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# Geographical variations and predictors of coronary artery disease mortality in Turkiye: an environmental and behavioral analysis

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## Abstract

**Objective** This study aims to analyze the geographical variations and identify key environmental and behavioral predictors of coronary artery disease (CAD) mortality in Turkiye.

**Methods** A 10-year longitudinal province-level data was used to identify change trajectories of CAD mortality. Environmental determinants (such as air quality and climatic conditions) and behavioral factors of alcohol consumption and smoking were examined for their association with CAD mortality change trajectories using Ordinal Logistic Regression models.

**Results** The study revealed significantly different trajectoriesof CAD mortality across Turkiye. Environmental factors, particularly air quality (Particulate Matter-10 variation) and climatic conditions (humidity and temperature variations), were heavily associated with the level of CAD mortality. Behavioral factors, notably alcohol consumption and smoking, also exhibited a significantly positive association. Humidity, sunlight, and temperature remained as key predictors of CAD after controlling for smoking and alcohol consumption.

**Conclusion** The study underscores the importance of addressing environmental and lifestyle factors in CAD management and prevention strategies. The findings suggest the necessity for region-specific interventions and public health policies tailored to the unique characteristics of each province in Turkiye. This research contributes to a deeper understanding of the multifactorial nature of CAD mortality, providing valuable insights for future research to investigate causal associations, healthcare planning, and policy-making.

**Trial registration** Our study has been registered in ClinicalTrials.GOV system with a procotol ID of CAD001.

**Keywords** Coronary artery disease, Mortality, Environmental factors, Behavioral factors, Geographical variations, Turkiye

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## Introduction

Coronary artery disease (CAD), also known as ischemic heart disease, remains a leading cause of mortality worldwide. According to World Health Organization (WHO), cardiovascular diseases cause the loss of 17.9 million lives each year [1]. Being the most common type of heart disease in the United States, CAD is a condition where plaque accumulates in the coronary arteries, restricting blood flow to the heart. The symptoms of CAD include chest, arm, or shoulder pain or discomfort and shortness of breath. The risks for CAD are physical inactivity, smoking tobacco, and many more behavioral factors that will be discused in the following Sect. [2]. Treatments include lifestyle changes such as regular exercise, angioplasty to prevent the narrowing of the arteries, and surgery [3].

The prevalence and impact of CAD vary significantly across different regions, influenced by a complex interplay of environmental and behavioral factors. Global trends indicate a shifting burden of CAD, with developing countries witnessing a surge in cases, possibly due to rapid urbanization and lifestyle changes [4]. In contrast, developed regions like Europe and North America have witnessed a relative decline in CAD mortality, attributed to improved healthcare systems and effective public health policies [5].

Environmental factors, including air pollution and urban living conditions, have emerged as critical determinants of CAD prevalence. Exposure to pollutants has been linked to increased cardiac events, emphasizing the need for environmental policies in disease management [6]. Behavioral factors such as diet, physical activity, and tobacco use also significantly contribute to CAD risk. Western diets high in saturated fats correlate with higher CAD rates, particularly in North America and parts of Europe [7]. In contrast, the traditional diets in some Asian countries, which are lower in saturated fats, may partly explain the lower incidence of CAD in these regions [8].

The Americas present a diverse picture, with South America grappling with rising CAD incidince rates due to increasing obesity and diabetes prevalence, unlike North America, where the rates are stabilizing [9]. Europe's experience with CAD incidince has been shaped by effective public health interventions, leading to a decline in smoking rates and better management of hypertension and hyperlipidemia [10]. In Asia, rapid urbanization and lifestyle westernization contribute to an increasing CAD burden, challenging the existing healthcare infrastructures [11].

Understanding these trends and factors is crucial for developing targeted interventions and policies to reduce the global burden of CAD mortality. This manuscript aims to delve into these aspects, offering insights into the complex dynamics of CAD mortality in Turkiye.

