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MORTALITY FROM CARDIOVASCULAR DISEASES IN THE MUNICIPALITIES OF MAINLAND PORTUGAL: SPATIOTEMPORAL EVOLUTION BETWEEN 1991 AND 2017

ABSTRACT. During the last decades, important efforts have been taken to tackle cardiovascular diseases, which resulted in important mortality and disability decreases. Despite this, cardiovascular diseases are still one of the major causes of death in Portugal. Thus, the aim of this study is to analyse the evolution of the spatial pattern of deaths by cardiovascular diseases, between 1991 and 2017, identifying areas of high risk, and its variation, in the 278 municipalities of Continental Portugal.

Secondary data on annual resident population and deaths by cardiovascular diseases (International Classification of Diseases 10th revision: I00-I99) was collected from the Portuguese National Statistics for the municipalities of Portugal Mainland, from the period under analysis.

To identify areas with significant high and low risk of mortality by cardiovascular diseases, towards time and space, and areas with significantly high or low temporal trends, retrospective spatial-temporal cluster and a spatial variation in temporal trends analysis were conducted.

In the spatial-temporal analysis 3 clusters of high risk and two of low risk were identified; municipalities forming the clusters of high risk tend to have rural characteristics while the municipalities in the clusters of low risk are located in the two metropolitan areas. The majority of the municipalities forming the clusters of low risk also present higher decreasing trends than the country average.

The results presented can contribute to support the development of future interventions on cardiovascular mortality.

KEY WORDS: Cardiovascular diseases mortality; space–time clustering; Spatial variation in temporal trends; Portugal

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INTRODUCTION

Circulatory system diseases are still the most common cause of death in the world (Bhatnagar 2017). According to the WHO (2017), more people die annually from Cardiovascular Diseases (CVD) than from any other cause, being responsible for 31% of all deaths worldwide. CVD are also associated with important morbidity and disability burdens (Roth et al. 2017). The term “CVD” is used to represent a group of disorders of the heart and blood vessels and it includes coronary heart disease, cerebrovascular disease, peripheral arterial disease, rheumatic and congenital heart diseases and venous thromboembolism (Stewart et al. 2017).

The increasing international awareness about CVD (among other noncommunicable disease) has contributed to the growing evidence on CVD (Mahmood et al. 2014), to track, and benchmark, opportunities for prevention and efforts to reduce its burden (Roth et al. 2017). According to Bhatnagar (2017), CVD are caused by a set of chronic conditions resulting from a complex interplay between genetic predisposition, life style factors and environmental influences that lead to a progressive deterioration of the structure of cardiovascular tissues; this process, at least until a certain extent, could be prevented by maintaining a healthy lifestyle (even though genetic defects underlie some infrequent forms of heart disease).

Several authors have been providing evidence on the association between several behavioral, environmental and

socioeconomic risk factors and CVD mortality and morbidity: unhealthy diet (Pekka et al. 2002, Åkesson et al. 2007; Jackson et al. 2019), insufficient physical activity (Matthews et al. 2012; Patterson et al. 2018), tobacco use (Huxley and Woodward 2011; Peters et al. 2013), harmful consumption of alcohol (Rehm et al. 2016; Ogunmoroti et al. 2019), air pollution (Brook et al. 2010; Hvidtfeldt et al. 2019), thermal discomfort (Vasconcelos et al. 2011, Almendra et al. 2017), socioeconomic deprivation (Chum and O’Campo 2015; Jimenez et al. 2019), unemployment (Naimi et al. 2009) and population density (Chaix et al. 2007), among others.

Environment can impact health in a direct way (e.g. through air quality) and also indirectly, through its influence on behaviors, and therefore on health (Malkhazova et al. 2014; Barton 2017; Mitsakou et al. 2019); for instance, living in municipalities with low job opportunities may lead to stress and poor mental health which in consequence may result in the adoption of unhealthier behaviors (Kamphuis et al. 2012; Loureiro et al. 2019). Studies assessing the impact of sudden and significant changes in the environment where people live, have been highlighting the consequences of environmental conditions on CVD (Bhatnagar 2017). Robertson et al (1977), found that the incidence of myocardial infarction and death from coronary heart disease was significantly higher among Japanese emigrants in the United States when compared to Japanese in Japan; material, behavioural and psychosocial factors were referred to as a major factor to explaining this inequality. More recently, Hedlund et al. (2007) studied pairs

of twins from Finland where one twin had lived one year, or more, in Sweden and found a reduced prevalence of coronary heart disease among the twins that migrated from Finland to Sweden; they highlighted that the change in the environment where the migrant lived may have contributed to the adoption of new dietary habits and physical activity patterns.

