Atención Primaria

ORIGINAL ARTICLE

The impact of chronic diseases on all-cause mortality in Spain: A population-based cohort study

Elena Caride-Miana[a,*], Domingo Orozco-Beltrán[b], Jose Antonio Quesada-Rico[b,c], Jose Joaquin Mira-Solves[d,e]

[a] *Doctoral Candidate, University Miguel Hernández de Elche, N332 87, 0330 Sant Joan Alicante, Spain*
[b] *Clinical Medicine Department, University Miguel Hernández de Elche, Spain*
[c] *Network for Research on Chronicity, Primary Care, and Health Promotion (RICAPPS), Spain*
[d] *Health Psychology Department, Universidad Miguel Hernandez, Elche, Spain*
[e] *ATENEA Research, Alicante-Sant Joan Health District, Spain*

Abstract

Objective: Our study aimed to assess the association between all-cause mortality and the most prevalent chronic diseases in Spain, including diabetes mellitus.

Design: Population-based retrospective cohort study.

Site: Spanish population (Spanish National Health Survey).

Participants: A population numbering 14,584 respondents of both sexes aged 40 years or older was selected.

Main measurements: The outcome variable was all-cause mortality over 6-year follow-up, measured by probabilistic cross-matching with the national death registry. Socioeconomic variables, health indicators, service use, and behavioral factors were collected. The main data source was the National Statistics Institute.

Results: Of the 14584 people included, 1346 (9.2%) died over 6-year follow-up. Regarding the most prevalent chronic diseases, those showing the strongest association with mortality were cancer (HR 1.74, 95% CI 1.40–2.16); chronic lung diseases (chronic obstructive pulmonary disease, bronchitis, or emphysema; HR 1.44, 95% CI 1.19–1.70); acute myocardial infarction (HR 1.33, 95% CI 1.08–1.65); and diabetes (HR 1.23, 95% CI 1.06–1.42). Less prevalent chronic diseases also increased mortality risk, including cirrhosis/liver disease (prevalence 1.5%; HR 1.67, 95% CI 1.22–2.29) and cerebrovascular diseases, including embolism and stroke (prevalence 2%; HR 1.39, 95% CI 1.07–1.81).

Conclusions: Chronic diseases affect over half the population aged 40 years and older in Spain. Some of the most prevalent conditions are closely associated with all-cause mortality. These include chronic lung diseases, acute myocardial infarction, and diabetes. Given their impact on mortality in the population, more efforts are needed in chronic disease prevention and management.

El papel de las enfermedades crónicas en la mortalidad total en España: un estudio de cohortes de base poblacional

Resumen

Objetivo: El objetivo fue analizar la asociación entre las principales enfermedades crónicas más prevalentes como la diabetes mellitus con la mortalidad por cualquier causa en la población española.

Diseño: Estudio de cohortes retrospectivo de base poblacional.

Emplazamiento: Población española (Encuesta Nacional de Salud de España).

Participantes: Catorce mil quinientos ochenta y cuatro participantes de ambos sexos mayores de 40 años.

Mediciones principales: La variable respuesta fue la mortalidad total durante el seguimiento a 6 años, medida mediante el cruce probabilístico con el registro nacional de defunciones. Se midieron variables socioeconómicas, de salud, uso de servicios y hábitos de vida. La fuente primaria de datos fue el Instituto Nacional de Estadística.

Resultados: Se analizaron a 14.584 sujetos, y se produjeron 1.346 fallecimientos por cualquier causa en 6 años de seguimiento, con una incidencia acumulada del 9,1%. Con respecto a las enfermedades crónicas más prevalentes la existencia de bronquitis crónica, enfisema o EPOC; de DM; la existencia de tumores, así como haber padecido un infarto agudo de miocardio (IAM), presentan mayor mortalidad. Hallándose un riesgo de muerte en 6 años (HR: 1,74; IC 95%: 1,40-2,16) en pacientes con tumores; HR: 1,44 e IC 95%: 1,19-1,70 en pacientes con enfermedad pulmonar crónica (bronquitis crónica, enfisema o EPOC), el IAM (HR: 1,33; IC 95%: 1,08-1,65) en pacientes con IAM y la diabetes (HR: 1,23; IC 95%: 1,06-1,42 en pacientes con DM).

Del mismo modo, se detectó un aumento de riesgo de mortalidad relacionado con la existencia de enfermedades crónicas menos prevalentes como la cirrosis o la disfunción hepática HR: 1,67; IC 95%: 1,22-2,29, con una prevalencia del 1,5% en la muestra, así como de las enfermedades cerebrovasculares (embolia, infarto cerebral, hemorragia cerebral) HR: 1,39; IC 95%: 1,07-1,81, con una prevalencia del 2%.

