An Ecological Study on the Geographic patterns of Ischemic Heart Disease in Portugal and its association with demography, economic factors and health resources distribution

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Complete List of Authors:	Ferreira-Pinto, Luis; Faculty of Medicine, University of Porto, CINTESIS Rocha-Gonçalves, Francisco; Faculty of Medicine, University of Porto, CINTESIS Teixeira-Pinto, Armando; Faculdade de Medicina da Universidade do Porto, Serviço de Biostatística e Informática Médica; Faculdade de Medicina da Universidade do Porto, CINTESIS
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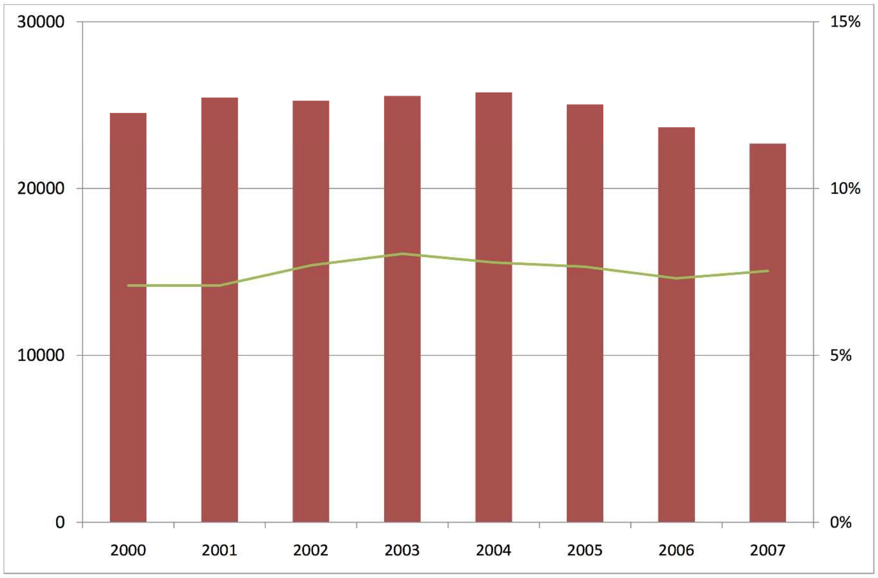

Figure 1 – Evolution of hospital admissions (bars) and fatality rate (line) of Ischemic Heart Disease in Portugal, through 2000 to 2007
297x209mm (300 x 300 DPI)

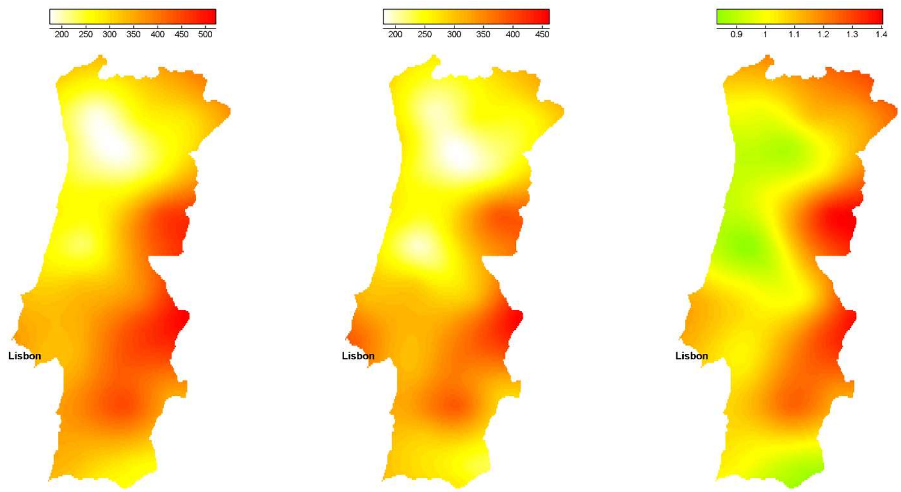

Figure 2. A – Geographical Distribution of the crude admission rate; B – Geographic Distribution of the SAR (Standardized Admission Rate); C – Geographical distribution of the residuals of the linear multiple regression. Legend refers to rates per 100.000 inhabitants.
328x169mm (300 x 300 DPI)

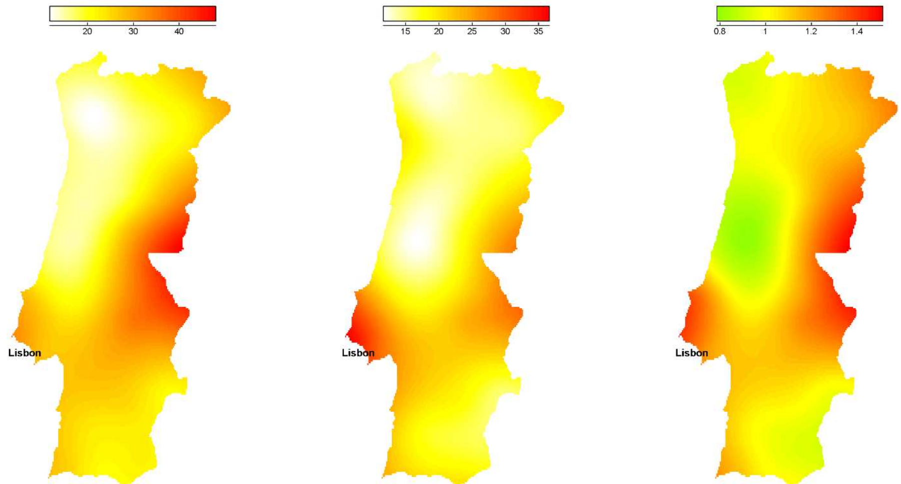

Figure 3. A – Geographical Distribution of the crude mortality rate; B – Geographic Distribution of the SMR (Standardized Mortality Rate); C – Geographical distribution of the residuals of the linear multiple regression. Legend refers to rates per 100.000 inhabitants
328x169mm (300 x 300 DPI)

An Ecological Study on the Geographic patterns of Ischemic Heart Disease in Portugal and its association with demography, economic factors and health resources distribution

Luís Ferreira-Pinto[1], Francisco Rocha-Gonçalves[1], Armando Teixeira-Pinto[1,2]

1 – CINTESIS, Faculty of Medicine - University of Porto, Portugal

2 – Department of Health Information and Decision Sciences, Unit of Biostatistics, Faculty of Medicine - University of Porto, Portugal

Correspondence:

Luis Ferreira-Pinto
Faculty of Medicine - University of Porto
4200-319 Porto
Portugal
Tel: +351 22 551 3622
Fax:+351 22 551 3623
luismanuelfpinto@gmail.com

ABSTRACT

OBJECTIVES: Being one of the main causes of morbidity and mortality in developed countries, Ischemic heart Disease's (IHD) incidence and mortality present clear differences between and within countries. Several authors already proposed possible explanations based on the demography, environmental factors, diet and level of urbanization. This study reflects the Portuguese reality concerning IHD, by analyzing the geographical distribution of hospital admissions and mortality due to this condition, in Portugal, and its association with demography, economical factors and the distribution of health care resources at the regional level.

