Heliyon 10 (2024) e28931

Contents lists available at ScienceDirect

Heliyon

journal homepage: www.cell.com/heliyon

Research article

Mortality risk factors in the dependent population of Castilla-La Mancha (Spain) before and during the first COVID-19 wave

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ARTICLE INFO

Keywords:
Mortality
Risk factors
COVID-19 pandemic
Central Spain
Long-term care system
Proportional hazards models

ABSTRACT

The coronavirus disease pandemic has had an important impact worldwide. The population aged over 65 years and aged dependent persons are the population groups which have suffered in a highest level the consequences of the pandemic in terms of cases and death. In Spain, the situation is similar to other countries, but regional studies are needed because competencies on long-term care depend on regional public administration. Thus, the aim of this work is to analyse social and individual factors associated with the risk of mortality of legally recognised dependent people during the pandemic compared to a non-pandemic period. The data were extracted from the administrative database on individuals included in Castilla-La Mancha's long-term care system and it was merged with the information from the Spanish National Death Index administered by the Ministry of Health, Consumption and Social Welfare. The results show that the risk of mortality between March and June 2020 was positively associated with being male; being older than 65, with an especially high impact in the group aged over 90; having a higher level of dependency; living in a nursing home; and living in a place with more population density. Intra-regional differences related to health areas also exists in both pandemic and non-pandemic periods. These findings are critical with a view to enhancing protocols for the care of the most vulnerable population groups.

1. Introduction

The latest global data and demographic projections continue to point to an increase in aging associated with a greater number of dependent persons [1–3]. Older adults and dependent persons are the population groups most likely to die since age, chronic diseases and functional limitations are the factors most commonly associated with mortality [4]. In the case of age, it should be considered that, despite generally being treated as a risk factor for mortality, it is the dynamic process of aging and not simply reaching the age of

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https://doi.org/10.1016/j.heliyon.2024.e28931
Received 26 October 2023; Received in revised form 26 March 2024; Accepted 27 March 2024
Available online 2 April 2024

majority that is the cause of the risk. This process can be defined as the sum of all the changes that occur in a human being over time and which lead to functional deterioration and, finally, to death [5].

These factors also explain why older people are more prone to getting an infection and suffering more severe consequences than other age groups [4]. This has been the case with the infection caused by the novel severe acute respiratory syndrome coronavirus 2 (SARS-COV-2 virus). Despite the coronavirus disease (COVID-19) pandemic having had a significant impact in terms of infections and deaths worldwide, the population aged over 65 years of age has shown the highest rate of incidence in terms of both the number of cases and deaths [6]. In particular, the over-80 age group presents a mortality rate 5 times higher than the average [7]. The study by Bonanad et al. (2020) found that, in China, Spain, Italy, the United Kingdom, and the State of New York, age was a determinant of mortality [8]. In the case of Spain, with 19.4% of its population aged over 65 years, more than 70% of COVID-19-related mortality is estimated to have occurred in this population group [9].

A considerable number of studies have shown that the most vulnerable groups have been those most affected by COVID-19 and, in particular, older adults living in nursing homes, as, for example, reported by Zunzunegui (2022) [10]. Despite limitations in the data and difficulties in counting cases of COVID-19 in the first wave of the pandemic [11], the data suggest that the impact of the pandemic on residential care facilities is common in many countries across the world, regardless of the type of health and welfare system [9]. The reports published by the International Long Term Care Policy Network, managed by the London School of Economics, point in the same direction [12]. During the first few months of the pandemic, mortality from COVID-19 in care homes worldwide ranged from 24 to 82% [13]. In many European countries, such cases account for between 30 and 60% of all COVID-19 deaths [14]. Studies confirm that long-term care home residents are more susceptible to infection and serious complications. In addition, COVID-19 is generally more severe in older adults, which may be explained by the functioning of the immune system [15]. Literature has also shown that mortality causes by COVID-19 are being male, socioeconomic inequalities, location —region or country differences— obesity and related comorbidities, type 2 diabetes and other chronic conditions [16–19].

In Spain, Law 39/2006, of December 14, 2006, on the Promotion of Personal Autonomy and Care for Persons in Situations of Dependence established the levels of dependence and the services for which persons recognised as dependent could qualify. In 2020, only 18.5% of persons recognised as dependent were users of residential care centers [20]. Despite this law has a national application, as in the health administration, the competency on social care lies in regional governments health outcomes can differ. To the best of our knowledge, no studies have analysed the dependent population in general. Numerous studies have aimed to enhance the information and knowledge about the situation in nursing homes, but there is also a need to extend the knowledge on the factors associated with the death of dependent persons in general. In addition to geographic issues and age, sex, marital status, and level of dependence are also relevant.

In this sense, so as to differentiate between the risks for older adults and to inform the policies that affect them, greater disaggregation by age group (60–69 years, 70–79 years and 80 years and older), sex and disability is crucial [7]. The availability of administrative data for all legally-recognised dependent persons in Castilla-La Mancha between 2018 and 2020 provides access to this information. Consequently, it is possible to establish the impact of the pandemic and to determine the risk factors associated with mortality of both those living in nursing homes and in the community at different points in time.

The aim of this study is, on the one hand, to show personal and some social characteristics of the legally recognised dependent population of Castilla-La Mancha during the first wave of COVID-19, between March and June 2020, and, on the other, to analyse the factors associated with the risk of mortality in that period, comparing both with their equivalents in non-pandemic times. Additionally, for descriptive purposes, graphical information will be provided on the evolution of the weekly mortality rate from May 2018 to the end of June 2020 and survival curves. Moreover, this is the first study using an administrative database provided by the technical staff of the Department of Social Welfare of the regional government. For this reason, an additional objective is to present the magnitude of the information provided by the database. Thus, the findings of the present work are of public interest and may allow the administrations responsible and policy makers for long-term care systems to improve their actions and policies in the dependent population, helping them to show the effect of the pandemic on risk of mortality, as well as to establish ad-hoc decisions to prevent the incidence of external effects, such as the pandemic caused by the novel SARS-COV-2 virus.

