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Regional Disparities and Trends in Venous Thromboembolism Mortality in Spain (1999-2022)

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PII: S0300-2896(24)00418-6

DOI: https://doi.org/doi:10.1016/j.arbres.2024.10.015

Reference: ARBRES 3683

To appear in: *Archivos de Bronconeumologia*

Received Date: 9 September 2024

Accepted Date: 22 October 2024

Please cite this article as: Cayuela L, Michela Gaeta A, Otero R, Jara-Palomares L, Mendo Pedrajas I, Cayuela A, Regional Disparities and Trends in Venous Thromboembolism Mortality in Spain (1999-2022), *Archivos de Bronconeumología* (2024), doi: https://doi.org/10.1016/j.arbres.2024.10.015

**ORIGINAL RESEARCH ARTICLE**

# Regional Disparities and Trends in Venous Thromboembolism Mortality in Spain (1999-2022)

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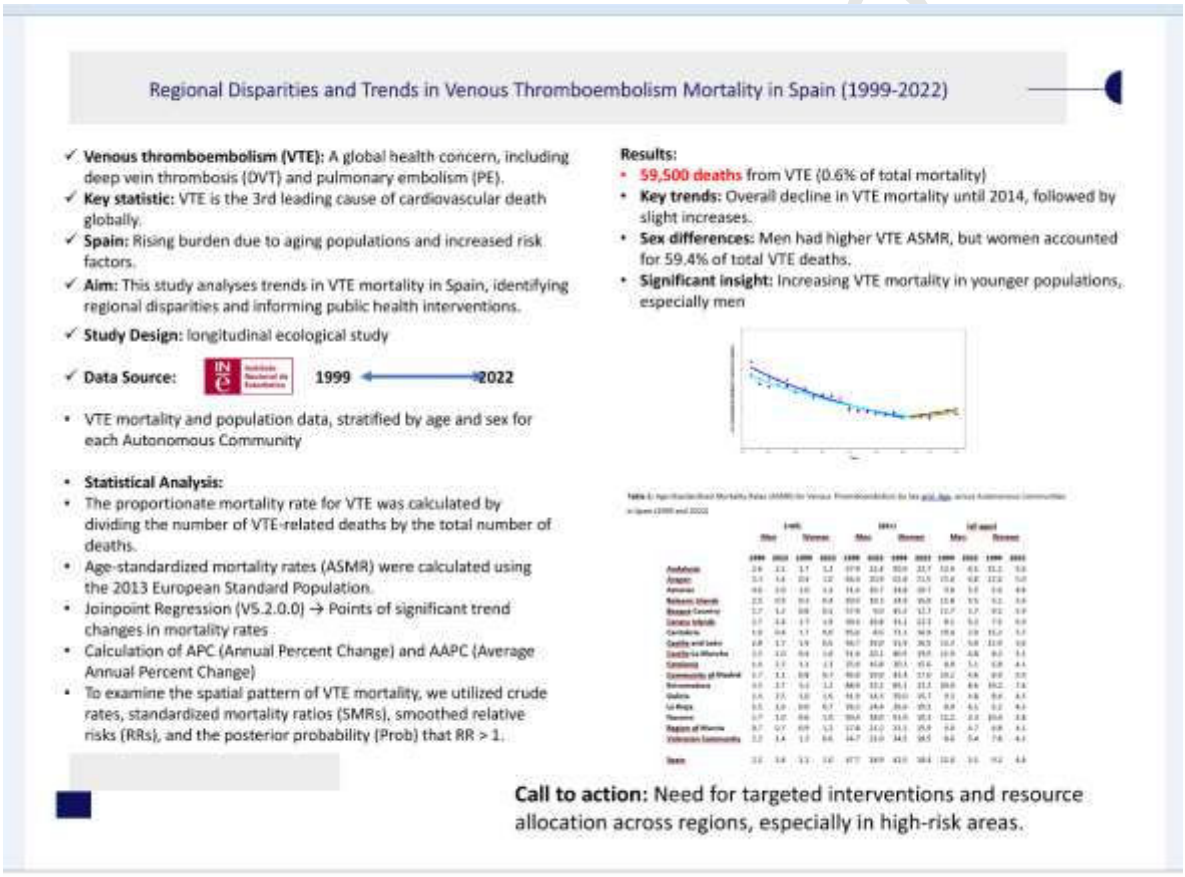
## Graphical Abstract




**Aim:** This study aims to analyse trends in Venous thromboembolism (VTE) mortality in the Spanish Autonomous Communities (ACs) from 1999 to 2022, with a focus on identifying regional disparities and informing targeted public health interventions.

**Methods:** Age-standardized mortality rates (ASMRs) were calculated using the European standard population as a reference. Joinpoint regression analysis was employed to identify significant changes in mortality trends, and geographical analysis was conducted using Bayesian inference to assess regional variations in mortality risk.

**Results:** From 1999 to 2022, Spain recorded 59,515 VTE-related deaths, with a higher proportion in women (59.4%) compared to men (40.6%). On a nationwide scale, VTE ASMRs showed a general decline for both men and women, with rates decreasing from 11.0 to 5.1 per 100,000 in men and from 9.2 to 4.4 per 100,000 in women. However, this decline was not uniform across all regions or demographic groups. Notably, mortality rates among younger individuals, particularly men, increased during the study period, highlighting the need for targeted interventions. Analysis revealed significant regional disparities, with higher mortality risks observed in Extremadura, Aragon, Navarre, and Andalusia, particularly for women.

**Conclusions:** This study provides valuable insights into the complex landscape of VTE mortality in Spain. While the overall decline in mortality is encouraging, persistent regional disparities and rising rates among younger individuals underscore the need for ongoing surveillance and targeted interventions.

**Keywords:** Venous thromboembolism, Deep vein thrombosis, Pulmonary embolism, Mortality trends, Spain, Regional disparities, public health.

**Regional Disparities and Trends in Venous Thromboembolism Mortality in Spain (1999-2022)**

## Introduction

Venous thromboembolism (VTE), encompassing deep vein thrombosis (DVT) and pulmonary embolism (PE), represents a critical global health concern[1]. With an annual incidence of 1-2 cases per 1,000 individuals[2], VTE is the third leading cause of cardiovascular mortality, placing substantial strain on healthcare systems globally[3].

