Special Issue: Lamination

Emina Kričković*, Tin Lukić, Zoran Kričković, Anastazija Stojšić-Milosavljević, Vladimir M. Cvetković and Milica Živanović

Spatio-temporal patterns and emerging trends of cardiovascular diseases in patients treated at the Institute of Cardiovascular Diseases of Vojvodina

https://doi.org/10.1515/geo-2025-0975
Received February 5, 2026; accepted March 23, 2026;
published online July 24, 2026

Abstract: Cardiovascular diseases represent one of the most dominant categories of non-communicable diseases, with a high prevalence both in Serbia and globally. Understanding their spatial distribution provides valuable insights for public health planning and disease prevention. This study applies geospatial analysis to examine the patterns of CVD among patients treated at the Institute for Cardiovascular Diseases of Vojvodina in Serbia, over the period 1995–2023. Beyond identifying spatial clusters, the analysis reveals long-term intensification of CVD burden in the South Bačka urban-suburban zone, indicating a sustained spatial polarization of cardiovascular morbidity over nearly three decades. Mann-Kendall trends per settlement were calculated. The spatial dimension of the research was addressed using the Emerging Hot Spot Analysis to detect statistically significant clusters of high and low values. To further refine the spatial representation of CVD clusters, the Kriging interpolation method was applied. The findings underscore the significance of geospatial methods in pinpointing high-risk areas in cardiovascular diseases, providing an evidence-based foundation for targeted healthcare interventions and resource allocation. Moreover, this study demonstrates the potential of integrating spatial geostatistics with health data to support the development of preventive strategies and to guide future epidemiological research on non-communicable diseases in Serbia and beyond.

Keywords: cardiovascular diseases; Institute for Cardiovascular Diseases of Vojvodina; emerging hot spot analysis; kriging method; Mann-Kendall test; public health

***Corresponding author: Emina Kričković**, Faculty of Geography, University of Belgrade, Studentski trg 3/3, Belgrade, Serbia, E-mail: emina.krickovic@gef.bg.ac.rs. https://orcid.org/0000-0002-0737-5636
Tin Lukić, Department of Geography, Tourism and Hotel Management, Faculty of Sciences, University of Novi Sad, Trg Dositeja Obradovića 3, Novi Sad, Serbia; Faculty of Geography, University of Belgrade, Studentski trg 3/3, Belgrade, Serbia; and Ruđer Bošković School, Kneza Višeslava 17, Belgrade, Serbia. https://orcid.org/0000-0001-5398-0928
Zoran Kričković, Military Geographical Institute –"General Stevan Bošković", Ministry of Defence of the Republic of Serbia, Mije Kovačevića 5, Belgrade, Serbia. https://orcid.org/0009-0006-1509-5008
Anastazija Stojšić-Milosavljević, Clinic of Cardiology, Institute of Cardiovascular Diseases of Vojvodina, Sremska Kamenica, Serbia. https://orcid.org/0000-0003-2092-4289
Vladimir M. Cvetković, Department of Disaster Management and Environmental Security, Faculty of Security Studies, University of Belgrade, Gospodara Vučića 50, Belgrade, Serbia; Scientific-Professional Society for Disaster Risk Management, Dimitrija Tucovića 121, Belgrade, Serbia; and Department of Environmental and Energy Process Engineering, Safety and Disaster Studies, Technical University of Leoben, Franz Josef-Straße 18, Leoben, Austria. https://orcid.org/0000-0002-3450-0658
Milica Živanović, Faculty of Geography, University of Belgrade, Studentski trg 3/3, Belgrade, Serbia. https://orcid.org/0009-0007-8294-7343

1 Introduction

Cardiovascular diseases (CVD) represent a critical public health issue, accounting for a substantial share of the global burden of disease in both high- and low-income countries [1, 2]. CVD in 2022 were responsible for approximately 19.8 million deaths, accounting for about 32 % of all deaths globally [3]. The majority of these fatalities-around 85 %-resulted from heart attacks and strokes [3]. Furthermore, among the 18 million premature deaths (before the age of 70) attributed to non-communicable diseases in 2021, at least 38 % were linked to cardiovascular conditions [3]. The global distribution of mortality from CVD shows pronounced regional differences [4]. The highest mortality rates in 2022 were observed in Eastern Europe, Central Asia, and certain parts of Africa and the Middle East, while the lowest rates were reported in Western Europe, North America, and Australia [4]. From the perspective of health geography, CVD are widely recognised as one of the leading causes of death in Europe [2, 5]. Multiple factors, including smoking, unhealthy dietary patterns, insufficient physical activity, psychological stress, and environmental pollution, substantially contribute to the development of non-communicable diseases [2, 6].

Analysis of CVD trends has been investigated in numerous studies [2, 7–15]. The non-parametric Mann-Kendall (MK) trend test and Sen's slope estimator are highly effective for analysing temporal trends in geospatial medical geography [2, 6, 16–18].

Numerous studies have applied GIS-based spatial analysis to examine cardiovascular disease patterns [2, 6, 19–25]. Kriging has been widely used in public health and environmental studies, particularly for mapping disease distribution, assessing exposure levels, and detecting spatial inequalities [2, 26–39].

GIS and spatial statistical methods have been widely employed to explore the spatial distribution and clustering of CVD, as well as to uncover patterns of health inequalities across different populations. These approaches have proven effective in identifying spatial clusters of high-risk areas, revealing temporal dynamics, and providing valuable evidence for targeted interventions in public health practice.

Non-communicable diseases – including CVD, malignant tumours, diabetes, chronic obstructive pulmonary disease, injuries, and others-have been the predominant contributors to the national disease burden in the population of the Republic of Serbia for decades [40]. They represent the leading causes of morbidity, disability, and premature mortality (before the age of 65) in the country [40]. In 2019, Serbia ranked 18th among 54 countries for CVD incidence, with a rate of 920 per 100,000 population [2, 6, 41]. Almost every second resident of Serbia dies from heart and blood vessel diseases [40]. In 2023, the leading causes of death among the population of Vojvodina were diseases of the circulatory system (51.0 %), neoplasms (21.8 %), and diseases of the respiratory system (6.8 %) [42].

Despite increasing use of GIS in cardiovascular epidemiology, long-term spatio-temporal trend analyses at the settlement level remain scarce in Southeast Europe, particularly for periods exceeding two decades. A relatively small number of studies in the territory of the Republic of Serbia used a geographical-medical approach in the study of CVD [2, 6, 25, 43–47]. Maksimović et al. examined how variations in magnesium and calcium content in drinking water relate to CVD across 65 municipalities in Serbia [43]. Šašić et al. analysed data from the 2019 National Health Survey of the Population of Serbia, which included a sample of 13,178 respondents aged 15 and older [48]. The analysis utilised data on socio-demographic characteristics, metabolic and behavioural risk factors, as well as self-reported health status and factors influencing health in relation to CVD [48]. Vulin et al. performed a retrospective study using data from the outpatient clinic of the Institute of Cardiovascular Diseases of Vojvodina in Sremska Kamenica (ICDV) collected in 2020 [49]. The research revealed an association between short-term fluctuations in blood pressure and left ventricular diastolic dysfunction among patients diagnosed with arterial hypertension [49]. Kričković et al. conducted a geographical medical analysis of non-communicable diseases – CVD (2010–2020) and diabetes (2010–2019) – in the AP Vojvodina (northern Serbia), aiming to identify the most and least burdened counties and to present trends in these diseases [6]. Kričković et al. employed artificial intelligence (ChatGPT) to create an interactive map showing the total number of patients examined at the ICDV, by settlement across the territory of the Republic of Serbia [25]. Also, Kričković et al. conducted a spatio-temporal analysis of hypertension among patients treated at the ICDV between 2000 and 2023 [2]. Petrović and Čanković focused on assessing obesity rates and the role of socio-demographic characteristics among adolescents in Vojvodina [47]. In addition, Jevtić et al. addressed the impact of air pollution on the occurrence of CVD within the same region [44]. These studies represent important initial steps in applying medical geography to better understand the distribution of CVD in Serbia, yet further research is needed to systematically assess spatio-temporal patterns, identify environmental and sociodemographic determinants, and provide actionable insights for public health policy.

This study applies geospatial analysis to examine the trends and patterns of CVD among patients treated at the ICDV in the Republic of Serbia, over the period 1995–2023. This research aims to identify CVD patterns across settlements in the Republic of Serbia, thereby providing insights into spatial disparities in disease burden and offering a methodological framework that can support future epidemiological analyses and public health planning. Understanding the spatial dimension of CVD occurrence is essential, as it enables the identification of geographic disparities, detection of high-burden areas, and provision of evidence to guide more efficient allocation of healthcare resources and targeted prevention strategies.

2 Methods

2.1 Demographic characteristics

According to the 2022 Census, the total population of the Republic of Serbia was 6,647,003, including 3,231,978 men and 3,415,025 women [50]. Women outnumbered men by approximately 183,000, accounting for 51.4 % of the total population. Between 2011 and 2022, the population of the Republic of Serbia decreased by 586,587 individuals (8.1 %) [50]. This decline was primarily driven by negative natural increase, which accounted for about 80 % of the total population decline. Additionally, negative net migration contributed to this trend, with an average annual outflow of approximately 11,000 people leaving the country more than entering [50].

In the Vojvodina region, the total population recorded in the 2022 Census was 1,740,230, comprising 845,739 men and 894,491 women, indicating an excess of 48,752 women compared to men [50].

Age structure by regions reveals notable spatial variations in the demographic composition of the Republic of Serbia during the period 2011–2022 [50]. Notably, the Belgrade region was the only one to record an increase in the share of children aged 0–14, rising from 14.0 % to 15.1 %, while other regions experienced stagnation or a slight decline in this indicator [50]. In the Vojvodina region, according to the 2022 Census, 254,971 individuals (14.7 %) were aged 0–14, 1,108,342 (63.7 %) were aged 15–64, and 376,917 (21.7 %) were aged 65 and over [50].

In 2022, incidence rates of myocardial infarction, unstable angina pectoris, and acute coronary syndrome in the Republic of Serbia were highest in the oldest age group (75+ years) for both men and women, with consistently higher values observed in men [51]. The same pattern was identified in the Vojvodina region, although for unstable angina pectoris the peak incidence occurred slightly earlier (70–74 years) in men [51]. A similar age-related trend was observed for mortality, with the highest rates for all three conditions recorded in the 75+ age group in both the Republic of Serbia and Vojvodina. Overall, men exhibited higher mortality rates than women [51].

2.2 Data set

For this study, a reference database from the ICDV and open data available from the Republic Geodetic Authority (RGA) were used [52, 53]. Spatial data downloaded from the RGA portal and stored in the geospatial database in ArcGIS Pro were in the UTM WGS84 coordinate system. These data were cleaned, processed and prepared for use in a geospatial database in ArcGIS Pro 3.2. The process of this study is presented in the Figure 1. After the pre-processing data, a Mann-Kendall analysis using Python was conducted. Afterwards, a space-time cube was implemented, and the Emerging Hot Spot (EHS) analysis conducted. In order to conduct the Kriging method, the settlement polygons were converted into points, and raster and contour maps were created.