Conclusiones: Las enfermedades crónicas afectan a más de la mitad de la población española mayor de 40 años, observándose asociación significativa de algunas de las enfermedades crónicas más prevalentes y que presentan mayor morbimortalidad en las consultas de atención primaria (la enfermedad pulmonar crónica, la bronquitis o el enfisema, el infarto agudo de miocardio y la diabetes) con la mortalidad total en España. Este estudio pone de manifiesto que son necesarios más esfuerzos en la prevención y en el manejo de estas enfermedades crónicas en las consultas de atención primaria debido a su relación con la mortalidad.

Introduction

Chronic diseases are an independent predictor of mortality.[1,2] They reduce an individual's life expectancy by an average of 1.8 years and together account for 63% of all deaths worldwide.[3] Two-thirds of these deaths are caused by just four conditions—cardiovascular disease (CVD), cancer, chronic obstructive pulmonary disease (COPD), and diabetes mellitus (DM)—which predominantly affect people over 64 years of age.[4] CVD, mental health disorders, and DM are associated with at least a 33% reduction in survival in the population over 65 years of age,[5] with CVD and DM representing the leading causes of premature death in the population.[6]

Diabetes is associated with an increased risk of all-cause mortality.[7] Different studies have tried to quantify this relationship, with heterogeneous results[8–10] that nevertheless confirm a clear increase in the risk of death from all causes in people with DM, with hazard ratios (HRs) that range from 1.15 to 3.15.[8–10] The few studies carried out in the Span-

ish population have taken place in geographically disparate regions, and none have assessed the contribution of DM to all-cause mortality throughout the territory.[11,12]

With respect to other chronic diseases such as COPD, published estimates of its association with all-cause mortality worldwide range from HR 1.41 (95% CI 1.32−1.50) to HR 1.61 (95% CI 1.32−1.95)[13,14] with most mortality studies focusing on understanding the factors involved in COPD mortality in order to develop prognostic risk scales in these patients.[15]

As for CVD, this is the leading cause of morbidity and mortality in industrialized countries, accounting for 45% of all deaths in people over 65 years of age. Numerous studies have estimated the risk of CVD mortality, and several cardiovascular risk scales have been developed In Spain, CVD is the leading cause of death, representing 24.3% of the total in 2020 according to data from the National Statistics Institute (INE).[16]

Data from the INE on demographic trends, specifically population aging, suggest that the percentage of the population over 65 years of age in Spain (which stood at 19.6% in 2021) will peak at 31.4% around 2050.[17] Despite the increasing burden of chronic diseases in the population and their economic impact, no recent studies have analyzed the effect of these diseases on mortality in Spain. Thus, this study aimed to assess the association between all-cause mortality and the most prevalent chronic diseases in Spain, including DM.

Material and methods

Study design and population

This retrospective population-based cohort study included respondents from the INE 2011–2012 National Health Survey.[18,19] This health survey provides representative data on all adults (≥15 years of age) residing in Spain and is conducted with a complex sample design. For this study, a population numbering 14,584 respondents of both sexes aged 40 years or older was selected. The recruitment period for the 2011–2012 National Health Survey was July 2011–June 2012. The duration of follow-up to measure mortality was 6.4 years (1 July 2011–31 December 2017).

Variables

The outcome variable was all-cause mortality (yes/no); the date of death was obtained from the INE, which cross-referenced information and data between the health survey and the national death registry by cause of death.

The explanatory variables collected in the National Health Survey were also analyzed.

- *Sociodemographic variables*: age, sex, social class (range I–VI, determined according to standard health survey methods and based on the respondent's occupation), size of municipality, autonomous community, nationality, educational attainment, marital status, and monthly income.
- *Behavioral and clinical characteristics*: body mass index (BMI), smoking habits (smoker/ex-smoker/never smoker), alcohol intake (yes/no, plus weekly intake in grams of pure alcohol), hours of sleep, physical activity, diet (intake of fruit, vegetables, legumes, dairy products, sweets, fast food), dental hygiene (tooth brushing), and self-perceived health according to both a Likert scale (very good/good/fair/poor/very poor) and a visual analog scale.
- *Chronic diseases*: dichotomously (yes/no/does not know) and in terms of specific disease groups: chronic CVD (hypertension, acute myocardial infarction, other cardiac diseases), respiratory diseases (asthma, chronic bronchitis, emphysema, chronic obstructive pulmonary disease [COPD]), metabolic diseases (DM, thyroid disease), cancer, and mental disorders (depression, anxiety, other).
- *Other clinical conditions*: varicose veins, osteoarthritis, chronic cervical pain, chronic lower back pain, allergy, stomach ulcer, urinary incontinence, high cholesterol, cataracts, skin problems, constipation, cirrhosis, stroke, migraine, hemorrhoids, osteoporosis, accidents in the last year, and mobility limitations.
- *Health services use*: use of glasses, use of hearing aids, hospital admissions in previous year, primary care visits, urgent care, specialist visits (physiotherapy, psychology, and radiology), and flu vaccination.