There remains a considerable gap in the global recognition and quality of epidemiological data for VTE when compared to conditions like myocardial infarction and stroke. Unlike these conditions, VTE is frequently omitted as a cause of preventable death in national reports and global epidemiological studies, resulting in substantial gaps in cause-specific mortality data[4]. Despite a decline in VTE mortality across Australasia, North America, and Western Europe from 1990 to 2013, many Eastern European countries did not witness comparable reductions[5]. Recent European data (2012-2020) reveal a complex VTE landscape with significant variability between countries. Although VTE-related mortality has generally declined, trends show significant variation, with most countries reporting decreases while some Eastern and Western European nations have experienced increases[6].

In Spain, the burden of VTE is increasing due to an ageing population, the increasing prevalence of risk factors [7–9] and advances in diagnostic capabilities. Between 1999 and 2022, the proportion of people aged 65 years and older will increase from 16.8% to 19.7%, highlighting the increasing prevalence of age-related conditions such as VTE.

While in-hospital and age-standardized mortality rates (ASMRs) for pulmonary embolism (PE) have improved[10–12], the broader effect on VTE mortality continues to be unclear[13]. Spain's decentralized healthcare system, with autonomous management by the Autonomous Communities (AC), leads to variations in resources, specialist availability, and diagnostics, potentially impacting VTE outcomes[14].

To optimize VTE treatment, prophylaxis, and resource allocation, a comprehensive understanding of temporal trends in VTE mortality across Spain's regions is essential.

Therefore, this study aims to examine VTE mortality patterns in the Autonomous Communities from 1999 to 2022.

## Methods

### Study Design

This longitudinal ecological study followed the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines.

### Data Source

VTE mortality and population data, stratified by age and sex for each AC, were obtained from the publicly accessible National Institute of Statistics dataset for 1999- 2022. VTE deaths were identified using ICD-10 codes I26 (Pulmonary embolism), I80 (Phlebitis and thrombophlebitis), or I82.9 (Embolism and thrombosis of unspecified vein) as the underlying cause of death on medical certificates, consistent with previous studies[6,15].

### Statistical analysis

The proportionate mortality for VTE was calculated by dividing the number of VTE-related deaths by the total number of deaths within each age group and sex. This allows for an understanding of the contribution of VTE to overall mortality trends in different demographic groups over time.

ASMRs, per 100,000 population were calculated for each AC by sex, using the European standard population as a reference and applying the direct method of standardization. This approach allows for the comparison of mortality rates over time and across ACs, independent of population age structures.

Joinpoint software (version 5.2.0.0) was used to identify statistically significant changes ("turning points") in VTE mortality trends and quantify their magnitude. We employed the software's default settings for the modelling approach, turning point identification criteria, and model selection. The software's default settings allow for a maximum of 4 joinpoints for 24 data points (years in our study), with a minimum of 2 observations between joinpoints. Joinpoint uses the Weighted Bayesian Information Criterion for the Model Selection Method. The confidence intervals for the Annual Percent Change (APC), Average

Annual Percent Change (AAPC), and locations of the joinpoints were estimated using a parametric method[16].

Joinpoint identified significant changes and calculated the APC for each resulting trend segment. The software also determined the AAPC across the entire study period (1999–2022), accounting for the varying lengths of each trend segment. Changes in mortality rates were considered statistically significant if the APC or AAPC was greater than zero (increasing; $P < .05$), less than zero (decreasing; $P < .05$), or non-significant for stable trends. Additionally, Joinpoint's "Pairwise Comparison" function was used to assess whether trends differed significantly between sexes. All mortality rates are presented per 100,000 individuals, and the male-to-female ratio was also calculated.

**Ethical Considerations**

We adhered to the Guidelines for Accurate and Transparent Health Estimates Reporting standards. As this study did not involve interventions or individual patient data, it was deemed exempt from ethical review or Institutional Review Board approval.

**Results**

Between 1999 and 2022, a total of 9.6 million people died in Spain, of whom 59,500 died from venous thromboembolism (VTE), representing only 0.6% of all deaths (0.5% in men and 0.8% in women). Women had a higher proportion of these VTE-related deaths (59.4%) than men (40.6%). VTE-related deaths initially decreased steadily from 1999 to 2014, but this downward trend reversed in the following years. The highest number of VTE-related deaths occurred in 1999 (3,130 deaths) and the lowest in 2014 (2,134 deaths).

Figure 1 shows the proportion of VTE-related deaths in Spain from 1999 to 2022, stratified by age and sex. Although VTE-related deaths account for a small proportion of total mortality, there are notable differences between sexes and age groups. In men, the proportion of VTE-related deaths gradually increases with age, peaking at 0.77% in the 35-39 age group and then declining to 0.48% in those aged 75 and over. Women show a

different pattern. The proportion of VTE-related deaths increases during adolescence and young adulthood, peaking at 1.46% in the 25-29 age group. After this peak, the proportion decreases but remains consistently higher than in men in most age groups.

Figure 2 shows VTE ASMR trends in Spain from 1999 to 2022, with joinpoint analysis results. Both men and women saw significant reductions in VTE mortality rates: men's ASMR dropped from 11.0 to 5.1 per 100,000, while women's decreased from 9.2 to 4.4 per 100,000. Joinpoint analysis identified different trends for each sex. For men, there was a notable decline from 1999 to 2016 (APC: -5.5%), followed by an increase from 2016 to 2022 (APC: 4.0%). Women had a significant decline from 1999 to 2017 (APC: -4.5%), with rates stabilizing afterward.

Table 1 shows age- and sex-specific ASMRs for VTE in Spanish ACs for 1999 and 2022. Both sexes and all age groups saw a significant decline in VTE ASMRs over these years, although disparities remained. Men consistently had higher VTE ASMRs than women across all age groups and ACs. The 65+ age group had notably higher ASMRs compared to those under 65, underscoring the increased risk with age. Despite a narrowing male-to-female mortality ratio, men remained disproportionately affected by VTE.