ICDV database was organised according to the International Classification of Diseases (ICD), as defined by the 10th Revision of the International Statistical Classification of Diseases and Related Health Problems, published by the WHO [2, 54]. Although the WHO released the 11th Revision of the ICD at the 72nd World Health Assembly in 2019, which came into effect on January 1, 2022 [the 10th Revision remains in use in the Republic of Serbia [2, 55]. CVD comprise a large and heterogeneous group of diseases including, according to the ICD-10 (codes I00 – I99) the following health disorders: acute rheumatic fever, chronic rheumatic diseases of the heart, hypertension induced diseases, ischemic heart diseases (coronary heart disease), lung-based heart diseases and diseases of the lung vessels, diseases of cerebral blood vessels, arterial diseases, diseases of arteriolae and capillaries, veins, lymphatic vessels and lymph nodes, and other unspecified diseases of the heart and circulation [56]. From 1995 to 2005, the data are quite limited, as these were the early years of the information system at the ICDV, and data entry was optional during that period [2, 52]. Starting in 2005, data entry became mandatory [2]. In Figure 2, the spatial distribution of patient counts across settlements is presented. The highest numbers of patients are depicted in pink shades, while the lowest numbers are shown in blue. The majority of patients originate from the metropolitan area of Novi Sad, where the ICDV is located. However, patients from other parts of the Republic are also represented. Although patients from settlements in the Autonomous Province of Kosovo and Metohija (AP KiM) were recorded in the ICDV database, they were excluded from this study due to the unavailability of settlement-level data from the open-access sources of the Republic Geodetic Authority of the Republic of Serbia. There were total 497 patients recorded from this Serbian province [52].

2.3 Emerging Hot Spot (EHS) analysis

This analysis was applied to identify spatial and temporal patterns of CVD cases among patients treated at the ICDV in the Republic of Serbia. This method, based on the Getis-Ord G_i^* statistic, detects statistically significant clusters of high (hot spots) and low (cold spots) values across space and time. By analysing sequential time periods, EHS classifies each location according to the stability and persistence of clustering, such as new, consecutive, intensifying, persistent, diminishing, sporadic, oscillating or historical hot or cold spots. This approach enables the identification of areas where disease intensity is increasing or decreasing over time, providing valuable insight into the spatial-temporal dynamics of cardiovascular morbidity.

The last time step is hot when the most recent time-step interval exhibits statistically significant clustering of high values. Within this category, several subtypes can be

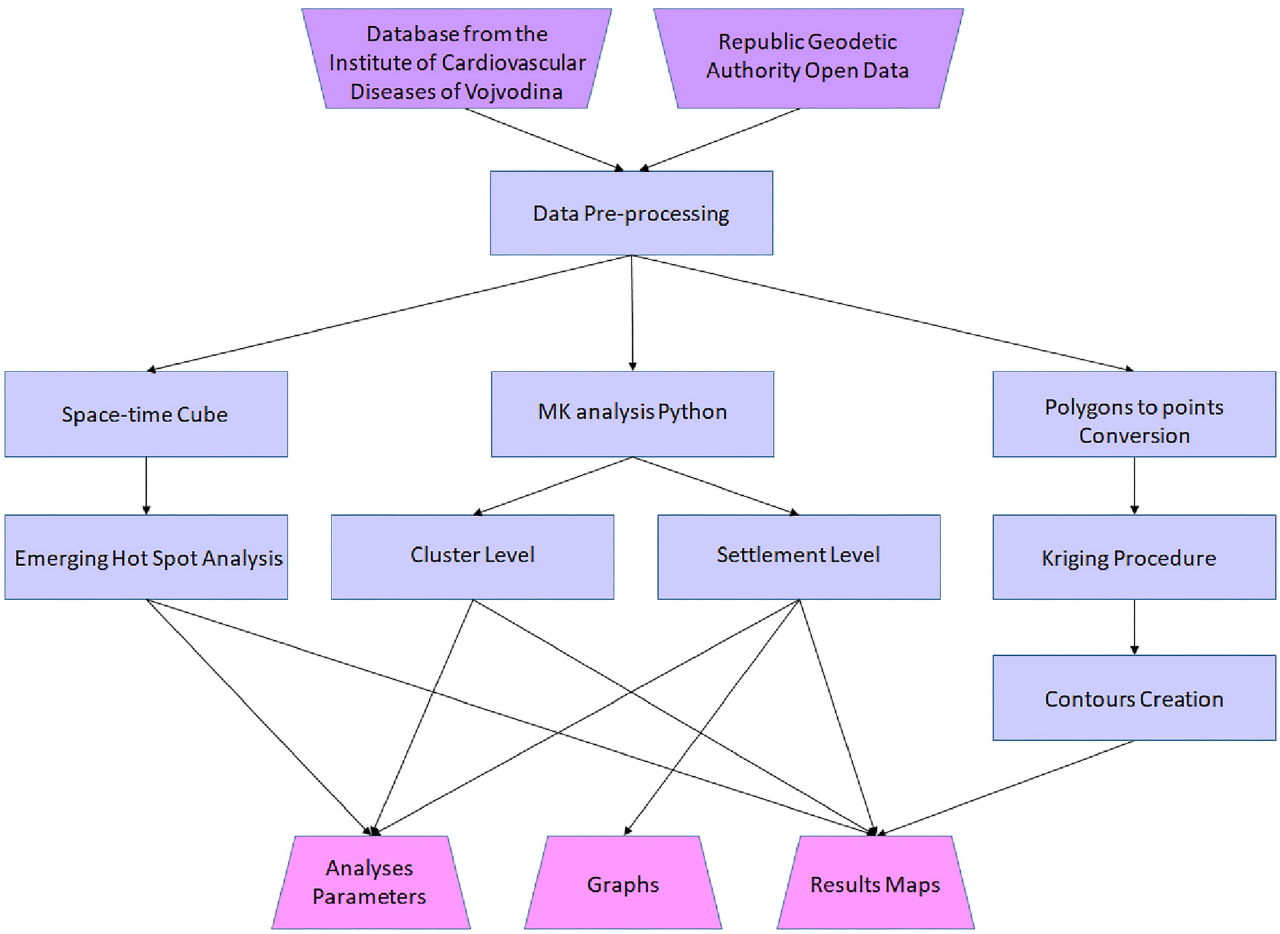


Figure 1: Schematic process of the research.

distinguished. The New Hot Spot indicates that the most recent time-step interval is hot for the first time. The Consecutive Hot Spot represents a single uninterrupted sequence of hot time-step intervals comprising less than 90 % of all intervals. The Intensifying Hot Spot occurs when at least 90 % of the time-step intervals are hot and the intensity of clustering increases over time. A Persistent Hot Spot is characterised by at least 90 % of the time-step intervals being hot, but with no significant upward or downward trend. The Diminishing Hot Spot also occurs in at least 90 % of time-step intervals, but the clustering intensity decreases over time. A Sporadic Hot Spot appears when only some of the time-step intervals are hot, while an Oscillating Hot Spot alternates between hot and cold intervals. If the last time-step interval is not hot, it is categorised as a Historical Hot Spot, indicating that at least 90 % of the intervals were hot, but the most recent one is not.

Conversely, the last time step is cold when the most recent time-step interval shows significant clustering of low values. Similar subtypes are recognised here as well. A New Cold Spot appears when the most recent time-step interval is cold for the first time. The Consecutive Cold Spot refers to a continuous sequence of cold time-step intervals making up less than 90 % of all intervals. The Intensifying Cold Spot type is characterized by at least 90 % of the time-step intervals being cold, with the clustering becoming colder over time. A Persistent Cold Spot maintains at least 90 % cold intervals with no trend up or down, while the Diminishing Cold Spot also spans at least 90 % of intervals but shows a weakening cold trend over time. The Sporadic Cold Spot occurs when only some time-step intervals are cold, and the Oscillating Cold Spot alternates between cold and hot intervals. Finally, if the last time-step interval is not cold, the pattern is identified as a Historical Cold Spot, indicating that at least 90 % of intervals were cold, but the most recent one is not. This analysis is based on the Gi* statistic, which is calculated using the formula [2, 6, 16, 18, 57]:

$$G_i^* = \frac{\sum_{j=1}^{n} \omega_{i,j} x_j - \overline{X} \sum_{j=1}^{n} \omega_{i,j}}{S\sqrt{\frac{\left[n \sum_{j=1}^{n} \omega_{i,j}^2 - \left(\sum_{j=1}^{n} \omega_{i,j}\right)^2\right]}{n-1}}} \tag{1}$$

where G_i^* is the spatial autocorrelation statistics of an event i

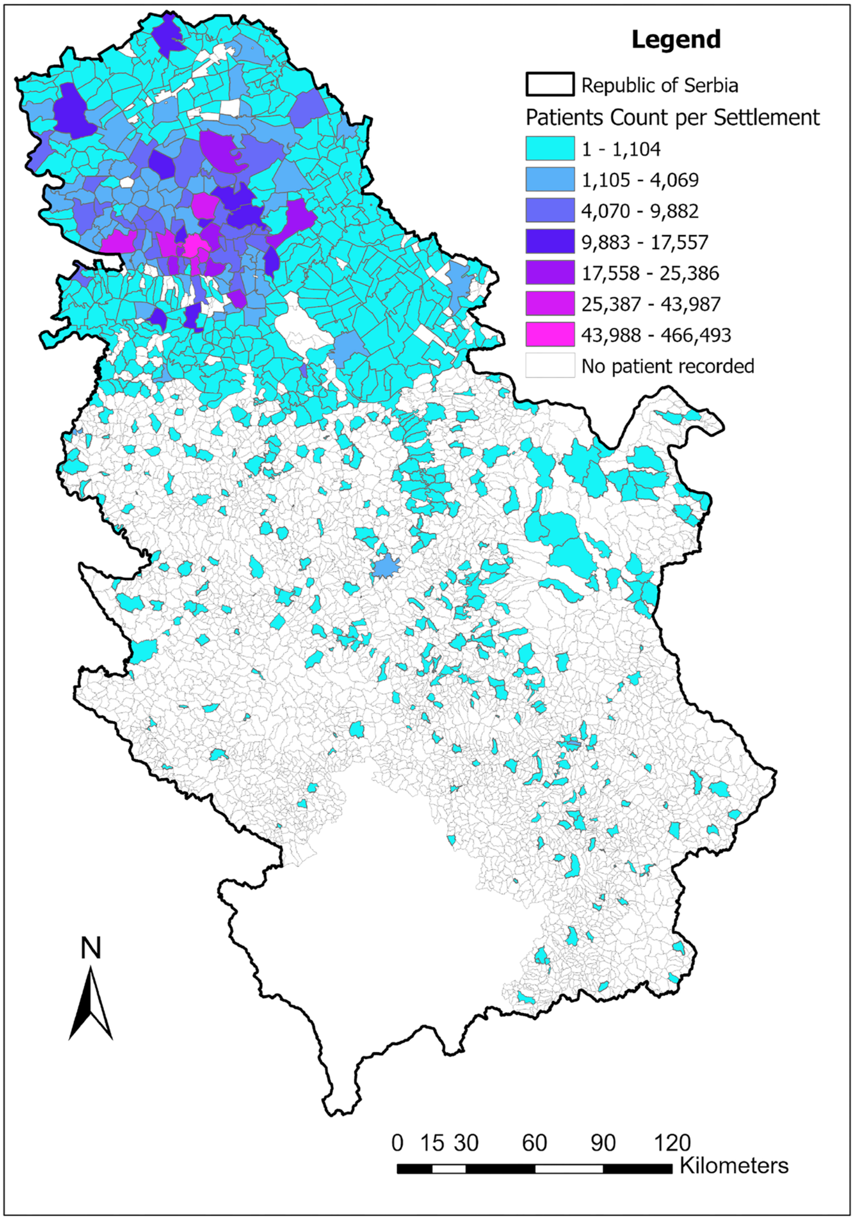


Figure 2: Spatial distribution of patient counts by settlement for the ICDV, Republic of Serbia.

over the n events, the term x_j defines the magnitude of the variable x at the events j over all n, and the term $w_{i,j}$ defines the weight value between the events i and j that represents their spatial interrelationship [2, 6, 16, 18, 57–59] and

$$\overline{X} = \frac{\sum_{j=1}^{n} x_j}{n} \tag{2}$$

$$S = \sqrt{\frac{\sum_{j=1}^{n} x_j^2}{n} - \left(\overline{X}\right)^2} \tag{3}$$

The G_i^* statistic quantifies the spatial association between a feature and its neighbouring values [2, 6, 16, 18, 57–59]. The local sum of a feature and its neighbours is compared to the sum of all features [2, 6, 16, 18, 57–59]. If the local sum differs significantly from the expected sum, with the difference being too large to attribute to random variation, a statistically significant z-score is obtained [2, 6, 16, 18, 57–59].