Mortality due to CVD is currently decreasing in nearly all European countries (Roth et al. 2017). This decreasing trend results from the positive evolution of some behaviour risk factors such as smoking and alcohol consumption and also the improvements of the disease treatment (Wilkins et al. 2017). The same trend is found in Portugal (Almendra et al. 2015), mostly in result of the significant improvements in healthcare and life conditions (Santana 2014). Nonetheless, despite this important decrease CVD are still one of the main causes of morbidity and mortality in Portugal and should be a priority to public health and urban planning stakeholders.

Assessing the unequal distribution of health outcomes between regions with deferent environmental conditions, and its evolution, can contribute to the identification of risk factors to be addressed in the planning of suitable public health interventions (Vardoulakis et al. 2014). Thus, this study analyses the evolution of the spatial patterns of deaths by CVD, between 1991 and 2017, identifying areas of high risk, and its geographical variation, in the 278 municipalities of Continental Portugal.

MATERIALS AND METHODS

Portugal mainland (hereinafter referred as Portugal) is constituted of 278 municipalities. In 2017, Portugal resident population was near 10 million inhabitants, 70% of whom reside in urban spaces (Santana and Almendra 2018); according to the national statistics (2018), at municipal level, the population density (hab/km²) varies between 4 and 7,641 (with an average population density of 109 hab/km²). Lisbon and Porto are the two most populous cities; the two cities are the capital of the correspondent metropolitan areas, accounting together for nearly 4.5 million inhabitants (Fig. 1a).

To identify areas with significant high risk of mortality by CVD, towards time and space and areas with significantly unusual high or low temporal trends, secondary data was collected for the 278 municipalities of Portugal mainland, for

26 years (1991–2017) from the Portuguese National Statistics Institute (National Statistics): 1. annual resident population and 2. deaths due to CVD (International Classification of Diseases 10th revision: I00-I99).

The retrospective spatial-temporal method of clusterization, developed by Martin Kulldorff, (Kulldorff 1997), was applied to cluster the municipalities with significant higher or lower CVD mortality rates, when compared to the expected value, considering the period under analysis. It assumes a Poisson probability model, estimating the Relative Risk (RR), with significant levels of 5%, through the Monte Carlo method. The spatial structure of the model was defined considering: i) the centroid of each municipality, ii) a circular spatial window, iii) 20% of the population, as the maximum cluster size, iv) 2 years as the minimum temporal cluster dimension, v) the impossibility of clusters overlapping.

The analysis of the spatial variation in temporal trends identifies if the temporal trend within a group of municipalities is significantly different than the expected value (e.g. if a cluster of municipalities is decreasing at a slower pace than the reference). In this analysis, a significant cluster does not necessarily mean that the CVD mortality rate is higher or lower, it reflects significant differences between the rhythms of the evolution of CVD mortality.

SaTScan v9.6 was used to develop the spatiotemporal analysis and ArcMap 10.6 to map the results.

RESULTS

In 2017, the crude CVD mortality rate was of 312.4 deaths per 100,000 inhabitants in Portugal (was of 468.1 in 1991) (Fig 1b and 1c). The spatial-temporal analysis of the CVD mortality allowed the identification of 3 clusters with high risk (represented by warm colours in Fig. 2a) and 2 clusters of lower risk (represented by cold colours in Fig. 2a). The high-risk clusters count 26% of the total deaths analysed.

High risk municipality clusters cover the several regions of Portugal (Fig 2a): cluster E includes municipalities from the North East region; Cluster B includes the majority of the municipalities from the Centre and Southern regions; Cluster D is constituted uniquely by the municipality of Lisbon. Cluster D, lasting from 1991 until 2007, has the longest temporal frame and the highest RR (1.81) with an average CVD mortality rate of 668 deaths per 100,000 inhabitants (Table 1). No clusters of high risk were identified after 2008 (Clusters