Joinpoint analysis identified substantial heterogeneity in VTE ASMR (all ages) trends across Spanish ACs (Table 2). While most ACs exhibited decreasing trends for both sexes, the pace and timing of these declines varied considerably. Interestingly, apart from Asturias, Cantabria, and Castile-La Mancha, ACs demonstrated parallel trends for men and women. Several ACs, including the Balearic Islands, Cantabria, Galicia, Navarra, and the Region of Murcia, consistently exhibited downward trends without significant changes. On a nationwide scale, trends were not parallel by gender.

VTE ASMRs among individuals under 65 displayed distinct sex-based trends (Table 3). While overall rates were relatively stable, joinpoint analysis revealed a shift in the early 2010s. Before this, both sexes experienced declining rates, but afterward, a significant increase occurred, more pronounced in men (5.2%) than women (3.7%). This disparity was evident nationally and in specific regions (Balearic Islands, Catalonia, Valencian Community), while other ACs showed parallel trends. At the regional level, most ACs initially showed declining

rates, but subsequent trends diverged, with some mirroring the national pattern and others stabilizing.

VTE mortality rates significantly decreased among individuals aged 65 and over, both nationally and across most Spanish ACs. However, notable heterogeneity existed in the magnitude and trajectory of these declines. (Table 4).

Most ACs exhibited declining VTE mortality rates, except Asturias and the Region of Murcia, where no significant reduction was observed in either sex. The pace of decline varied widely across regions, ranging from a modest -2.5% in the Valencian Community to a more pronounced -8.6% among men in Cantabria.

Joinpoint analysis revealed diverse regional trends. Six ACs maintained consistent downward trajectories (Andalusia, Aragon, Canary Islands, Extremadura, La Rioja, and Navarra). Other ACs experienced an inflexion point around the 2000s-2010s, followed by either stabilization (Asturias, Balearic Islands, Cantabria, Castile and León, Castile-La Mancha, Madrid, and Valencian Community) or an increase (Catalonia). The Basque Country, Galicia, and the Region of Murcia initially had stable rates before declining.

**Discussion**

This study presents a comprehensive analysis of VTE mortality trends in Spain from 1999 to 2022, revealing a complex picture marked by overall declines but significant regional disparities and concerning increases in younger populations.

The observed reduction in ASMRs for VTE aligns with recent European studies reporting decreases in VTE and PE-related mortality[4,6,11]. These improvements are likely attributable to heightened VTE awareness, enhanced prevention strategies, and the advent of direct oral anticoagulants (DOACs), which have revolutionized VTE management[17,18]. Although DOACs are recommended for VTE management due to their effectiveness and safety profile, Spain does not currently fund these medications, posing a challenge for their widespread use[19]. However, the persistence of regional and demographic differences underscores the need for tailored interventions.

Gender significantly impacts the risk, symptoms, and outcomes of VTE[20,21]. Our analysis confirms that men have consistently higher VTE ASMRs than women across all age groups and regions. This disparity persists despite a reduction in the male-to-female mortality ratio over time.

Age is a significant risk factor for VTE and its outcomes. Individuals aged 65 and older are at notably higher risk of VTE-related mortality compared to younger populations[18]. This highlights the importance of developing tailored prevention and management strategies for older adults. Conversely, the increasing rates of VTE mortality among younger individuals, particularly men, are alarming. This trend parallels the rise observed over the past two decades in the United States[15] among adults aged 25 to 44. Lifestyle factors such as increased obesity[7], physical inactivity[8], and smoking[9] may contribute to this trend. Moreover, the COVID-19 pandemic could have exacerbated the issue by disrupting healthcare services and increasing the risk of thrombotic events[22].

Our results show a significant gender difference in the proportional mortality from VTE, with women having higher values, especially in reproductive and middle-aged years. This difference is most pronounced in young and middle-aged adults. In the 20-24 age group, the proportion of VTE-related mortality in women is more than four times higher than in men (Figure 1). This marked difference can be attributed to several sex-specific risk factors[23]. These findings highlight the need for gender-specific risk assessment and prevention in VTE management. Healthcare providers should focus on identifying and managing VTE risks in young and middle-aged women, especially during hormonal changes or when using hormone therapy. This may involve better screening, early symptom education, and careful consideration of hormone therapy for high-risk individuals.

Although VTE affects both sexes in older age groups, its relative contribution to overall mortality tends to decrease with age. This may be attributed to the increasing prevalence of other competing causes of death in the elderly population[24]. The observed age-related shift in VTE mortality emphasises the need for age-specific prevention and treatment strategies. While younger women may benefit from hormonal risk factors, older adults may require approaches that address mobility, comorbidities and the interplay between age and VTE risk.

Our analysis highlights significant regional differences in VTE mortality rates among Spain's ACs. While some regions have shown a steady decline, others continue to struggle with persistently high mortality rates. Factors such as socio-economic status, access to healthcare and the quality of clinical management play a key role in these differences.

Regions like Extremadura and Andalusia, with higher socioeconomic deprivation, may have limited access to healthcare resources, including preventive services and anticoagulant therapies, leading to higher VTE mortality[19]. These areas also face higher obesity rates, a key VTE risk factor[7] . In contrast, regions with better healthcare infrastructure, such as Madrid and the Basque Country, benefit from specialized services, early diagnosis, and advanced treatments like direct oral anticoagulants, contributing to lower mortality rates. Moreover, differences in hospital admission rates, the speed of diagnosis, and patient adherence to treatment regimens may vary across regions, affecting mortality trends[10].

Trends in VTE mortality also vary over time. While most regions show a steady decline, some, such as Asturias and Murcia, have seen stable or even increasing mortality since 2016. In Murcia, for example, there has been no significant reduction for either sex, while in Cantabria there has been a sharp decline in male mortality, with an annual rate of -8.6%. These differences highlight the need to understand region-specific health factors that influence outcomes.

Some regions, such as Andalusia and Extremadura, show consistent downward trends in mortality for both men and women, indicating the success of regional public health strategies. However, regions such as Catalonia experienced an increase in VTE mortality after 2016, which may be related to changing epidemiological patterns and the impact of the COVID-19 pandemic, which increased the risk of VTE due to prolonged hospitalization and sedentary lifestyles. Further research is needed to investigate the impact of the pandemic on VTE mortality, particularly in regions with a high burden of disease[25].