For the Emerging Hot Spot (EHS) analysis in ArcGIS Pro, specific parameters were applied to ensure consistent spatial and temporal evaluation. The Neighbourhood Time Step was set to 1, meaning that each time-step interval was compared only to its immediate temporal neighbours. Spatial relationships were conceptualised using the K-Nearest Neighbours (K_NEAREST_NEIGHBORS) approach, with the number of spatial neighbours set to 8, ensuring that each location was evaluated in relation to its eight closest neighbours. The Global Window was defined as the

ENTIRE_CUBE, indicating that the statistical analysis considered all locations and time steps across the full space-time cube, rather than applying a localised window. These settings allowed for the detection of significant clusters and emerging patterns throughout the study area over the entire 29-year period.

2.4 Mann-Kendal (MK) analysis

To quantify temporal trends in cardiovascular disease burden, the non-parametric Mann-Kendall test was applied to annual patient counts at the settlement and cluster levels. The MK test [60–63] is designed to evaluate statistically whether a variable exhibits a consistent upward or downward trend over time [2]. According to the MK test, two hypotheses were tested: the null hypothesis, H0, that there is no trend in the time series; and the alternative hypothesis, Ha, that there is a significant trend in the series, for a given significance level limit [2, 6, 16–18, 64].

This model evaluates trends by analysing the sequence of data points in the series [2, 6, 16–18, 60–62, 64]:

$$S = \sum_{i=2}^{n} \sum_{j=1}^{i-1} \operatorname{sign}(x_i - x_j) \tag{4}$$

where sign(x_i−x_j) is

$$\operatorname{sign}(x) = \begin{cases} 1, \; for\; x_i - x_j > 0 \\ 0, \; for\; x_i - x_j = 0 \\ -1, \; for\; x_i - x_j < 0 \end{cases} \tag{5}$$

The statistic S tends to normality for large n; with mean and variance defined as follows [2, 6, 16–18, 64]

$$E(S) = 0 \tag{6}$$

$$V(S) = 1\Big/18\left[n(n-1)(2n+5) - \sum_{P=1}^{q} t_P(t_P - 1)(2t_P + 5)\right] \tag{7}$$

where n is the length of the times-series, t_P is the number of ties for the p value and q is the number of tied values (i.e. equals values). The second term represents an adjustment for tied or censored data. The standardised test statistic Z is given by [2, 6, 16–18, 60–62, 64]:

$$Z = \begin{cases} \dfrac{S-1}{\sqrt{\operatorname{Var}(S)}} & if\; S > 0, \\ 0 & if\; S = 0, \\ \dfrac{S+1}{\sqrt{\operatorname{Var}(S)}} & if\; S < 0, \end{cases} \tag{8}$$

The Z value is used to assess whether a trend in the data is statistically significant [2, 17, 18]. For this analysis, the *pymannkendall* Python module was used, among other tools, to read data from the ArcGIS Pro geodatabase, export parameters to an Excel file, and generate graphs with the data and corresponding trend lines. The MK analysis was performed using Python within the PyCharm 2023 Community Edition environment [2, 17, 18]. Only settlements with a statistically identified trend were included in the analysis. Given that Python is widely used for automating geospatial processes, developing geoprocessing tools, managing data, and integrating with other software systems, its application in medical geographical research is of considerable importance. In addition to the pymannkendall library, the arcpy, NumPy, collections, and xlutils libraries were used in this analysis.

The MK trend test is highly effective for analysing temporal trends in geospatial medical geography [17]. MK detects monotonic trends without assuming data normality, making it robust to non-normal distributions, missing values, irregular time intervals, and outliers – common features of epidemiological datasets [17]. Its rank-based approach captures subtle, long-term increases or decreases in CVDS, even when short-term fluctuations occur due to changes in reporting or population shifts [17]. For a comprehensive geospatial analysis of CVDS patterns, the MK test is most effective when used in conjunction with spatial statistical techniques and models that can accommodate non-linearities and spatial dependencies [17].

2.5 Kriging procedure

The kriging method, named after Daniel G. Krige, a mining engineer who in the 1950s developed statistical approaches for estimating ore deposits [65, 66]. The French scientist Georges Matheron, inspired by Krige's work, extended the Wiener–Kolmogorov theory of stochastic processes to spatial phenomena and, in Krige's honour, named the method kriging [66–68]. Kriging represents a commonly applied method for interpolating spatial data [2, 69]. It utilises input data composed of measurements or observations that describe a spatially continuous phenomenon, obtained from sampling locations distributed throughout the study area [2, 69]. The Kriging method was applied to generate a continuous spatial surface illustrating the estimated distribution of CVD cases across the study area. The resulting raster was converted into contour lines to improve visual interpretation and to emphasise spatial gradients in disease intensity.

The accuracy of the model is limited if the data aren't spatially correlated, if they are limited in spread, or if the number of data points is small [70]. The weights for each interpolated point are computed based on the spatial structure of the interpolated location in relation to all sampled points [2, 71]. These weights are derived from the variogram, which reflects the spatial characteristics of the data, and are applied to the sampled points using the following formula [2, 71]:

$$\widehat{Z}(x_0) = \sum_{i=1}^{N} \lambda_i Z(x_i) \tag{9}$$

where the value of the predicted point (z-hat, at location x-nought) is equal to the sum of the value of each sampled point (x, at location i) times that point's unique weight (lambda, for location i) [2, 71].

Low values in the optional output variance of the prediction raster indicate a high level of confidence in the predicted values, whereas high values may suggest the need for additional data points [2, 72]. In this study the ordinary Kriging method was used, with a spherical model applied for the semi-variogram model [2].

3 Results

3.1 Results of the EHS analysis

As previously mentioned, to perform the EHS analysis, a space-time cube was created. All bins within the space-time cube had a defined date field for time, the time step interval was set to one year, the time step alignment was set to the end time, and a fishnet grid was used as the aggregation shape type. The coordinate system applied was WGS 1984 UTM Zone 34N. The analysed time period spanned 29 years, from 1995, when the first patient was recorded in the database, to 2023.

The space-time cube aggregated 1,386,348 points into 936 fishnet grid locations over 29 time-step intervals. Each grid cell measured 11,925 m by 11,925 m. The entire cube covered an area of 310,050 m from west to east and 429,300 m from north to south. Each time-step interval represented one year, so the total time span of the cube was 29 years. Of the 936 total locations, 395 (42.20 %) contained at least one point during at least one time-step interval. These 395 locations comprised 11,455 space-time bins, of which 7,448 (65.02 %) had point counts greater than zero. A statistically significant increase in point counts was observed over time. Table 1 in Appendix 1 presents the main characteristics of the space-time cube.

Each cluster in this analysis covered 142.21 km^2 area. The results revealed 3 clusters categorised as Consecutive Hot Spots, 9 clusters categorised as Intensifying Hot Spot and 3 clusters categorised as Sporadic Hot Spots, including 16, 35, and 9 settlements in those clusters, respectively (Table 2 in Appendix 1). The remaining clusters showed no patterns.

In the Consecutive Hot Spots category, the first cluster was identified in the settlements of Bački Petrovac, Kulpin, and Maglić ($Z = 5.95$, $p = 2.74 \times 10^{-9}$). The second cluster was detected in Banoštor, Begeč, Čelarevo, Čerević, and Gložan ($Z = 6.15$, $p = 7.57 \times 10^{-10}$), while the third encompassed Grabovo, Grgurevci, Ležimir, Lug, Manđelos, Sviloš, Šišatovac, and Šuljam ($Z = 6.21$, $p = 5.34 \times 10^{-10}$).

In the Intensifying Hot Spot category, the first cluster included Čenej, Kisač, Rumenka, and Stepanovićevo ($Z = 5.31$, $p = 1.11 \times 10^{-8}$), the second covered Bački Jarak and Kać ($Z = 5.27$, $p = 1.36 \times 10^{-7}$), the third covered Gospođinci, Đurđevo, and Žabalj ($Z = 5.12$, $p = 3.04 \times 10^{-7}$), the fourth covered Beočin, Futog, Ledinci, Rakovac, and Veternik ($Z = 5.38$, $p = 7.30 \times 10^{-8}$), the fifth covered Novi Sad and Petrovaradin ($Z = 5.27$, $p = 1.36 \times 10^{-7}$), the sixth cluster was observed in Budisava, Kovilj, and Šajkaš ($Z = 5.16$, $p = 2.49 \times 10^{-7}$), whereas the seventh was concentrated in Bešenovački Prnjavor, Jazak, Mala Remeta, Stari Ledinci, and Vrdnik ($Z = 5.27$, $p = 1.36 \times 10^{-7}$). The eighth cluster comprised Bukovac, Grgetek, Irig, Krušedol Selo, Neradin, Sremska Kamenica, Sremski Karlovci, and Velika Remeta ($Z = 5.12$, $p = 3.04 \times 10^{-7}$). The ninth cluster included Beška, Čortanovci, and Maradik ($Z = 5.05$, $p = 4.51 \times 10^{-7}$).

In the Sporadic Hot Spot, the first cluster included Bačko Dobro Polje, Sirig, and Zmajevo ($Z = 4.90$, $p = 9.79 \times 10^{-7}$), the second cluster occurred in Nadalj, Temerin, and Turija ($Z = 4.78$, $p = 1.72 \times 10^{-6}$), and the third was recorded in Inđija, Jarkovci, and Ljukovo ($Z = 4.37$, $p = 1.24 \times 10^{-5}$). Figure 3 represents the number of patients in the ICDV, according to EHS analysis.

The results indicate that consecutive hot spot clusters are spatially concentrated on the west of Novi Sad. Apart from this, intensifying hot spot clusters are around the urban and suburban areas of Novi Sad. In contrast, sporadic clusters are more dispersed across rural settlements, reflecting localised variations in disease intensity.