There are several studies in literature focusing on the effect of environmental and behavioral factors on CAD mortality rates. In Turkiye, there are also considerable literature that tried to explore mainly the behavioral factors that have effects on CAD. However, the research that focuses on both the behavioral and the environmental factors that have effects on CAD is limited.

This study, with the use of new variables (environmental: particulate matter, humidity, temperature, air pressure, sunlight and behavioral factors: alcohol and smoking) looked to explore the factors that affect CAD mortality rates in Turkiye. This study will contribute to the literature and help public policy makers make decisions for public health.

The main research question we are addressing in this study is the following: What are the main environmental (particulate matter, humidity, temperature, air pressure, sunlight) and behavioral factors (alcohol and smoking) that affect CAD mortality rates?

## Materials and methods

Annual death counts due to coronary artery diseases (CAD) based on the ICD10 Codes I20-I25 were obtained from the national mortality reports by Turkish Statistical Association for 81 provinces of Turkiye for a 10-year period from 2010 to 2019. Standardized by the population size of each provinvc in each year, CAD death rate was expressed as the number of deaths per 100,000 population and used as the primary outcome variable in this study.

The primary predictors include Particulate Matter 10 ($PM_{10}$), sulfur dioxide ($SO_2$), Carbon Monoxide (CO), Nitrogen Dioxide ($NO_2$), and Ozone ($O_3$), air pressure, humidity, rainy days in a year, maximum-average-minimum temperatures, wind speed as well as total sunlight, sun radiation, and electromagnetic field were obtained from the Turkish Ministry of Environment, Urbanisation, and Climate Change, and were expressed as the medians of the measurements between 2010 and 2019. To investigate the impact of the environmental variations on the CAD mortality, the variation representations of these markers were also defined as the standard deviations (SD) and coefficient of variation (CV) from 2010 to 2019 as additional markers. Lastly, to represent the known behavioral domain at the province-level, smoking, alcohol consumption, and exposure to second-hand smoke data were obtained from with CAD mortality were also investigated. Elderly age (age$\geq$65 years) and male proportions compare to the province population were also considered as potential predictors.

In the first step of our analyses, we aimed to identify different change trajectories of the CAD mortality. The

TRAJ procedure developed by Jones, Nagin, and Roeder (2001) suggested four change-profiles for CAD mortality based on the goodness of fit diagnostics [12]. As these change-profiles are of ordered nature (e.i., low, intermediate, high, etc.), Ordinal Logistic Regression modelling framework was used to model the likelihood of being in a higher ordinal category of CAD trajectories for each unit-increase in the univariable predictor.

A total of 38 predictors were included in these univariable models. To control for the increased Type-1 Error rate due to high number of univariable testing, the multiplicity has been corrected using the False Discovery Rate (FDR) technique by Benjamini, Y., & Hochberg, Y [13]. To graphically illustrate the association of the significant predictors on the same panel, the response variable and the predictors were standardized to have mean zero and variance one. All analysis were conducted using SAS (R) Version 9.4 (Cary, North Carolina, USA).

## Results

Analysis through SAS TRAJ procedure identified 4-trajectories in CAD mortality across the 81 provinces of Turkiye as presented in Fig. 1. The figure demonstrates a pronounced variation in CAD mortality rates, where Trajectory-1 has more stable CAD mortality while the other three trajectories have sharper increases and stabilization afterwards.

The Logistic Regression modelling revealed several key predictors of CAD mortality. Size of the elderly population (age ≥ 65 years) in a given province was highly significantly associated with the CAD death rate as anticipated. Similarly, the size of the male population was also found to be negatively associated with the CAD deaths, indicating higher CAD mortaliy likelihood for females. In terms of environmental factors, higher median air pressure and higher median humidity levels were positively associated with increased CAD mortality, as shown in Table 1; Figure 2 (OR estimates are 1.09 with 95% CI of (1.02,1.17) and 1.08 with 95% CI of (1.03,1.13), respectively). The positive association between these factors indicates that