DESIGN: Ecological Study

SETTING: Data from all Portuguese Public Hospitals were obtained using the National Registry of Hospital Admissions, between 2000 and 2007.

PARTICIPANTS: Almost 250 000 patients had the diagnosis of IHD (ICD codes 410-414). After excluding patients with less than 18yrs or patients discharged alive in less than 24hrs, almost 200 000 were included in the final analysis.

PRIMARY AND SECONDARY OUTCOME MEASURES: Mortality rate; Hospital admissions rate.

RESULTS: The geographical distribution of non-adjusted mortality and hospital admission showed an inner/ coastal pattern but no North/ South gradient was clear. Counties with higher economical development had significantly higher mortality and admission rates. However, health care resources distribution was not significantly associated with IHD hospital admission and mortality. When adjusted for age, gender, economic development and health resources distribution there was still unexplained geographical variation both in hospital admissions and mortality rates.

CONCLUSION: A pattern in the geographic distribution of incidence and mortality of IHD was clear even after the adjustment for age and gender. Economical variables were the ones presenting the strongest association. These type of analysis may be very helpful for the definition of health policies, in particular to identify priority regions for disease prevention and guidelines for health care resources distribution.

ARTICLE SUMMARY

ARTICLE FOCUS:

- The Geographic Distribution of both Hospital admissions and mortality rate due to Ischemic Heart Disease in Portugal
- The association of hospital admissions and fatality rate due to IHD and demography, economical factors and the distribution of health care resources at regional level

KEY MESSAGES

- Ischemic Heart Disease was positively associated with economical power
- The distribution of health care resources presented no statistically significant association with both hospital admissions and mortality rate due to Ischemic Heart Disease

STRENGTHS AND LIMITATIONS

- Data used was originated from a National database containing hospital admissions to all Portuguese Public Hospitals between 2000 and 2007
- There is no recent information about geographical differences in diet in Portugal

ABREVIATION LIST

ICD-9 – International Classification of Diseases, Ninth Revision

IHD – Ischemic Heart Disease

NHS – National Health System

NYC – New York City

OECD – Organization for Economic Co-operation and Development

PPI – Purchasing Power Index

SAR – Standardized Admission Rate

SMR – Standardized Mortality Rate

INTRODUCTION

Ischemic heart disease (IHD) is one of the leading causes of death in Europe but large variations on both mortality and incidence rates are observed between(1, 2) and within(3-5) countries. For example, Muller-Nordhorn et al.(1) showed substantial differences in the standardized mortality rate (SMR) between countries in a recent report of cardiovascular mortality across European countries. France had the lowest rate of 65 deaths per 100 000 inhabitants and Latvia the highest one with 461 deaths per 100 000 inhabitant. In this list, Portugal appears with the second lowest SMR (87/ 100 000). Nevertheless, IHD remains as a leading cause of death and major cause of disability in Portugal(6). Additionally, cardiovascular diseases represent the main source of expense for the Portuguese National Health System according to OECD Health Data 2005(7) and, as a result, have been a concern for both clinicians and health policy authorities.

The variation of SMR across countries has been explained by heterogeneity in the geographical distribution of risk factors such as demography, diet, smoking, obesity, sedentary behavior and environment(8), but also differences in the economical development of the regions and distribution of medical care resources(9, 10). These associations can be found at country level as well, and their report may provide valuable directions for research and public health measures. This study reflects the Portuguese reality but its methodology can be generalized to other applications. Moreover, in this study we exploit a specific direction and we explore statistical associations between demographic factors, socioeconomic indicators, availability of health resources and geographical location and the incidence and mortality of IHD in Portugal, based on hospital admissions.

In this article, we describe the Portuguese geographical pattern of IHD incidence and mortality and exploit its association with demographic, economic power and distribution health resources distribution across regions. An innovative feature of this work is the combination of demand-side and supply-side variables with the objective of explaining the regional variation. From the perspective of socioeconomic differences (demand-related attributes), we use the Purchasing Power Index of each county to characterize its economical power. From the perspective of the supply we collected data referring to health care facilities, such as hospitals and human resources available in each county. Our main practical implication will be that having identified high and low risk regions, we will acknowledge at what extent can demography, economical and health resources distribution affect the incidence and mortality of IHD. A distinctive point of this paper is that we propose that income or income inequality, as in Massing et al.(11), are important factors for explaining differences among mortality rates. In fact, the more affluent societies are known to suffer from a higher incidence of certain diseases such as cardiovascular diseases. This is indicative of a different lifestyle, which is more prone to higher cardiovascular risk.

Overall, in other industrialized countries, previous studies have showed that there is significant variation of the incidence and mortality rate of IHD between and within European Countries. Portugal lacks a specific study of this problem, which is another of the innovative features of this paper. Additionally, several factors have been described as associated with these observed distributions of cardiovascular mortality. This paper enhances the current knowledge regarding the problem of explaining in the observed regional differences in mortality due to IHD. It explains mortality due to IHD in the Portuguese NHS hospitals. For this purpose, we developed several hypotheses, namely the heterogeneity of demographical and geographical characteristics across and within Portuguese counties.

Next we explain our methodology and the database that we have used. It follows a discussion of the main findings and a presentation of the conclusions and some guidelines for future research.

METHODS

Data sources

The national registry of Hospital Admissions includes information on all patients admitted to Portuguese Public Hospitals. We used all admissions, between 2000 to 2007, of adult patients (18yrs or older) with main diagnosis of Ischemic Heart Disease (ICD-9 codes: 410 – 414). Patients discharged alive in less than 24 hours were excluded given the improbability of having suffered any acute episode of IHD and thus, presenting a high risk of misdiagnosis. The information retrieved included age, sex, patient's address, admission hospital, dates of admission and discharge, outcome at discharge (death or alive).

The average number of hospital admissions per year and the number of hospital deaths were used as proxies of the national incidence and mortality rate for IHD(12). We computed the crude incidence and mortality rates by dividing the number of patients admitted for each county by the total population of the county. Patient's county was determined by his residency address. The term fatality rate is sometimes used in the results section to distinguish in-hospital deaths among patients admitted with IHD.

Regional data on demography, economics and Health care resources distribution were obtained through the National Institute of Statistics (http://www.ine.pt). We used the size of population per county, together with age and sex, as the demographic characterization of the counties. The county's population also provides some indication about the degree of urbanization. The Purchasing Power Index (PPI) was the economical variable used and served as a proxy of the Economical status of the population across the regions. The PPI indicates the purchasing power level of a region per inhabitant, in the comparison to the national average (base=100). Regarding the Health Care resources, several indicators were obtained for each county: existence of a hospital in the county, existence of more than one primary care center (all counties have at least one primary care center), number of physicians per inhabitant, number of nurses per inhabitant, number pharmacies and the average number of medical appointments per year and per inhabitant. The choice of these variables was driven by their availability at county level.