3.2 Results of the MK analysis – settlement level

From the set of outputs provided by the Python module used in this analysis, the following parameters were extracted: trend type, p-value, z-value, slope, and intercept. Table 3 in Appendix 1 presents the parameters for each settlement used in this analysis. Overall, trends were detected in 333 settlements, of which 287 exhibited an increasing trend and 46 a decreasing trend. Figure 4 clearly shows that settlements with an increasing trend are predominantly

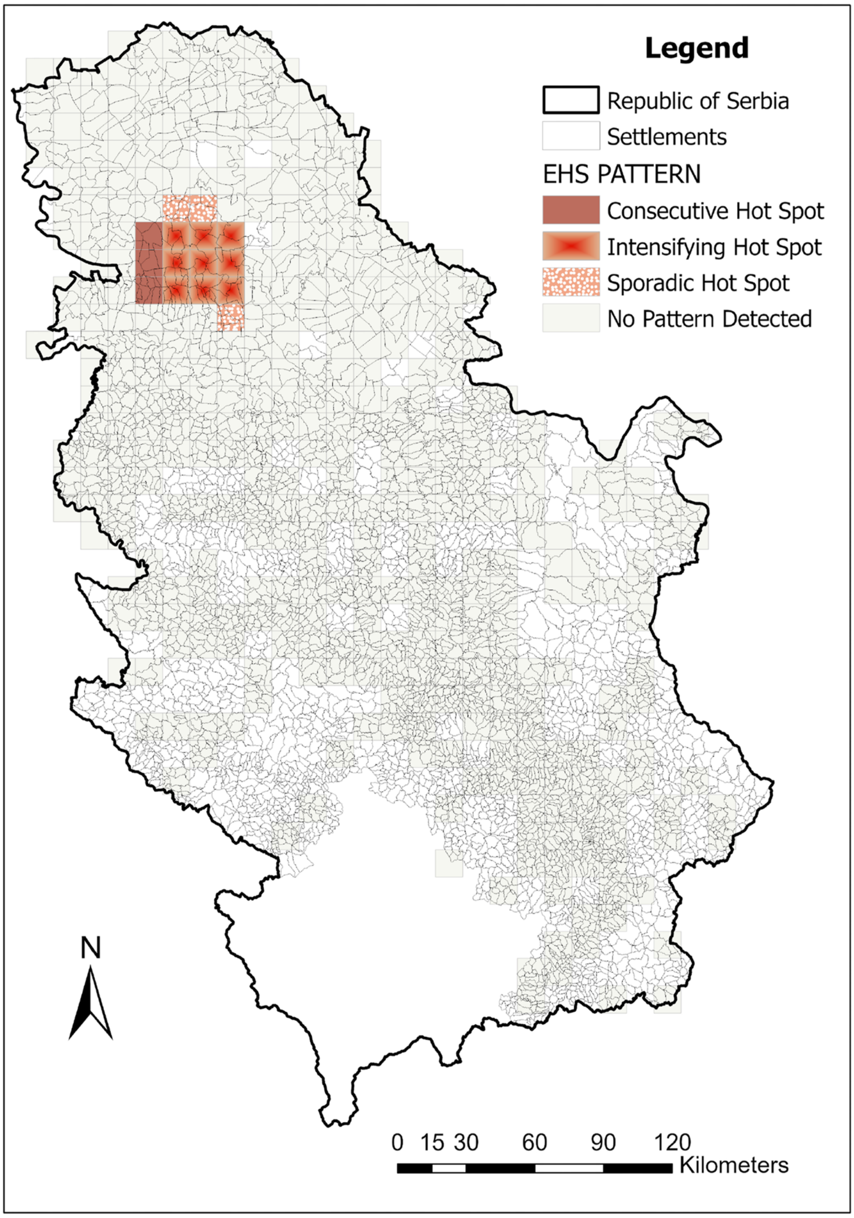


Figure 3: Number of patients in the ICDV – EHS analysis.

concentrated in the northern part of the study area, which is consistent with the results of two other analyses. Furthermore, the majority of settlements with an identified decreasing trend are located outside the AP Vojvodina, as the ICDV is not their primary medical facility at this level of healthcare provision.

3.3 Results of the MK analysis on the EHS clusters

In addition to the EHS analysis conducted at the settlement level, a MK trend analysis was performed on the EHS clusters. To enable this analysis, a spatial intersection was carried out between the EHS cluster polygons and patient records aggregated by settlement. For each cluster, the MK analysis was applied to the corresponding subset of patient records.

Where a statistically significant trend was identified, the relevant parameters from both the EHS and MK analyses were compiled, and the EHS cluster polygons were updated to reflect the detected trend. These parameters are presented in Table 4 in Appendix 1 as a comparison of the EHS and MK analysis parameters at the cluster level.

As shown in Figure 5, only one decreasing trend was detected among the 91 clusters analysed, while the remaining 90 clusters exhibited an increasing trend. Furthermore, an increasing trend was identified in 10 out of the 15 clusters

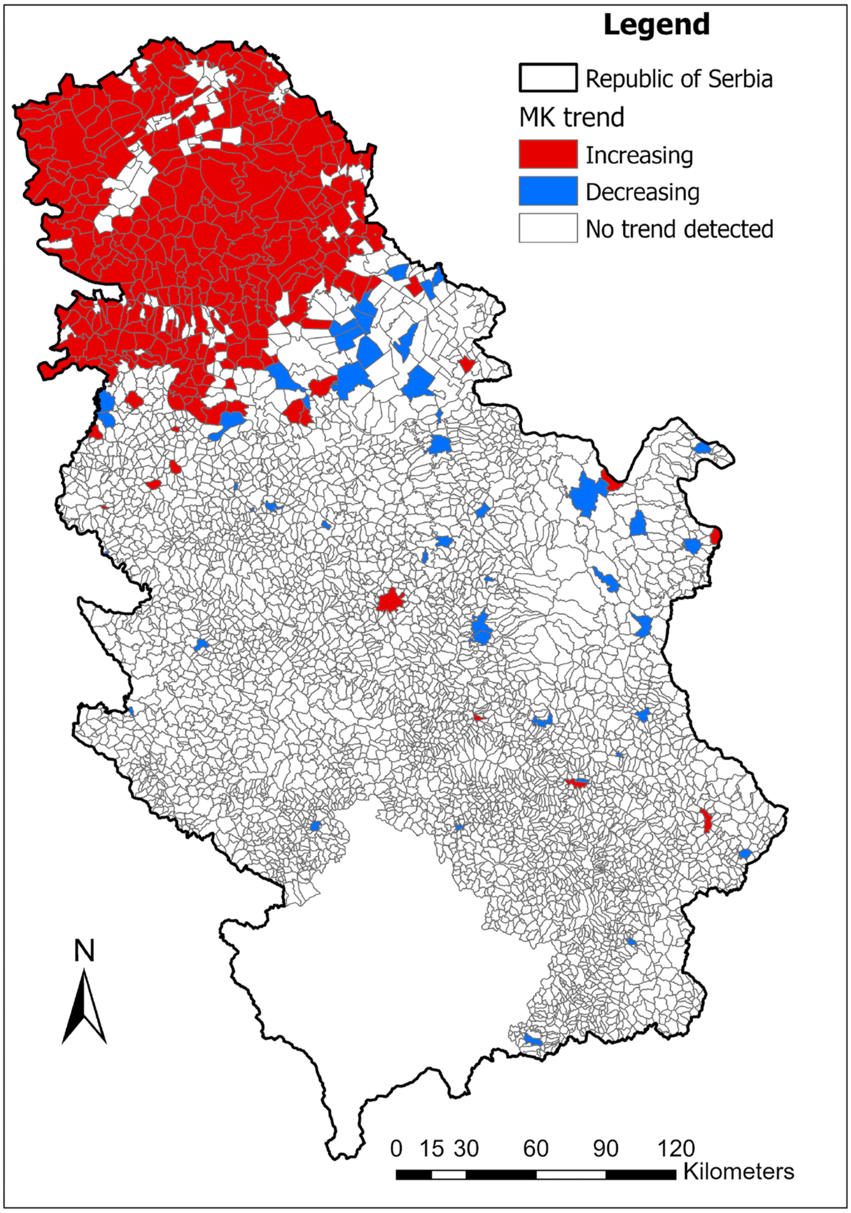


Figure 4: The MK trends in the number of patients in the ICDV – settlement level.

with a defined EHS pattern. Clusters classified as Intensifying and Consecutive Hot Spots consistently exhibited statistically significant positive MK trends, indicating that both the spatial concentration and temporal burden of CVD are increasing simultaneously.

The presence of a single cluster with a statistically significant decreasing trend suggests that localised reductions in ICDV patient counts are possible, likely reflecting changes in referral patterns, availability of alternative tertiary care centres, or demographic shifts rather than true epidemiological decline. The statistically significant upward trend reflects a sustained increase in recorded CVD cases across the majority of active space-time bins, with the steepest increases observed in urban and peri-urban settlements surrounding Novi Sad. The consistency between settlement-level and cluster-level MK results indicates that the observed upward trends are not artefacts of spatial aggregation, but represent a robust, scale-independent increase in CVD burden.

3.4 Results of kriging procedure

Given the strong spatial autocorrelation of patient counts and the absence of a deterministic trend surface, ordinary

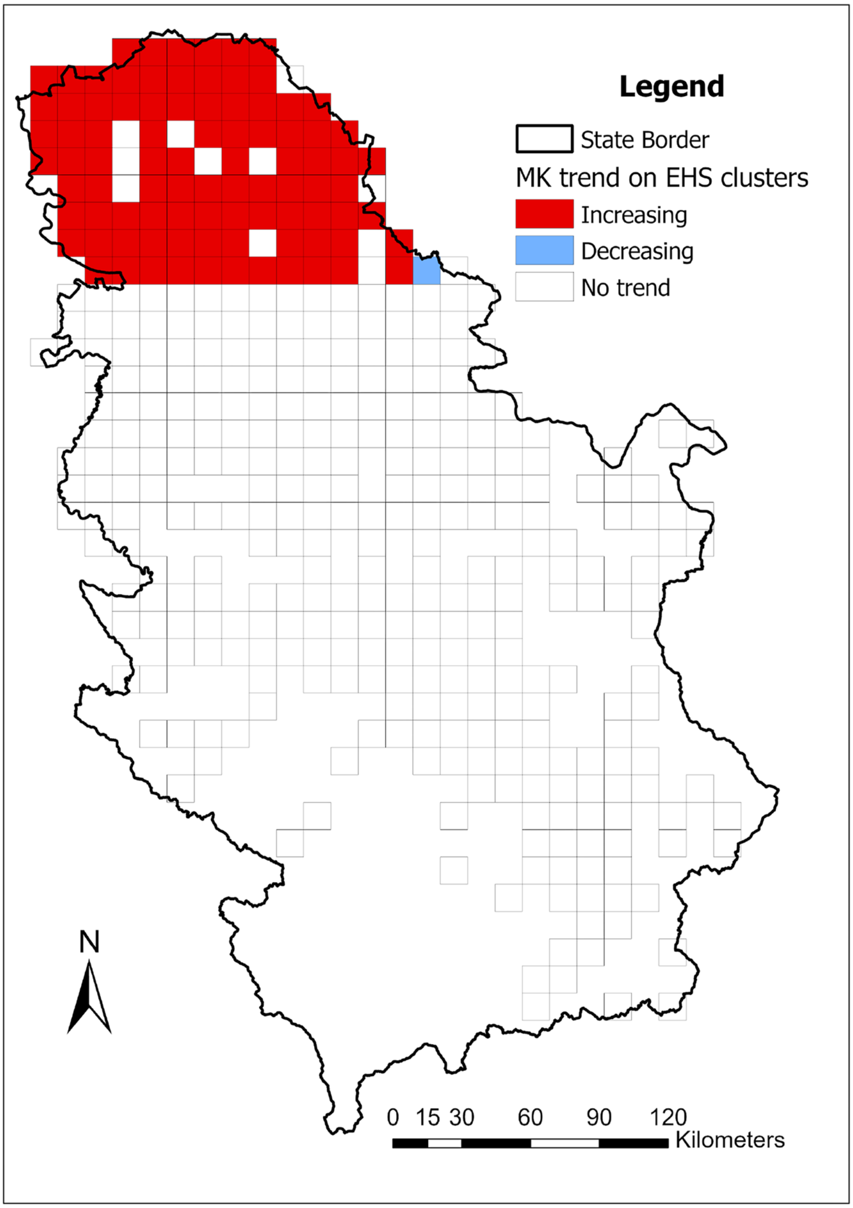


Figure 5: The MK trends in the number of patients in the ICDV – cluster level.