2. Methodology

2.1. Databases

This work uses two combined databases. First, we used information extracted from the administrative database (digital administrative record) of long-term care system of Castilla-La Mancha (Spain), which included all persons with the legal recognition of dependency by the regional public administration. The data has been provided by a third party, the Consejería de Bienestar Social de la Junta de Comunidades de Castilla-La Mancha (Spain) —regional government— which is the owner of the intellectual property of the data.

Secondly, information collected from the National Death Index, administered by the Spanish Ministry of Health, Consumption and Social Welfare [21], was used to obtain the date of death of the dependent persons included in the first database. The search was conducted in April 2021. All the data obtained from the different sources was anonymized.

2.2. Population

The data delivery process was conducted on a six-monthly basis from December 31, 2017, creating a series of waves, with each six-monthly wave including the total number of people included in the system up to that date. Table 1 shows the process of data reception. The different waves were combined into a single database based on the anonymized individual files. The combined database from waves II to VI was used as the basis for this study. Given the nature of the information received, the combination of data from each wave makes this database an unbalanced longitudinal panel. Cumulative information was obtained for 78,648 subjects.

2.3. Data cleaning and establishment of cohorts

Fig. 1 shows the data cleaning process and the individuals excluded and the reasons for exclusion. Thirty-six individuals were discarded for not submitting the date of birth or submitting it wrongly, and 248 because they appeared in one wave, and not in the subsequent one, but appeared again in others due to a technical problem in the system. Additionally, 46 people who died before May 28, 2018 were discarded. These individuals were excluded because we considered that the information, they provided was not consistent with the rest of the information. A total of 1706 individuals were discarded as they did not appear in wave VI and their date of death was also unavailable. The total number of valid subjects included in this database, or the main cohort, after data cleaning was 76,612. Knowing the date, they were registered in the system and also the date of death, the information available allowed us to determine the total dependent population in the region on any given date.

At this point, drawing on the main cohort (total subjects in the database, n = 76,612), we constructed two cohorts to study their mortality in two time periods. The first cohort (the reference cohort) included information on subjects who were in the database at some point in the 17-week reference period (weeks 10–26 of 2019), for whom we analysed deaths in that period (reference period). The second one (the study cohort) comprised subjects in the database during a time of COVID-19, weeks 10–26 of 2020 —first wave of the pandemic. Thus, 68,848 subjects were obtained for the reference cohort and 63,786 for the cohort exposed to COVID-19 (study cohort).

2.4. Variables included in the long-term care system database

The database includes a series of variables that are shown in Table 2. Not all these variables have been introduced in the analysis and we show them in order to present the information of this database.

Given that the level of dependence is related to the basic and instrumental activities of daily living that individuals are able to perform, it can be considered a proxy variable for health/quality of life. The extent of dependence is divided into three levels: level 1 is mild dependence; level 2 is moderate dependence; and level 3 is severe dependence. In Spain, all regions use the same scale to assess dependency —established by Real Decreto 174/2011 on February 18, 2011—. In summary, level 1 is assigned when people need help for daily basic activities once for day; level 2 is assigned when people need help for daily basic activities 2–3 times a day; level 3 is assigned when people need help for daily basic activities many times a day and there is a full lack of autonomy. A higher level of dependence is considered to represent a lower level of quality of life. Additionally, in this study, we allocated the highest level registered in any of the waves, since as each wave was delivered, the level of an individual's dependence was updated accordingly. It is important to highlight that the database provided by the regional administration does not include medical records —comorbidities, medication, or socioeconomic status— because health care system and long-term care system are independent.

We used the information provided by the LTC system in the statistical analysis as follows: we included sex, age (using date of birth), level of dependence, living in a nursing home, and municipality/province (to find the health area, calculating population density and to include ageing index).

2.5. Variables built upon those included in the long-term care system

The variables included in the long-term care system were used to construct a number of others, which are shown in Table 3. As we explained in the last section, not all these variables have been introduced in the analysis for the same reason. For the present study, age was calculated using two different reference date, one for each cohort −2 March 2020 for the exposed cohort; March 4, 2019 for the reference cohort—, whereby the dependent persons' ages were calculated as the difference between this date and their date of birth, divided by 365.25 days.

Table 1
Data reception process.

Date	Wave	Description	N
June 30, 2018	II	Included in the database until June 30, 2018	54,359
December 31, 2018	III	Included in the database until December 31, 2018	57,610
June 30, 2019	IV	Included in the database until June 30, 2019	59,492
December 31, 2019	V	Included in the database until December 31, 2019	61,597
June 30, 2020	VI	Included in the database until June 30, 2020	59,516

Note: Wave I was received on December 31, 2017, but in a format that was incompatible with the other waves and was therefore not used in this study.