Finally, the geographic coordinates of each county were taken as the geometric center of the county and were used to model the geographic variations of incidence and mortality.

Statistical Analysis

Geographically, the Portuguese population is not uniformly distributed regarding age and sex. Therefore, we calculated the Standardized Admission Ratio (SAR) and the Standardized Mortality Ratio (SMR) for each county using direct standardization for sex and age group. The variables PPI, number of pharmacies, number of physicians, number of nurses and number of medical appointments were log-transformed given the skewness of their distribution.

The association between demographic, economical and health resources variables with SAR and SMR, was analyzed using Pearson's correlations and simple linear regressions. The geographic distribution of both crude admission and mortality rates and SAR and SMR were modeled using a semi-parametric regression for latitude and longitude. The predictive values of the semi-parametric model were plotted in a heat-color map of Portugal. Multivariable linear regression was then used to simultaneously adjust the association of the different covariates with SAR and SMR. The variables for the final model were selected in a stepwise fashion according to their statistical significance. Finally, the residuals of the linear model, representing the unexplained variation of SAR and SMR across the counties, were modeled using a semi-parametric model for latitude and longitude. The fitted values of this model were again presented as a heat-color map.

The statistical analysis was performed using SPSS 19.0 and R2.10.1 and the significance level was set at 0.05 for all the inferences.

RESULTS

From 2000 to 2007, there were almost 200 000 admissions to 95 public hospitals in mainland Portugal, with Ischemic Heart Disease (ICD-9 410-414) as main diagnosis, 65.4% of which were men. Seven and a half percent of the admitted patients died (n=14 912). Fatality was significantly higher in women (10.5% vs. 6.0% in men, $p<0.001$). Admitted patients had a mean (sd) age of 67 (12) yrs old, a median (5^{th} percentile, 95^{th} percentile) length of in-hospital stay of 6 (1, 21). In this period, the number of hospital admissions showed a slight decline, especially in the last years (24 527 admissions in 2000 versus 22 665 in 2007). Fatality rate remained relatively constant over the years, around 7.5% (Figure 1).

Admission and mortality rates were compared across the 278 counties. Admission rate presented a high geographic variability (Figure 2A). A coast-interior pattern is clearly identified, especially in the center region. Overall the north coast region presented the lowest admission rate, while the center-interior region presented the highest. The lowest admission rate was registered in Vizela (14.3 admissions per 100 000 inhabitants per year), a county located in the north interior. On the other hand, Covilhã, a county located in the center-interior, registered the highest admission rate (701 admissions per 100 000 inhabitants per year).

The county with lowest fatality rate was also Vizela (no deaths in 20 admissions) and the county with highest fatality rate is located in the north interior (Aguiar da Beira with 18.6% in 70 admissions). There was a high variability of the crude mortality rate across the country (Figure 3A). The north half of the country presented a clear coast-interior pattern with the north coast showing the lowest mortality rate. Although not as clearly defined, the bottom half of the country suggests an opposite coast-interior pattern. The region around Lisbon, with the highest population density, also showed an elevated crude mortality rate.

After adjustment for age and gender, the patters observed in the distribution of standardized admission rate (SAR) were in general similar to those observed with the crude rate. The patterns of standardized mortality rate (SMR) were generally intensified. However, the crude mortality rate in the interior regions tended to smooth out, when adjusted for age and gender. Also, the counties around Lisbon area were among the highest SMR in the country (e.g., one of its counties, Loures, had the highest SMR - 53 deaths per 100 000 inhabitants per year – in the country). Figures 2B and 3B show the geographical distribution of SAR and SMR, respectively.

Health resources distribution and socio-demographic indicators are presented in Table 1. The Purchasing Power Index shows large differences across the counties with a minimum of 46 (in Vinhais) and a maximum of 236 (in Lisbon), indicating large disparities regarding the distribution of the economical power in mainland Portugal. The uneven distribution of population also points out the great differences found between regions; a pattern of coast-interior is clear with higher population density in the coast regions. Also, a north-south pattern may be identified, even though Lisbon has the highest population density, north regions tend to be more densely populated than south regions.

The distribution of health resources across the country was also markedly different. The country average number of physicians observed was 3.6 per 1000 inhabitants, ranging from 0 in two counties of the centre interior (Oleiros and Pampilhosa da Serra) to 23.6 in a county of the centre coast (Coimbra). Along with the physicians, the mean of nurses per 1000 inhabitants in Portugal was 5.0, ranging from 0.1 in three counties located in the interior of the country (Reguengos de Monsaraz, Sardoal e Vizela) to 24.7 also in Coimbra. Concerning pharmacies per 1000 inhabitants, 0.3 was the country mean, also ranging from 0.2 in several counties to 1.3. Seventy one percent (n=197) of the counties do not have a hospital (neither public nor private) and most of the counties (90%, n=250) have only one Primary Health Care Centre.

Table 2 presents the univariate associations between SAR and socio-demographic, economical and health care resources variables. Counties presenting a higher purchasing power, as well as more population, showed a significantly higher SAR ($p<0.001$ and $p=0.010$, respectively). Also, the existence of a hospital in the county, as well as more than one Primary Health Care Centre and more pharmacies were associated with the higher SAR ($p=0.017$, $p<0.001$ and $p=0.009$, respectively). Counties with more physicians and more nurses presented a higher SAR ($p<0.001$). Finally, the number of medical appointments was the only covariate presenting a negative association with SAR ($p=0.045$).

The association between the socio-demographic, economical and health care resources variables and SMR is described in Table 3. Counties with higher purchasing power index and more population had significantly higher SMR ($p<0.001$). Also, the number of physicians and nurses was positively associated with the SMR ($p<0.001$ and $p=0.019$, respectively). Having more than one Primary Health Care Centre was also associated with higher SMR ($p<0.001$). Similarly to the SAR, the number of medical appointments was the only negative association with SMR ($p<0.001$). The number of pharmacies and the existence of a hospital in the county were not significantly associated with SMR.

Multivariable analysis

When adjusting the geographic distributions of socio-demographic characteristics and economical and health resources availability to each other, the results obtained were substantially different from those obtained in the univariate analysis. Purchasing power index and the number of pharmacies remained positively associated with the SAR ($p<0.001$ for both variables) when adjusting to the other covariates. The remaining variables were not significantly associated with the geographical distribution of SAR after adjustment for purchasing power index and number of pharmacies.

Concerning the analysis of SMR, counties with higher purchasing power index and having more than one Primary Health Care Centre had a higher SMR ($p<0.001$ and $p=0.017$, respectively) after adjustment. The existence of a hospital in the county, which was not statistically significant in the univariate analysis, became negatively associated with SMR ($p=0.020$) indicating that counties with a hospital had lower SMR. Also, pharmacies became positively associated with SMR ($p=0.030$) when adjusting for the other covariates. The remaining variables (physicians, nurses, medical appointments and population size), which alone presented a significant association with SMR, were no longer significant after adjustment for purchasing power index, more than one Primary Health Care Centre, existence of a hospital and number of pharmacies in the county.