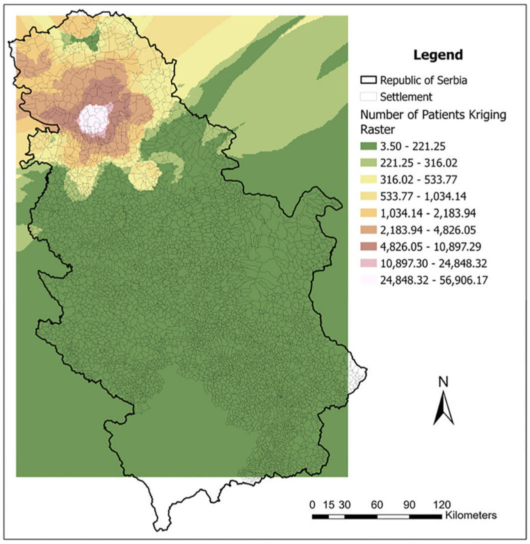
kriging was selected. Cross-validation indicated acceptable prediction errors, supporting its use for exploratory visualization rather than precise risk estimation.

As previously noted, to perform this analysis the settlement polygons were converted into points, after which a Kriging raster was generated. Figure 6a) illustrates the spatial distribution of the number of ICDV patients per settlement based on the Kriging interpolation. Lower patient counts are represented by green shades, whereas higher counts are shown in brown and white, with values ranging from 3.50 to 56,906.17. Figure 6b) shows the final contour lines, with number of patients ranging from 200 to 56,800. Contours interval was set to 200, so the lowest contour is the same value.

3.5 Discussion

The findings of this study provide important insights into the geospatial distribution of CVD in the Republic of Serbia, based on patient data from the ICDV between 1995 and 2023. Trend analysis was detected in 333 settlements, of which 287 exhibited an increasing trend and 46 a decreasing trend. The settlements with an increasing trend are predominantly concentrated in the northern part of the study area, which is consistent with the results of two other analyses. Furthermore, the majority of settlements with an identified decreasing trend are located outside the AP Vojvodina, as the ICDV is not their primary medical facility at this level of healthcare provision.

a)



b)

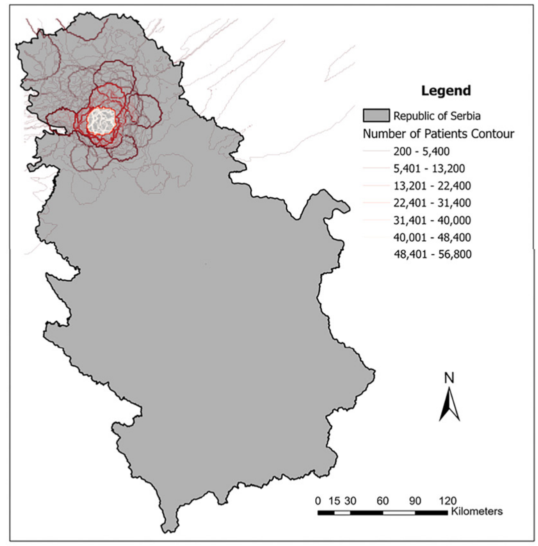


Figure 6: Spatial distribution of ICDV patient counts derived from: a) the kriging raster, b) Contours.

The application of the EHS analysis revealed distinct clusters of CVD, with 3 clusters categorised as Consecutive Hot Spots, 9 clusters categorised as Intensifying Hot Spot and 3 clusters categorised as Sporadic Hot Spots, including 16, 35, and 9 settlements in those clusters, respectively. The persistence and intensification of hot spots in the Novi Sad metropolitan region suggest cumulative effects of urbanization, healthcare accessibility, and lifestyle risk factors, reinforcing spatial health inequalities rather than diffusing them over time. These findings suggest a significantly higher burden of CVD settlements within South Bačka County. The identification of settlements that consistently appear within hot spot clusters is particularly relevant for directing public health interventions, as it allows for prioritisation of resources and targeted prevention strategies.

Figure 7 provides an integrated spatial perspective by combining cluster-based trend analysis with continuous surface interpolation. The convergence of intensifying EHS clusters, positive MK trends, and kriging-derived high-value zones highlights a pronounced spatial core of CVD burden centred on the Novi Sad metropolitan area. Importantly, the gradual attenuation of interpolated values away from this core suggests a spatial gradient rather than abrupt boundaries, indicating transitional zones between high- and low-burden areas. Such patterns are characteristic of urban-suburban health polarization and point to cumulative effects of population density, healthcare utilization, and long-term exposure to CVD risk factors.

The use of Kriging interpolation further enhanced the spatial representation of disease burden. This approach enables interpretation of geographic variation in CVD occurrence and highlights transitional zones between high- and low-burden areas. Taken together, the results underline the value of geospatial methods for public health surveillance, as they not only detect statistically significant clustering but also allow for a nuanced understanding of spatial gradients. This is clearly illustrated in Figure 8, which integrates these three methods. These analyses indicate the same centre of gravity for the CVD patient distribution.

The present study has not sought to investigate the etiological factors underlying the occurrence of CVD. Instead, its primary objective has been to delineate areas characterised by relatively high and low levels of disease burden. This spatial perspective allows for the detection of geographic inequalities in cardiovascular health and serves as a preliminary step toward more comprehensive analyses that could integrate sociodemographic, environmental, and lifestyle-related risk factors. By identifying the most and least affected regions, the study provides valuable evidence to guide targeted public health interventions and future epidemiological research.

From 1995 to 2005, the data are quite limited, as these were the early years of the information system at the ICDV, when data entry was optional and therefore incomplete. This limitation mirrors broader systemic challenges in Serbia, where, although a coronary heart disease register had been legally mandated since 1980, the initial system faced significant weaknesses that compromised its effectiveness [56]. Although a coronary heart disease register has been legally mandated in Serbia since 1980, the initial system faced significant limitations that compromised its effectiveness [56]. The use of inadequate reporting forms, insufficiently precise methodological instructions, limited training of health

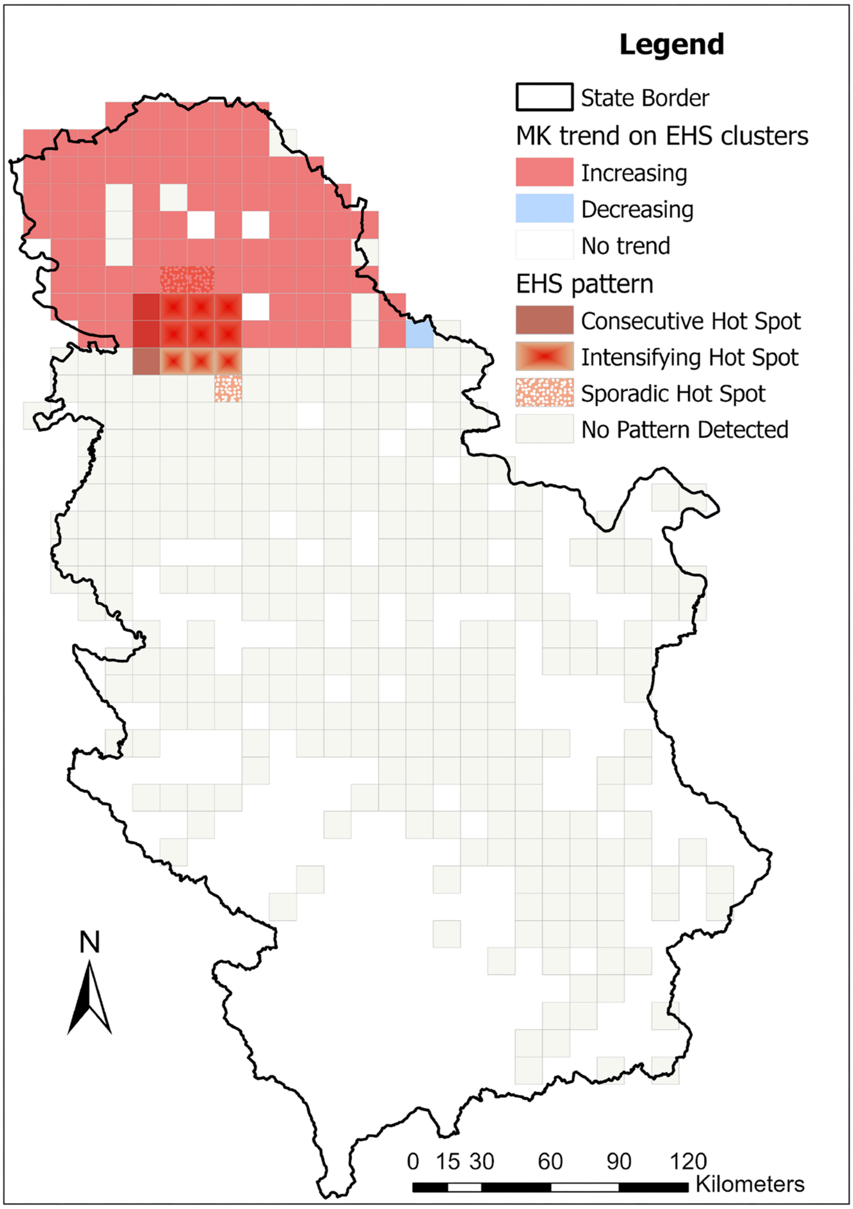


Figure 7: Integrated spatial distribution of ICDV patient counts derived from the MK and EHS analyses.

personnel, and the absence of adequate informatics support all contributed to systematic underreporting of newly diagnosed cases effectiveness [56]. By the end of the 1990s, the number of registered patients was markedly lower than mortality data suggested and up to 20 times below the estimated prevalence of ischemic heart disease [56]. These shortcomings highlight the discrepancy between the intended scope of registration and the actual epidemiological burden of CVD, raising concerns about the reliability of early surveillance data for research and policy planning.

In response to these challenges, a series of legal and regulatory measures were introduced to improve data quality, coverage, and standardisation. A major milestone was the establishment of the population-based Acute Coronary Syndrome Register (RAKSS) in 2006, initiated by the Institute of Public Health of Serbia “Dr Milan Jovanović Batut” in collaboration with the national Expert Team for ACS effectiveness [56]. The reorganisation emphasised decentralisation and the inclusion of multiple data sources beyond the existing hospital-based REAKS registry, with regional institutes of public health tasked with managing local registries and Batut responsible for centralised analysis effectiveness [56]. These efforts significantly strengthened cardiovascular disease surveillance and created a more robust epidemiological foundation for monitoring CVD.