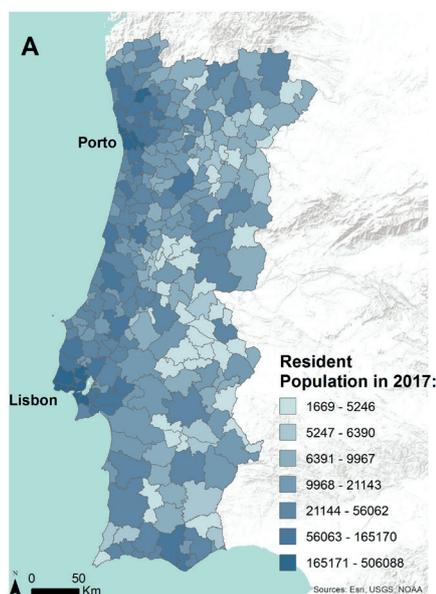


Fig. 1a. Resident population in 2017

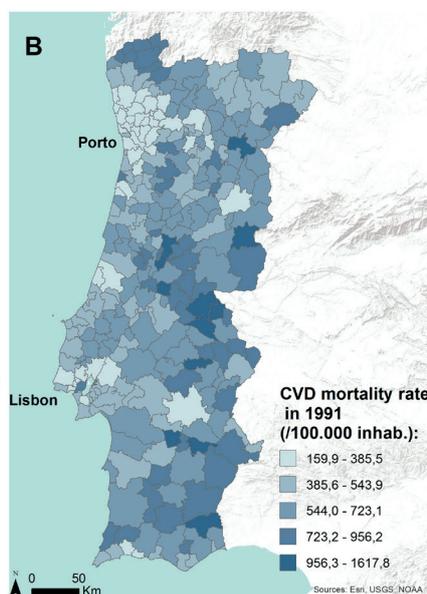


Fig. 1b. Cardiovascular mortality rate in 1991

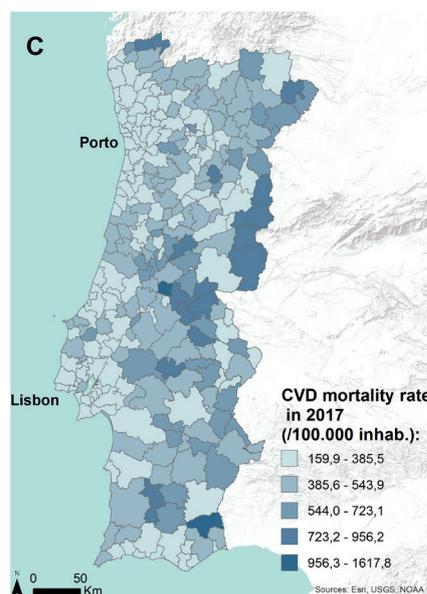


Fig. 1c. Cardiovascular mortality rate in 2017

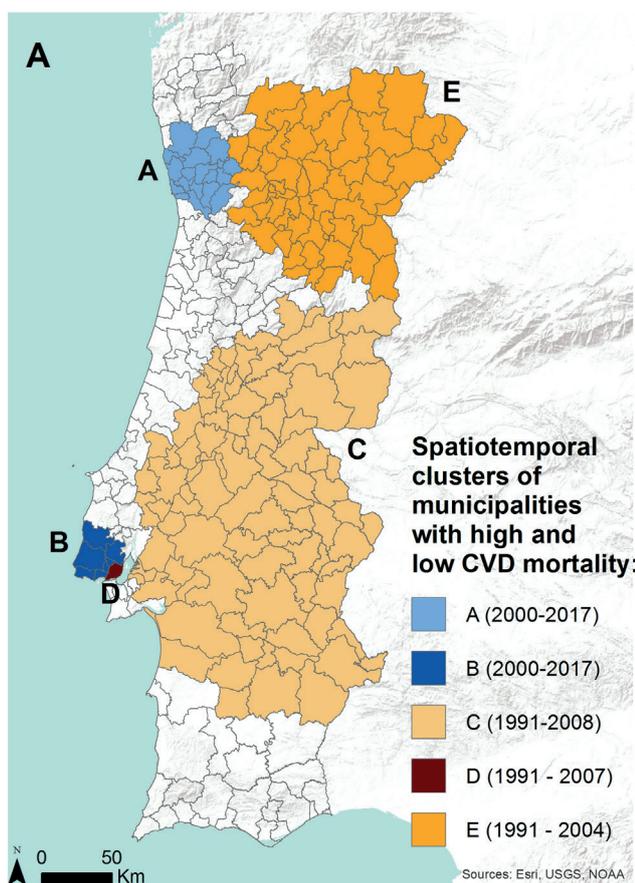


Fig. 2a. Spatiotemporal clusters of cardiovascular mortality

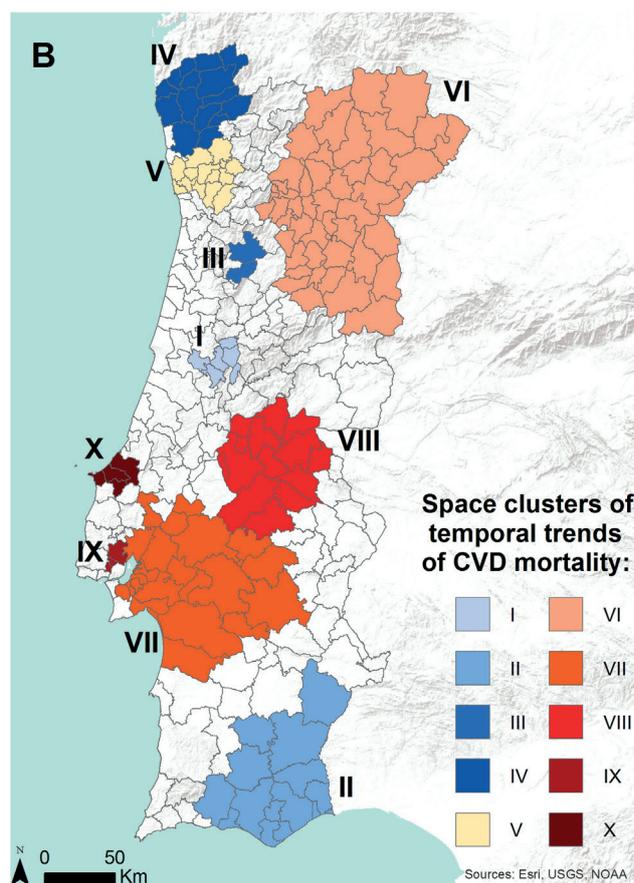


Fig. 2b. Space clusters of temporal trends of cardiovascular mortality

C, D and E last until 2008, 2007 and 2004, respectively) while clusters of low risk are identified from 2000 onwards, lasting until the end of the period under analysis.

Low risk clusters are mainly constituted by municipalities of the two metropolitan areas; Porto Metropolitan Area Cluster (Cluster A) includes the Porto municipality. On the opposite direction, Lisbon Metropolitan Area Cluster (Cluster B) does not include the municipality of Lisbon (which forms Cluster D of high risk).

Clusters A and Cluster B have the same temporal dimension (from 2000 until 2017) but the RR in cluster A is lower (0.58) when compared to cluster B (0.74).

In the temporal analysis of the spatial variation an annual average decrease of 1.8%, in the CVD mortality rate, was found between 1991 and 2017.

Table 2 presents the results of the spatial variation in temporal trend of CVD mortality. Despite the observed decline of CVD mortality in all municipalities, there are important inequalities in the pace of decrease. Clusters V to X are decreasing at a slower pace than what would be expected while clusters I to IV are decreasing faster than the rest of the country (Table 2, Fig 2b). In the municipalities