Unexplained variation of the SAR and SMR

Figures 2C and 3C present the geographic distribution of the unexplained variation of the SAR and SMR obtained through the regression residuals. Regions colored in green indicate lower levels of hospital admissions and mortality than the one predicted by the model; regions colored in yellow present a number of hospital admissions and mortality similar to those predicted by the multiple linear regression and regions colored in red indicate areas where hospital admissions and mortality were higher than predicted by the respective models. It can be observed a clear coast-interior pattern with the interior regions presenting higher SAR and SMR than the ones explained by socio-demographic, economical and health resources factors.

DISCUSSION

We found a high variability, within the country, in the mortality and hospital admissions rates of patients with IHD. This heterogeneity was attenuated when the rates were adjusted for age and sex but large discrepancies can still be observed among the different counties. Economical differences and geographic distribution of health resources were associated with both mortality and admission rates, but did not fully explain the regional variation of these rates. In any case, the PPI as a proxy of economical development and urbanization of a region, appeared as one of the strongest factors associated with both mortality and hospital admissions.

An urban effect associated to IHD mortality has been proposed in different countries. For example, in Perisse et al.(13) and in McNutt, L. et al.(14), the suggested explanations for that phenomenon are lifestyle, socio-economic differences, eating habits and professional stress. A Norwegian study, by Nafstad et al.(15) showed that urban air pollution might increase the risk of men dying, due to respiratory diseases, cancer or from IHD with an adjusted risk factor of 1,08%. This is also a plausible explanation for the current findings, since there are more research findings of this sort, however none in the Portuguese case. A confirmation will depend on future work involving data regarding air pollution and others.

Another interesting finding was the positive association of mortality rate with the number pharmacies and primary health care centers, when adjusting for other factors, suggesting a higher mortality in counties with more pharmacies and more than one primary Health care center. A possible explanation for this association may be the residual confounding of an urban effect. In fact, counties with more pharmacies and more primary health care centers correspond to those with higher level of urbanization and the adjustment using the multivariable regression may not have fully eliminated this bias.

There was no association between the number of physicians or nurses and the mortality rates. These variables represent the supply side and the quantity of care. Although there are differences in the quantity of physicians and nurses across the hospitals, this was not validated as an explanation for the differences in mortality. This predicted effect was probably offset by other variables, since there is a significant relationship if they are the single regressors of SMR.

We lack data on potential confounders. If such data was available we would have been able to evaluate their role. The economic dimension, here depicted by PPI, is a relevant explanation for the SMR that is usually absent from the published literature. One of the main goals of this research – to test the role of that variable – is then fully achieved. Other explanations are left for future research.

Given that data was collected by each hospital prior to being integrated into a single database by health authorities, some errors may have occurred during these processes. However, we have no notice of any such problem and they would be very limited: for example, a patient being classified as a new patient at a readmission. From our experience the potential for these problems and their potential impact is not significant.

Clearly, if appropriate data becomes available for future studies, risk factors should be considered (namely cholesterol and glycemia(16)), The explanation for an increased risk or proportion of deaths by IHD can rely in factors associated to urbanization: nutrition, exercise, professional stress, or pollution. In this research we discounted the effects of age and sex. We also tested variables such as the intensity of demand and offer of specialized medical care. The residual explanations (X% of the observed variance of observed deaths levels, remains unexplained) can be the former arguments. But further work will be necessary in order to test them properly and such a task will depend on the existence of databases. Finally, exposure to city stress is the explanation provided by Christenfeld et al.(17) for the fact that both residents and visitors to NYC were 155% and 134% above the expected proportion (i.e., the national average). However they don't report actual measures of such stressed lifestyle.

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COMPETING INTERESTS

The authors have no competing interests

AUTHOR'S CONTRIBUTERSHIP

Luis Ferreira-Pinto - Literature review, statistical analysis, article writing

Francisco Rocha-Goncalves - Interpretation of the results, article writing

Armando Teixeira-Pinto - Statistical analysis, article writing

DATA SHARING STATEMENT

There is no additional data available

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Table 1 – Distribution of health resources and social-economic indicators in the country.

Male, *nb. (%)*	129445	(65.4)
Age, *mean (SD)*	67.4	(12.4)
Length of stay, *median (P5, P95)*	6	(1, 21)
Population size, *median (P5, P95)*	12946	(3110, 122174)
Purchasing Power Index, *median (P5, P95)*	67.9	(49.2, 119.1)
Number of medical appointments (inhabit/year), *median (P5, P95)*	3.2	(2.0, 4.8)
Number of nurses (1000 inhabit/county), *median (P5, P95)*	2.0	(0.9, 9.4)
Number of physicians (1000 inhabit/county), *median (P5, P95)*	1.1	(0.3, 4.6)
Number of pharmacies (1000 inhabit/county), *median (P5, P95)*	0.3	(0.2, 0.8)
No hospital in the county, *nb (%)*	197	(70.9)
Only one primary health care centre in the county, *nb (%)*	250	(89.9)

Table 2 - Association between Cardiovascular SAR and health resources availability (Primary health centers, pharmacies, nurses, medical appointments, hospitals, and physicians), economic factors (PPI) and demographic characteristics (Population) across 278 the counties.

	Univariate			Multivariable	
	r	B	*p-value*	B	*p-value*
Purchasing power Index	0.441	1.255	***<0.001***	1.476	***<0.001***
Population size	0.153	0.117	***0.010***	-	-
More than one primary health centre in the county	0.230	0.270	***<0.001***	-	-
Existence of a hospital in the county	0.144	0.112	***0.017***	-	-
Number of Pharmacies (1000 inhabit/county)	0.156	0.279	***0.009***	0.525	***<0.001***
Number of nurses (1000 inhabit/county)	0.220	0.254	***<0.001***	-	-
Number of medical appointments (inhabit/county)	-0.120	-0.392	***0.045***	-	-
Number of physicians (1000 inhabit/county)	0.352	0.272	***<0.001***	-	-

r - Pearson's correlation, B – linear regression coefficient

Table 3 - Association between Cardiovascular SMR and health resources availability (Primary health centers, pharmacies, nurses, medical appointments, hospitals, physicians), economic factors (PPI) and demographic characteristics (Population) across 278 counties.