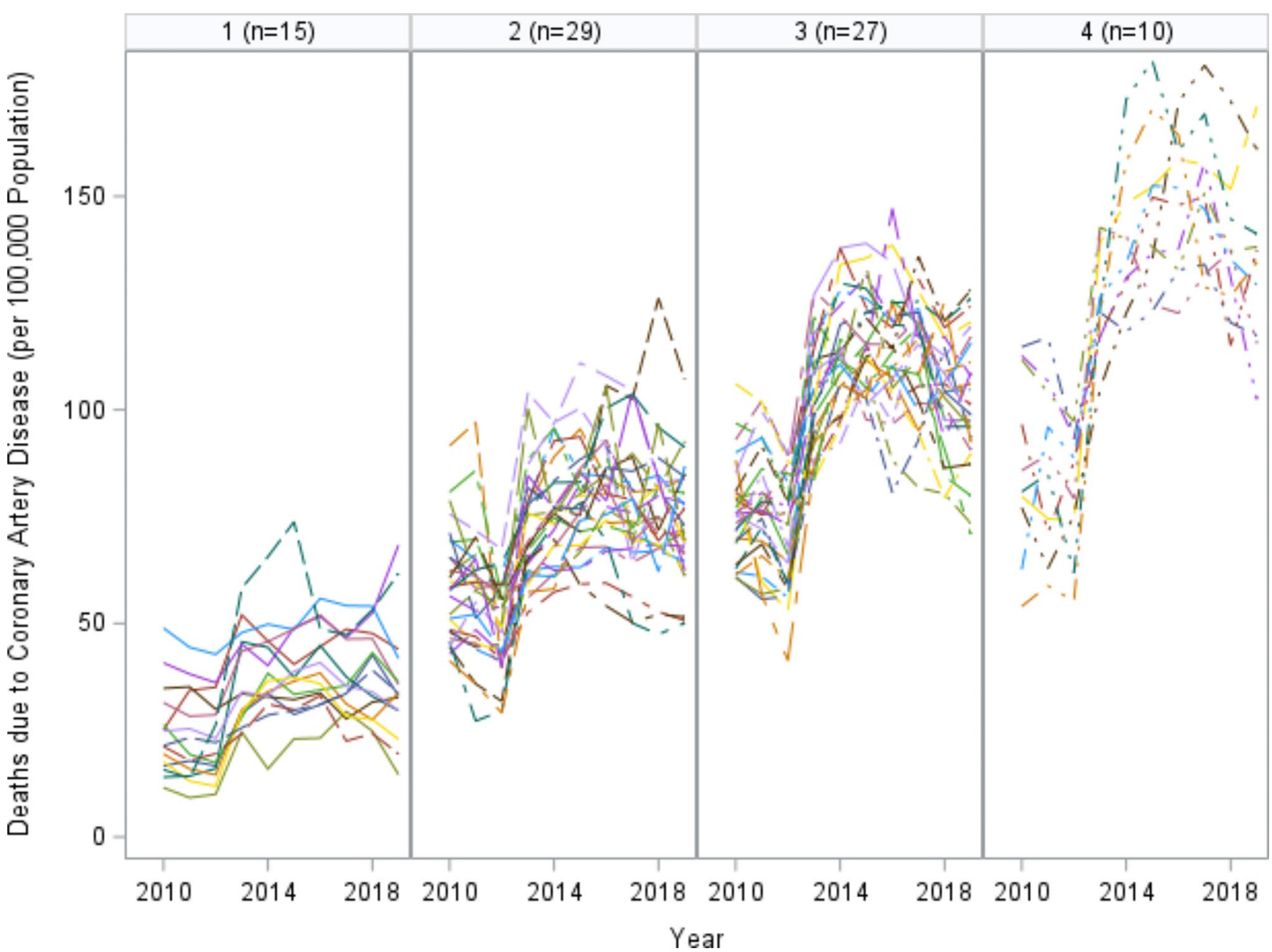


**Fig. 1** Coronary artery disease mortality profiles clustered by SAS TRAJ procedure utilizing the CAD deaths over a 10-year period (Each line represents a province)