constituting Cluster I, CVD mortality has declined faster than in any other municipality; despite this evolution the CVD mortality rate in this cluster is still higher than the country average.

DISCUSSION

This study analysed the evolution of the spatial pattern of deaths by CVD, between 1991 and 2017. The methods adopted in this study combine space–time clustering and spatial variation in temporal trends, allowing the identification of municipalities (space or space–time) characterized by higher CVD mortality, and of municipalities with temporal trends different from the rest of the country. The spatiotemporal pattern of CVD mortality in Portugal has been changing between 1991 and 2017. A general decreasing trend was identified between 1991 and 2017 (annual average decrease of 1.8%); this trend is also represented in the evolution of the spatiotemporal clusters as no cluster of high risk is identified after 2008. Municipalities forming the lower risk clusters tend to be more urban when compared to the municipalities forming clusters of high

Table 1. Relative Risk of the spatiotemporal clusters of cardiovascular mortality

Clusters (p-value <0.05)	Temporal frame (years)	N.º of municipalities	Av. Year Population	Population density (hab./km ²)	RR	Cluster CVD mortality rate (per 100,000 inhab.)
A	2000-17	19	1,946,680	774.0	0.58	229
B	2000-17	7	1,284,042	1,321.4	0.74	288
C	1991-08	91	1,373,008	34.9	1.54	543
D	1991-07	1	562,593	5,622.9	1.81	668
E	1991-04	54	749,505	42.1	1.37	517