These findings highlight the importance of region-specific public health strategies. High-risk regions such as Extremadura may benefit from initiatives to improve access to anticoagulation therapy, hospital care and lifestyle interventions to reduce obesity, smoking and physical inactivity. Meanwhile, regions with lower VTE mortality, such as Madrid, should continue to implement preventive measures such as risk assessment for surgical patients and management of hospital-acquired thrombosis.

Personalized VTE prevention strategies tailored to local needs and healthcare resources could significantly improve outcomes across Spain.

Variations in VTE ASMRs may partly reflect differences in the accuracy and consistency of cause-of-death reporting. Although efforts like the IRIS automatic codification system aim to standardize and validate death data, discrepancies in reporting practices or coding accuracy could still influence regional mortality statistics[26].

Addressing these risk factors through region-specific public health initiatives may help mitigate some of the mortality differences.

Strengths of the study include the use of a large, population-based dataset and rigorous statistical methodologies. However, limitations such as the ecological study design and potential misclassification of VTE-related deaths should be acknowledged.

Due to the unavailability of incidence data, we relied on mortality data, a standard practice in similar studies. While epidemiological mortality studies have inherent limitations, they provide valuable insights into disease burden and its determinants. When interpreting trends, it is essential to consider the potential impact of small sample sizes on estimates in specific age and sex groups. Despite these considerations, the chosen analytical approach remains suitable for addressing the research objectives.

Future research should focus on identifying specific regional risk factors and determinants of VTE mortality. Prospective studies incorporating individual-level data are needed to evaluate the impact of prevention and treatment strategies. Long-term monitoring of VTE trends is essential to assess the effectiveness of public health interventions.

A comprehensive approach is essential to account for the complex interactions between age, sex, and regional factors in VTE mortality. Efforts should include addressing socioeconomic disparities, improving access to care, and promoting healthy lifestyles. The findings have important implications for public health policy, suggesting a need for renewed focus on VTE prevention and treatment strategies, tailored interventions for men, and localized public health strategies to address regional challenges.

In conclusion, this study provides valuable insights into the complex landscape of VTE mortality in Spain. While the overall decline in mortality is encouraging, persistent regional

disparities and rising rates among younger individuals underscore the need for ongoing surveillance and targeted interventions.

**Final Declarations**

**Ethics Statement:** This study utilized anonymized data obtained from the INE database. The research adhered to the principles of good clinical practice (GCP) and the Declaration of Helsinki. As participant identification was not possible and no personal information was accessed, informed consent or ethics committee approval was not required. Additionally, the Guidelines for Accurate and Transparent Health Estimation Reporting for Population Health Research (GATHER) were followed to ensure the credibility and integrity of the findings.

**Funding:** This research received no specific funding from public, commercial or not-for-profit organisations.

**Authors' Contributions:** All authors made substantial contributions to the conception and design of the study, acquisition, analysis, and interpretation of data. They were involved in drafting and critically revising the manuscript for significant intellectual content. All authors approved the final version to be published and agree to be accountable for all aspects of the work, ensuring that any questions regarding the accuracy or integrity of any part are thoroughly investigated and resolved.

**Conflict of Interest:** The authors declare no conflicts of interest related to the contents of this manuscript.

**Data Availability:** The data for this study are publicly available through the https://www.ine.es/

**Artificial intelligence involvement:** No artificial intelligence tools or technologies were used in the drafting, editing, or production of this manuscript. All aspects of the work, including writing, analysis, and interpretation, were conducted solely by the authors.

# Ethics in publishing

1. Does your research involve experimentation on animals?:
**No**
2. Does your study include human subjects?:
**Yes**
If yes; please provide name of the ethical committee approving these experiments and the registration number. :
**Ethics Statement: This study utilized anonymized data obtained from the INE database. The research adhered to the principles of good clinical practice (GCP) and**
**the Declaration of Helsinki. As participant identification was not possible and no personal information was accessed, informed consent or ethics committee approval was not required. Additionally, the Guidelines for Accurate and Transparent Health Estimation Reporting for Population Health Research (GATHER) were followed to ensure the credibility and integrity of the findings. Data Availability: The data for this study are publicly available through the https://www.ine.es/**
If yes; please confirm authors compliance with all relevant ethical regulations. :
**Yes**
If yes; please confirm that written consent has been obtained from all patients. :
**Yes**
3. Does your study include a clinical trial?:
**No**
Ethics Statement: This study utilized anonymized data obtained from the INE database. The
research adhered to the principles of good clinical practice (GCP) and the Declaration of Helsinki. As
participant identification was not possible and no personal information was accessed, informed
consent or ethics committee approval was not required. Additionally, the Guidelines for Accurate
and Transparent Health Estimation Reporting for Population Health Research (GATHER) were
followed to ensure the credibility and integrity of the findings. Data Availability: The data for this
study are publicly available through the https://www.ine.es/
4. Are all data shown in the figures and tables also shown in the text of the Results section and
discussed in the Conclusions?:
**Yes**

**Table 1:** Age-Standardised Mortality Rates (ASMR) for Venous Thromboembolism by Sex and Age, across Autonomous Communities in Spain (1999 and 2022)