Statistical analysis

A descriptive analysis of the variables was performed, calculating frequencies for categorical variables and mean, standard deviation (SD), and range for quantitative variables. An analysis of missing data was carried out using a simple imputation process, stratified by the mortality outcome (yes/no). For quantitative variables, imputation was performed using the mean value, and for categorical variables using the most frequent category.

Factors associated with mortality were analyzed using contingency tables, applying the Chi-squared test for categorical variables and the Student's t test for quantitative variables. The magnitude of the associations was estimated by fitting multivariate Cox proportional hazards models, using a stepwise variable selection procedure based on the Akaike information criterion. The proportional hazards hypothesis was tested, applying a time-dependent term in the variables that did not comply with these hypotheses. Results were expressed as HRs and their 95% confidence intervals (CIs). Goodness-of-fit indicators and predictive indicators such as Harrell's C-index[20] are shown.

To obtain estimates representative of the Spanish population, a complex sampling strategy was applied, using as a weighting factor the survey elevation factor divided by its mean, obtaining weights centered on its mean.[21] All analyses were carried out using SPSS v.28 and R v.4.2.2.

Results

A total of 14,584 respondents aged 40 years or older from the National Health Survey were included, with a mean age of 58.9 years. Overall, 52.6% were women, 89.9% had Spanish nationality, and 55.2% self-reported having some chronic disease (Table S1). The most prevalent were hypertension (32.5%), DM (11.4%), and chronic lung disease (6.5%) (Table 1).

Table 1 Six-year mortality according to the presence of different chronic diseases.

Chronic disease or condition	Total (N = 14,584)		Survived (N = 13,239)		Died (N = 1345)		
	n	%	n	%	n	%	P
Any chronic disease or health problem							
No	6527	44.8%	6254	95.8%	273	4.2%	<0.001
Yes	8057	55.2%	6984	86.7%	1073	13.3%	
Hypertension							
No	9844	67.5%	9181	93.3%	663	6.7%	<0.001
Yes	4740	32.5%	4058	85.6%	682	14.4%	
Myocardial infarction							
No	14,123	96.8%	12,921	91.5%	1202	8.5%	<0.001
Yes	461	3.2%	318	68.8%	144	31.2%	
Other heart diseases							
No	13,289	91.1%	12,271	92.3%	1018	7.7%	<0.001
Yes	1295	8.9%	967	74.7%	328	25.3%	
Varicose veins in the legs							
No	12,152	83.3%	11,078	91.2%	1075	8.8%	<0.001
Yes	2432	16.7%	2161	88.9%	271	11.1%	
Arthrosis, arthritis, or rheumatism							
No	10,252	70.3%	9591	93.5%	662	6.5%	<0.001
Yes	4332	29.7%	3648	84.2%	684	15.8%	
Chronic cervical pain							
No	11,400	78.2%	10,430	91.5%	970	8.5%	<0.001
Yes	3184	21.8%	2808	88.2%	376	11.8%	
Chronic lumbar pain							
No	10,765	73.8%	9864	91.6%	901	8.4%	<0.001
Yes	3819	26.2%	3374	88.4%	445	11.6%	
Chronic allergy (excluding allergic asthma)							
No	12,967	88.9%	11,726	90.4%	1241	9.6%	<0.001
Yes	1617	11.1%	1513	93.6%	104	6.4%	
Asthma							
No	13,918	95.4%	12,676	91.1%	1243	8.9%	<0.001
Yes	666	4.6%	563	84.5%	103	15.5%	
Chronic bronchitis, emphysema, chronic obstructive pulmonary disease							
No	13,633	93.5%	12,537	92.0%	1095	8.0%	<0.001
Yes	951	6.5%	701	73.7%	250	26.3%	
Diabetes							
No	12,925	88.6%	11,906	92.1%	1019	7.9%	<0.001
Yes	1659	11.4%	1333	80.3%	326	19.7%	
Stomach or duodenal ulcer							
No	13,704	94.0%	12,481	91.1%	1222	8.9%	<0.001
Yes	880	6.0%	757	86.0%	123	14.0%	
Urinary incontinence							
No	13,764	94.4%	12,692	92.2%	1072	7.8%	<0.001
Yes	820	5.6%	547	66.7%	273	33.3%	
High cholesterol							
No	10,581	72.6%	9620	90.9%	961	9.1%	0.34
Yes	4003	27.4%	3618	90.4%	384	9.6%	
Cataracts							
No	12,641	86.7%	11,794	93.3%	847	6.7%	<0.001