Table 2. Space clusters of temporal trends of cardiovascular mortality

Clusters (p-value <0.05)	N.º of municipalities	Av. Year Population	Population density (hab./km ²)	Trend inside Cluster (%), 1991-2017	Trend outside Cluster (%), 1991-2017	CVD mortality rate in 1991	CVD mortality rate in 2017
I	6	61,519	89.2	-3.23	-1.79	677.8	336.6
II	14	334,389	45.4	-2.78	-1.77	594.5	350.0
III	2	29,314	54.0	-2.66	-1.80	826.9	471.2
IV	15	606,629	180.1	-2.23	-1.78	461.7	301.4
V	14	1,180,155	695.3	-1.28	-1.82	293.0	225.4
VI	47	602,960	36.4	-1.13	-1.84	513.7	416.8
VII	21	895,301	84.0	-1.07	-1.87	401.6	314.2
VIII	14	120,213	21.7	-0.91	-1.81	702.3	556.8
IX	3	517,334	2377.8	-0.70	-1.85	300.6	257.9
X	4	100,702	177.9	-0.52	-1.82	416.1	385.1

risk; it is noteworthy that Cluster D, with the higher risk, is constituted by the Lisbon Municipality alone. The majority of the municipalities in the rural clusters present a lower decreasing trend than what would be expected if they would be evolving at the same pace as the other municipalities.

A continuous and rapid decline in CVD mortality has been observed during the last years in the more developed regions (Roth et al. 2017). The decreasing trend found in this study is in line with previous works (Almendra et al. 2015; Santana, 2005; Santana and Almendra 2018). In Portugal, CVD mortality has been evolving positively for some decades as a result of improvements in living conditions in terms of basic sanitation, housing condition, education, for instance (Santana and Almendra 2018). The growing adoption of strategic and preventive measures and the improvements of diagnosis and treatment of stroke and myocardial infarction are also contributing to the trend identified (Direção-Geral da Saúde, 2017). In addition, important improvements in lifestyles determinants such as the decrease of tobacco and alcohol consumption have been registered during the last years and its impact must also be considered (Santana 2005; Santana and Almendra 2018). As an example, a set of public health initiatives were implemented to reduce salt intake which positively impacted the evolution of the number of CVD events, and eventually also impacted premature deaths (Abreu et al. 2018). Measures addressing excessive tobacco and alcohol consumption were implemented and may also have impacted the evolution of the CVD mortality.

The association between socioeconomic conditions and health is often assessed under the rationale that people living in more deprived areas people will present worst health outcomes (Nogueira 2010; Santana et al. 2015b). As referred before, the majority of the municipalities forming the Clusters E and C are located in the inland of the country which is characterized by higher material deprivation (Almendra et al. 2017), a more pronounced ageing pattern (Santana and Almendra, 2018) and lower geographical access to healthcare (Santana et al. 2015a). The conjugation of these factors may contribute to a higher mortality rate found in these municipalities. Santana (2005) and Correia et al. (2004) identified a similar pattern during the 1990', highlighting that CVD mortality was associated with rurality (e.g. more manual workers, lower education levels).

On the other hand, clusters with low risk are constituted by municipalities of the metropolitan areas, where the

population density tend to be higher; Winkleby et al. (2007), in a study developed in Sweden, also found lower risk of coronary heart disease incidence in areas with higher population density. Malkhazova et al. (2014), refers that cities create the most favorable conditions for life: people living in urban spaces may benefit from better developed social and health structures, providing more opportunities for education and career choices.

Lisbon municipality was classified as a cluster of high risk, contrasting with the other municipalities of the metropolitan area. Possible explanations may be related with the high number of migrants living in Lisbon in worst health conditions (Harding et al. 2008) and with a high ageing population recorded in Lisbon; according to the national statistics (INE, 2019), in 2001, the ageing index in Lisbon was of 198, being the highest of the Lisbon metropolitan area (the country average was 105).

Roth et al. (2017) refer that political and social unrest may be in the origin of discontinuities in the evolution of CVD mortality, highlighting that further attention is needed to understand how CVD is influenced by rapid changes in material living conditions. In consequence of the "Great Recession", and the following implementation of the Economic Adjustment Programme, portuguese social and economic structures were shaken (e.g. such as strong unemployment increases, loss of purchasing power, important emigration flows) (Doetsch et al. 2017; Almendra et al. 2019). This may also have contributed to the observed spatial variation in temporal trend, since the decreasing trend of the CVD mortality may have been slowed down in the municipalities more affected by the consequences of the economic downturn.

Other factors influencing the spatial variation in temporal trend may be related to the different ageing rhythms recorded throughout the country as there is a positive association between CVD mortality and the ageing rate (Casper et al. 2016). The decline of CVD mortality may have been smoothed by the demographic evolution, mostly in municipalities where the ageing process has been more intense.