| | (<65) | | | | (65+) | | | | (all ages) | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Men | | Women | | Men | | Women | | Men | | Women | |
| | 1999 | 2022 | 1999 | 2022 | 1999 | 2022 | 1999 | 2022 | 1999 | 2022 | 1999 | 2022 |
| **Andalusia** | 2.6 | 2.1 | 1.7 | 1.2 | 57.9 | 22.4 | 50.0 | 23.7 | 13.4 | 6.1 | 11.1 | 5.6 |
| **Aragon** | 3.3 | 3.4 | 0.4 | 1.0 | 66.4 | 20.9 | 62.8 | 21.5 | 15.6 | 6.8 | 12.6 | 5.0 |
| **Asturias** | 4.6 | 2.0 | 1.0 | 1.2 | 31.4 | 19.7 | 24.8 | 19.7 | 9.8 | 5.5 | 5.6 | 4.8 |
| **Balearic Islands** | 2.5 | 0.9 | 0.3 | 0.4 | 50.5 | 19.3 | 24.9 | 16.9 | 11.8 | 4.5 | 5.1 | 3.6 |
| **Basque Country** | 1.7 | 1.2 | 0.8 | 0.5 | 57.9 | 9.0 | 45.3 | 12.7 | 12.7 | 2.7 | 9.5 | 2.9 |
| **Canary Islands** | 2.7 | 2.4 | 1.7 | 1.9 | 30.4 | 16.8 | 31.2 | 22.3 | 8.1 | 5.2 | 7.5 | 5.9 |
| **Cantabria** | 1.0 | 0.4 | 1.7 | 0.0 | 95.6 | 8.6 | 71.1 | 16.9 | 19.4 | 2.0 | 15.2 | 3.3 |
| **Castile and León** | 2.8 | 1.7 | 1.9 | 0.5 | 56.7 | 19.0 | 52.9 | 16.5 | 13.3 | 5.0 | 11.9 | 3.6 |
| **Castile-La Mancha** | 2.3 | 1.0 | 0.4 | 1.6 | 51.6 | 20.1 | 40.5 | 19.5 | 11.9 | 4.8 | 8.2 | 5.1 |
| **Catalonia** | 1.4 | 2.3 | 1.1 | 1.3 | 35.0 | 16.8 | 30.3 | 15.6 | 8.0 | 5.1 | 6.8 | 4.1 |
| **Community of Madrid** | 1.7 | 1.1 | 0.8 | 0.7 | 45.0 | 19.0 | 42.4 | 17.0 | 10.2 | 4.6 | 8.9 | 3.9 |
| **Extremadura** | 3.3 | 2.7 | 3.2 | 1.2 | 88.9 | 33.2 | 85.1 | 33.2 | 20.0 | 8.6 | 19.2 | 7.4 |
| **Galicia** | 1.4 | 2.5 | 1.0 | 1.6 | 41.9 | 14.3 | 39.0 | 15.7 | 9.3 | 4.8 | 8.4 | 4.3 |
| **La Rioja** | 1.1 | 1.6 | 0.0 | 0.7 | 36.3 | 24.4 | 26.6 | 19.2 | 8.0 | 6.1 | 5.2 | 4.3 |
| **Navarre** | 1.7 | 1.0 | 0.6 | 1.0 | 50.4 | 18.0 | 51.0 | 10.1 | 11.2 | 4.3 | 10.4 | 2.8 |
| **Region of Murcia** | 0.7 | 0.7 | 0.9 | 1.2 | 17.8 | 21.2 | 31.1 | 15.9 | 4.0 | 4.7 | 6.8 | 4.1 |
| **Valencian Community** | 2.2 | 1.4 | 1.3 | 0.6 | 34.7 | 22.0 | 34.5 | 18.5 | 8.6 | 5.4 | 7.8 | 4.1 |
| **Spain** | 2.1 | 1.8 | 1.2 | 1.0 | 47.7 | 18.9 | 42.5 | 18.4 | 11.0 | 5.1 | 9.2 | 4.4 |

**Table 2:** Joinpoint Analysis Results for Venous thromboembolism Mortality in Spain (1999-2022) by Sex and Age Groups (all ages), across Autonomous Communities

| | | | Trend 1 | | | Trend 2 | | |
|---|---|---|---|---|---|---|---|---|
| | | **AAPC** | **Period** | **APC** | **(CI)** | **Period** | **APC** | **(CI)** |
| Andalusia | Men-Women | -2.5* | 1999-2013 | -5.6* | (-6.7;-4.6) | 2013-2022 | 2.5* | (0.4;4.6) |
| Aragon | Men-Women | -3* | 1999-2018 | -5.2* | (-6.1;-4.3) | 2018-2022 | 8.4 | (-3.5;21.7) |
| Asturias | Men | -1.7 | 1999-2014 | -4.4* | (-6.6;-2.1) | 2014-2022 | 3.7 | (-2.4;10.2) |
| | Women | -2.8* | 1999-2022 | -2.8* | (-3.8;-1.7) | | | |
| Balearic Islands | Men-Women | -4.7* | 1999-2022 | -4.7* | (-5.5;-3.8) | | | |
| Basque Country | Men-Women | -5* | 1999-2011 | -8.8* | (-10.5;-7.1) | 2011-2022 | -0.7 | (-3.1;1.8) |
| Canary Islands | Men-Women | -3.3* | 1999-2013 | -7.4* | (-9.6;-5.2) | 2013-2022 | 3.5 | (-0.5;7.7) |
| Cantabria | Men | -7.9* | 1999-2022 | -7.9* | (-9.7;-6.2) | | | |
| | Women | -6* | 1999-2022 | -6* | (-7.3;-4.7) | | | |
| Castile and León | Men-Women | -4.1* | 1999-2014 | -6.7* | (-7.9;-5.6) | 2014-2022 | 1.1 | (-2.6;4.9) |
| Castile-La Mancha | Men | -4.2* | 1999-2012 | -7.7* | (-9.8;-5.6) | 2012-2022 | 0.6 | (-3;4.4) |
| | Women | -2.4* | 1999-2016 | -5.1* | (-6.3;-3.8) | 2016-2022 | 5.5 | (-1.4;13) |
| Catalonia | Men-Women | -1.9* | 1999-2017 | -4.1* | (-4.7;-3.6) | 2017-2022 | 6.8* | (2.5;11.2) |
| Community of Madrid | Men-Women | -3.6* | 1999-2018 | -5.8* | (-6.5;-5.1) | 2018-2022 | 7.4 | (-1.2;16.7) |
| Extremadura | Men-Women | -4.5* | 1999-2001 | -18.4 | (-36.7;5.1) | 2001-2022 | -3* | (-3.8;-2.3) |
| Galicia | Men-Women | -3* | 1999-2022 | -3* | (-3.5;-2.5) | | | |
| La Rioja | Men-Women | -3.3 | 1999-2017 | -6.3* | (-8.5;-4.1) | 2017-2022 | 8.4 | (-8.4;28.3) |
| Navarre | Men-Women | -4.8* | 1999-2022 | -4.8* | (-5.7;-3.8) | | | |
| Region of Murcia | Men-Women | -2.7* | 1999-2022 | -2.7* | (-3.6;-1.9) | | | |
| Valencian Community | Men-Women | -2.8* | 1999-2014 | -4.4* | (-5.3;-3.4) | 2014-2022 | 0.2 | (-2.3;2.7) |
| Spain | Men | -3.1* | 1999-2016 | -5.5* | (-6.1;-4.9) | 2016-2022 | 4.0* | (0.8;7.2) |
| | Women | -2.9* | 1999-2017 | -4.5* | (-5.1;-4.0) | 2017-2022 | 3 | (-1.1;7.4) |