Table 1 (*Continued*)

Chronic disease or condition	Total (*N* = 14,584)		Survived (*N* = 13,239)		Died (*N* = 1345)		
	n	%	*n*	%	*n*	%	*P*
Yes	1943	13.3%	1445	74.4%	498	25.6%	
Chronic skin problems							
No	13,763	94.4%	12,523	91.0%	1240	9.0%	<0.001
Yes	821	5.6%	715	87.2%	105	12.8%	
Cirrhosis, liver dysfunction							
No	14,364	98.5%	13,068	91.0%	1295	9.0%	<0.001
Yes	220	1.5%	170	77.3%	50	22.7%	
Chronic depression							
No	13,045	89.4%	11,910	91.3%	1135	8.7%	<0.001
Yes	1539	10.6%	1328	86.3%	211	13.7%	
Chronic anxiety							
No	13,103	89.8%	11,919	91.0%	1184	9.0%	0.021
Yes	1481	10.2%	1320	89.1%	161	10.9%	
Other mental disorder							
No	14,255	97.7%	13,053	91.6%	1202	8.4%	<0.001
Yes	329	2.3%	185	56.3%	144	43.7%	
Stroke, cerebral infarction, cerebral hemorrhage							
No	14,298	98.0%	13,066	91.4%	1233	8.6%	<0.001
Yes	286	2.0%	173	60.5%	113	39.5%	
Migraine or frequent headache							
No	13,012	89.2%	11,791	90.6%	1221	9.4%	0.055
Yes	1572	10.8%	1447	92.1%	124	7.9%	
Malignant tumors							
No	13,935	95.6%	12,762	91.6%	1173	8.4%	<0.001
Yes	649	4.4%	476	73.4%	172	26.6%	
Osteoporosis							
No	13,576	93.1%	12,406	91.4%	1170	8.6%	<0.001
Yes	1008	6.9%	833	82.6%	176	17.4%	
Thyroid disease							
No	13,567	93.0%	12,301	90.7%	1266	9.3%	0.098
Yes	1017	7.0%	937	92.2%	79	7.8%	

Altogether, 1346 people died over six-year follow-up, for a cumulative incidence of all-cause mortality of 9.2%. The mean age in the deceased group was 76.6 years. The mortality rate was 13.3% in people who self-reported having some type of chronic disease, compared to 4.2% in those who did not. With respect to the individual assessment of each of the 27 chronic diseases studied, statistically significant differences in mortality at six years were detected for 25 diseases, including several of those most commonly encountered in clinical practice: 31.2% versus 8.5% in people with versus without a history of acute myocardial infarction (AMI), 26.3% versus 8% in patients with COPD, 26.6% versus 8.4% in those with malignant tumors, and 19.7% versus 7.9% in people with a diagnosis of DM.

Among the most prevalent chronic diseases, those showing a significant association with mortality in the multivariate Cox model included chronic bronchitis, emphysema, or COPD (HR 1.43, 95% CI 1.19–1.70); DM (HR 1.23, 95% CI 1.06–1.42); cancer (HR 1.74, 95% CI 1.40–2.16); and history of AMI (HR 1.33, 95% CI 1.08–1.65) (Table 2). Some of the less prevalent chronic diseases showed similar or even higher-magnitude associations, including cirrhosis/liver dysfunction (prevalence 1.5% in the sample; HR 1.67, 95% CI 1.22–2.29) and cerebrovascular diseases including embolism and stroke (prevalence 2%; HR 1.39, 95% CI 1.07–1.81) (Table 2).

Other factors associated with an increased risk were smoking (HR 1.66, 95% CI 1.32–2.09), no fruit intake (HR1.84, 95% CI 1.30–2.61), and very poor self-perceived health (HR 2.55, 95% CI 1.67–3.99). Hospital admission in the previous year was also associated with a two-fold risk of death (HR 2.10, 95% CI 1.51–2.93), although the magnitude of this risk decreased over time, depending on the length of follow-up (Fig. 1). On the other hand, protective factors were female sex (HR 0.59, 95% CI 0.50–0.70), marriage (HR

Table 2 Multivariate Cox proportional hazards model for mortality at 6 years.