An important limitation of this study is related with the unavailability of deaths by age at municipal level, which did not allow the age-standardization of the results. This study applied spatiotemporal scan statistic to detect clusters in different space and periods but did not consider covariables

that could help to understand these patterns. Further studies should build up from our results and include covariables on demographic and socioeconomic characteristics.

CONCLUSIONS

The spatiotemporal pattern of the CVD mortality in Portugal has been decreasing since 1991. Municipalities with rural characteristics tend to present higher CVD mortality risk and, simultaneously, a slower decreasing trend.

The joint analysis of the spatiotemporal clustering and spatial variation on temporal trends can contribute to support the development of future interventions to control this challenging problem. Strategies directed to the municipalities where the CVD mortality is higher and the

decreasing trend is slower can have a high impact on the CVD burden. On the other hand, municipalities where the CVD decreased significantly faster than the country can be important study cases to identify conditions that contributed to the positive evolution.

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REFERENCES

- Abreu D., Sousa P., Matias-Dias C., Pinto F.J.(2018). Cardiovascular disease and high blood pressure trend analyses from 2002 to 2016: after the implementation of a salt reduction strategy. *BMC Public Health* 18, 722. DOI: 10.1186/s12889-018-5634-z.
- Åkesson A., Weismayer C., Newby P.K., Wolk A. (2007). Combined Effect of Low-Risk Dietary and Lifestyle Behaviors in Primary Prevention of Myocardial Infarction in Women. *Arch. Intern. Med.* 167, 2122. DOI: 10.1001/archinte.167.19.2122.
- Almendra R., Santana P., Vasconcelos J., Freire E. (2015). Seasonal mortality patterns due to diseases of the circulatory system in Portugal. *Geogr. Environ. Sustain.* 1, 71-77, DOI: 10.24057/2071-9388-2015-8-1-71-78.
- Almendra R., Santana P., Vasconcelos J. (2017). Evidence of social deprivation on the spatial patterns of excess winter mortality. *Int. J. Public Health* 62, 849-856. DOI: 10.1007/s00038-017-0964-7.
- Almendra R., Perelman J., Vasconcelos J., Santana P. (2019). Excess winter mortality and morbidity before, during, and after the Great Recession: the Portuguese case. *Int. J. Biometeorol.* 63, 873-883. DOI: 10.1007/s00484-019-01700-6.
- Barton H. (2017). *City of well-being : a radical guide to planning*, Routledge. ed. New York.
- Bhatnagar A. (2017). Environmental Determinants of Cardiovascular Disease. *Circ. Res.* 121, 162-180. DOI: 10.1161/CIRCRESAHA.117.306458.
- Brook R.D., Rajagopalan S., Pope C.A., Brook J.R. et. al. (2010). Particulate Matter Air Pollution and Cardiovascular Disease. *Circulation* 121, 2331-2378. DOI: 10.1161/CIR.0b013e3181d8e1.
- Casper M., Kramer M.R., Quick H., Schieb L.J. et al. (2016). Changes in the Geographic Patterns of Heart Disease Mortality in the United States: 1973 to 2010. *Circulation* 133, 1171-80. DOI: 10.1161/CIRCULATIONAHA.115.018663.
- Chaix B., Rosvall M., Merlo J. (2007). Assessment of the magnitude of geographical variations and socioeconomic contextual effects on ischaemic heart disease mortality: a multilevel survival analysis of a large Swedish cohort. *J. Epidemiol. Community Heal.* 61, 349-355. DOI: 10.1136/jech.2006.047597.
- Chum A., O'Campo P. (2015). Cross-sectional associations between residential environmental exposures and cardiovascular diseases. *BMC Public Health* 15, 438. DOI: 10.1186/s12889-015-1788-0.
