cardiovascular disease: A prospective cohort study in the UK Biobank. *Environment International*, 193, 109110. <a href="https://doi.org/10.1016/j.envint.2024.109110">https://doi.org/10.1016/j.envint.2024.109110</a>
- Jaber, A. S., Hussein, A. K., Kadhim, N. A., & Bojassim, A. A. (2022). A Moran's I autocorrelation and spatial cluster analysis for identifying Coronavirus disease COVID-19 in Iraq using GIS approach. *Caspian Journal of Environmental Sciences*, 20(1), 55–60. <a href="https://doi.org/10.22124/cjes.2022.5392">https://doi.org/10.22124/cjes.2022.5392</a>
- Jordan, G., Ridder, D., Joost, S., Vollenweider, P., Preisig, M., Marques-Vidal, P., Guessous, I., & Vaucher, J. (2024). Spatial analysis of 10-year predicted risk and incident atherosclerotic cardiovascular disease: the CoLaus cohort. *Scientific Reports*, 14(1), 4752. <a href="https://doi.org/10.1038/s41598-024-54900-5">https://doi.org/10.1038/s41598-024-54900-5</a>
- Keys, A., Aravanis, C., Blackburn, H. W., Van Buchem, F. S., Buzina, R., Djordjević, B. D., Dontas, A. S., Fidanza, F., Karvonen, M. J., Kimura, N., Lekos, D., Monti, M., Puddu, V., & Taylor, H. L. (1966). Epidemiological studies related to coronary heart disease: characteristics of men aged 40-59 in seven countries. *Acta Socio-Medica Scandinavica Supplement*, 460, 1–392. https://doi.org/10.1111/j.0954-6820.1966.tb04737.x
- Li, J., & Siegrist, J. (2012). Physical Activity and Risk of Cardiovascular Disease—A Meta-Analysis of Prospective Cohort Studies. *International Journal of Environmental Research and Public Health*, 9(2), 391–407. https://doi.org/10.3390/jierph9020391
- Liu, X. X., Ma, X. L., Huang, W. Z., Luo, Y. N., He, C. J., Zhong, X. M., Dadvand, P., Browning, M. H. E. M., Li, L., Zou, X. G., Dong, G. H., & Yang, B. Y. (2022). Green space and cardiovascular disease: a systematic review with meta-analysis. *Environmental Pollution*, 301, 118990. <a href="https://doi.org/10.1016/j.envpol.2022.118990">https://doi.org/10.1016/j.envpol.2022.118990</a>
- Mena, C., Sepúlveda, C., Fuentes, E., Ormazábal, Y., & Palomo, I. (2018). Spatial analysis for the epidemiological study of cardiovascular diseases: A systematic literature search. *Geospatial Health*, 13(1), 11–19. https://doi.org/10.4081/gh.2018.587
- Michas, G., Karvelas, G., & Trikas, A. (2019). Cardiovascular disease in Greece, the latest evidence on risk factors. *Hellenic Journal of Cardiology*, 60(5), 271-275. <a href="https://doi.org/10.1016/j.hjc.2018.09.006">https://doi.org/10.1016/j.hjc.2018.09.006</a>
- Moran, P. A. P. (1950). Notes on continuous stochastic phenomena. Biometrika, 37(1-2), 17-23. https://www.jstor.org/stable/2332142
- Moulopoulos, S. D., Adamopoulos, P. N., Diamantopoulos, E. I., Nanas, S. N., Anthopoulos, L. N., & Iliadi-Alexandrou, M. (1987). Coronary heart disease risk factors in a random sample of Athenian adults. The Athens Study. *American Journal of Epidemiology, 126*(5), 882-92. <a href="https://doi.org/10.1093/oxfordjournals.aje.a114725">https://doi.org/10.1093/oxfordjournals.aje.a114725</a>