**AAPC:** Average Annual Percentage of Change

**APC**: Annual Percentage Change

*****:P<0.05

**CI:** Confidence Intervals

**Table 3:** Joinpoint Analysis Results for Venous Thromboembolism Mortality in Spain (1999-2022) by Sex and Age Group (<65), across Autonomous Communities.

| | | | Trend 1 | | | Trend 2 | | |
|---|---|---|---|---|---|---|---|---|
| | | **AAPC** | **Period** | **APC** | **(CI)** | **Period** | **APC** | **(CI)** |
| Andalusia | Men-Women | -0.2 | 1999-2010 | -7.4* | (-10.1;-4.5) | 2010-2022 | 6.8* | (4.2;9.5) |
| Aragon | Men-Women | -0.5 | 1999-2001 | -35.2 | (-72.7;53.7) | 2001-2022 | 3.6* | (1.6;5.7) |
| Asturias | Men | -1.3 | 1999-2008 | -13.3* | (-20.1;-6) | 2008-2022 | 7.3* | (2.6;12.2) |
| | Women | -0.7 | 1999-2022 | -0.7 | (-2.9;1.6) | | | |
| Balearic Islands | Men | -2.3 | 1999-2022 | -2.3 | (-5.3;0.8) | | | |
| Basque Country | Men-Women | -1.7 | 1999-2006 | -10.8* | (-19.9;-0.7) | 2006-2022 | 2.5 | (-0.7;5.7) |
| Canary Islands | Men-Women | 0.5 | 1999-2019 | -2.8* | (-4.5;-1.1) | 2019-2022 | 25.6 | (-2.3;61.5) |
| Cantabria | | | | n.a. | | | | |
| Castile and León | Men-Women | -2.9 | 1999-2003 | -17.3* | (-31.5;-0.2) | 2003-2022 | 0.4 | (-1.6;2.4) |
| Castile-La Mancha | Men-Women | -1.7 | 1999-2012 | -7.7* | (-11.8;-3.5) | 2012-2022 | 6.8* | (0.5;13.4) |
| Catalonia | Men | 1.4 | 1999-2020 | -0.8 | (-2.3;0.7) | 2020-2022 | 27.3 | (-22.3;108.6) |
| | Women | 2.1* | 1999-2022 | 2.1* | (0.7;3.6) | | | |
| Community of Madrid | Men-Women | -2.3 | 1999-2018 | -4.6* | (-6.1;-3) | 2018-2022 | 9.6 | (-8;30.5) |
| Extremadura | Men-Women | -0.5 | 1999-2016 | -5.2* | (-8;-2.2) | 2016-2022 | 13.9 | (-0.8;30.6) |
| Galicia | Men-Women | 0.4 | 1999-2011 | -5.6* | (-9.1;-1.9) | 2011-2022 | 7.4* | (3.4;11.6) |
| La Rioja | | | | n.a. | | | | |
| Navarre | | | | n.a. | | | | |
| Region of Murcia | Men | -0.2 | 1999-2022 | -0.2 | (-3;2.6) | | | |
| Valencian Community | Men | -2.7* | 1999-2009 | -8* | (-12.2;-3.7) | 2009-2022 | 1.6 | (-1.6;4.8) |
| | Women | -0.7 | 1999-2006 | -9.1* | (-17.1;-0.4) | 2006-2022 | 3.2* | (0.4;6) |
| Spain | Men | -0.9 | 1999-2012 | -5.4* | (-6.3;-3.7) | 2012-2022 | 5.2* | (3.4;7.1) |
| | Women | 0 | 1999-2010 | -4.0* | (-6.4;-1.4) | 2010-2022 | 3.7* | (1.6;5.9) |

**AAPC:** Average Annual Percentage of Change

**APC**: Annual Percentage Change

*****:P<0.05

**CI:** Confidence Intervals

**Table 4:** Joinpoint Analysis Results for Venous Thromboembolism Mortality in Spain (1999-2022) by Sex and Age Group (65+), across Autonomous Communities