Chronic disease or condition	HR[a]	95% CI	p
Myocardial infarction	1.33	(1.08–1.65)	0.008
Arthrosis, arthritis or rheumatism	0.80	(0.70–0.93)	0.003
Chronic allergy	0.73	(0.59–0.91)	0.006
Chronic bronchitis, emphysema, or COPD	1.43	(1.19–1.70)	<0.001
Diabetes	1.23	(1.06–1.42)	0.006
High cholesterol	0.72	(0.62–0.83)	<0.001
Cirrhosis, liver dysfunction	1.67	(1.22–2.29)	0.002
Other mental disorders	1.64	(1.30–2.09)	<0.001
Embolism, cerebral infarction, cerebral hemorrhage	1.39	(1.07–1.81)	0.013
Malignant tumors	1.74	(1.40–2.16)	<0.001
Activity restriction in the last 2 weeks	1.19	(1.00–1.42)	0.051
Hospital admission in the previous year	2.10	(1.51–2.93)	<0.001
Self-perceived health (VAS)	0.99	(0.989–0.997)	0.001
Follow-up time x hospital admission in year prior to survey	0.99	(0.982–0.996)	0.004

CI: confidence interval; COPD: chronic obstructive pulmonary disease; HR: hazard ratio; VAS: visual analog scale.

$N = 14{,}584$; n deaths = 1345; likelihood ratio test = 3583 ($p < 0.001$); C-index = 0.891, 95% CI 0.882–0.900.

[a] Adjusted for autonomous community, sex, age, BMI, marital status, tobacco use, hours of sleep, main daily activity, leisure-time physical activity, fruit intake, dental hygiene, and self-perceived health.
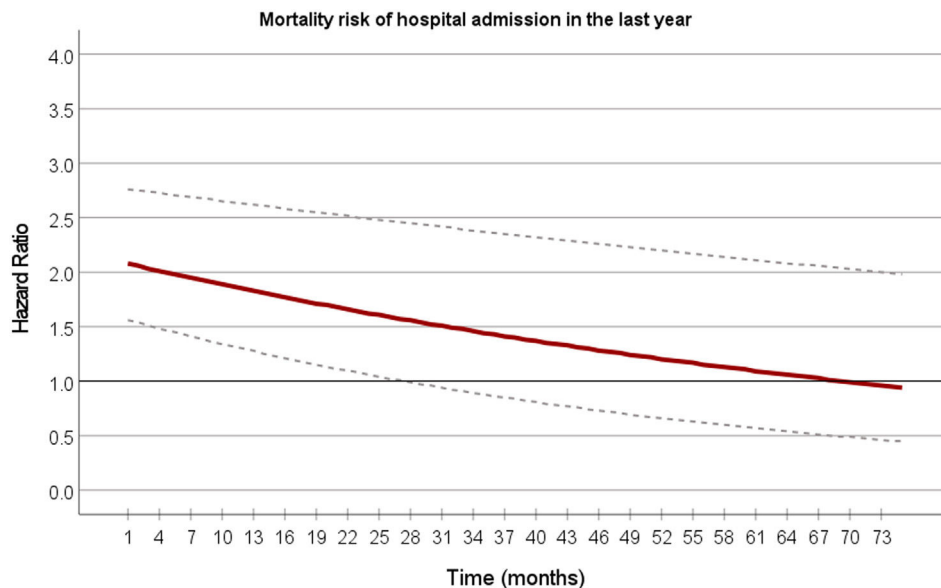
Figure 1 Multivariate Cox model for the association between risk of mortality and hospital admission in the year preceding the survey, according to length of follow-up.

0.63, 95% CI 0.51–0.79), and occasional physical activity (HR 0.73, 95% CI 0.62–0.86).

Discussion

Our study underscores the high prevalence of chronic diseases in people aged 40 years or more in Spain and provides a more accurate and current picture of the impact of these diseases on overall mortality. Well over half (55.2%) the sample had at least one chronic disease, and the all-cause mortality in this group was over three times higher (13.3%) than in those without (4.2%). Four diseases stand out for the considerable impact they have on population mortality,

arising from the combination of high prevalence and significantly increased risk of death: cancer, chronic lung disease, AMI, and DM.