	Univariate			Multivariable	
	r	B	*p-value*	B	*p-value*
Purchasing power Index	0.452	1.585	***<0.001***	1.696	***<0.001***
Population size	0.279	0.262	***<0.001***	-	-
More than one primary health centre in the county	0.296	0.429	***<0.001***	0.210	***0.017***
Existence of a hospital in the county	0.115	0.110	*0.056*	-0.128	***0.030***
Number of Pharmacies (1000 inhabit/county)	-0.001	-0.002	*0.988*	0.286	***0.020***
Number of nurses (1000 inhabit/county)	0.140	0.200	***0.019***	-	-
Number of medical appointments (inhabit/county)	-0.212	-0.855	***<0.001***	-	-
Number of physicians (1000 inhabit/county)	0.307	0.292	***<0.001***	-	-

r - Pearson's correlation, B – linear regression coefficient

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Luís Ferreira-Pinto[1], Francisco Rocha-Gonçalves[1], Armando Teixeira-Pinto[1,2]

1 – CINTESIS, Faculty of Medicine - University of Porto, Portugal

2 – Department of Health Information and Decision Sciences, Unit of Biostatistics, Faculty of Medicine - University of Porto, Portugal

Correspondence:

Luis Ferreira-Pinto
Faculty of Medicine - University of Porto
4200-319 Porto
Portugal
Tel: +351 22 551 3622
Fax:+351 22 551 3623
luismanuelfpinto@gmail.com

ABSTRACT

OBJECTIVES: Being one of the main causes of morbidity and mortality in developed countries, Ischemic heart Disease's (IHD) incidence and mortality present clear differences between and within countries. Several authors already proposed possible explanations based on the demography, environmental factors, diet and level of urbanization. This study reflects the Portuguese reality concerning IHD, by analyzing the geographical distribution of hospital admissions and mortality due to this condition, in Portugal, and its association with demography, economical factors and the distribution of health care resources at the regional level.

DESIGN: Ecological Study

SETTING: Data from all Portuguese Public Hospitals were obtained using the National Registry of Hospital Admissions, between 2000 and 2007 and data on demography, economical factors and health resources distribution was obtained from the National Institute of Statistics .

PARTICIPANTS: Aggregated statistics on hospital admissions and mortality were computed for 278 counties based on almost 200 000 admissions.

PRIMARY AND SECONDARY OUTCOME MEASURES: Mortality rate; Hospital admissions rate.

RESULTS: The geographical distribution of non-adjusted mortality and hospital admission showed an inner/ coastal pattern but no North/ South gradient was clear. Counties with higher economical development had significantly higher mortality and admission rates. However, health care resources distribution was not significantly associated with IHD hospital admission and mortality. When adjusted for age, gender, economic development and health resources distribution there was still unexplained geographical variation both in hospital admissions and mortality rates.

CONCLUSION: A pattern in the geographic distribution of incidence and mortality of IHD was clear even after the adjustment for age and gender. Economical variables were the ones presenting the strongest association. These type of analysis may be very helpful for the definition of health policies, in particular to identify priority regions for disease prevention and guidelines for health care resources distribution.

ARTICLE SUMMARY

ARTICLE FOCUS:

- The Geographic Distribution of both Hospital admissions and mortality rate due to Ischemic Heart Disease in Portugal
- The association of hospital admissions and fatality rate due to IHD and demography, economical factors and the distribution of health care resources at regional level

KEY MESSAGES

- Ischemic Heart Disease was positively associated with economical power
- The distribution of health care resources presented no statistically significant association with both hospital admissions and mortality rate due to Ischemic Heart Disease

STRENGTHS AND LIMITATIONS

- Data used was originated from a National database containing hospital admissions to all Portuguese Public Hospitals between 2000 and 2007
- There is no recent information about geographical differences in diet in Portugal

ABREVIATION LIST

ICD-9 – International Classification of Diseases, Ninth Revision

IHD – Ischemic Heart Disease

NHS – National Health System

NYC – New York City

OECD – Organization for Economic Co-operation and Development

PPI – Purchasing Power Index

SAR – Standardized Admission Rate

SMR – Standardized Mortality Rate

INTRODUCTION

In this article, we describe the Portuguese geographical pattern of Ischemic heart disease (IHD) incidence and mortality and exploit its association with demographic, economic power and distribution health resources distribution across regions. IHD is one of the leading causes of death in Europe but large variations on both mortality and incidence rates are observed between[1 2] and within[3-5] countries. For example, Muller-Nordhorn et al.[1] showed substantial differences in the standardized mortality rate (SMR) between countries in a recent report of cardiovascular mortality across European countries. France had the lowest rate of 65 deaths per 100 000 inhabitants and Latvia the highest one with 461 deaths per 100 000 inhabitant. In this list, Portugal appears with the second lowest SMR (87/100 000). Nevertheless, IHD remains as a leading cause of death and major cause of disability in Portugal. [6] Additionally, cardiovascular diseases represent the main source of expense for the Portuguese National Health System according to OECD Health Data 2005 [7] and, as a result, have been a concern for both clinicians and health policy authorities.

The variation of SMR across countries has been explained by heterogeneity in the geographical distribution of risk factors such as demography, diet, smoking, obesity, sedentary behaviour and environment [8], but also differences in the economical development of the regions and distribution of medical care resources [9 10]. These associations can be found at country level as well, and their report may provide valuable directions for research and public health measures.

This study reflects the Portuguese reality but its methodology can be generalized to other applications. Moreover, in this study we exploit a specific direction and we explore statistical associations between demographic factors, socioeconomic indicators, availability of health resources and geographical location and the incidence and mortality of IHD in Portugal, based on hospital admissions. From the perspective of socioeconomic differences, we use the

Purchasing Power Index of each county to characterize its economical power. From the perspective of the supply we collected data referring to health care facilities, such as hospitals and human resources available in each county. Our main practical implication will be that having identified high and low risk regions, we will acknowledge at what extent demography, economical and health resources distribution are associated with incidence and mortality of IHD. A distinctive point of this paper is that we propose that income or income inequality, as in Massing et al.[11], are important factors are associated with mortality rates. In fact, the more affluent societies are known to suffer from a higher incidence of certain diseases such as cardiovascular diseases. This is indicative of a different lifestyle, which is more prone to higher cardiovascular risk.

Overall, in other industrialized countries, previous studies have showed that there is significant variation of the incidence and mortality rate of IHD between and within European Countries. Portugal lacks a specific study of this problem, which is another of the innovative features of this paper. Additionally, several factors have been described as associated with these observed distributions of cardiovascular mortality.

Next we explain our methodology and the database that we have used. It follows a discussion of the main findings and a presentation of the conclusions and some guidelines for future research.

METHODS

Data sources

The national registry of Hospital Admissions includes information on all patients admitted to Portuguese Public Hospitals. We used all admissions, between 2000 to 2007, of adult patients (18yrs or older) with main diagnosis of Ischemic Heart Disease (ICD-9 codes: 410 –

414). Patients discharged alive in less than 24 hours were excluded given the improbability of having suffered any acute episode of IHD and thus, presenting a high risk of misdiagnosis. The information retrieved included age, sex, patient's address, admission hospital, dates of admission and discharge, outcome at discharge (death or alive). It was not possible to identify multiple episodes of hospital admissions occurring for the same patient. Therefore, one patient my contribute multiple times for the number of events used in the calculation of the incidence rate.