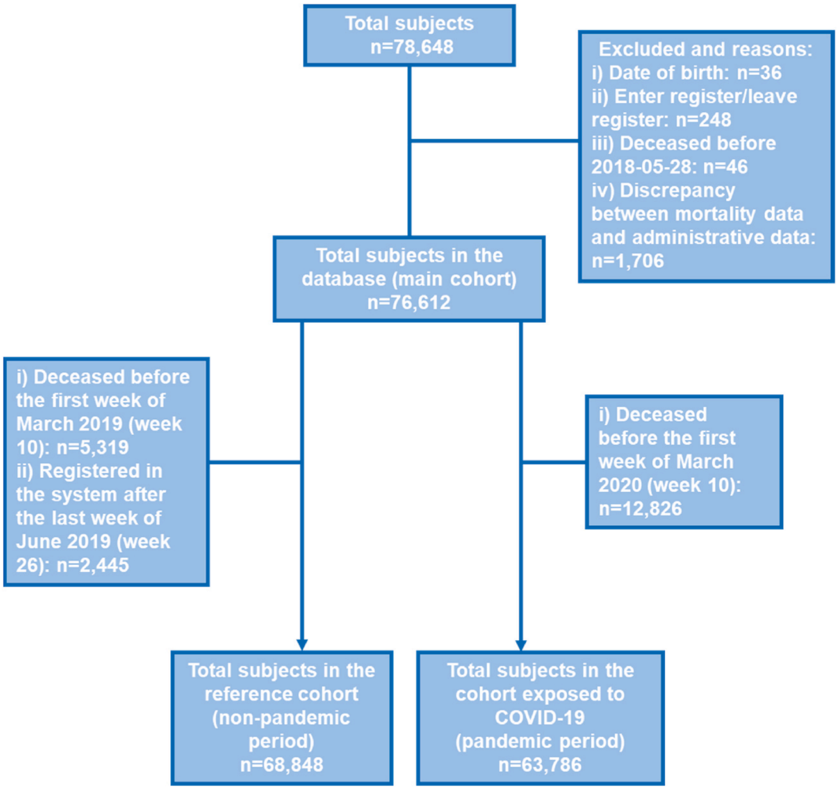

Fig. 1. Data cleaning process.

Table 2
Variables included in the LTC system.

Type of variable	Variable
Sociodemographic	Sex
	Date of birth
	Municipality and code for municipality
	Province
	Nationality
	Size of household
	Date of death (by National Death Index)
In the system	Date registered in the system
	Date the benefit was determined
	Level of dependence
Economic benefits	For family care
	Linked to the service
	Personal care
Provision of services	Residential care
	Home help
	Telecare
	Day-care/Night-care centre
	Promotion of personal autonomy

2.6. *Weekly crude mortality rate*

Obtaining the date of death of the subjects and combining it with the database of dependent persons allowed us to calculate crude mortality rates at different points in time. Using the subjects in the main cohort (n = 76,612), weekly crude mortality rates were calculated for dependent persons from May 28, 2018 (week 22) to the last full week of June 2020 (week 26). Once the crude mortality rate was calculated, it was expressed as the crude mortality rate per 1000 inhabitants.

Table 3
Variables built upon those included in the system.

Type of variable	Variable
Sociodemographic	Age (on any date of reference)
	Number of inhabitants in the municipality
	Number of inhabitants in the municipality by sex
	Area of municipality (km^2)
	Number of nursing homes in the municipality
	Ownership of nursing home at municipal level[a]: public/private
	Number of nursing home places in the municipality
	Health area: 8 health areas in Castilla-La Mancha
	Ageing index (population ≥65/population <16)

[a] In numerous municipalities the distinction between public and private management was not possible, as both forms of management coexist.

2.7. Statistical analysis

To study the factors associated with death from the first full week of March 2020 (week 10) to the last week of June 2020 (week 26), as well as from the first full week of March 2019 (week 10) to the last week of June 2019 (week 26), a Cox proportional hazards regression model was performed using the R's package survival [22]. Survival curves were plotted with survminer package [23,24]. All our calculations were performed using the R statistical software and a spreadsheet [25–27].

The event of interest was death and, if it did not occur until week 26, subjects were censored. The time to event was calculated in days. The covariates were sex (male = 1, female = 0), categorized age for each cohort at week 10 (<65 = 1, 65–80 = 2, 80–90 = 3, >90 = 4), level of dependence (level 1 = 1, level 2 = 2, level 3 = 3), living in a nursing home or not (yes = 1, no = 0), ageing index and population density at municipal level for year 2020 [28], and health area (8 categories: Albacete, Ciudad Real, Cuenca, Guadalajara, Mancha-Centro, Puertollano, Talavera de la Reina and Toledo) as a dummy variable [29]. In the regression, we introduced health area and not the province because each municipality belongs to one health area and health area is a level of the organization of the regional health system and it includes municipalities of different provinces (see Appendix, Fig. A2). We also introduced the natural logarithm of the ageing index and the population density to test if municipal demographic characteristics constitute a significant factor. Population density was categorized into two groups by employing the median value for the year 2020 as threshold.

We developed the analysis in the subsequent manner: 1) we calculated hazard ratios for the unadjusted univariate models; 2) we calculated hazard ratios for the multivariate full model for both cohorts exposed and reference in a separate way. We presented survival curves for the first. We also assess the accomplishment of the proportional hazards assumption for the covariates through the utilization of the Schoenfeld residuals test. In instances, where this assumption was found to be violated, we proceeded to employ time-

