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BMJ Open Association of socioeconomic status with prognosis in hypertensive patients over age 65: a cohort study in the community setting

Jesus Martin-Fernandez ,^{1,2,3,4} Tamara Alonso-Safont,^{5,6} Patricia Elena Gestri-Mora,⁶ Elena Polentinos-Castro,^{2,3,4,7} Gemma Rodríguez-Martínez,⁸ Amaia Bilbao,^{4,9,10} M^a Isabel del Cura-Gonzalez ^D ^{2,3,4,7,11}

To cite: Martin-Fernandez J. ABSTRACT

Objective To examine whether socioeconomic status is associated with prognosis after the diagnosis of hypertension (HTN), in a population older than 65 years, in the community setting.

Design Retrospective cohort study.

Setting All the primary care centres of the Community of Madrid (n=392).

Participants All patients (>65 years) with a new diagnosis of HTN in 2007-08, without previous kidney or cardiovascular (K/CV) events (n=21754).

Patient records from primary care electronic health records and Spanish mortality database were analysed from January 2007 through December 2018. Sociodemographic data such as age, gender, Area Deprivation Index (MEDEA—Mortalidad en áreas pequeñas Españolas y Desigualdades Socioeconómicas y Ambientales—Index in quintiles), and characteristics, such as smoking, type 2 diabetes mellitus and hypercholesterolaemia, were collected at the time of enrolment.

Primary and secondary outcome measures The occurrence of K/CV events (including mortality from these causes) and total mortality were evaluated using Cox rearession.

Results Patients had a mean age of 73.5 (SD 6.5) years, and 63.5% were women. The median follow-up was 128.7 months (IQR: 110.6-136.7 months). There were 10648 first K/CV events, including 1508 deaths from these causes and 4273 deaths from other causes. Adjusted for age. gender, smoking, diabetes and hypercholesterolaemia, when comparing the third, fourth and last quintiles (less affluent) of the Deprivation Index with respect to the first quintile, the hazard of K/CV events increased by 14.8% (95% CI: 3.3 to 27.6%), 16.0% (95% CI: 6.4 to 26.4%) and 19.1% (95% CI: 8.9 to 30.2%), respectively. The MEDEA Index was not associated with differences in adjusted total mortality.

Conclusion Living in a low socioeconomic status area is associated with an increase in kidney or cardiovascular events in hypertensive patients diagnosed after age 65 years, which will result in a significant increase in disease burden even if not related to an increase in total mortality.

STRENGTHS AND LIMITATIONS OF THIS STUDY

- \Rightarrow The combination of mortality regional registries and 'hard events' recorded in electronic health records can be a powerful method for monitoring outcomes.
- \Rightarrow As elderly individuals may be more likely to have stable housing situations, the identification of socioeconomic level based on area of residence may be more plausible.
- \Rightarrow In 2018, the closing date of the study, 80% of the assigned population visited their family doctor on a primary care centre, which enhance study generalisability.
- \Rightarrow Some potential confounders as social support or individual socioeconomic variables have not been included.
- \Rightarrow The accuracy and completeness of registries in electronic health records have been only validated for hypertension, diabetes mellitus, acute myocardial infarction and stroke diagnosis.

INTRODUCTION

data mining, Al training, Hypertension (HTN) is one of the most and prevalent cardiovascular risk factors in the community environment, and the number of <u>0</u> diagnoses has doubled in the past 30 years.¹ HTN is associated with an excess of mortality, mainly mediated by cardiovascular (CV) disease.2 ³ Although the control of hypertension through pharmacological and lifestyle measures has been shown to decrease g mortality from these causes,⁴⁻⁷ it seems that hypertensive patients have an excess risk of cardiovascular events⁸ ⁹ and overall mortality.⁹⁻¹³ HTN is attributed to a large disease burden, making it responsible for the loss of 143 million disability-adjusted life years globally in 2015.³ Most of this burden of disease is due to cardiovascular and renal complications and mortality from these causes associated with the HTN diagnosis.¹⁴