The average number of hospital admissions per year and the number of hospital deaths were used as proxies of the national incidence and mortality rate for IHD [12]. We computed the crude incidence and mortality rates by dividing the number of patients admitted for each county by the total population of the county above 18 years old. Patient's county was determined by his residency postal code. The term fatality rate is sometimes used in the results section to distinguish in-hospital deaths among patients admitted with IHD.

Regional data on demography, economics and Health care resources distribution were obtained through the National Institute of Statistics (http://www.ine.pt). We used the size of population per county, together with age and sex, as the demographic characterization of the counties. The county's population also provides some indication about the degree of urbanization. The Purchasing Power Index (PPI) was the economical variable used and served as a proxy of the Economical status of the population across the regions. The PPI indicates the purchasing power level of a region per inhabitant, in the comparison to the national average. It is a summary index of 17 economical variables that include, for example, income per capita, electric consumption, taxes and number of vehicles per capita, among others. It is represented as a base 100 index, meaning that if a region as a PPI of 110 it is 10% above the national average.

Regarding the Health Care resources, several indicators were obtained for each county: existence of a hospital in the county, existence of more than one primary care center (all counties have at least one primary care center), number of physicians per inhabitant, number of nurses per inhabitant, number pharmacies and the average number of medical appointments per year and per inhabitant. The choice of these variables was driven by their availability at county level.

Finally, the geographic coordinates of each county were taken as the geometric center of the county and were used to model the geographic variations of incidence and mortality.

Statistical Analysis

Geographically, the Portuguese population is not uniformly distributed regarding age and sex. Therefore, we calculated the Standardized Admission Ratio (SAR) and the Standardized Mortality Ratio (SMR) for each county using direct standardization for sex and age group. The variables PPI, number of pharmacies, number of physicians, number of nurses and number of medical appointments were log-transformed given the skewness of their distribution. For the same reason, the dependent variables SAR and SMR where also log-transformed.

The association between demographic, economical and health resources variables with SAR and SMR, was analyzed using Pearson's correlations and simple linear regressions. The geographic distribution of both crude admission and mortality rates and SAR and SMR were modeled using a semi-parametric regression for latitude and longitude. The predictive values of the semi-parametric model were plotted in a heat-color map of Portugal. Multivariable linear regression was then used to simultaneously adjust the association of the different covariates with SAR and SMR. The variables for the final model were selected in a stepwise fashion according to their statistical significance. Finally, the residuals of the linear model, representing the unexplained variation of SAR and SMR across the counties, were modeled using a semi-parametric model for latitude and longitude. The fitted values of this model were again presented as a heat-color map.

The statistical analysis was performed using SPSS 19.0 and R2.10.1 and the significance level was set at 0.05 for all the inferences.

RESULTS

From 2000 to 2007, there were almost 200 000 admissions to 95 public hospitals in mainland Portugal, with Ischemic Heart Disease (ICD-9 410-414) as main diagnosis, 65.4% of which were men. Seven and a half percent of the admitted patients died (n=14 912). Fatality was significantly higher in women (10.5% vs. 6.0% in men, p<0.001). Admitted patients had a mean (sd) age of 67 (12) yrs old, a median (5^{th} percentile, 95^{th} percentile) length of in-hospital stay of 6 (1, 21). In this period, the number of hospital admissions showed a slight decline, especially in the last years (24 527 admissions in 2000 versus 22 665 in 2007). Fatality rate remained relatively constant over the years, around 7.5% (Figure 1).

Admission and mortality rates were compared across the 278 counties. Admission rate presented a high geographic variability (Figure 2A). A coast-interior pattern is clearly identified, especially in the center region. Overall the north coast region presented the lowest admission rate, while the center-interior region presented the highest. The lowest admission rate was registered in Vizela (14.3 admissions per 100 000 inhabitants per year), a county located in the north interior. On the other hand, Covilhã, a county located in the center-interior, registered the highest admission rate (701 admissions per 100 000 inhabitants per year).

The county with lowest fatality rate was also Vizela (no deaths in 20 admissions) and the county with highest fatality rate is located in the north interior (Aguiar da Beira with 18.6% in 70 admissions). There was a high variability of the crude mortality rate across the country (Figure 3A). The north half of the country presented a clear coast-interior pattern with the north coast showing the lowest mortality rate. Although not as clearly defined, the bottom half of the country suggests an opposite coast-interior pattern. The region around Lisbon, with the highest population density, also showed an elevated crude mortality rate.

After adjustment for age and gender, the patters observed in the distribution of standardized admission rate (SAR) were in general similar to those observed with the crude rate. The patterns of standardized mortality rate (SMR) were generally intensified. However, the crude mortality rate in the interior regions tended to smooth out, when adjusted for age and gender. Also, the counties around Lisbon area were among the highest SMR in the country (e.g., one of its counties, Loures, had the highest SMR - 53 deaths per 100 000 inhabitants per year – in the country). Figures 2B and 3B show the geographical distribution of SAR and SMR, respectively.

Health resources distribution and socio-demographic indicators are presented in Table 1. The Purchasing Power Index shows large differences across the counties with a minimum of 46 (in Vinhais) and a maximum of 236 (in Lisbon), indicating large disparities regarding the distribution of the economical power in mainland Portugal. The uneven distribution of population also points out the great differences found between regions; a pattern of coast-interior is clear with higher population density in the coast regions. Also, a north-south pattern may be identified, even though Lisbon has the highest population density, north regions tend to be more densely populated than south regions.

The distribution of health resources across the country was also markedly different. The country average number of physicians observed was 3.6 per 1000 inhabitants, ranging from 0 in two counties of the centre interior (Oleiros and Pampilhosa da Serra) to 23.6 in a county of the centre coast (Coimbra). Along with the physicians, the mean of nurses per 1000 inhabitants in Portugal was 5.0, ranging from 0.1 in three counties located in the interior of the country (Reguengos de Monsaraz, Sardoal e Vizela) to 24.7 also in Coimbra. Concerning pharmacies per 1000 inhabitants, 0.3 was the country mean, also ranging from 0.2 in several counties to 1.3. Seventy one percent (n=197) of the counties do not have a hospital (neither public nor private) and most of the counties (90%, n=250) have only one Primary Health Care Centre.

Table 2 presents the univariate associations between SAR and socio-demographic, economical and health care resources variables. Counties presenting a higher purchasing power, as well as more population, showed a significantly higher SAR ($p<0.001$ and $p=0.010$, respectively). Also, the existence of a hospital in the county, as well as more than one Primary Health Care Centre and more pharmacies were associated with the higher SAR ($p=0.017$, $p<0.001$ and $p=0.009$, respectively). Counties with more physicians and more nurses presented a higher SAR ($p<0.001$). Finally, the number of medical appointments was the only covariate presenting a negative association with SAR ($p=0.045$).