Our results are consistent with the literature, confirming the important impact of chronic diseases on population morbidity and their status as independent risk factors for mortality.[1–5] In our study, people with DM carried a 22.7% higher risk of dying at six years than those without. This risk is lower than that estimated in previous studies, such as the ASTURIAS study, which found a nearly three-fold higher risk of cardiovascular death in people with versus without DM. Similarly, the FRESCO study reported that people with diabetes carried over twice the risk of all-cause death than those without (HR 1.56, 95% CI 1.39–1.75 in men and HR

1.85, 95% CI 1.59–2.14 in women).[12,13] This difference in the mortality risk may be attributable to the differences in study periods: the ASTURIAS study started in 1998 and the FRESCO study included population cohorts from 1991, 13 and 21 years, respectively, prior to our study. In light of previous studies showing a decrease in the mortality trends associated with DM in our country,[22] our study allows us to update our data on the mortality impact of the different chronic diseases in Spain, in line with the results obtained elsewhere in Europe.[23,24]

With respect to chronic lung diseases, some older studies analyzed all-cause mortality in patients with COPD in Spain, estimating that mortality in people aged 65–70 years is 33% to 47% at 4–7 years[25,26]; however, no recent studies have updated these estimates. Our data show that chronic lung diseases are associated with a mortality risk of 42% in people aged 40 or older over 6.4 years in Spain. Likewise, we observed a 33.4% higher risk of six-year mortality in people with versus without a history of AMI, contributing new data on this relationship in the Spanish population.

Our survival analysis also identified certain protective factors: female sex, marriage, and physical activity. In contrast, tobacco use and ''very poor'' self-perceived health were associated with a higher mortality risk. Hospital admission in the previous year also increased the mortality risk (Fig. 1). These results agree with those obtained in previous studies elsewhere,[27–30] confirming that these factors are also relevant for mortality in the Spanish population.

The strengths of the study include the population-based nature of the health survey and the use of the elevation factor to make the estimates, which are representative of the population over 40 years of age in Spain in 2011. The minimum age cutoff of 40 years enables the study of a larger population than other studies, which have included only those over 60 years of age, and the six-year follow-up is adequate for identifying mortality risk factors. Moreover, the National Statistics Institute devised the methodology used to collect information from both the National Health Survey and the mortality registry, ensuring the validity of both the methods and the data.

The study also has some limitations, mainly related to the survey itself. Data on chronic diseases were from self-report, so there may be some discrepancies compared to clinical diagnoses. However, this risk of information bias is inherent to national health surveys, which are nevertheless recognized as a common and reliable source of research. Moreover, some predictors of mortality may not have been included in the survey, and it was not possible to distinguish between subtypes within the same disease entities.

Conclusions

Chronic diseases affect more than half of the Spanish population over 40 years of age and are associated with a six-year cumulative all-cause mortality of 13.3%, compared to 4.2% in people reporting no chronic disease. Four conditions have special relevance: cancer, chronic lung diseases (COPD, chronic bronchitis or emphysema), AMI, and DM. Among these, DM and chronic lung diseases stand out both because of their high prevalence and the significantly increased risk of mortality (22.7% and 42.5%, respectively). The results

of our study highlight the need for more research into the factors involved in these four major chronic diseases and possible strategies to reduce their impact on population mortality. This study also demonstrates the usefulness of combining different sources of information, such as the National Health Survey and the National Death Registry, to perform population-based health research.

What is known about the topic?

- The results of our study highlight the impact of 4 chronic diseases on mortality in the Spanish population: cancer, chronic lung diseases, acute myocardial infarction and diabetes.
- Our study highlights the importance of directing more studies to design strategies that reduce the impact of these chronic diseases on population mortality.
- This study also demonstrates the usefulness of combining different sources of information, such as the National Health Survey and the National Death Registry, to perform population-based health research.

Ethical considerations

Ethics approval and consent to participate: Not applicable.

Funding

Consent for publication

Not applicable.

Conflict of interests

The authors have no relevant financial or non-financial interests to disclose.

The authors have no conflicts of interest to declare that are relevant to the content of this article.

All authors certify that they have no affiliations with or involvement in any organization or entity with any financial interest or non-financial interest in the subject matter or materials discussed in this manuscript.

The authors have no financial or proprietary interests in any material discussed in this article.

Availability of data and materials

The datasets analyzed during the current study are not publicly available but are available from the corresponding author on reasonable request.

Acknowledgments

Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.aprim.2024.103112.

References

1. Lee SJ, Lindquist K, Segal MR, Covinsky KE. Development and validation of a prognostic index for 4-year mortality in older adults. JAMA. 2006;295:801–8, http://dx.doi.org/10.1001/jama.295.7.801. Erratum in: JAMA. 2006 Apr 26;295(16):1900. PMID: 16478903.

2. Centers for Disease Control The Power of Prevention: Chronic Disease the Public Health Challenge of the 21st Century. Available from: www.cdc.gov/chronicdisease/pdf/2009-Power-of-Prevention.pdf [accessed 31.12.17].