- Panagiotakos, D. B., Pitsavos, C., Chrysohoou, C., Skoumas, I., & Stefanadis, C., ATTICA Study group. (2008). Five-year incidence of cardiovascular disease and its predictors in Greece: The ATTICA study. Vascular Medicine, 13(2), 113–121. https://doi.org/10.1177/1358863x07087731
- Panagiotakos, D. B., Georgousopoulou, E. N., Pitsavos, C., Chrysohoou, C., Metaxa, V., Georgiopoulos, G. A., Kalogeropoulou, K., Tousoulis, D., Stefanadis, C., & ATTICA Study group. (2015). Ten-year (2002-2012) cardiovascular disease incidence and all-cause mortality, in urban Greek population: The ATTICA study. *International Journal of Cardiology*, 180, 178–184. https://doi.org/10.1016/j.ijcard.2014.11.206
- Pitsavos, C., Panagiotakos, D. B., Chrysohoou, C., & Stefanadis, C. (2003). Epidemiology of cardiovascular risk factors in Greece: Aims, design and baseline characteristics of the ATTICA study. *BMC Public Health*, *3*, 32. <a href="https://doi.org/10.1186/1471-2458-3-32">https://doi.org/10.1186/1471-2458-3-32</a>
- Rajabi, M., Mansourian, A., Pilesjö, P., Oudin Åström, D., Cederin, K., & Sundquist, K. (2018). Exploring spatial patterns of cardiovascular disease in Sweden between 2000 and 2010. *Scandinavian Journal of Public Health*, 46(6), 647–658. https://doi.org/10.1177/1403494818780845
- Ren, H., Wan, X., Wei, C., & Yang, G. (2019). Spatiotemporal variations in cardiovascular disease mortality in China from 1991 to 2009. *BMC Cardiovascular Disorders*, 19(1), 159. <a href="https://doi.org/10.1186/s12872-019-1128-x">https://doi.org/10.1186/s12872-019-1128-x</a>
- Roth, G. A., Mensah, G. A., Johnson, C. O., Addolorato, G., Ammirati, E., Baddour, L. M., Barengo, N. C., Beaton, A. Z., Benjamin, E. J., Benziger, C. P., Bonny, A., Brauer, M., Brodmann, M., Cahill, T. J., Carapetis, J., Catapano, A. L., Chugh, S. S., Cooper, L. T., Coresh, J.,...Fuster, V. (2020). Global Burden of Cardiovascular Diseases and Risk Factors, 1990-2019: Update From the GBD 2019 Study. *Journal of the American College of Cardiology*, 76(25), 2982–3021. https://doi.org/10.1016/j.jacc.2020.11.010
- Şener, R., & Türk, T. (2021). Spatiotemporal Analysis of Cardiovascular Disease Mortality with Geographical Information Systems. *Applied Spatial Analysis and Policy*, 14(4), 929–945. <a href="https://doi.org/10.1007/s12061-021-09382-7">https://doi.org/10.1007/s12061-021-09382-7</a>
- Seo, S., Choi, S., Kim, K., Kim, S. M., & Park, S. M. (2019). Association between urban green space and the risk of cardiovascular disease: A longitudinal study in seven Korean metropolitan areas. *Environment International*, 125, 51–57. <a href="https://doi.org/10.1016/j.envint.2019.01.038">https://doi.org/10.1016/j.envint.2019.01.038</a>
- Smallman-Raynor, M.R., Cliff, A.D., & Stickler, P.J. (2022a). Meningococcal Meningitis and Coal Mining in Provincial England: Geographical Perspectives on a Major Epidemic, 1929–33. *Geographical Analysis*, 54(1), 197–216. https://doi.org/10.1111/gean.12272
- Smallman-Raynor, M.R., Cliff, A.D., & The COVID-19 Genomics UK (COG-UK) Consortium. (2022b). Spatial growth rate of emerging SARS-CoV-2 lineages in England, September 2020-December 2021. *Epidemiology and Infection*, 150, e145. https://doi.org/10.1017/S0950268822001285.