The association between the socio-demographic, economical and health care resources variables and SMR is described in Table 3. Counties with higher purchasing power index and more population had significantly higher SMR ($p<0.001$). Also, the number of physicians and nurses was positively associated with the SMR ($p<0.001$ and $p=0.019$, respectively). Having more than one Primary Health Care Centre was also associated with higher SMR ($p<0.001$). Similarly to the SAR, the number of medical appointments was the only negative association with SMR ($p<0.001$). The number of pharmacies and the existence of a hospital in the county were not significantly associated with SMR.

Multivariable analysis

When adjusting the geographic distributions of socio-demographic characteristics and economical and health resources availability to each other, the results obtained were substantially different from those obtained in the univariate analysis. Purchasing power index and the number of pharmacies remained positively associated with the SAR ($p<0.001$ for both variables) when adjusting to the other covariates. The remaining variables were not significantly associated with the geographical distribution of SAR after adjustment for purchasing power index and number of pharmacies. The adjusted r^2 for the SAR is 0.27.

Concerning the analysis of SMR, counties with higher purchasing power index and having more than one Primary Health Care Centre had a higher SMR ($p<0.001$ and $p=0.017$, respectively) after adjustment. The existence of a hospital in the county, which was not statistically significant in the univariate analysis, became negatively associated with SMR ($p=0.020$) indicating that counties with a hospital had lower SMR. Also, pharmacies became positively associated with SMR ($p=0.030$) when adjusting for the other covariates. The remaining variables (physicians, nurses, medical appointments and population size), which alone presented a significant association with SMR, were no longer significant after adjustment for purchasing power index, more than one Primary Health Care Centre, existence of a hospital and number of pharmacies in the county. The adjusted r^2 for the SMR is 0.24.

Unexplained variation of the SAR and SMR

Figures 2C and 3C present the geographic distribution of the unexplained variation of the SAR and SMR obtained through the regression residuals. Regions colored in green indicate lower levels of hospital admissions and mortality than the one predicted by the model; regions colored in yellow present a number of hospital admissions and mortality similar to those predicted by the multiple linear regression and regions colored in red indicate areas where hospital admissions and mortality were higher than predicted by the respective models. It can be observed a clear coast-interior pattern with the interior regions presenting higher SAR and SMR than the ones explained by socio-demographic, economical and health resources factors.

DISCUSSION

We found a high variability, within the country, in the mortality and hospital admissions rates of patients with IHD. This heterogeneity was attenuated when the rates were adjusted for age and sex but large discrepancies can still be observed among the different counties. Economical differences and geographic distribution of health resources were associated with both mortality and admission rates, but did not fully explain the regional variation of these rates. In any case, the PPI as a proxy of economical development and urbanization of a region, appeared as one of the strongest factors associated with both mortality and hospital admissions.

An exposure to city stress is the explanation provided by Christenfeld et al.[13] for the fact that both residents and visitors to NYC were 155% and 134% above the expected proportion (i.e., the national average). However they don't report actual measures of such stressed lifestyle. Also, an urban effect associated to IHD mortality has been proposed in several countries. For example, in Perisse et al.[14] and in McNutt, L. et al.[15], the suggested explanations for that phenomenon are lifestyle, socio-economic differences, eating habits and professional stress. A Norwegian study, by Nafstad et al.[16] showed that urban air pollution might increase the risk of men dying, due to respiratory diseases, cancer or from IHD with an adjusted risk factor of 1,08%. Also, a Northern Irish study by O'Rilley et al[17]. suggested that urban areas tend to have higher mortality rates from all causes, mainly from Respiratory diseases, Ischemic Heart Diseases and Circulatory diseases, being air pollution the explanation pointed out to these findings. This is also a plausible explanation for the current findings, since there are more research findings of this sort, however none in the Portuguese case. A confirmation will depend on future work involving data regarding air pollution and others.

Another interesting finding was the positive association of mortality rate with the number pharmacies and primary health care centers, when adjusting for other factors, suggesting a higher mortality in counties with more pharmacies and more than one primary Health care center. A possible explanation for this association may be the residual confounding of an urban effect. In fact, counties with more pharmacies and more primary health care centers correspond to those with higher level of urbanization and the adjustment using the multivariable regression may not have fully eliminated this bias.

There was no association between the number of physicians or nurses and the mortality rates. These variables represent the supply side and the quantity of care. Although there are differences in the quantity of physicians and nurses across the hospitals, this was not validated as an explanation for the differences in mortality. This predicted effect was probably offset by other variables, since there is a significant relationship if they are the single regressors of SMR.

There are important limitations in this study. We used hospital mortality of patients admitted with IHD as a proxy of the real IHD mortality rate. Also, we were not able to identify readmissions so a patient may contribute more than one time to the incidence of IHD. However, these two errors are likely to be similar across all regions and therefore not affecting the comparability across counties

Finally, given the nature of the ecological design. All the significant results found in the analysis are limited to statistical interpretation and no causality should be drawn from these associations. Even if we had data on all confounders, the adjustments that in the multivariable model would not remove the ecological bias, as explained by Greenland et al [18]..

However, these results are useful to point new directions for research. Some interesting associations with SMR were observed, in particular, the economic dimension (here depicted by PPI) which are usually absent from the published literature and should be further investigated.

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COMPETING INTERESTS

The authors have no competing interests

AUTHOR'S CONTRIBUTERSHIP

Luis Ferreira-Pinto - Literature review, statistical analysis, article writing

Francisco Rocha-Goncalves - Interpretation of the results, article writing

Armando Teixeira-Pinto - Statistical analysis, article writing

DATA SHARING STATEMENT

There is no additional data available

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Table 1 **–** Distribution of health resources and social-economic indicators in the country.

Male, *nb. (%)*	129445	(65.4)
Age, *mean (SD)*	67.4	(12.4)
Length of stay, *median (P5, P95)*	6	(1, 21)
Population size, *median (P5, P95)*	12946	(3110, 122174)
Purchasing Power Index, *median (P5, P95)*	67.9	(49.2, 119.1)
Number of medical appointments (inhabit/year), *median (P5, P95)*	3.2	(2.0, 4.8)
Number of nurses (1000 inhabit/county), *median (P5, P95)*	2.0	(0.9, 9.4)
Number of physicians (1000 inhabit/county), *median (P5, P95)*	1.1	(0.3, 4.6)
Number of pharmacies (1000 inhabit/county), *median (P5, P95)*	0.3	(0.2, 0.8)
No hospital in the county, *nb (%)*	197	(70.9)
Only one primary health care centre in the county, *nb (%)*	250	(89.9)

Table 2 - Association between Cardiovascular SAR and health resources availability (Primary health centers, pharmacies, nurses, medical appointments, hospitals, and physicians), economic factors (PPI) and demographic characteristics (Population) across 278 the counties.