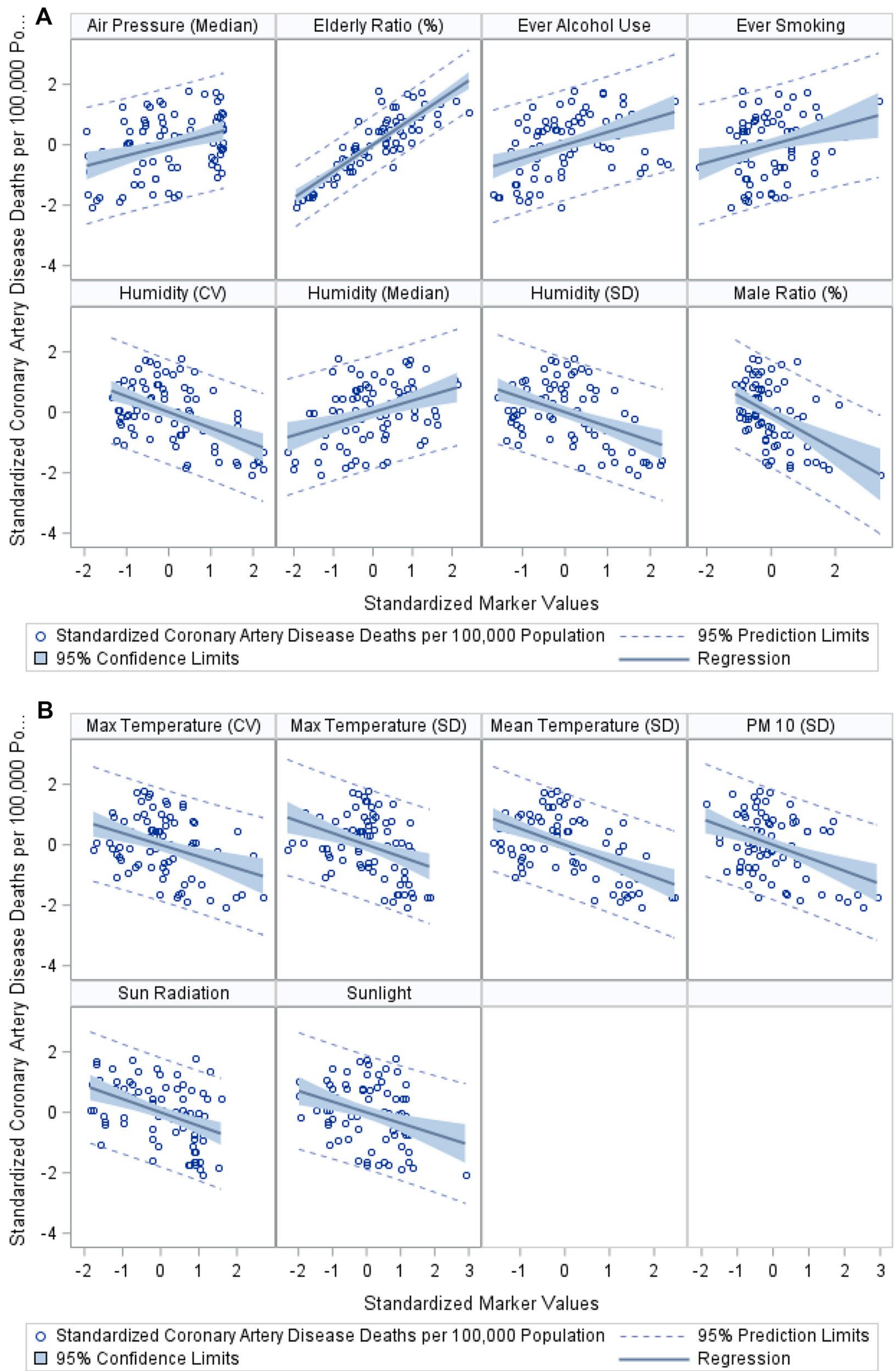


**Fig. 2** **A**: Significant markers indicative of an association with deaths due to Coronary Artery Disease. CV: Coefficient of Variation, SD: Standard of Deviation. **B**: Additional Significant markers indicative of an association with deaths due to Coronary Artery Disease. CV: Coefficient of Variation, SD: Standard of Deviation