3. DuGoff EH, Canudas-Romo V, Buttorff C. Multiple chronic conditions and life expectancy: a life table analysis. Med Care. 2014;52:688–94, http://dx.doi.org/10.1097/MLR.0000000000000166.

4. Rizzuto D, Melis RJF, Angleman S, Qiu C, Marengoni A. Effect of chronic diseases and multimorbidity on survival and functioning in elderly adults. J Am Geriatr Soc. 2017;65:1056–60, http://dx.doi.org/10.1111/jgs.14868. Epub 2017 Mar 17. PMID: 28306158.

5. Caughey GE, Ramsay EN, Vitry AI, Gilbert AL, Luszcz M, Ryan P, et al. Comorbid chronic diseases, discordant impact on mortality in older people: a 14-year longitudinal population study. J Epidemiol Community Health. 2010;64:1036–42, http://dx.doi.org/10.1136/jech.2009.088260. Epub 2009 Oct 23. PMID: 19854745.

6. Jagger C, Matthews R, Matthews F, Robinson T, Robine JM, Brayne C, et al. The burden of diseases on disability-free life expectancy in later life. J Gerontol A Biol Sci Med Sci. 2007;62:408–14, http://dx.doi.org/10.1093/gerona/62.4.408. PMID: 17452735.

7. Dal Canto E, Ceriello A, Rydén L, Ferrini M, Hansesn TB, Schnell O, et al. Diabetes as a cardiovascular risk factor: an overview of global trends of macro and micro vascular complications. Eur J Prev Cardiol. 2019;26 2 Suppl.:25–32, http://dx.doi.org/10.1177/2047487319878371. Epub 2019 Nov 13. PMID: 31722562.

8. Rao Kondapally Seshasai S, Kaptoge S, Thompson A, Di Angelantonio E, Gao P, Sarwar N, et al. Diabetes mellitus, fasting glucose, and risk of cause-specific death. N Engl J Med. 2011;364:829–41, http://dx.doi.org/10.1056/NEJMoa1008862. Erratum in: N Engl J Med. 2011 Mar 31;364(13):1281. PMID: 21366474; PMCID: PMC4109980.

9. Tancredi M, Rosengren A, Svensson AM, Kosiborod M, Pivodic A, Gudbjörnsdottir S, et al. Excess mortality among persons with type 2 diabetes. N Engl J Med. 2015;373:1720–32, http://dx.doi.org/10.1056/NEJMoa1504347. PMID: 26510021.

10. Yu OH, Suissa S. Identifying causes for excess mortality in patients with diabetes: closer but not there yet. Diabetes Care. 2016;39:1851–3, http://dx.doi.org/10.2337/dci16-0026. PMID: 27926885.

11. Valdés S, Botas P, Delgado E, Díaz-Cadórniga F. Mortality risk in spanish adults with diagnosed diabetes, undiagnosed diabetes, or pre-diabetes. The Asturias study 1998–2004. Rev Esp Cardiol (Engl Ed). 2009;62:528–34, http://dx.doi.org/10.1016/S1885-5857(09)71835-3, 1885-5857.

12. Baena-Díez JM, Peñafiel J, Subirana I, Ramos R, Elosua R, Marín-Ibáñez A, et al. Risk of cause-specific death in individuals with diabetes: a competing risks analysis. Diabetes Care. 2016;39:1987–95, http://dx.doi.org/10.2337/dc16-0614. Epub 2016 Aug 4. PMID: 27493134.

13. Park HY, Kang D, Lee H, Shin SH, Kang M, Kong S, et al. Impact of chronic obstructive pulmonary disease on mortality: a large national cohort study. Respirology. 2020;25:726–34, http://dx.doi.org/10.1111/resp.13678. Epub 2019 Aug 19. PMID: 31426128.

14. Martinez CH, Mannino DM, Jaimes FA, Curtis JL, Han MK, Hansel NN, et al. Undiagnosed obstructive lung disease in the United States. Associated factors and long-term mortality. Ann Am Thorac Soc. 2015;12:1788–95, http://dx.doi.org/10.1513/AnnalsATS.201506-388OC. PMID: 26524488; PMCID: PMC4722830.

15. Martinez FJ, Foster G, Curtis JL, Criner G, Weinmann G, Fishman A, et al. Predictors of mortality in patients with emphysema and severe airflow obstruction. Am J Respir Crit Care Med. 2006;173:1326–34, http://dx.doi.org/10.1164/rccm.200510-1677OC. Epub 2006 Mar 16. PMID: 16543549; PMCID: PMC2662972.