- Timmis, A., Vardas, P., Townsend, N., Torbica, A., Katus, H., De Smedt, D., Gale, C. P., Maggioni, A. P., Petersen, S. E., Huculeci, R., Kazakiewicz, D., de Benito Rubio, V., Ignatiuk, B., Raisi-Estabragh, Z., Pawlak, A., Karagiannidis, E., Treskes, R., Gaita, D., Beltrame, J.F.,...Achenbach, S. (2022). European Society of Cardiology: cardiovascular disease statistics 2021. European Heart Journal, 43(8), 716–799. <a href="https://doi.org/10.1093/eurhearti/ehab892">https://doi.org/10.1093/eurhearti/ehab892</a>
- Tsiampalis, T., Faka, A., Psaltopoulou, T., Pitsavos, C., Chalkias, C., & Panagiotakos, D. B. (2023). The Spatial Variability of the Sex and Age- Specific 10-Year Incidence of Cardiovascular Diseases and its Clinical Risk Factors in Athens Metropolitan Area: a Local Statistical Modelling Approach in the Context of the ATTICA Epidemiological Study. *Applied Spatial Analysis and Policy*, 16(2), 939–965. https://doi.org/10.1007/s12061-023-09508-7
- Wang, T., Li, Y., & Zheng, X. (2024). Association of socioeconomic status with cardiovascular disease and cardiovascular risk factors: a systematic review and meta-analysis. *Journal of Public Health (Germany)*, 32(3), 385–399. https://doi.org/10.1007/s10389-023-01825-4
- Weimann, A., Dai, D., & Oni, T. (2016). A cross-sectional and spatial analysis of the prevalence of multimorbidity and its association with socioeconomic disadvantage in South Africa: A comparison between 2008 and 2012. Social Science and Medicine, 163, 144-56. https://doi.org/10.1016/j.socscimed.2016.06.055
- Wieland, T. (2020). Flatten the curve! modeling SARS-CoV-2/COVID-19 growth in Germany at the county level. *Region*, 7(2), 43–83. <a href="https://doi.org/10.18335/region.v7i2.324">https://doi.org/10.18335/region.v7i2.324</a>



- Wieland, T. (2022). Spatial patterns of excess mortality in the first year of the COVID-19 pandemic in Germany. *European Journal of Geography*, 13(4), 18–33. <a href="https://doi.org/10.48088/eig.t.wie.13.4.018.033">https://doi.org/10.48088/eig.t.wie.13.4.018.033</a>
- Yang, J., Zhang, Y., Luo, L., Meng, R., & Yu, C. (2018). Global mortality burden of cirrhosis and liver cancer attributable to injection drug use, 1990—2016: An age-period-cohort and spatial autocorrelation analysis. *International Journal of Environmental Research and Public Health*, 15(1), 170. https://doi.org/10.3390/ijerph15010170
- Yeh, C. T., Cheng, Y. Y., & Liu, T. Y. (2020). Spatial characteristics of urban green spaces and human health: An exploratory analysis of canonical correlation. *International Journal of Environmental Research and Public Health*, 17(9), 3227. https://doi.org/10.3390/ijerph17093227
- Zhang, H., Yang, L., Li, L., Xu, G., & Zhang, X. (2019). The epidemic characteristics and spatial autocorrelation analysis of hand, foot and mouth disease from 2010 to 2015 in Shantou, Guangdong, China. BMC Public Health, 19(1), 998. https://doi.org/10.1186/s12889-019-7329-5
- Zhang, M., Shi, Y., Shi, O., Zhao, Z., Zhang, X., Li, C., Huang, Z., Zhao, L., Wang, L., Li, Y., & Li, X. (2020). Geographical variations in cardiovascular health in China: A nationwide population-based survey of 74,726 adults. *The Lancet Regional Health Western Pacific, 3,* 100033. <a href="https://doi.org/10.1016/j.lanwpc.2020.100033">https://doi.org/10.1016/j.lanwpc.2020.100033</a>

**Disclaimer/Publisher's Note:** The statements, opinions and data contained in all publications are solely those of the individual author(s) and contributor(s) and not of EUROGEO and/or the editor(s). EUROGEO and/or the editor(s) disclaim responsibility for any injury to people or property resulting from any ideas, methods, instructions, or products referred to in the content.

## \*# European Journal of Geography