	Univariate			Multivariable	
	r	B	*p-value*	B	*p-value*
Purchasing power Index	0.441	1.255	***<0.001***	1.476	***<0.001***
Population size	0.153	0.117	***0.010***	-	-
More than one primary health centre in the county	0.230	0.270	***<0.001***	-	-
Existence of a hospital in the county	0.144	0.112	***0.017***	-	-
Number of Pharmacies (1000 inhabit/county)	0.156	0.279	***0.009***	0.525	***<0.001***
Number of nurses (1000 inhabit/county)	0.220	0.254	***<0.001***	-	-
Number of medical appointments (inhabit/county)	-0.120	-0.392	***0.045***	-	-
Number of physicians (1000 inhabit/county)	0.352	0.272	***<0.001***	-	-

r - Pearson's correlation, B – linear regression coefficient

Table 3 - Association between Cardiovascular SMR and health resources availability (Primary health centers, pharmacies, nurses, medical appointments, hospitals, physicians), economic factors (PPI) and demographic characteristics (Population) across 278 counties.

	Univariate			Multivariable	
	r	B	*p-value*	B	*p-value*
Purchasing power Index	0.452	1.585	***<0.001***	1.696	***<0.001***
Population size	0.279	0.262	***<0.001***	-	-
More than one primary health centre in the county	0.296	0.429	***<0.001***	0.210	***0.017***
Existence of a hospital in the county	0.115	0.110	*0.056*	-0.128	***0.030***
Number of Pharmacies (1000 inhabit/county)	-0.001	-0.002	*0.988*	0.286	***0.020***
Number of nurses (1000 inhabit/county)	0.140	0.200	***0.019***	-	-
Number of medical appointments (inhabit/county)	-0.212	-0.855	***<0.001***	-	-
Number of physicians (1000 inhabit/county)	0.307	0.292	***<0.001***	-	-

r - Pearson's correlation, B – linear regression coefficient

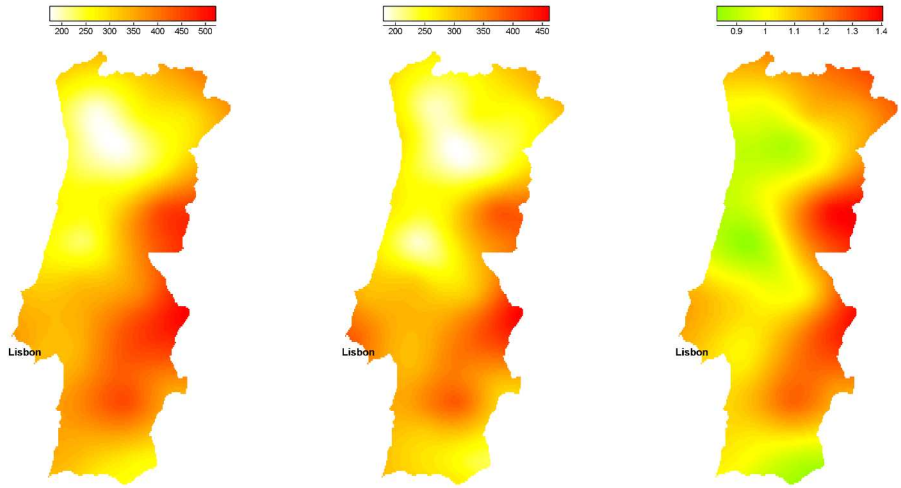

Figure 2. A – Geographical Distribution of the crude admission rate; B – Geographic Distribution of the SAR (Standardized Admission Rate); C – Geographical distribution of the residuals of the linear multiple regression. Legend refers to rates per 100.000 inhabitants.
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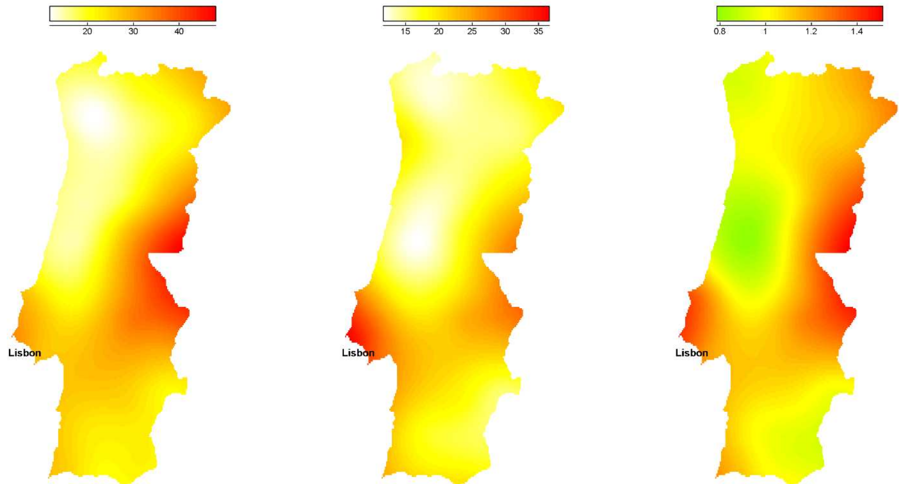

Figure 3. A – Geographical Distribution of the crude mortality rate; B – Geographic Distribution of the SMR (Standardized Mortality Rate); C – Geographical distribution of the residuals of the linear multiple regression. Legend refers to rates per 100.000 inhabitants
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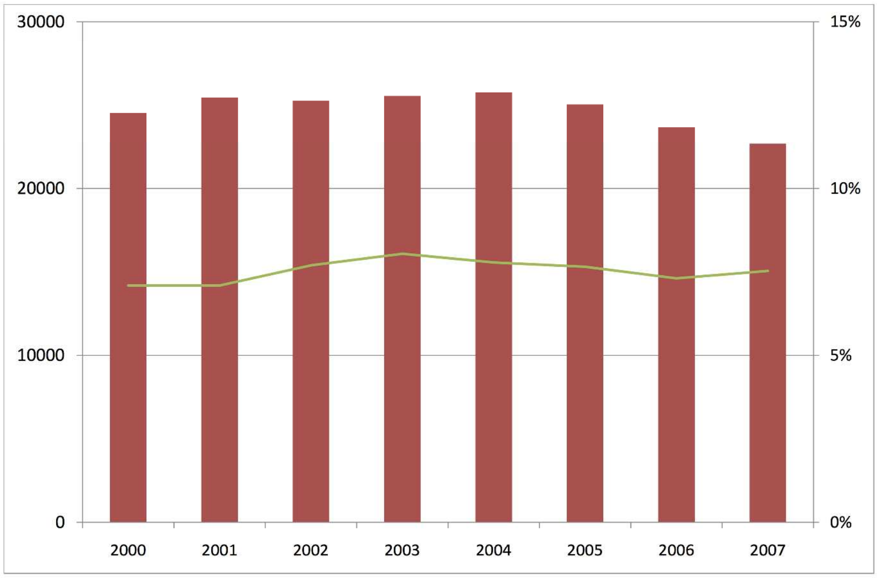

Figure 1 – Evolution of hospital admissions (bars) and fatality rate (line) of Ischemic Heart Disease in Portugal, through 2000 to 2007
297x209mm (300 x 300 DPI)