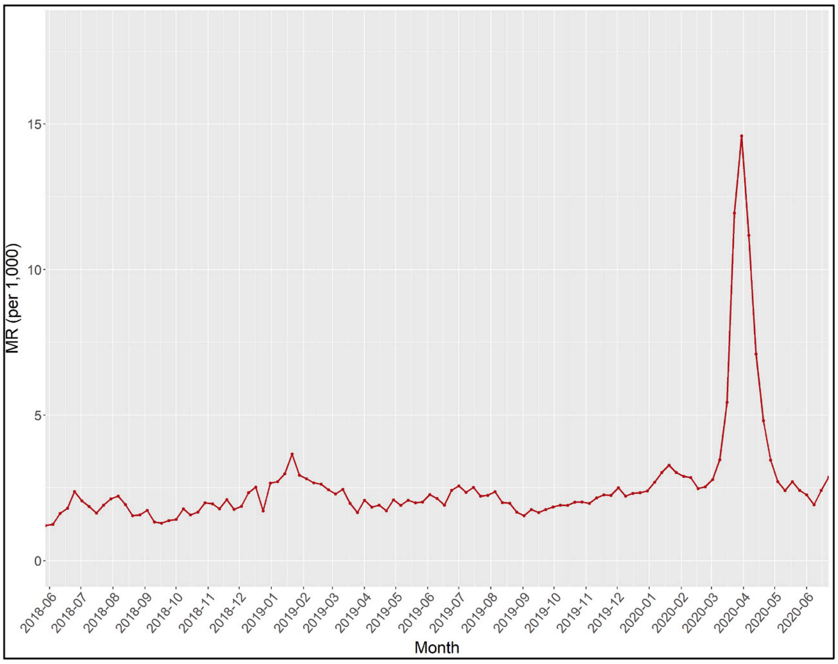

Fig. 2. Weekly crude mortality rate (MR) per 1000 inhabitants from June 2018 to June 2020.
Note: MR: Mortality rate.

varying coefficient models, allowing the covariates to show linear temporal variations [30–32].

3. Results

The results of this study are novel because it is the first time that the administrative database of the dependent population of Castilla-La Mancha is exploited. We present the results as follows. First, we show the evolution of the weekly mortality rate of dependent persons between May 2018 and June 2020. Three descriptive analyses on the dependent and population during the pandemic period are then presented, showing their general characteristics and differences by sex. Finally, we present the results of the statistical analysis conducted by applying the univariate and multivariate Cox regression model —with time-varying effects, when necessary— for the reference and the COVID-exposed.

3.1. Weekly crude mortality rate for dependent persons

Fig. 2 shows the evolution over time of the weekly crude mortality rate per 1000 dependent persons. The graph shows a more or less constant trend until March 2020. Between week 22 of 2018 and week 9 of 2020, the mean weekly mortality rate was 2.11 deaths per 1000 (SD = 0.47). However, from week 10 of 2020, the trend begins to change due to the effects of the pandemic, peaking in week 14 (March 30 to April 5). Up to the last full week of June, the mean weekly mortality rate was 4.97 deaths per 1000 (SD = 3.91).

3.2. Descriptive analysis of the cohorts exposed and not exposed to COVID-19

Table 4 shows the characteristics of the subjects in the cohort exposed to COVID-19 (n = 63,786) and that not exposed (n = 68,848), differentiated by sex. In both cohorts, 65% of the population are women. Across the total population, the largest age group is 80–90 years, followed by the group aged over 90. However, there exist age-related sex differences: in the group aged 80–90 years and that of individuals aged over 90 years, the number of women is larger than that of men, while the percentage of men under 65 years is about 20% higher than the percentage of women in the same age group in both cohorts. Regarding the level of dependence, in the cohort exposed to COVID-19, the largest percentage of dependent persons is that with level 1 dependence, while in the reference cohort it is those with level 3. In both cohorts, there is a higher percentage of women than men with level 1, while for the other levels, the percentage of men is higher. The percentage of people in residential care is around 20% for men and women in both cohorts. The geographic distribution is similar in both cohorts and both sexes, with the majority of the dependent population located in Toledo and

Table 4
Characteristics of the subjects in the cohort exposed to COVID-19 (n = 63,786) and the reference cohort (n = 68,848).

Variables		Cohort in COVID-19 pandemic period*				Cohort in pre-COVID-19 pandemic period			
		Total (n = 63,786)	Men (n = 22,221)	Women (n = 41,565)	P	Total (n = 68,848)	Men (n = 24,086)	Women (n = 44,762)	P
		%	%	%		%	%	%	
Deceased (crude mortality rate)		8.13	8.64	7.85	<0.001	3.39	3.72	2.00	<0.001
Age	<65	21.80	35.57	14.44	<0.001	19.83	33.23	13.76	<0.001
	65–80	17.90	18.25	17.72		16.03	18.59	18.40	
	80–90	39.64	30.80	44.38		38.78	33.77	46.32	
	>90	20.64	15.38	23.45		25.36	14.42	21.52	
Level	Level 1	34.84	32.83	35.91	<0.001	32.48	30.85	33.35	<0.001
	Level 2	33.66	34.75	33.08		33.64	34.67	33.09	
	Level 3	31.5	32.42	31.01		33.88	34.48	33.56	
Nursing home	No	80.12	80.12	80.13	0.991	78.28	78.35	78.25	0.778
	Yes	19.88	19.88	19.87		21.72	21.65	21.75	
Population density	<43.3	49.85	48.97	50.32	0.001	50.15	49.31	50.59	0.001
	>43.3	50.15	51.02	49.68		49.85	50.69	49.41	
Ageing index (mean)		216.14	215.52	216.48	0.771	216.14	217.38	215.88	0.636
Health area	Albacete	24.24	24.94	23.88	<0.001	24.02	24.49	23.77	<0.001
	Ciudad Real	14.24	13.55	14.60		13.87	13.22	14.23	
	Cuenca	11.89	11.98	11.84		11.94	12.13	11.83	
	Guadalajara	9.66	10.07	9.44		9.80	10.20	9.59	
	Mancha-Centro	11.80	11.43	11.99		11.74	11.28	11.99	
	Puertollano	4.04	3.72	4.22		3.89	3.65	4.03	
	Talavera de la Reina	9.03	8.92	9.09		9.25	9.30	9.23	
	Toledo	15.08	15.39	14.93		15.47	15.72	15.33	

Note: An χ^2 and t-Student analysis were performed to examine differences by sex.
a. The number of deceased in this table includes persons whose death was registered between the first week of March (week 10) and the last full week of June (week 26) in 2019 (cohort in pre-COVID-19 pandemic period) and 2020 (cohort in covid-19 pandemic period). In this sense, the value can be interpreted as the crude mortality rate for the period.