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Dr Jesus Martin-Fernandez; jmfernandez@salud.madrid.org However, neither the incidence of HTN nor its prognosis is homogeneous in all social groups. Almost two decades ago, potential associations between population characteristics and individual blood pressure figures began to emerge, and these figures were influenced by circumstances such as lower educational levels.¹⁵ Social deprivation in the place of residence was significantly associated with the appearance of hypertension, even after adjusting for demographic variables and lifestyles.¹⁶ Some studies showed that the probability of suffering HTN increased by up to 30% when comparing those who had spent their childhood among the most disadvantaged social classes with people who lived in advantaged areas.¹⁷ The association between socioeconomic status and HTN seems clear, and some authors proposed that it is strongly mediated by education level¹⁸ and that the risk of HTN increases with age.¹⁹ Subsequently, it has been shown that a lower socioeconomic situation across the lifecourse was associated with a higher incidence of HTN and that both the accumulation of socioeconomic risks and the models of social mobility with more adverse socioeconomic trajectories increased the incidence rate of HTN.^{20 21}

The mechanisms that explain this association are not entirely clear. It seems that unhealthy lifestyles and other risk factors (eg, smoking and obesity), which are more frequently found in subjects from lower socioeconomic classes, could partly explain these relationships.¹⁷ In studies carried out in our environment, it has been observed that the differences in the prevalence of hypertension according to socioeconomic factors in an older population are small, and it is suggested that, in women, the direct effect of socioeconomic status and level of education on hypertension are negligible. However, in men education and socioeconomic status are related to hypertension without being mediated by the usual risk factors.²²

More recent studies show that a higher number of social vulnerabilities are associated with a progressively greater risk of developing HTN.²³ The association of a lower socioeconomic situation and the incidence of cardiovascular disease is well described.^{17 24} Additionally, it is associated with higher mortality from these causes²⁵ and with total mortality. Inverse association between educational level and cardiovascular mortality has been found in our country and it was particularly strong among women.²⁶ Some studies relate this inequity to worse healthcare received by people with low socioeconomic status.²⁷ However, it is not clear whether patients with HTN in a setting with universal access to healthcare suffer from these potential differences in their prognosis associated with socioeconomic situation.

The study of socioeconomic status can be approached from an individual or contextual perspective. There are multiple characteristics that can define the socioeconomic situation, which can be considered from a multidimensional perspective.²⁸ Many of the studies mentioned use indicators of individual socioeconomic status.^{23 25 29} Others use the socioeconomic status of the area and evaluate its

relationship with survival after a cardiovascular event.³⁰ In fact, the deprivation of the area has been shown to be a better predictor than the individual socioeconomic situation when studying the occurrence of cardiovascular events.³¹ In our setting, the MEDEA project ('Mortalidad en áreas pequeñas Españolas y Desigualdades Socioeconómicas y Ambientales') generated an Area Deprivation Index capable of detecting areas of low socioeconomic level, which has been shown to explain differences in mortality.³² Addressing socioeconomic differences from a contextual perspective has been successful in investigating differences in cardiovascular mortality due to certain diseases.³⁰

In this framework, the evidence of the association between socioeconomic status and risk factors for cardiocopyright, vascular events was stronger in older subjects.^{19 25} Therefore, we aimed to evaluate the potential association between the area-level socioeconomic status and the risk of kidney and cardiovascular events and mortality after the diagnosis of HTN, in a population aged 65 and older in the community setting.

METHODS

This is a retrospective observational study.

We studied a cohort of all patients aged 65 years or older diagnosed with HTN without evidence of kidney or cardiovascular disease at inclusion in their electronic health record (EHR) in the primary care centres (PCC) of the Community of Madrid from 1 January 2007 to 31 January 2008. We used the code ICP-2 K86, which has been previously validated for the HTN diagnosis.³³ (figure 1).

The exclusion criteria were being under 65 years of age, having suffered from kidney or cardiovascular disease, having been diagnosed with hypertension or taking antihypertensive medication, before the start of the observa- \triangleright tion period.

training, The follow-up lasted until 31 December 2018 or until the moment in which the patient died or was discharged from the health records of the Autonomous Community.

Variables

Exposure variable: area socioeconomic status. The Deprivation Index assigned to each census area in the MEDEA project is calculated from indicators related to work tion (total insufficient education among young people).³² The index was categorised into quintiles, with the first see being the most favoured and the fifth the least f

Covariates

Demographic and clinical variables were collected. Age at inclusion and gender were collected from clinical records. The following clinical conditions were also collected as covariates: (1) diabetes mellitus type 2 (DM, ICPC-2 T89 and T90); (2) smoking history (any review that the patient smokes or diagnosis of active smoking-ICPC-2P17-at

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Figure 1 Cohort generation flow diagram. CIBELES, centre of strategic basic information for health environments; EHR, electronic health record.

the time or in the year prior to inclusion); and (3) hypercholesterolaemia (ICPC-2 T93).

Age, gender and these three clinical conditions were recorded at the time of inclusion.