**Table 1** Summary of markers significantly associated with coronary artery disease mortality profiles (CV is coefficient of Variance, SD is standard deviation)

| Predictor | OR (95% CI) | *P*-value | FDR Corrected *P*-value |
|---|---|---|---|
| Age >= 65 Ratio (%) | 2.46 (1.89,3.20) | < 0.0001 | 9.18E-10 |
| Air Pressure (Median) (Every 10-units) | 1.09 (1.02,1.17) | 0.0129 | 0.030537 |
| Ever Alcohol Use | 1.11 (1.05,1.16) | 0.0001 | 0.001114 |
| Ever Smoking | 1.10 (1.03,1.19) | 0.0066 | 0.016746 |
| Humidity (CV) | 0.91 (0.87,0.95) | < 0.0001 | 0.000258 |
| Humidity (Median) | 1.08 (1.03,1.13) | 0.0019 | 0.007079 |
| Humidity (SD) | 0.83 (0.75,0.91) | 0.0002 | 0.001234 |
| Male Ratio (%) | 0.51 (0.32,0.83) | 0.0064 | 0.016746 |
| Maximum Temperature (CV) | 0.93 (0.89,0.98) | 0.0059 | 0.016746 |
| Maximum Temperature (SD) | 0.69 (0.54,0.89) | 0.0043 | 0.014902 |
| Mean Temperature (SD) | 0.44 (0.30,0.64) | < 0.0001 | 0.000258 |
| Minimum Temperature (SD) | 0.50 (0.34,0.72) | 0.0003 | 0.001422 |
| Particulate Matter-10 (SD) | 0.88 (0.82,0.94) | 0.0002 | 0.001422 |
| Rainy Days (CV) | 0.95 (0.92,0.98) | 0.0012 | 0.005248 |
| Sun Radiation (Every 10-units) | 0.93 (0.89,0.97) | 0.0008 | 0.003883 |
| Sunlight (Every 10-units) | 0.98 (0.97,0.99) | 0.0064 | 0.016746 |

provinces with higher air pressure or greater humidity tend to report higher rates of CAD mortality. Behavioral factors such as ever alcohol use (OR = 1.11, 95% CI: 1.05,1.16) and ever smoking (OR = 1.1, 95% CI: 1.03,1.19) were likewise positively associated with higher CAD mortality, suggesting that provinces with higher rates of alcohol consumption and smoking have a greater likelihood of increased CAD mortality.

Conversely, factors like variability in maximum temperature (Coefficient of Variation, CV) and standard deviation (SD) in particulate matter-10 (PM-10) levels and rainy days indicated a negative association with CAD mortality. This implies that provinces with greater variability in temperature, PM-10 levels, and rainy days have comparatively lower CAD mortality rates. Provinces with higher sunligh and sun radiation exposures were also more likely to report lower level of CAD mortality.

Figure 2 visually represents these associations, illustrating the positive correlation between higher median air pressure, higher humidity, alcohol use, and smoking with increased CAD mortality. In contrast, the negative association of temperature variability, sunlight, sun radiation, and PM-10 levels with CAD mortality is also depicted, offering a comprehensive view of the environmental and behavioral factors influencing CAD mortality in Turkiye.

We further constructed a multivariable model controlling for smoking and alcohol consumption, in which median humidity and its variability metrics, sunlight, and variation of the minimum temperature kept their significant associations with the likelihood of higher level of CAD mortality (Area Under the Curve estimation = 0.80).