Ciudad Real, followed by Albacete, Cuenca and Guadalajara. Finally, the percentage of deaths, or the mortality rate, for the period studied in each cohort, that is, weeks 10–26 of 2019 and 2020, is 8.13% in the COVID-exposed cohort and 3.39% in the reference cohort, with this percentage being significantly lower among women.

3.3. Factors associated with dying in a time of pandemic and a time without pandemic

Tables 5–6 show the results of the univariate and multivariate Cox regression models respectively with time-varying coefficients when it was necessary, and Fig. 3 shows the survival curves of the univariate models. Proportional hazard assumptions —by Schoenfeld residuals test— were met for all univariate models except for sex, and health area in the exposed cohorts —we included time-varying coefficients for these variables at the bottom of the table—. On the other hand, the assumptions of the multivariate models are only met for the non-exposed cohort. The other multivariate model, exposed cohort—stratifying by exposure—, unmet the assumptions for sex, population density and ageing index and some health areas in the first one, and living in a nursing home, population density, ageing index, and some health areas in the second one (see Appendix). All multivariate models showed an acceptable goodness-of-fit and significance in global test statistics.

Regarding Table 5 —univariate models—, factors such as sex (being male), age, level of dependence and living in a nursing home are factors positively associated with mortality, indicating a higher risk of mortality. The impact of the level of dependence and living in a nursing home is more pronounced in the exposed cohort. Population density exhibits no effect during pandemic, but it is negatively associated with mortality in the reference cohort. In contrast, ageing index is negatively associated with mortality during the pandemic period but positively in the non-pandemic period. Health area shows both positive and negative effects in some areas during pandemic: with higher mortality risk in Ciudad Real, Guadalajara, and Mancha-Centro, and lower risk in Puertollano and Talavera de la Reina compared to Albacete. However, during the non-pandemic period, health area's effect is limited. When adjusting covariates by time effect in the exposed cohorts, the risks were higher and lower compared to the non-adjusted models, and the time effect indicated that

Table 5
Univariate Cox regression models for all cause-mortality for each cohort (years 2020 and 2019).

		Cohort in COVID-19 pandemic period[a]		Cohort in pre-COVID-19 pandemic period	
Variables (univariate results)		HR	95% CI	HR	95% CI
Sex	*Woman (reference)*	1.00	Ref.	1.00	Ref.
	Man	1.23	(1.11; 1.37)	1.16	(1.07; 1.26)
Age	*<65*	1.00	Ref.	1.00	Ref.
	65–80	4.81	(4.04; 5.72)	5.01	(3.81; 6.59)
	80–90	8.49	(7.23; 9.96)	8.12	(6.29; 10.47)
	>90	14.53	(12.37; 17.07)	17.20	(13.33; 22.19)
Level	*Level 1*	1.00	Ref.	1.00	Ref.
	Level 2	1.91	(1.76; 2.07)	1.63	(1.45; 1.83)
	Level 3	3.73	(3.13; 3.64)	2.39	(2.15; 2.67)
Nursing home	*No (reference)*	1.00	Ref.	1.00	Ref.
	Yes	3.11	(2.95; 3.29)	1.92	(1.76; 2.09)
Population density	*<43.3 (reference)*	1.00	Ref.	1.00	Ref.
	>43.3	1.04	(0.98; 1.10)	0.92	(0.85; 0.997)
Log(Ageing index)		0.95	(0.91; 0.99)	1.07	(1.01; 1.13)
Health area (HA)	*Albacete (reference)*	1.00	Ref.	1.00	Ref.
	Ciudad Real	1.12	(1.03; 1.23)	1.085	(0.94; 1.25)
	Cuenca	1.04	(0.95; 1.14)	1.192	(1.04; 1.37)
	Guadalajara	1.13	(1.02; 1.25)	1.07	(0.92; 1.25)
	Mancha-Centro	1.16	(1.06; 1.27)	1.058	(0.91; 1.23)
	Puertollano	0.82	(0.7; 0.96)	1.05	(0.84; 1.31)
	Talavera de la Reina	0.79	(0.70; 0.89)	1.077	(0.92; 1.26)
	Toledo	0.93	(0.84; 1.01)	1.112	(0.97; 1.27)
Covariate[a] × Time (linear)	*Sex*	1.23	(1.11; 1.37)	–	–
	Sex × Time	0.998	(0.996; 0.999)	–	–
	Population density	1.18	(1.06; 1.30)	–	–
	Population density × Time	0.997	(0.995; 0.999)	–	–
	Log*(Ageing index)*	0.9998	(0.9997; 0.9999)	–	–
	Log*(Ageing index)* × Time	1.001	(0.999; 1.002)	–	–
	HA Mancha-Centro	1.54	(1.31; 1.81)	–	–
	HA Talavera de la Reina	0.66	(0.53; 0.81)	–	–
	HA Toledo	0.80	(0.69; 0.94)	–	–
	HA Mancha-Centro × Time	0.993	(0.990; 0.997)	–	–
	HA Talavera de la Reina × Time	1.004	(1.001; 1.008)	–	–
	HA Toledo × Time	1.003	(1.001; 1.006)	–	–

Abbreviations: CI: confidence interval; HR: hazard ratio; Ref.: reference.
Note: Mortality was only measured from weeks 10–26 in each case.
[a] Applying time-varying coefficients when proportional hazard assumption was not met.