Outcome variables

In the follow-up, the following study outcomes were collected: (1) kidney events: urinary microalbuminuria (yes/no), defined as a urine albumin/creatinine ratio greater than 30, existence of proteinuria (yes/ no) defined as the presence of 300 mg/dL of protein in urine in at least two consecutive samples in the absence of concomitant disease or the presence of chronic kidney disease (ICPC-2 U99.1); (2) CV events: ischaemic heart disease (acute myocardial infarction—ICPC-2 K75, angina—ICPC-2K74, cardiac ischaemia, chronic—ICPC-2 K76, cerebrovascular disease—ICPC-2 K90, peripheral arterial disease—ICPC-2 K92; and (3) death from any cause and kidney or CV death. Deaths due to chronic kidney disease (ICD10: N18), cerebrovascular accident (ICD10: G46; I60-I69), ischaemic heart disease (ICD10: I20-I25), heart failure (ICD10: I50) and peripheral arterial disease (ICD10: I70, I71, I72, I74) were classified as kidney/cardiovascular mortality.

For the definition of different diagnoses, the records of the primary care (PC) clinical history were used and coded according to the International Classification of Primary Care (ICPC-2).³⁴

The International Classification of Diseases 10th edition (ICD-10) was used to study the causes of mortality.³⁵

The data sources linked using a matching algorithm were the EHR of PC and the registry of mortality by specific cause of the National Institute of Statistics. This study followed the guidelines for cohort studies, described in the Strengthening the Reporting of Observational

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Studies in Epidemiology (STROBE) reporting guideline and the RECORD statement (online supplemental additional file 1).

Analysis

The database construction involved several steps to enhance data quality (figure 1).

The distribution of the independent variables of the subject, the mean area of residence and the follow-up times were described.

Cox proportional hazards models were adjusted to study the risks associated with the context in which the subjects lived.³⁶ The proportional hazards assumption in a Cox proportional hazards model was not met when using conventional tests, but HRs over time were assessed and were found to be stable enough to proceed with the analysis. Additionally, other concerns such as influential outliers, missing data or significant model misspecification were considered. The 95% CIs for the Cox regression coefficients were estimated using bootstrap resampling. This approach has been suggested in large sample sizes or complex clinical scenarios.³⁷

The models were constructed including the MEDEA Index as an independent variable and were adjusted for patient demographic and clinical variables. Two types of models were constructed. The first used the occurrence of kidney or cardiovascular events as the outcome, including mortality from these causes. In this model, follow-up was considered to end when the first of these events occurred, or when the subject was lost, or on 31 December 2018, whichever came first. The second type of models considered all-cause mortality as the event to be studied. The final models were also built separately for men and women. Gender differences play an influential role in multiple health-related outcomes. The importance of studying gender in investigating the role of the cultural and social environment in the prognosis of HTN has been highlighted.³⁸

The estimated size for the cohort of 20000 subjects would allow finding differences in event occurrences of 2% at 10 years in each of the Deprivation Index guintiles (between 12% and 20%) even in the presence of very high variance inflation factors.³⁹

Stata 14.2 software was used for data analysis.

Patient and public involvement

None.

RESULTS

Protected We included 21754 patients over age 65 with new diagnoses of uncomplicated HTN in 392 centres and clinics: 12335 in 2007 and 9419 in 2008 (figure 1).

by copyright Table 1 shows the characteristics of the studied cohort, in which women predominate (63.5%), with a mean age at inclusion of 73.5 years (SD 6.5 years, range 65-101 years; median 72 years, IQR 68-78 years). The median follow-up of the cohort was 128.7 months (IQR 110.6including 136.7 months).

Occurrence of kidney or CV events included death from these causes

During follow-up, 10648 first kidney/CV events occurred (including 1508 deaths due to these causes without a previous event). A total of 1937655 person-months were observed, and the incidence rate of these events was 54/10000 person-months. The median time of occurrence of the event was 62.6 months (IQR 33.6-92.3 months). text

Table 2 shows the results of the best model explaining the association between the Deprivation Index and the occurrence of kidney/CV events (including death from these causes).

Adjusted for age, gender, smoking, diabetes mellitus and hypercholesterolaemia, an association is observed between greater deprivation and the greater occurrence d of kidney or CV events, starting from the third quintile \geq of the MEDEA Index. This association increases slightly in intensity as the Deprivation Index worsens; the more unfavourable this index is, the stronger the association.