The model results for the insignificant markers at FDR of 0.05 are presented in Supplementary Table-2.

## Discussions

Coronary artery disease is one of the most common cardiovascular diseases worldwide. Despite its high prevalence, CAD has not been well observed with the consideration of environmental (particulate matter, humidity, temperature, air pressure, sunlight) and behavioral factors (alcohol and smoking) in Turkiye. Our study aimed to explore the correlation of the factors with CAD using limited data. Using the result of this observation, we aimed to see if our findings aligned with previous studies from Turkiye and other countries around the world.

Some of the environmental factors that are considered are environmental markers such as air quality (Particulate Matter-10) and climatic conditions (humidity, temperature variations), which were found to be significantly associated with CAD mortality. In terms of particulate matter, the findings of this study showed similarity with Brook et al.'s studies. Their study had experimental evidence showing biological mechanisms where particulate matter can cause cardiovascular diseases. Through different pathways and cascade of inflammatory responses, some cardiovascular events can be initiated [14].

Some behavioral factors were also considered. Behavioral factors like alcohol consumption and smoking, as shown in Table 1, also emerged as significant predictors of CAD mortality. In their studies, Salehi et al. found out that smoking was associated with the severity of CAD. The increase in dose of smoking and duration would lead to an increase in the likelihood of occlusion in coronary arteries [15]. One finding in this study showed very similar results, a strong positive correlation of smoking with CAD.

In another study conducted by Song et al. discovered that an excess consumption of alcohol led to a worse prognosis for coronary artery disease [16]. Their research findings support this study findings which show of a positive correlation of CAD with excess alcohol consumption in Turkiye.

The leading strength of this study is its comprehensive analysis of various influential environmental and behavioral predictors, and their association with CAD mortality in Turkiye. The use of province-level data (Fig. 3) allows for a nuanced understanding of the different levels of CAD burden, illustrated as a strong spatial autocorrelation where provinces in different regions have similar CAD mortality burden.