Table 6
Multivariate Cox regression models for all-cause mortality: cohort exposed to COVID-19 (year 2020) and reference cohort (year 2019).

		Cohort in COVID-19 pandemic period[a]		Cohort in pre-COVID-19 pandemic period	
Variables		HR	95% CI	HR	95% CI
Sex	*Woman*	1.00	Ref.	1.00	Ref.
	Man	1.73	(1.56; 1.93)	1.56	(1.44; 1.7)
Age	*<65*	1.00	Ref.	1.00	Ref.
	65–80	5.51	(4.63; 6.56)	5.71	(4.34; 7.51)
	80–90	10.43	(8.84; 12.26)	9.45	(7.31; 12.22)
	>90	15.64	(13.29; 18.40)	18.43	(14.25; 23.85)
Level	*Level 1*	1.00	Ref.	1.00	Ref.
	Level 2	1.74	(1.60; 1.89)	1.54	(1.37; 1.73)
	Level 3	2.64	(2.44; 2.86)	2.02	(1.80; 2.27)
Nursing home	*No*	1.00	Ref.	1.00	Ref.
	Yes	2.15	(2.03; 2.28)	1.36	(1.24; 1.49)
Population density	*<43.3 (reference)*	1.00	Ref.	1.00	Ref.
	>43.3	1.24	(1.09; 1.41)	1.03	(0.93; 1.14)
Log(Ageing index)		0.893	(0.81; 0.99)	0.99	(0.92; 1.07)
Health area (HA)	*Albacete*	1.00	Ref.	1.00	Ref.
	Ciudad Real	1.19	(1.09; 1.30)	1.11	(0.97; 1.28)
	Cuenca	1.07	(0.97; 1.18)	1.17	(1.01; 1.35)
	Guadalajara	1.00	(0.90; 1.10)	0.96	(0.82; 1.13)
	Mancha-Centro	1.78	(1.52; 2.09)	1.20	(1.03; 1.39)
	Puertollano	0.91	(0.77; 1.06)	1.13	(0.90; 1.42)
	Talavera de la Reina	0.65	(0.53; 0.81)	1.03	(0.88; 1.22)
	Toledo	0.79	(0.67; 0.93)	1.15	(1.00; 1.31)
Covariate ×	*Sex × Time*	0.998	(0.990; 1.000)	–	–
	Nursing home × Time	0.998	(0.995; 1.000)	–	–
Time (linear)	*Population density × Time*	0.998	(0.995; 1.00)	–	–
	Log*(Ageing index) × Time*	1.001	(0.999; 1.00)	–	–
	HA Mancha-Centro × Time	0.994	(0.99; 0.997)	–	–
	HA Talavera de la Reina × Time	1.004	(0.99; 1.01)	–	–
	HA Toledo × Time	1.004	(1.001; 1.006)	–	–

Abbreviations: CI: confidence interval; HR: hazard ratio; Ref.: reference.
Note: Mortality was only measured from weeks 10–26 in each case.
[a] Results for multivariate models does include time-varying coefficients when proportional hazard assumption was not met.

over time, the risks become lower and higher, i.e., if a variable presented a HR > 1, time effect was <1 and vice versa.

Fig. 3 shows that the probability of survival was relatively low during the first 40 days, with a subsequent trend towards stabilization. When comparing both the exposed and non-exposed cohorts, the risk of mortality was higher in the former group, particularly affecting vulnerable groups, such as the elderly, those with higher levels of dependence, and residents of nursing homes.

Regarding Table 6, for both exposed cohort and reference cohort, and after controlling for all covariates and adjusting by time, when necessary, similar patterns emerge: sex (being male) and age are associated with a higher risk of mortality, while level of dependence and living in a nursing home show a lower risk compared to univariate models. Population density and ageing index show a higher effect in risks compared to univariate models: living in a place with a higher population density increases risk of mortality during the pandemic period, and living in a place with an older population implies lower risk of mortality. However, significance of these variables was lost in the reference cohort model. Finally, the effect in the risk of mortality of living in a particular health area is also increased for the areas which showed greater risk in the univariate model, but also decreased for the areas which showed lower risk compared to the reference category. The time effect is similar to that the univariate models: over time, risk values tend to equilibrium, showing higher and lower hazard ratio during the first 45 days.

4. Discussion

The COVID-19 crisis has revealed the importance of the availability of specific data to improve policies affecting older adults, including, together with disaggregation by age, sex, disability, marital status, household structure and housing type [7]. The results of our work are aligned with this vision and are novel in terms of geographical location and in the analysed population.

Our analysis shows that the weekly mortality rate per 1000 dependent persons increased during the pandemic period under study (weeks 10–26). With respect to the characteristics of the population, the cohorts exposed and not exposed to COVID-19 presented similar characteristics, with slight variations. The finding that differentiates one cohort from the other is the death rate, namely, 8.13% during the pandemic period and 3.39% during the non-pandemic period, with significant sex-related differences in both cohorts. These results are in line with the deaths recorded in Spain in 2020, where deaths increased by 17.9% compared to 2019. Additionally, 34% of the total number of deaths occurred in the period between March and June [33]. Specifically, 50% of the COVID-19-related deaths were concentrated in these months.