Table 1 Characteristics of the studied cohort (n=21754)									
Medea Index	First Q	Second Q	Third Q	Fourth Q	Fifth Q	Total*			
Age									
65 to 74 years	2562 (57.2%)	2571 (59.2%)	2655 (62.6%)	2828 (64.7%)	2797 (64.9%)	13413 (61.7%)			
75 to 84 years	1503 (33.5%)	1433 (33.0%)	1301 (30.7%)	1302 (29.8%)	1304 (30.3%)	6843 (31.5%)			
≥85	417 (9.3%)	340 (7.8%)	283 (6.7%)	240 (5.5%)	207 (4.8%)	1487 (6.8%)			
Median (IQR)	73 (69–79)	73 (68–78)	72 (68–77)	72 (68–77)	72 (68–77)	72 (68–78)			
Woman	3000 (63.9%)	2811 (64.7%)	2666 (62.9%)	2726 (62.4%)	2598 (60.3%)	13801 (63.5%)			
Smokers	296 (6.6%)	272 (6.3%)	254 (6.0%)	268 (6.1%)	295 (6.9%)	1385 (6.4%)			
Diabetes mellitus	518 (11.6%)	569 (13.1%)	585 (13.8%)	685 (15.8%)	673 (15.6%)	3030 (13.9%)			
Hypercholesterolaemia	1221 (27.2%)	1150 (26.51%)	1168 (27.6%)	1264 (28.9%)	1240 (28.8%)	6043 (27.8%)			

*It was not possible to assign the MEDEA Index to 11 subjects. Q, quintile.

Table 2 Cox model for kidney of shown	or cardiovascula	r events, including mortality from thes	e causes, adjusted for the covariates
Variable	HR	HR 95% CI	p>z
Age			
75–84 vs 65–74 years	1.767	1.686 to 1.851	<0.001
≥85 vs. 65–74 years	2.980	2.731 to 3.25	<0.001
Female vs male	0.966	0.927 to 1.006	0.097
Diabetes mellitus	1.357	1.283 to 1.435	<0.001
Baseline smoking	1.208	1.122 to 1.301	<0.001
Hypercholesterolaemia	1.066	1.023 to 1.111	0.002
Socioeconomic group			
Second vs first quintile	1.009	0.916 to 1.112	0.849
Third vs first quintile	1.148	1.033 to 1.276	0.010
Fourth vs first quintile	1.160	1.064 to 1.264	0.001
Fifth vs first quintile	1.191	1.089 to 1.302	<0.001
Included subjects=21743. Number of clusters (centres): 392.			

Number of events: 10648.

Figure 2 shows the cumulative hazard function by quintiles adjusted for the variables (at means) shown in the model in table 2. The second quintile is not clearly different from the first, but there is an evident increase in cumulative hazard in the third, fourth and fifth quintiles, with respect to the first, after adjusting for the aforementioned variables.

The best model was run separately for men and women but no significant differences were found with the overall model (see online supplemental tables).

Occurrence of mortality from any cause

During follow-up, 5781 deaths occurred from any cause, 1508 deaths from kidney/CV causes and 4273 from other



Figure 2 Cumulative hazard function of suffering a kidney or cardiovascular event (including death from these causes) according to MEDEA quintile, adjusted for age, gender, presence of diabetes mellitus, smoking and hypercholesterolaemia (model in table 2).

Variable	HR	HR CI 95%	p>z
Age			
75–84 vs 65–74 years	3.446	3.255 to 3.649	< 0.001
≥85 vs. 65–74 years	13.115	12.214 to 14.083	<0.001
Female vs male	0.695	0.656 to 0.736	<0.001
Diabetes mellitus	1.319	1.223 to 1.422	< 0.001
Baseline smoking	1.418	1.269 to 1.583	<0.001
Hypercholesterolaemia	0.782	0.731 to 0.837	<0.001
Socioeconomic group			0.391
Second vs first quintile	0.942	0.82 to 1.081	0.395
Third vs first quintile	0.913	0.798 to 1.044	0.183
Fourth vs first quintile	0.866	0.781 to 1.006	0.062
Fifth vs first quintile	0.952	0.846 to 1.072	0.420
Included subjects=21743. Number of clusters (centres): 392. Number of events: 5781.			

causes. and the incidence rate of these events was 23/10000person-months. The median time to death in those who died during the study period was 85.4 months (IQR 55.4-109.5 months).

The best model to study the association between the Deprivation Index and all-cause mortality shows no association (table 3). Regarding the adjustment variables, the association of age with mortality was very strong; female sex and hypercholesterolaemia were associated with lower mortality; smoking and DM were associated with higher mortality.