- Correia M., Silva M.R., Matos I., Magalhães R. et al. (2004). Prospective community-based study of stroke in Northern Portugal: Incidence and case fatality in rural and urban populations. *Stroke* 35, 2048-2053. DOI: 10.1161/01.STR.0000137606.34301.13.
- Direção-Geral da Saúde (2017). *Programa Nacional para as Doenças Cérebro-Cardiovasculares*. Lisbon.
- Doetsch J., Pilot E., Santana P., Krafft T. (2017). Potential barriers in healthcare access of the elderly population influenced by the economic crisis and the troika agreement: A qualitative case study in Lisbon, Portugal. *Int. J. Equity Health* 16, 184. DOI: 10.1186/s12939-017-0679-7.
- Harding S., Teyhan A., Rosato M., Santana P. (2008). All cause and cardiovascular mortality in African migrants living in Portugal: evidence of large social inequalities. *Eur. J. Cardiovasc. Prev. Rehabil.* 15, 670-676, DOI: 10.1097/HJR.0b013e32830fe6ce.
- Hedlund E., Kaprio J., Lange A., Koskenvuo M. et al. (2007). Migration and coronary heart disease: A study of Finnish twins living in Sweden and their co-twins residing in Finland. *Scand. J. Public Health* 35, 468-474, DOI: 10.1080/14034940701256875.
- Huxley R.R., Woodward M. (2011). Cigarette smoking as a risk factor for coronary heart disease in women compared with men: A systematic review and meta-analysis of prospective cohort studies. *Lancet* 1297-1305. DOI: 10.1016/S0140-6736(11)60781-2.
- Hvidtfeldt U.A., Geels C., Sørensen M., Kettel M. et al. (2019). Long-term residential exposure to PM2.5 constituents and mortality in a Danish cohort. *Environ. Int.* 133, 105268. DOI: 10.1016/j.envint.2019.105268.
- Jackson J.K., MacDonald-Wicks L.K., McEvoy M.A., Forder P.M. et al. (2019). Better diet quality scores are associated with a lower risk of hypertension and non-fatal CVD in middle-aged Australian women over 15 years of follow-up. *Public Health Nutr.* 1-12. DOI: 10.1017/S1368980019002842.
- Jimenez M.P., Wellenius G.A., Subramanian S.V., Buka S. et al. (2019). Longitudinal associations of neighborhood socioeconomic status with cardiovascular risk factors: A 46-year follow-up study. *Soc. Sci. Med.* 241, 112574. DOI: 10.1016/j.socscimed.2019.112574.
- Kamphuis C.B.M., Turrell G., Giskes K., Mackenbach J.P., van Lenthe F.J. (2012). Socioeconomic inequalities in cardiovascular mortality and the role of childhood socioeconomic conditions and adulthood risk factors: a prospective cohort study with 17-years of follow up. *BMC Public Health* 12, 1045. DOI: 10.1186/1471-2458-12-1045
- Kulldorff M. (1997). A spatial scan statistic. *Commun. Stat. – Theory Methods* 26, 1481-1496. DOI: 10.1080/03610929708831995.
- Loureiro A., Santana P., Nunes C., Almendra R. (2019). The Role of Individual and Neighborhood Characteristics on Mental Health after a Period of Economic Crisis in the Lisbon Region (Portugal): A Multilevel Analysis. *Int. J. Environ. Res. Public Health* 16, 1-16.
- Mahmood S.S., Levy D., Vasan R.S., Wang T.J. (2014). The Framingham Heart Study and the epidemiology of cardiovascular disease: a historical perspective. *Lancet* 383, 999-1008. DOI: 10.1016/S0140-6736(13)61752-3.
- Malkhazova S.M., Linsheng Y., Wuyi W., Orlov D.S., Shartova N.V. et al. (2014). HEALTH OF URBAN POPULATION IN MOSCOW AND BEIJING AGGLOMERATIONS. *Geogr. Environ. Sustain.* 7, 41-53. DOI: 10.24057/2071-9388-2014-7-4-41-53.
- Matthews C.E., George S.M., Moore S.C., Bowles H.R. et al. (2012). Amount of time spent in sedentary behaviors and cause-specific mortality in US adults. *Am. J. Clin. Nutr.* 95, 437-445. DOI: 10.3945/ajcn.111.019620.