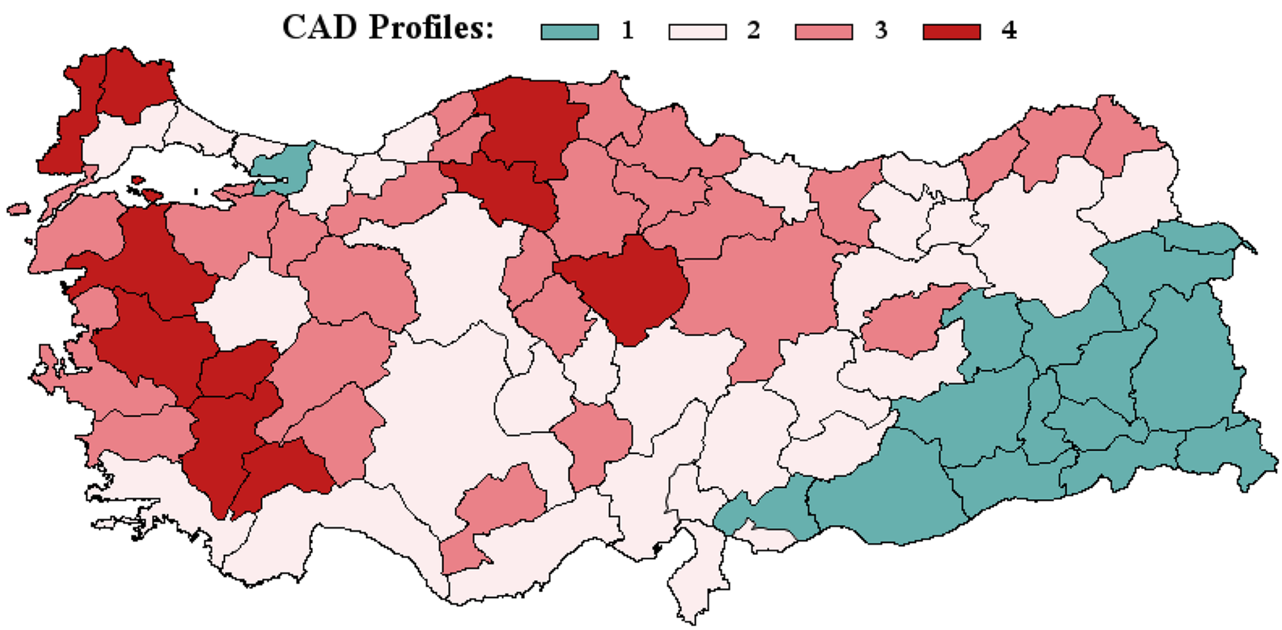


**Fig. 3** Map of Turkiye with the CAD Mortality Trajectores to illustrate the spatial autocorrelation

However, the study has several limitations. The reliance on secondary data sources and its overall observational nature may hinder the accuracy of some measurements, and preclude causal inferences. In addition, environmental impact occurs potentially slowly over time and having the outcome and predictor coming from the same time frame does not provide associatiations beyond correlation hypotheses, not necessarily indicating any form of causal association.

Secondly, even as an ecological data, our data has depth only at the province level, not at smaller geographical definitions like counties, zip-codes, etc., which limits the capturing of true variation of both the exposure and outcome. Such higher level of aggregation naturally limits the statistical power as well.

Not but not least, the study does not account for potential genetic predispositions, which could play a role in CAD mortality outcomes. Lack of data at the province-level on obesity prevalence, level of physical activity, and dietary patterns is another restriction preventing the examination of their relation with the incidince of CAD.

Future research should focus on longitudinal studies to understand the causal pathways of these associations better. Investigating the genetic factors and their interplay with environmental and lifestyle factors (i.e., epigenetics) could also provide deeper insights into CAD etiology and prevention strategies.

In conclusion, this study presents a comprehensive analysis regarding the influence of the geographical and predictor-based variations on coronary artery disease (CAD) mortality rates in Turkiye. The significant associations between environmental factors, behavioral patterns, and CAD mortality emphasize the need for multifaceted public health strategies. While the study highlights essential regional disparities in CAD outcomes, it also points to universal risk factors such as air pollution and lifestyle choices. Having a good understanding of each of the environmental and behavioral factors at the regional level where geographical units such as provinces, cities, towns etc. that are closer to each other are likely to have similar exposure and health outcome profiles may succesfully lead to targeted interventions that take into account both the unique regional characteristics and the shared risk factors. Ultimately, this study contributes to a growing body of evidence that can inform public health authorities, researchers, and individuals so that more effective and timely healty policies for disease prevention and disease intervention can be developed and life style changes can be implemented such as increasing physical exercise and decreasing smoking and alcohol consumption. The conclusions derived from this study extend beyond Turkiye to include other regions with similar demographic and environmental profiles and provide the hypotheses to be tested in a well-designed prostective cohort studies.

## Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s12872-024-04240-z.

Supplementary Material 1

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**Author contributions**
MT generated the research idea, carried out the literature search, wrote the initial and final draft of the manuscript, HGK helped with the literature search, manuscript writing, and detailing the discussions; MK acquired the research data, carried out the data analyses and modeling, provided the materials and methods section of the manuscript, and approved the final manuscript.

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**Data availability**
As the death records data utilized in this report were granted access only to the corresponding author, we do not have the permission to share these data components; however, we can share the environmental data upon request. Please contact Dr. Mehmet Kocak at mehmetkocak@medipol.edu.tr regarding such data requests.

**Code availability**
Not applicable

## Declarations

**Ethics approval and consent to participate**
Our research protocol was approved by Istanbul Medipol University Ethics Committee (Application number: 10840098-604.01.01-E.53819). The Ethics Committee waived the need for Informed Consent as there is no human subject involved in this research. Data is simply province-level mortality data provided by the Turkish Statistical Institute per year.

**Consent for publication**
Not applicable.

**Competing interests**
The authors declare no competing interests.

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