Again, the best model for total mortality was run separately for men and women and no relevant differences were found with the overall model (see online supplemental tables).

DISCUSSION

The Deprivation Index of the area in which one lives is associated with an increase in kidney/CV events in hypertensive patients diagnosed after age 65 and without previous cardiovascular history, in follow-up in the community environment for more than 10 years. This association remained after adjusting for other potential demographic and metabolic risk factors, such as diabetes or hypercholesterolaemia, or lifestyle indicators, such as smoking. This association was not found when mortality from all causes was studied. It should also be noted that no gender differences were found when studying the aforementioned relationships between socioeconomic status and prognosis in older patients with hypertension.

In this study, an increased hazard of almost 20% of kidney/CV events (including death due to these causes) was found in patients residing in areas in the least affluent quintile compared with those who inhabited the most

Protected by copyright, including for use: oured areas. The association between the incidence of HTN and social group is already known,^{16 17} also in the elderly.²² In addition, an association between a lower socioeconomic status and an increased risk of cardiovascular and total mortality was found, and it seems that the factors that mediated this association had to do mainly **5** with habits and inflammatory markers rather than with psychosocial risk.²⁵ Other authors support that the role $\frac{1}{2}$ of conventional risk factors might be minor in explaining relationship between social and psychological factors and cardiovascular disease.⁴⁰ The study of the association between socioeconomic status and mortality in hypertensive patients has been recently reported at the individual level, but it was not evident when the socioeconomic ٩ status of the area was studied.²³ Suggested mechanisms to explain the association between socioeconomic disadvantaged environments and cardiovascular disease relate to dietary habits, physical activity resources and other cardiovascular risk factors.²⁸ In this paper, we evaluated the association between area-level socioeconomic status and kidney and cardiovascular events in hypertensive patients, adjusting for the effect of other risk factors such as diabetes, smoking and hypercholesterolaemia.

We found no apparent relationship between the socioeconomic status of the area and total mortality in newly diagnosed hypertensive patients over age 65 years. When the relationship between socioeconomic status and total mortality in older patients is studied, the differences in the Spanish population are lower than in the rest of Europe.⁴¹ These differences with respect to patterns of other countries have been explained by lifestyles and the existence of stronger social networks, regardless of social class. It has been mentioned how social support can be a protective factor against cardiovascular mortality in older people.⁴² In our country, individuals over age 65

who lived in provinces with the most adverse socioeconomic context had the highest mortality from cardiovascular diseases and the lowest mortality from cancer and external causes.⁴³ This may mean that the association between socioeconomic status and total mortality is not as strong as expected. In general, the trend of the past two decades is that inequalities in total mortality reduced in all European countries and, especially, in Spain. This change is attributed more to improvements in lifestyle and access to preventive activities than to policies aimed at reducing health inequalities.⁴⁴ A previous study conducted in the same region as ours reported a differential use of more intensive PC services in those subjects with lower economic situations.45 This could indicate that there are no major problems with accessibility to healthcare and preventive activities and would partly explain why no association was found between the socioeconomic status of the area and total mortality in this group of patients.

This study was subjected to several potential limitations. Given its design, causal inferences cannot be made, individual socioeconomic variables have not been included, other variables such as marital status have not been considered, underlying diseases have not been controlled and there are limitations inherent to studies that use registries not designed for research. Among its potential strengths, this study points out that the monitoring of the outcomes could be done exhaustively by combining two independent sources. We included all patients newly diagnosed of HTN in 2 years in a region of Spain (Madrid) where more than 6 million people live which resulted in a very large sample size and less concern for selection bias as compared with usual cohort studies or surveys. Since the study population is elderly, the identification of the socioeconomic status with that of the area of residence may be more plausible. Also, the generalisability of the results is good enough, as accessibility to the health system, specifically to the PC doctor, is very high in our environment. In 2018, the closing date of the study, 80% of the assigned population visited their family doctor on a PCC.⁴⁶

The implications of the results discussed relate to practice, health policies and research. First, older patients diagnosed with hypertension in socioeconomic disadvantaged settings should be monitored particularly closely. Second, as has been suggested, to reduce the burden of disease derived from HTN, strategies are needed to accelerate the socioeconomic improvements of the most vulnerable population and the development of environments that promote health.⁴⁷ Public health policies should focus on reducing social inequalities as a mechanism for improving individual health, with special attention to elderly patients. Finally, these results encourage further study of the role of social support, the cultural context of care and the healthcare system in the prognosis of these diseases.

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