Nevertheless, ongoing challenges such as ensuring data completeness and sustaining long-term registry infrastructure remain important considerations for

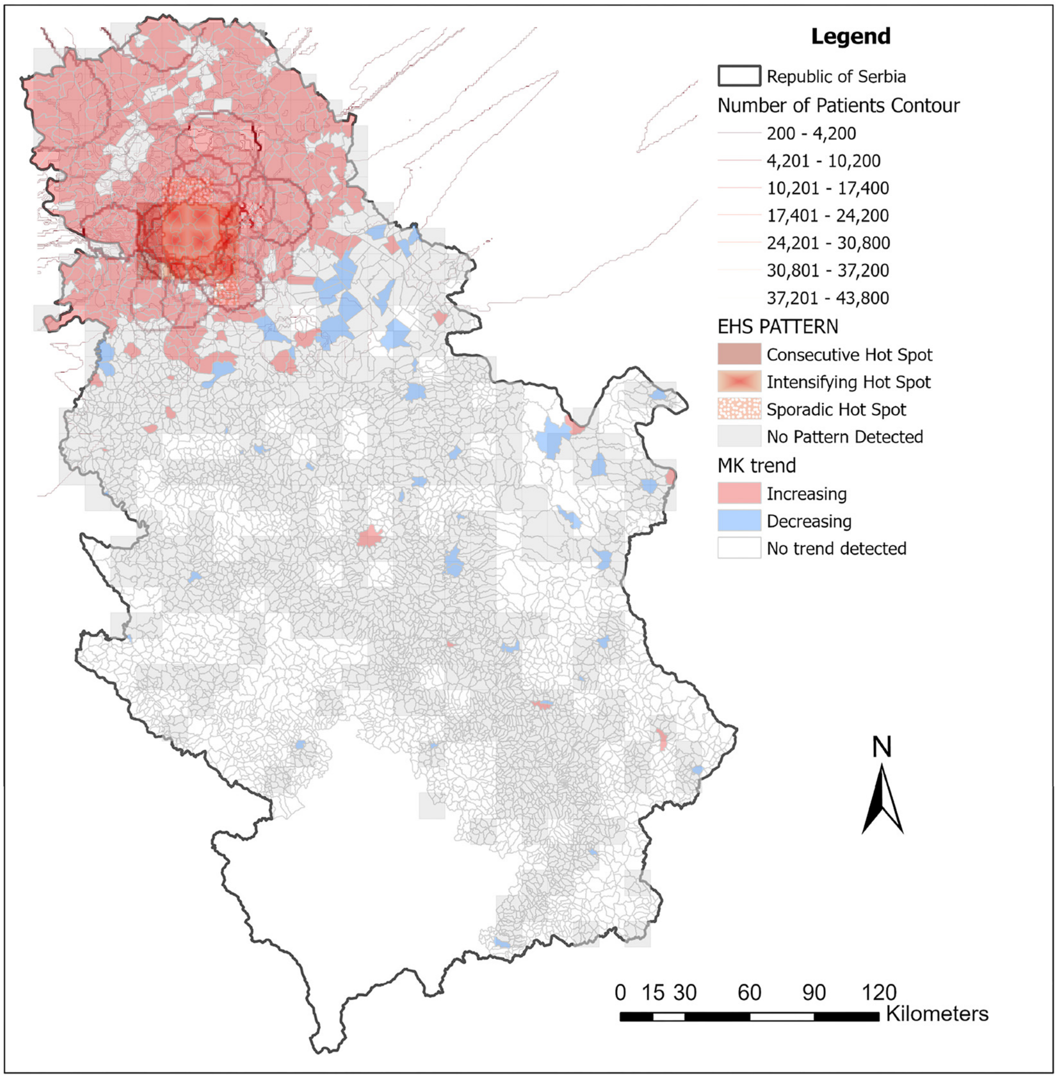


Figure 8: Integrated spatial distribution of ICDV patient counts derived from the MK and EHS analyses and kriging interpolation.

further development. In addition to improving data quality and registry infrastructure, further progress in CVD surveillance in Serbia will require strengthening inter-institutional collaboration and coordination. Effective monitoring of disease trends depends not only on the efforts of individual hospitals or public health institutes, but also on the establishment of systematic communication channels, standardised reporting procedures, and integrated information systems across all levels of healthcare. Closer cooperation between clinical centres, regional public health institutes, and national authorities would enhance the completeness and reliability of data, reduce duplication of effort, and ensure timely data sharing for both clinical practice and public health policy. Such a coordinated approach is essential for building a sustainable and comprehensive surveillance framework that can support evidence-based decision-making and targeted interventions.

As already noted, although ICD-10 was used in this study and remains officially implemented in Serbia, ICD-11 came into effect on January 1, 2022. Unlike ICD-10, ICD-11 is fully digital, includes more diagnoses and more precise codes, features updated medical terminology, and introduces new diagnostic categories, enabling more detailed monitoring and internationally comparable statistics. Its implementation in Serbia has not yet begun due to the need for adjustments in legislation, information systems, and national adaptation of the classification.

Kričković et al. analysed some of the CVD and found that the North Bačka County had a lower mortality rate for acute coronary syndrome and myocardial infarction, despite an above-average number of new cases [6]. They also reported the highest incidence of unstable angina pectoris in the Severnobački, Severnobanatski, and Srednjobanatski counties, while the Zapadnobački county showed higher mortality [6]. However, their study was limited to three CVD within Vojvodina, whereas the present study encompassed all CVD recorded among patients of the ICDV. These methodological and scope-related differences significantly affect the comparability of the results.

According to Institute of Public Health of Serbia Dr Milan Jovanović Batut [51], in 2022, standardized incidence rates of acute coronary syndrome per 100,000 population in the AP Vojvodina were highest in the Zapadnobački and Severnobački counties. In central Serbia, the highest incidence rates were observed in the Kolubarski, Braničevski, Borski, Nišavski, and Toplički counties, while the lowest rates were recorded in the Južnobački, Sremski, Mačvanski, Beogradski, Zlatiborski, and Šumadijski counties [51]. Similarly, in 2022, standardized mortality rates from acute coronary syndrome in Vojvodina were highest in the Severnobački and Severnobanatski counties, whereas in Central Serbia, the highest mortality was observed in the Kolubarski, Zlatiborski, and Raški counties [51]. The lowest mortality rates were reported in the Zapadnobački, Sremski, Beogradski, Moravički, and Jablanički counties [51].

These data, which are publicly available from the Institute of Public Health of Serbia "Dr Milan Jovanović Batut," cannot be directly compared with the results of the present study, as it focuses on patients from a single healthcare institution and considers all CVD collectively, rather than acute coronary syndrome alone.

Kričković et al. utilized artificial intelligence to develop an interactive map depicting the spatial distribution of patients examined at the ICDV [23]. The results indicated that the largest proportion of patients originated from the Južnobački County, which was anticipated considering the Institute's location within this administrative area [25]. Furthermore, the majority of admitted patients were residents of the AP Vojvodina, which is consistent with the findings of the present research. Research conducted by Kričković et al. where investigated patients at the ICDV indicated higher trends in hypertension cases in settlements within Južnobački County [2], which is consistent with the findings of the present research.

The study "Research on the Health of the Population of Serbia in 2019", conducted by the Statistical Office of the Republic of Serbia in collaboration with the Institute of Public Health of Serbia and the Ministry of Health of the Republic of Serbia, reveals notable health inequalities [2, 6, 46, 73]. Women, particularly those with lower education and socioeconomic status, more often report poor health. In Vojvodina, a higher prevalence of obesity (25.4 %) was observed, likely associated with diets rich in saturated fats, salt, and high-calorie foods [2, 6, 46, 73]. Unfavourable patterns are also present in other regions. Southern and Eastern Serbia show higher levels of obesity, greater daily bread consumption, and higher rates of smoking and alcohol use, while Šumadija and Western Serbia have lower rates of these behaviours [2, 6, 46, 73]. The latest National Health Survey for 2025, conducted on a sample of 4,800 households, is expected to provide further insights once results are published [74]. These findings highlight the importance of promoting healthier lifestyles – including better nutrition, increased physical activity, weight control, and reduced tobacco and alcohol use, to lower cardiovascular risk.

In 2023, the Institute of Public Health of Vojvodina, in collaboration with six county institutes, implemented the program "Monitoring the Sodium Chloride Content in Meals Provided through Organised Nutrition for Preschool Children and Adolescents in Vojvodina" [42]. Data from 2012 to 2022 indicated that salt intake among preschool children was consistently excessive in all examined facilities, in both urban and rural areas [42]. Elevated sodium chloride levels were also found in meals for school-aged children, adolescents, and university students [42]. Since 2008, all European Union member states, in cooperation with the World Health Organisation (WHO), have been implementing national programs aimed at reducing salt intake. The WHO recommends a 30 % reduction by 2025 [42]. In Serbia, the Strategy for the Prevention of Non-Communicable Diseases and its 2009–2015 Action Plan identified improved nutrition and reduced salt intake as specific goals; however, implementation programs have not been developed [42, 75]. Evidence from countries with established national salt reduction programs shows that achieving the recommended daily sodium intake is a long-term and challenging process requiring multisectoral support [42]. Effective collaboration between public health institutions and organised nutrition services for children and youth is essential for sustainable progress [42].

Petrović and Čanković found that both general and abdominal obesity are highly prevalent among adolescents in Vojvodina, with a higher occurrence observed among boys [47]. These results are concerning since obesity during adolescence significantly increases the likelihood of developing CVD later in life [47]. The study by Tomašević et al. indicated an increase in the prevalence of obesity and hypertension in Vojvodina, with obese individuals being nearly twice as likely to develop hypertension [45]. These findings are particularly important given that obesity and elevated blood pressure are key risk factors contributing to the onset and progression of CVD [45].

Jevtić et al. reveal a significant positive correlation between hospital admissions due to CVD and outdoor NO_2

concentrations in the Novi Sad area, Serbia [44]. Exposure to nitrogen dioxide and other air pollutants has been widely recognised as a contributing factor to the onset and exacerbation of cardiovascular conditions [44]. These findings underscore the importance of addressing environmental determinants of health, in conjunction with behavioural and risk factors, to reduce the overall burden of CVD in the population. In this context, the spatial distribution of air quality in Vojvodina during 2024 indicates notable regional disparities that may contribute to unequal CVD risk. While most of the territory was characterized by Category I air quality (clean or slightly polluted), elevated pollution levels were identified in urban agglomerations such as Novi Sad and Pančevo, where air was classified as Category III (over-polluted) due to exceedances of PM_{10} limit values [76]. Additionally, increased concentrations of particulate matter were recorded in Subotica, Beočin, Sombor, and Zrenjanin [76].

These findings are partially consistent with the results of the MK analysis, which indicate an increasing trend in most observed regions, suggesting a possible association between higher pollution levels and elevated CVD burden. However, an exception is observed in Pančevo, where, despite high levels of air pollution, the increasing trend was not confirmed. This discrepancy may be explained by the fact that Pančevo belongs to a different administrative county than the analysed hospital catchment area, which may influence patient flow, case registration, and the spatial attribution of health outcomes. From a public health perspective, populations residing in areas with elevated PM_{10} and NO_2 levels remain at higher cardiovascular risk, underscoring the importance of integrating environmental indicators into spatial health analyses [76].