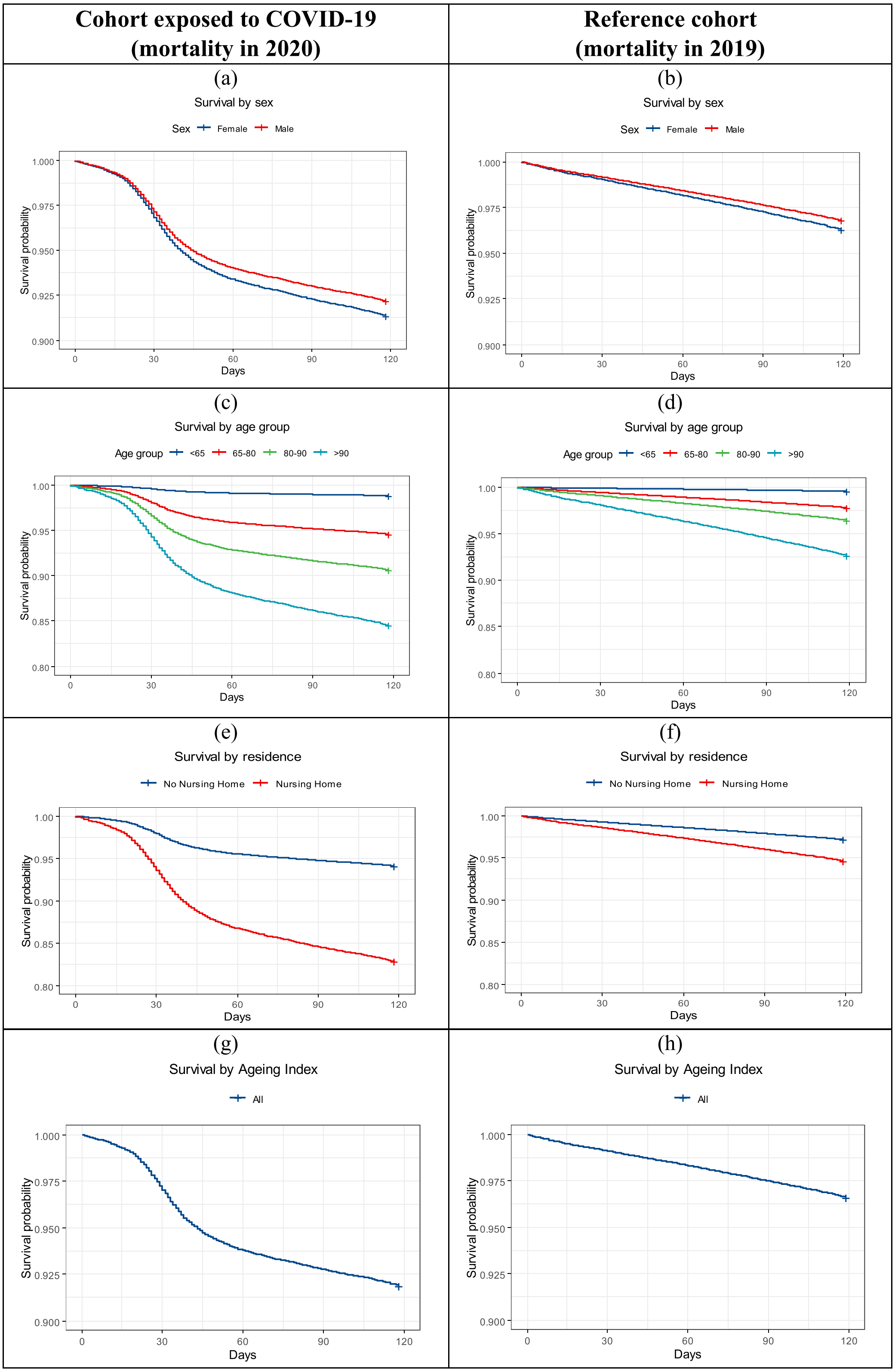

Fig. 3. Survival curves for all-cause mortality for the unadjusted univariate Cox regression models and null models in exposed (year 2020) and reference cohorts (year 2019)
Note: None of the survival functions included time-varying coefficients. Note also that mortality was only measured from weeks 10–26 in each case.