| | | | Trend 1 | | | Trend 2 | | |
|---|---|---|---|---|---|---|---|---|
| | | **AAPC** | **Period** | **APC** | **(CI)** | **Period** | **APC** | **(CI)** |
| Andalusia | Men-Women | -3* | 1999-2022 | -8.6* | (-10.4;-6.8) | | | |
| Aragon | Men-Women | -4* | 1999-2022 | -5.9* | (-7.1;-4.6) | | | |
| Asturias | Men-Women | -1.9 | 1999-2014 | -5.5* | (-6.4;-4.6) | 2014-2022 | 1.8 | (-0.5;4.3) |
| Balearic Islands | Men-Women | -4.9* | 1999-2018 | -6* | (-6.9;-5.1) | 2018-2022 | 5.9 | (-6.8;20.3) |
| Basque Country | Men-Women | -5.8* | 1999-2002 | 10.5 | (-8.8;33.8) | 2002-2022 | -3.6* | (-4.5;-2.7) |
| Canary Islands | Men-Women | -4.9* | 1999-2022 | -4.9* | (-5.9;-4) | | | |
| Cantabria | Men | -8.6* | 1999-2011 | -9.4* | (-11.1;-7.7) | 2011-2022 | -1.6 | (-4.1;1) |
| | Women | -5.9* | 1999-2013 | -8* | (-10.6;-5.3) | 2013-2022 | 2.7 | (-2.2;7.8) |
| Castile and León | Men-Women | -4.6* | 1999-2014 | -7.1* | (-8.3;-5.9) | 2014-2022 | 0.2 | (-3.8;4.3) |
| Castile-La Mancha | Men-Women | -3.8* | 1999-2013 | -6.3* | (-7.6;-5) | 2013-2022 | 0.2 | (-2.7;3.1) |
| Catalonia | Men-Women | -2.7* | 1999-2017 | -5.1* | (-5.7;-4.4) | 2017-2022 | 6.2* | (1.4;11.2) |
| Community of Madrid | Men-Women | -3.9* | 1999-2018 | -6* | (-6.7;-5.2) | 2018-2022 | 6.9 | (-2.1;16.7) |
| Extremadura | Men-Women | -3.9* | 1999-2022 | -3.9* | (-4.6;-3.2) | | | |
| Galicia | Men-Women | -3.7* | 1999-2009 | -0.9 | (-2.5;0.6) | 2009-2022 | -5.8* | (-6.9;-4.7) |
| La Rioja | Men-Women | -4.6* | 1999-2022 | -4.6* | (-6.1;-3.1) | | | |
| Navarre | Men-Women | -5.4* | 1999-2022 | -5.4* | (-6.4;-4.3) | | | |
| Region of Murcia | Men-Women | -2.2 | 1999-2003 | 7.7 | (-7.3;25.2) | 2003-2022 | -4.2* | (-5.4;-3) |
| Valencian Community | Men-Women | -2.5* | 1999-2020 | -4* | (-4.7;-3.4) | 2020-2022 | 15 | (-10.1;47.1) |
| Spain | Men | -3.7* | 1999-2017 | -5.7* | (-6.3;-5.1) | 2017-2022 | 4.2 | (-0.4;8.9) |
| | Women | -3.4* | 1999-2018 | -4.8* | (-5.3;-4.4) | 2018-2022 | 3.6 | (-2.4;9.9) |

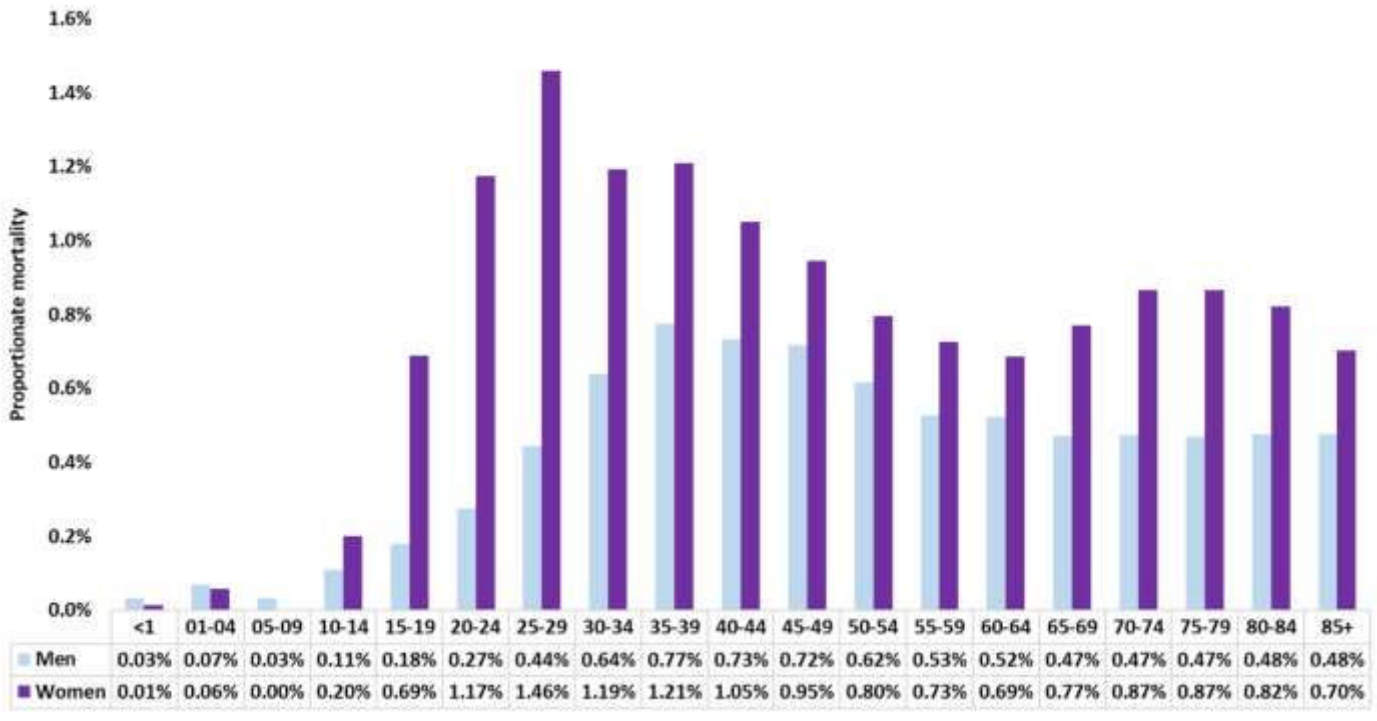
**AAPC:** Average Annual Percentage of Change