Effective prevention and control of CVD requires a continued emphasis on health promotion and education, particularly targeting vulnerable populations and the health issues that contribute most to the local disease burden [42]. Successful implementation depends on modern health education tools, trained educators, and a multidisciplinary, multisectoral approach involving partnerships with schools, social services, local communities, media, and NGOs [42]. Additionally, leveraging modern technologies and communication channels, especially when engaging children and youth, can enhance the reach and impact of these interventions [42]. Moreover, greater emphasis should be placed on the implementation of structured preventive strategies, given that CVD are largely preventable. This includes the early detection and effective management of major risk factors such as hypertension, diabetes, smoking, physical inactivity, and unhealthy diet. In this context, strengthening primary health care systems and introducing organized screening programs, particularly for high-risk populations, are essential steps toward reducing disease burden. Additionally, population-based health promotion interventions aimed at encouraging healthier lifestyles, along with efforts to reduce health inequalities and improve access to preventive services, are crucial for achieving sustainable public health outcomes.

Comprehensive implementation of national strategies, regulations, and programs for the prevention and control of chronic non-communicable diseases, along with the provision of material and human resources [42], should constitute an imperative for the Republic of Serbia in the fight against CVD. Strengthening collaboration among institutions specialized in the treatment of CVD across the Republic of Serbia, particularly through the establishment of a unified database, would provide a more comprehensive foundation for spatial-temporal analyses. Such integration could enable researchers to obtain a complete overview of CVD patterns at the national level, thus improving the accuracy of epidemiological insights. Greater emphasis should be placed on regional cooperation.

Equally important is the need for multidisciplinary cooperation. Experts from various fields-clinicians, epidemiologists, geographers, statisticians, and public health professionals-should not work in isolation but rather engage in joint studies. This integrated approach would allow for a more in-depth examination of the multifactorial causes of CVD, including demographic, environmental, behavioural, and socioeconomic determinants. Interdisciplinary collaboration may foster innovative research directions, including the application of advanced geospatial techniques, machine learning, and predictive modelling to better understand disease dynamics. Finally, the development of such an integrated system would support evidence-based decision-making, offering policymakers a robust tool for designing prevention strategies and allocating healthcare resources more efficiently.

In the context of global development priorities, population health represents a key indicator of societal progress and is directly linked to the 2030 Agenda for Sustainable Development adopted by the United Nations, particularly Sustainable Development Goal 3 (SDG 3: Good Health and Well-being) [77]. This goal emphasizes the need to reduce mortality from non-communicable diseases, among which CVD remain the leading cause of death at both global and national levels [77]. CVD constitute one of the most significant public health challenges; therefore, their prevention, early diagnosis, and adequate treatment play a crucial role in achieving the targets of SDG 3, especially those related to reducing premature mortality from non-communicable diseases through prevention and treatment, as well as promoting mental health and well-being [77].

4 Conclusions

This spatial analysis of CVD reveals pronounced geographical disparities in disease occurrence, demonstrating an uneven distribution of cardiovascular burden across settlements in the Republic of Serbia. The marked concentration of cases in South Bačka County, particularly within the Novi Sad metropolitan area, points to the existence of persistent high-risk zones that warrant targeted preventive measures and improved accessibility to healthcare services. While this spatial pattern reflects genuine differences in disease burden, it must also be interpreted in light of the study design, as the analysis is based on patients treated at a single tertiary medical institution. The location of the ICDV likely influenced the observed spatial distribution, with proximity to the Institute contributing to higher recorded patient numbers in adjacent settlements.

The application of geostatistical and GIS-based methods proved highly effective in elucidating the spatial and temporal dynamics of cardiovascular morbidity, providing insights that extend beyond those obtainable through conventional epidemiological approaches. Incorporating trend analysis transforms spatial clustering from a descriptive tool into an early-warning mechanism capable of supporting proactive cardiovascular disease prevention. By integrating the EHS analysis with Kriging interpolation within a long-term spatio-temporal framework, this study offers a robust and transferable methodological approach for monitoring cardiovascular disease burden at the settlement level. The ability to identify persistent, emerging, and spatially concentrated high-risk areas provides policymakers with an evidence-based foundation for prioritizing preventive programs, optimizing the allocation of healthcare resources, and strengthening early-warning capacities within public health systems. In this context, spatially explicit analyses can support more effective, place-based interventions and contribute to the reduction of regional health inequalities.

Beyond its immediate empirical findings, the study underscores the broader value of incorporating advanced spatial analytics into the surveillance of non-communicable diseases. The methodological framework presented here is readily applicable to other disease groups and geographic settings, particularly in regions where long-term clinical registries exist but remain underutilized for spatial epidemiological research. Future studies should aim to integrate data from multiple healthcare institutions to achieve a more comprehensive and representative national overview of CVD in Serbia, thereby minimizing biases related to healthcare accessibility and institutional proximity. The incorporation of population-normalized indicators, advanced spatio-temporal analyses, and machine learning techniques holds considerable potential for improving predictive modelling and supporting the early detection of emerging risk areas. Additionally, longitudinal investigations linking spatial patterns with demographic, socioeconomic, environmental, and clinical determinants are essential for evaluating the effectiveness of preventive measures and for informing evidence-based public health strategies aimed at reducing the long-term burden of CVD.

Research ethics: Not applicable.
Informed consent: Not applicable.
Author contributions: Conceptualization, E.K. and T.L; Methodology, E.K. and T.L.; Software, Z.K.; Formal analysis, V.M.C., M.Ž.; Investigation, E.K., T.L., Z.K., A.S.M., V.M.C. and M.Ž.; Resources, A.S.M. All authors have read and agreed to the published version of the manuscript.
Use of Large Language Models, AI and Machine Learning Tools: None declared.
Conflict of interest: The authors state no conflict of interest.
Research funding: This study was supported by the Program of Cooperation with the Serbian Scientific Diaspora- Joint Research Projects – DIASPORA 2023, from the Science Fund of the Republic of Serbia, under the project LAMINATION (The Loess Plateau Margins: Towards Innovative Sustainable Conservation), Project number: 17807 and the support of the Ministry of Science, Technological Development and Innovation of the Republic of Serbia (Grants No 451-03-33/2026-03/200125 & 451-03-34/2026-03/200125 and 451-03-33/2026-03/200091). Furthermore, this study was supported by the Scientific-Professional Society for Disaster Risk Management and ProSafeNet – The Global Hub for Safety, Security, Risk & Emergency Professionals and Scientists (https://prosafenet.com/). Also, this study was supported by the project of the Ministry of Defence of the Republic of Serbia and the Serbian Armed Forces – Application of Digital Geotopograpchic Data in Multi-Criteria Analysis for Identifying Safe Helicopter Landing Zones in the Republic of Serbia (Project number: 1.18-2026).
Data availability: Not applicable.

References

1. Rudasingwa G, Cho S, Ishimwe NC. Regional prevalence and spatial modeling of hypertension in South Africa. Open Health 2024;5:20230030.
2. Kričković E, Lukić T, Kričković Z, Stojšić-Milosavljević A. Hypertension in AP Vojvodina (Northern Serbia): a spatio-temporal analysis of patients at the institute for cardiovascular diseases of Vojvodina. Open Geosci 2025;17:20250843.

3. World Health Organization. Cardiovascular diseases (CVDs) [internet]; 2025. Available from: https://www.who.int/news-room/fact-sheets/detail/cardiovascular-diseases-(cvds).
4. Mensah GA, Fuster V, Murray CJL, Roth GA, Abate YH, et al. Global burden of cardiovascular diseases and risks, 1990–2022. J Am Coll Cardiol 2023;82:2351–473.
5. Levine DA, Lewis CE, Williams OD, Safford MM, Liu K, Calhoun DA, et al. Geographic and demographic variability in 20-year hypertension incidence. Hypertension 2010;57:39–47.
6. Kričković E, Lukić T, Jovanović-Popović D. Geographic medical overview of non-communicable diseases (cardiovascular diseases and diabetes) in the territory of the AP Vojvodina (Northern Serbia). Healthcare 2023; 11:1–35.
7. Wang MS, Deng JW, Geng WY, Zheng R, Xu HL, Dong Y, et al. Temporal trend and attributable risk factors of cardiovascular disease burden for adults 55 years and older in 204 countries/territories from 1990 to 2021: an analysis for the global burden of disease study 2021. Eur J Prev Cardiol 2025;32:539–52.
8. Hu T, Yang X, Du Y, Zhao Y, Chen L, Sun N, et al. Trends in the global, regional, and national burden of cardiovascular diseases attributed to high systolic blood pressure from 1990 to 2021 and projections to 2045: a systematic analysis based on GBD 2021 data. BMC Cardiovasc Disord 2025;25:390.
9. Kang Y, Wang X, Yin P, Chen Z, Jiang L, Dong W, et al. Nationwide spatiotemporal trends in blood pressure and the attributable cardiovascular burden from 2005 to 2018: a pooled analysis of 13.1 million participants in China. J Hypertens 2021;39:e84.
10. Gupta R. Trends in hypertension epidemiology in India. J Hum Hypertens 2004;18:73–8.
11. Gupta R, Gaur K, Ram CV. Emerging trends in hypertension epidemiology in India. J Hum Hypertens 2019;33:575–87.
12. Heaton J, Alshami A, Imburgio S, Mararenko A, Schoenfeld M, Sealove B, et al. Current trends in hypertension identification and management: insights from the national health and nutrition examination survey (NHANES) following the 2017 ACC/AHA high blood pressure guidelines. J Am Heart Assoc 2024;13:1–10.
13. Aekplakorn W, Chariyalertsak S, Kessomboon P, Assanangkornchai S, Taneepanichskul S, Goldstein A, et al. Trends in hypertension prevalence, awareness, treatment, and control in the Thai population, 2004 to 2020. BMC Public Health 2024;24:3149.
14. Cherla A, Kyriopoulos I, Pearcy P, Tsangalidou Z, Hajrulahovic H, Theodorakis P, et al. Trends in avoidable mortality from cardiovascular diseases in the European Union, 1995–2020: a retrospective secondary data analysis. The Lancet Reg Health Europe 2024;47:101079.
15. Woodruff RC, Tong X, Khan SS, Shah NS, Jackson SL, Loustalot F, et al. Trends in cardiovascular disease mortality rates and excess deaths, 2010–2022. Am J Prev Med 2024;66:582–9.
16. Kričković E, Lukić T, Srejić T, Stojšić-Milosavljević A, Stojanović V, Kričković Z. Spatial-temporal and trend analysis of traffic accidents in AP Vojvodina (North Serbia). Open Geosci 2024;16:20220630.
17. Kričković E, Cvetković VM, Kričković Z, Lukić T. Spatial-temporal trends of cancer among women in central Serbia, 1999–2021: implications for disaster and public health preparedness. Helthcare 2025;13:1–36, 2169.
18. Kričković E, Lukić T, Kričković Z, Stojšić-Milosavljević A, Živanović M, Srejić T. Spatiotemporal and trend analysis of common cancers in men in central Serbia (1999–2021). Open Geosci 2025;17:20250802.
19. White K, Stewart JE, Lòpez-DeFede A, Wilkerson RC. Small-area variation in hypertension prevalence among black and white medicaid enrollees. Ethn Dis 2016;26:331–8.
20. Laohasiriwong W, Puttanapong N, Singsalasang A. Prevalence of hypertension in Thailand: hotspot clustering detected by spatial analysis. Geospat Health 2018;13:20–7.
21. Xu L, Jiang Q, Lairson DR. Spatio-temporal variation of genderspecific hypertension risk: evidence from China. Int J Env Res Public Health 2019;16:4545.
22. Murad A, Khashoggi BF. Using GIS for disease mapping and clustering in Jeddah, Saudi Arabia. ISPRS Int J Geo-Inf 2020;9:328.
23. Leroux D, Cloutier L. Geographical analysis of hypertension in Canadian population. J Hypertens 2022;40:e211.
24. Kamath R, Brand H, Arun HR, Lakshmi V, Sharma N, D'Souza RMC. Spatial patterns in the distribution of hypertension among men and women in India and its relationship with health insurance coverage. Healthcare (Basel) 2023;11:1630.
25. Kričković E, Lukić T, Kričković Z, Stojšić-Milosavljević A, Srejić T. Use of health information systems and artificial intelligence for environmental and public health protection. In: Proceedings of the 13th scientific and professional conference with international participation "planning and normative protection of space and the environment". Vršac, Serbia: Association of Spatial Planners of Serbia; University of Belgrade – Faculty of Geography; 2025:143–9 pp.
26. Oliver MA, Webster R. Kriging: a method of interpolation for geographical information systems. Int J Geogr Inf Sci 1990;4:313–32.
27. Carrat F, Valleron AJ. Epidemiologic mapping using the "Kriging" method: application to an influenza-like epidemic in France. Am J Epidemiol 1992;135:1293–300.
28. Wartenberg D. Some epidemiologic applications of Kriging. In: Soares A, editor. Geostatistics Tróia '92. Quantitative Geology and Geostatistics. Dordrecht: Springer; 1993:911–22 pp.
29. Mercer LD, Szpiro AA, Sheppard L, Lindström J, Adar SD, Allen RW, et al. Comparing universal kriging and land-use regression for predicting concentrations of gaseous oxides of nitrogen (NOx) for the multi-ethnic study of atherosclerosis and air pollution (MESA Air). Atmos Env (1994) 2011;45:4412–20.
30. Oliver MA, Webster R, Lajaunie C, Muir KR, Parkes SE, Cameron AH, et al. Binomial cokriging for estimating and mapping the risk of childhood cancer. Math Med Biol 1998;15:279–97.
31. Berke O. Exploratory disease mapping: kriging the spatial risk function from regional count data. Int J Health Geogr 2004;3:18.
32. Jerrett M, Burnett RT, Ma R, Pope CA, Krewski D, Newbold KB, et al. Spatial analysis of air pollution and mortality in Los Angeles. Epidemiology 2005;16:727–36.
33. Ali M, Goovaerts P, Nazia N, Haq MZ, Yunus M, Emch M. Application of poisson kriging to the mapping of cholera and dysentery incidence in an endemic area of Bangladesh. Int J Health Geogr 2006;5:45.
34. Auchincloss AH, Diez Roux AV, Brown DG, Raghunathan TE, Erdmann CA. Filling the gaps: spatial interpolation of residential survey data in the estimation of neighborhood characteristics. Epidemiology 2007;18:469–78.
35. Goovaerts P, Gebreab S. How does poisson kriging compare to the popular BYM model for mapping disease risks. Int J Health Geogr 2008; 7:6.
36. Pouliou T, Kanaroglou PS, Elliott SJ, Pengelly LD. Assessing the health impacts of air pollution: a re-analysis of the Hamilton children's cohort