16. Conroy RM, Pyörälä K, Fitzgerald AP, Sans S, Menotti A, De Backer G, et al. Estimation of ten-year risk of fatal cardiovascular disease in Europe: the SCORE project. Eur Heart J. 2003;24:987–1003, http://dx.doi.org/10.1016/s0195-668x(03)00114-3. PMID: 12788299.

17. National Statistics Institute. Madrid: INE. Deaths by death's cause 2020. Population projections 2020–2070. Available from: https://www.ine.es.

18. National Health Survey of Spain. 2017. Available from: https://www.ine.es/dyngs/INEbase/es/operacion.htm?c=Estadistica_C&cid=1254736176783&menu=ultiDatos&idp=1254735573175 [accessed 24.5.23].

19. National Statistics Institute. Madrid: INE. 2023. Available from: https://www.ine.es [accessed 24.5.23].

20. Harrell FE, Lee KL, Califf RM, Pryor DB, Rosati RA. Regression modeling strategies for improved prognostic prediction. Stat Med. 1984;3:143–52, http://dx.doi.org/10.1002/sim.4780090503.

21. Gómez-Beneyto M, Nolasco A, Moncho J, Pereyra-Zamora P, Tamayo-Fonseca N, Munarriz M, et al. Psychometric behaviour of the strengths and difficulties questionnaire (SDQ) in the Spanish national health survey 2006. BMC Psychiatry. 2013;13:95, http://dx.doi.org/10.1186/1471-244X-13-95. PMID: 23522343; PMCID: PMC3623874.

22. Orozco-Beltrán D, Sánchez E, Garrido A, Quesada JA, Carratalá-Munuera MC, Gil-Guillén VF. Trends in mortality from diabetes mellitus in Spain: 1998–2013. Rev Esp Cardiol (Engl Ed). 2017;70:433–43, http://dx.doi.org/10.1016/j.rec.2016.09.022. English, Spanish. Epub 2016 Nov 5. PMID: 27825716.

23. Barnett KN, McMurdo ME, Ogston SA, Morris AD, Evans JM. Mortality in people diagnosed with type 2 diabetes at an older age: a systematic review. Age Ageing. 2006;35:463–8, http://dx.doi.org/10.1177/1474651413495703. Epub 2006 May 5. PMID: 16679336.

24. Nwaneri C, Cooper H, Bowen-Jones D. Mortality in type 2 diabetes mellitus: magnitude of the evidence from a systematic review and meta-analysis. Br J Diabetes Vasc Dis. 2013;13:192–207, http://dx.doi.org/10.1177/1474651413495703.

25. Solanes Garcia I, Casan Clarà P. Causas de muerte y predicción de mortalidad en la EPOC [Causes of death and prediction of mortality in COPD]. Arch Bronconeumol. 2010;46:343–6, http://dx.doi.org/10.1016/j.arbres.2010.04.001. Spanish. Epub 2010 May 14. PMID: 20471740.

26. Domingo-Salvany A, Lamarca R, Ferrer M, Garcia-Aymerich J, Alonso J, Felez M, et al. Health-related quality of life and mortality in male patients with chronic obstructive pulmonary disease. Am J Respir Crit Care Med. 2002;166:680–5.

27. García CM, González-Jurado JA. Impacto de la inactividad física en la mortalidad y los costos económicos por defunciones cardiovasculares: evidencia desde Argentina [Impact of physical inactivity on mortality and the economic costs of cardiovascular deaths: evidence from Argentina]. Rev Panam Salud Publica. 2017;41:e92, http://dx.doi.org/10.26633/RPSP. 2017.92. Spanish. PMID: 28902280; PMCID: PMC6645184.

28. Pérez-Ríos M, Schiaffino A, Montes A, Fernández E, López MJ, Martínez-Sánchez JM, et al. Smoking-attributable mortality in Spain in 2016. Arch Bronconeumol. 2020;56:559–63, http://dx.doi.org/10.1016/j.arbr.2020.07.005. Epub 2020 Jul 18. PMID: 35373765.

29. Carter P, Uppal H, Chandran S, Potluri R. Married patients with modifiable cardiovascular risk factors have lower mortality rates. Heart. 2017;103:A68–9, http://dx.doi.org/10.1136/heartjnl-2017-311726.92.

30. Kommuri NV, Koelling TM, Hummel SL. The impact of prior heart failure hospitalizations on long-term mortality differs by baseline risk of death. Am J Med. 2012;125, http://dx.doi.org/10.1016/j.amjmed.2011.06.014, 209.e9–e15. PMID: 22269626.