**APC**: Annual Percentage Change

*:P<0.05

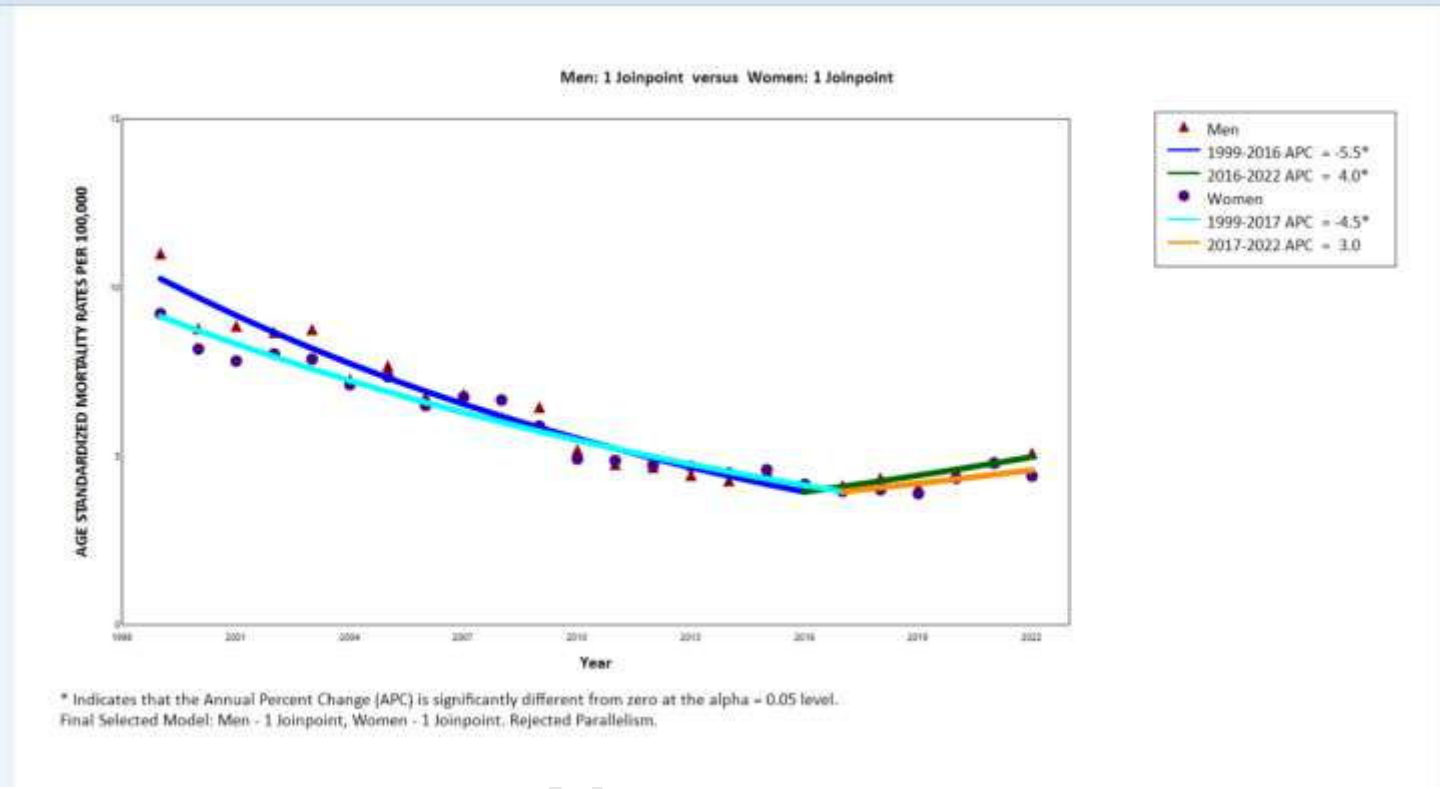
**CI:** Confidence Intervals

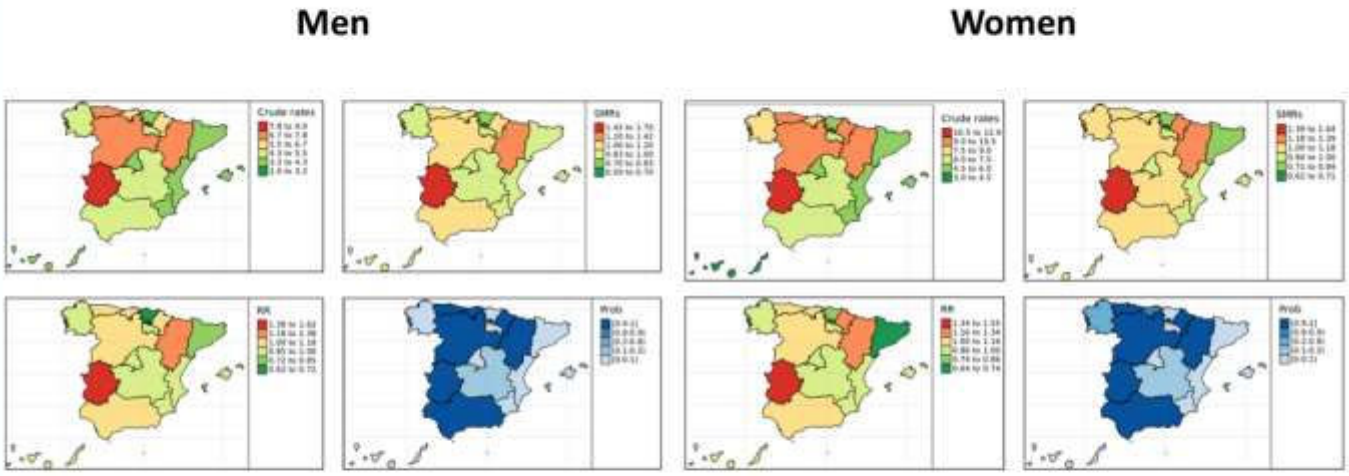
**Figure 1:** Proportion of VTE-Related Deaths in Spain (1999–2022), Stratified by Age and Sex.




| | <1 | 01-04 | 05-09 | 10-14 | 15-19 | 20-24 | 25-29 | 30-34 | 35-39 | 40-44 | 45-49 | 50-54 | 55-59 | 60-64 | 65-69 | 70-74 | 75-79 | 80-84 | 85+ |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Men | 0.03% | 0.07% | 0.03% | 0.11% | 0.18% | 0.27% | 0.44% | 0.64% | 0.77% | 0.73% | 0.72% | 0.62% | 0.53% | 0.52% | 0.47% | 0.47% | 0.47% | 0.48% | 0.48% |
| Women | 0.01% | 0.06% | 0.00% | 0.20% | 0.69% | 1.17% | 1.46% | 1.19% | 1.21% | 1.05% | 0.95% | 0.80% | 0.73% | 0.69% | 0.77% | 0.87% | 0.87% | 0.82% | 0.70% |

**Figure 2:** Trends in Age-Standardized Mortality Rates (ASMR) for Venous Thromboembolism in Spain (1999-2022), with Joinpoint Analysis






**SMR:** Standardized Mortality Ratios ; **RR:** Smoothed relative risks (RRs) ; **Prob:**posterior probability (PP) that RR > 1.

Figure 3

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