data using a spatial analytic approach. Int J Env Health Res 2008;18: 17–35.
37. Sampson PD, Richards M, Szpiro AA, Bergen S, Sheppard L, Larson TV, et al. A regionalized national universal kriging model using partial least squares regression for estimating annual PM2.5 concentrations in epidemiology; 2012. UW Biostatistics Working Paper Series. Working Paper 387. https://biostats.bepress.com/uwbiostat/paper387.
38. Casella V, Manzino A, Bellazzi R, Franzini M. Filtering and mapping public health data with an innovative Kriging approach, accounting for single observation variance. Procedia Environ Sci 2015;26:57–61.
39. Hsu CC, Tsai DR, Su SY, Jhuang JR, Chiang CJ, Yang YW, et al. A stabilized kriging method for mapping disease rates. J Epidemiol 2023;33:201–8.
40. Institute of Public Health of Serbia “Dr Milan Jovanović Batut”. Selected health indicators for 2021. Belgrade: Institute of Public Health of Serbia “Dr Milan Jovanović Batut”; 2022. https://www.batut.org.rs/download/publikacije/Odabrani%20zdravstveni%20pokazatelji%202021.pdf.
41. Timmis A, Vardas P, Townsend N, Torbica A, Katus H, De Smedt D, et al. European society of cardiology: cardiovascular disease statistics 2021. Eur Heart J 2022;43:716–99.
42. Institute of Public Health of Vojvodina. Health status of the population of AP Vojvodina in 2023. Novi Sad: Institute of Public Health of Vojvodina; 2024.
43. Maksimović Z, Jovanović T, Ršumović M, Đorđević M. Magnesium and calcium in drinking water in relation to cardiovascular mortality in Serbia. In: Magnesium in the Environment and Organisms; SANU, Scientific Meetings; Book 1; Department of Mathematics, Physics and Geo-Sciences, Department of Chemical and Biological Sciences. Belgrade, Serbia. Belgrade: Serbian Academy of Sciences and Arts; 1999, vol XCII:21–7 pp.
44. Jevtić M, Dragić N, Bijelović S, Popović M. Cardiovascular diseases and air pollution in Novi Sad, Serbia. Int J Occup Med Env Health 2014;27: 153–64.
45. Tomasevic T, Milijasevic D, Ac Nikolic E, Ukropina S, Topalov Z. Obesity and hypertension as a growing public health problem in Province of Vojvodina, Serbia. Eur J Public Health 2015;25:ckv175–248.
46. Kričković E. The influence of geographical and medical factors on the health of the population of AP Vojvodina. PhD thesis. Belgrade, Serbia: University of Belgrade, Faculty of Geography; 2022.
47. Petrović V, Čanković S. Prevalence of obesity and impact of socio demographic factors on obesity in 15-19 years old adolescents in Vojvodina, Serbia. Cent Eur J Public Health 2023;31:287–95.
48. Šašić B, Čanković DK, Mijatović-Jovanović VP, Ukropina SN, Ostojić ZZ, Milijašević DS, et al. Socio-demographic differences in the prevalence of cardiovascular diseases and the association with risk factors in the population of Serbia. Hosp Pharmacol 2024;11:1555–64.
49. Vulin A, Sucur N, Delic Z, Poljak JP, Ljubotina A, Todic VD, et al. Short-term blood pressure variability and left ventricular diastolic dysfunction in patients with arterial hypertension. J Hypertens 2022;40: e109.
50. Marinković I, Galjak M, Nikitović V, Magdalenić I, Despić J, Sekulić M. Population of Serbia – dynamics and structure. In: Nikitović V, editor. Census of population, households and dwellings 2022. Belgrade: Statistical Office of the Republic of Serbia; 2025:1–152 pp.
51. Institute for Public Health of Serbia “Dr. Milan Jovanović Batut”. Serbian acute coronary syndrome registry. Incidence and mortality of acute coronary syndrome in Serbia 2022. Report No. 17. Belgrade: Institute for Public Health of Serbia “Dr. Milan Jovanović Batut”; 2022: 1–101 pp.
52. Institute for Cardiovascular Diseases of Vojvodina. Database (1995–2003). Sremska Kamenica.
53. Republic Geodetic Authority. Open data of the national spatial data infrastructure (NSDI). https://download.geosrbija.rs/.
54. World Health Organization. International statistical classification of diseases and related health problems, 10th revision, edition 2010. Geneva, Switzerland: WHO; 2011, vol 1. https://www.who.int/standards/classifications/classification-of-diseases.
55. Institute for Public Health of Serbia “Dr. Milan Jovanović Batut”. International statistical classification of diseases and related health problems. Belgrade: Institute for Public Health of Serbia “Dr. Milan Jovanović Batut”. Tenth Revision, Book 1, 2010 Edition; 2013.
56. Institute of Public Health of Serbia “Dr Milan Jovanović Batut”. Incidence and mortality of acute coronary syndrome in Serbia 2022. Report No. 17. Belgrade: Institute of Public Health of Serbia “Dr Milan Jovanović Batut”; 2022.
57. Said SNBM, Zahran E-SMM, Shams S. Forest fire risk assessment using hotspot analysis in GIS. Open Civ Eng J 2017;11:786–801.
58. Getis A, Ord JK. The analysis of spatial association by use of distance statistics. Geogr Anal 1992;24:189–206.
59. Ord JK, Getis A. Local spatial autocorrelation statistics: distributional issues and an application. Geogr Anal 1995;27:286–306.
60. Mann HB. Nonparametric tests against trend. Econom. J. Econom. Soc. 1945;13:245–59.
61. Kendall MG. Rank correlation methods, 4th ed. London, UK: Charles Griffin; 1975.
62. Gilbert RO. Statistical methods for environmental pollution monitoring. New York: Van Nostrand Reinhold; 1987:320 p.
63. Salmi TMA, Anttila P, Ruoho-Airola T, Amnell T. Detecting trends of annual values of atmospheric pollutants by the Mann-Kendall test and Sen’s slope estimates – the excel template application MAKESENS. In Publications on Air Quality; No. 31. Helsinki, Finland: bFinnish Meteorological Institute; 2002:35 p.
64. Gavrilov MB, Marković SB, Jarad A, Korać VM. The analysis of temperature trends in Vojvodina (Serbia) from 1949 to 2006. Therm Sci 2015;19:S339–50.
65. Krige DG. A statistical approach to some basic mine valuation problems on the Witwatersrand. J Chem Metall Min Soc S Afr 1951;52:119–39. https://journals.co.za/content/saimm/52/6/AJA0038223X_4792.
66. Bajat B, Blagojević B. Application of geostatistics in spatial analysis. Bull Serbian Geogr Soc 2007;2:143–52.
67. Matheron G. Principles of geostatistics. Econ Geol 1963;58:1246–66.
68. Goodchild M, Haining R. GIS and spatial data analysis: converging perspectives. Pap Reg. Sci. 2004;83:363–85.
69. Pouliou T. Air pollution and respiratory health: re- analysis of the Hamilton children’s cohort study. Master thesis. Hamilton, Ontario; 2005.
70. Statistics How To. Kriging: Definition, Limitations [Internet]. https://www.statisticshowto.com/kriging/.
71. Columbia University Mailman School of Public Health. Kriging interpolation [Internet] https://www.publichealth.columbia.edu/research/population-health-methods/kriging-interpolation.

72. Esri. How Kriging works [internet]. https://pro.arcgis.com/en/pro-app/latest/tool-reference/3d-analyst/how-kriging-works.
73. Milić N, Stanisavljević D, Krstić M, Jovanović B, Brcanski J, Kilibarda B, et al. Research on the health of the population of Serbia in 2019. Belgrade: OMNIA BGD; 2021:1–144 pp.
74. Institute for Public Health of Serbia "Dr. Milan Jovanović Batut". Research on the health of the population of Serbia; 2025. https://www.batut.org.rs/index.php?content=3090.
75. Official Gazette Republic of Serbia (No. 22/09). Strategy for the prevention of non-communicable diseases. https://pravno-informacioni-sistem.rs/eli/rep/sgrs/vlada/strategija/2009/22/2.
76. Ministry of Environmental Protection; Environmental Protection Agency of the Republic of Serbia. Annual report on air quality status in the Republic of Serbia 2024. Belgrade: Environmental Protection Agency of the Republic of Serbia; 2025:112 p.
77. United Nations: The Sustainable Development Goals Report; 2023. https://data.unicef.org/sdgs/goal-3-good-health-wellbeing/.

Supplementary Material: This article contains supplementary material (https://doi.org/10.1515/geo-2025-0975).