- Mitsakou C., Dimitroulopoulou S., Heaviside C., Katsouyanni K. et. al. (2019). Environmental public health risks in European metropolitan areas within the EURO-HEALTHY project. *Sci. Total Environ.* 658, 1630-1639. DOI: 10.1016/J.SCITOTENV.2018.12.130.
- Naimi A.I., Paquet C., Gauvin L., Daniel M. (2009). Associations between area-level unemployment, body mass index, and risk factors for cardiovascular disease in an urban area. *Int. J. Environ. Res. Public Health* 6, 3082-96, DOI: 10.3390/ijerph6123082.
- Nogueira H.G. (2010). Deprivation amplification and health promoting resources in the context of a poor country. *Soc. Sci. Med.* 70, 1391-1395. DOI: 10.1016/j.socscimed.2010.01.011.
- Ogunmoroti O., Osibogun O., McClelland R.L., Burke G.L. et al. (2019). Alcohol and ideal cardiovascular health: The Multi-Ethnic Study of Atherosclerosis. *Clin. Cardiol.* 42, 151-158. DOI: 10.1002/clc.23125.
- Patterson R., McNamara E., Tainio M., de Sá T.H., Smith A.D. et. al. (2018). Sedentary behaviour and risk of all-cause, cardiovascular and cancer mortality, and incident type 2 diabetes: a systematic review and dose response meta-analysis. *Eur. J. Epidemiol.* 33, 811-829. DOI: 10.1007/s10654-018-0380-1.
- Pekka, P., Pirjo, P., Ulla, U. (2002). Influencing public nutrition for non-communicable disease prevention: from community intervention to national programme—experiences from Finland. *Public Health Nutr.* 5, 245-51.
- Peters S.A.E., Huxley R.R., Woodward M. (2013). Smoking as a risk factor for stroke in women compared with men: A systematic review and meta-analysis of 81 cohorts, including 3 980 359 individuals and 42 401 strokes. *Stroke* 44, 2821-2828. DOI: 10.1161/STROKEAHA.113.002342.
- Rehm J., Shield K.D., Roerecke M., Gmel G. (2016). Modelling the impact of alcohol consumption on cardiovascular disease mortality for comparative risk assessments: an overview. *BMC Public Health* 16, 363. DOI: 10.1186/s12889-016-3026-9
- Robertson T.L., Kato H., Rhoads G.G., Kagan A. et. al. (1977). Epidemiologic studies of coronary heart disease and stroke in Japanese men living in Japan, Hawaii and California: Incidence of myocardial infarction and death from coronary heart disease. *Am. J. Cardiol.* 39, 239-243. DOI: 10.1016/S0002-9149(77)80197-5.
- Roth G.A., Johnson C., Abajobir A., et al. (2017). Global, Regional, and National Burden of Cardiovascular Diseases for 10 Causes, 1990 to 2015. *J. Am. Coll. Cardiol.* 70, 1-25. DOI: 10.1016/J.JACC.2017.04.052.
- Santana P. (2005). *Geografias da Saúde e do Desenvolvimento. Evolução e Tendências em Portugal*, Almedina. ed. Coimbra.
- Santana P. (2014). A saúde dos portugueses, in: Simões, J. (Ed.), *40 Anos de Abril Na Saúde*. Almedina, Coimbra, 69-92.
- Santana P., Costa C., Cardoso G., Loureiro A., Ferrão J. (2015a). Suicide in Portugal: Spatial determinants in a context of economic crisis. *Heal. Place* 35, 85-94. DOI: 10.1016/j.healthplace.2015.07.001.
- Santana P., Costa C., Marí-Dell'Olmo M., Gotsens M., Borrell C. (2015b). Mortality, material deprivation and urbanization: exploring the social patterns of a metropolitan area. *Int. J. Equity Health* 14, p. 55. DOI: 10.1186/s12939-015-0182-y.
- Santana P., Almendra R. (2018). The health of the Portuguese over the last four decades. *Méditerranée*. DOI: 10.4000/mediterranee.10348.
- Stewart J., Manmathan G., Wilkinson P. (2017). Primary prevention of cardiovascular disease: A review of contemporary guidance and literature. *JRSM Cardiovasc. Dis.* 6. DOI: 10.1177/2048004016687211.
- Vardoulakis S., Dear K., Hajat S., Heaviside C., Eggen B. (2014). Comparative Assessment of the Effects of Climate Change on Heat- and Cold-Related Mortality in the United Kingdom and Australia. *Environ. Health Perspect.* DOI: 10.1289/ehp.1307524.
- Vasconcelos J., Freire E., Morais J., MacHado J.R., Santana P. (2011). The health impacts of poor housing conditions and thermal discomfort. *Procedia Environ. Sci.* 4, 158-164. DOI: 10.1016/j.proenv.2011.03.019.
- WHO (2017). Fact sheet on Cardiovascular diseases [https://www.who.int/news-room/fact-sheets/detail/cardiovascular-diseases-(cvds)]. WHO Fact sheet.
- Wilkins E., Wickramasinghe K. (2017). *European Cardiovascular Disease Statistics 2017 edition*, European Heart Network. Brussels.
- Winkleby M., Sundquist K., Cubbin C. (2007). Inequities in CHD incidence and case fatality by neighborhood deprivation. *Am. J. Prev. Med.* 32, 97-106. DOI: 10.1016/j.amepre.2006.10.002.