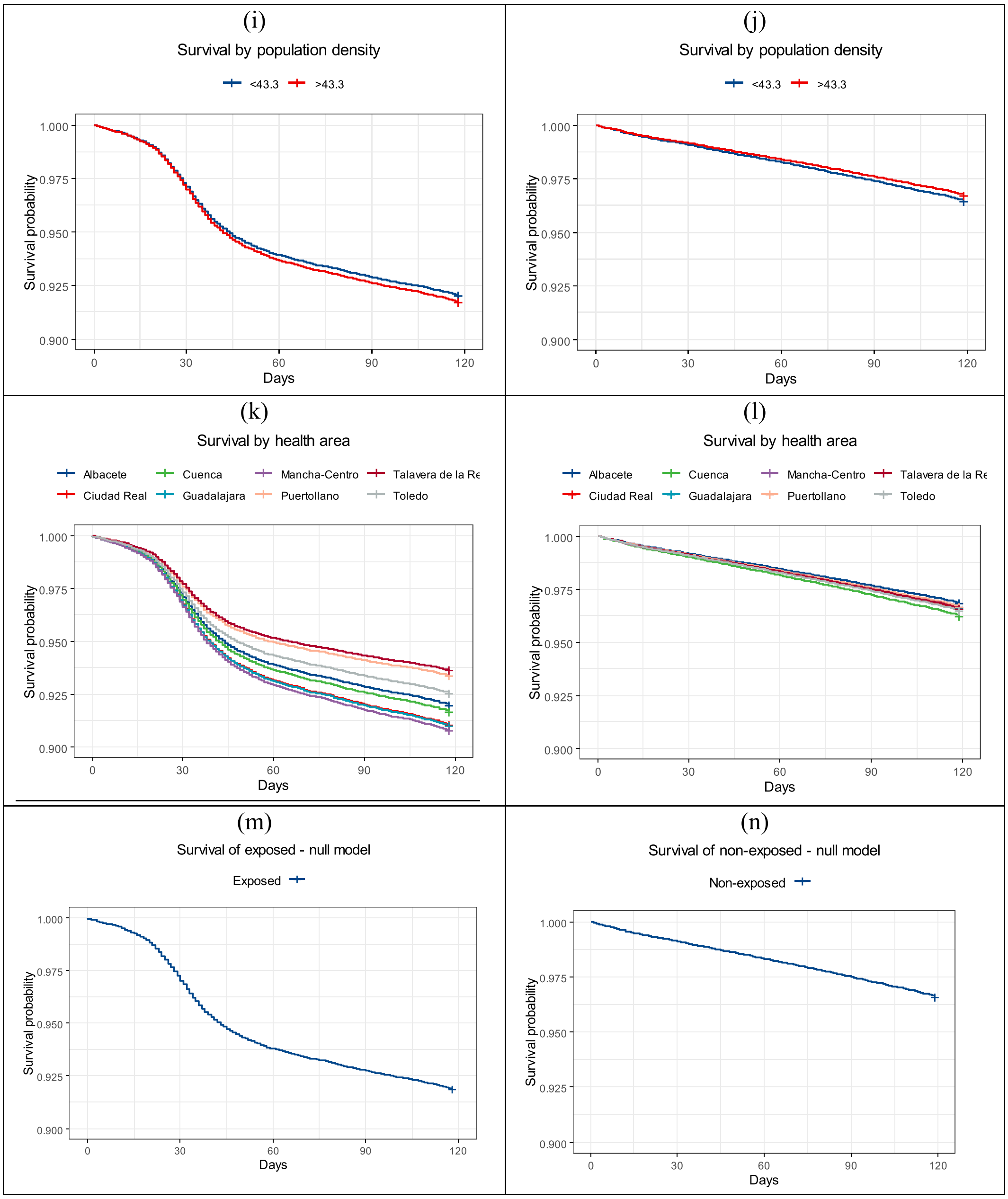

Fig. 3. (*continued*).

In our study, both exposed and reference cohorts, show similar patterns regarding risk of mortality. Being male, a higher level of dependence or living in a care home are positively associated with the risk of mortality, but the exposure to COVID-19 accounts and extra increase in these terms. In general, age had an impact on mortality. In both the European Union and the European Economic Area, most deaths occurred among the oldest age groups, that is 70 years and older [14]. A study on a set of countries reporting more than 200 cases of COVID-19 found no association between the percentage of persons aged 65 years and over and the death or fatality rate [34]. Furthermore, previous longitudinal studies have shown that the level of dependence explains the risk of mortality, even when adjusting for other factors, such as age [35]. Finally, various authors have suggested that, in the case of COVID-19, an effort should also be made to determine the unequal incidence rate by sex [36].

In our work there is a change in the risk of mortality by age, being lower in the >90 group during the pandemic period. This contrasts with the results for Spain as a whole in 2020, where the number of deaths in the populations aged 60–69 years, 70–79 years and 80 years and over rose by 14.5%, 20.5% and 19.5%, respectively. Data are also similar for other countries. In China, the death rate for those aged over 80 was 14.8% [37], while in the United Kingdom, the rate of mortality for those aged 65 years or over was 89% and for those over 85 years of age 43% [38]. The rate of mortality also varies by level of dependence, with the population most affected being that with the highest degree of dependence, that is, level 3. Nonetheless, the COVID-19 pandemic has disproportionately affected older adults and especially those living in long-term care facilities [39].

Mortality in nursing homes is key information for policy makers. While in the non-pandemic period, 34.40% of deaths occurred in these institutions, in the pandemic, this percentage increased to 42%. This finding is in line with events in most European countries, where deaths in long-term care facilities (LTCF) accounted for between 30 and 60 % of COVID-19-related deaths, with this rate reaching as high as 80% for high-income countries [14,39,40]. In the United States LTCF the situation was similar to Europe [41]. These high percentages of deaths and extra increase in the risk of mortality in nursing homes do not correspond to the percentage of population represented by the number of residents. In Spain, less than 4% of older adults live in residential care facilities [10], yet, in the period under study, the number of residents who died in nursing homes ranged from 30 to 60% [42]. In this sense, it is worth noting that studies prior to the pandemic showed that surveillance in long-term care facilities is an added value for enhancing infection control [4], given that the prevalence of vulnerable individuals in residential facilities is high [9]. During the pandemic, greater frailty was associated with a higher risk of COVID-19-related death [43]. Nonetheless, effective management of such crises is vital. For example, in Spain, a larger number of nursing homes is not necessarily associated with a higher number of deaths [44]. as different types of factors play a role in the impact of COVID-19 in nursing homes [45].

Regional differences in health outcomes are usual in Spain, and also during the pandemic period [46], but intraregional differences are not usually assessed. Our analysis incorporating information about health area, population density or the ageing index also suggests that the risk of mortality varied in the pandemic period compared to that prior to the virus. In our study living in a place with higher population density or a lower ageing index presented higher risk of mortality. These results are expected: population density —which in our region inversely correlates inversely with ageing index— is associated with a higher risk of transmission [47]. Moreover, the place where people live and receive healthcare services, the health area, can also condition the risk of mortality in the dependent population, with an extra risk for areas as Mancha-Centro during pandemic or without pandemic —and an extra improvement in the survival in other areas as Talavera de la Reina or Toledo during pandemic—. Additionally, and according to various articles, in the case of COVID-19 pandemic, we should consider the social determinants of the communities in which individuals live, since inequalities in health associated with socioeconomic status are a consequence of inequalities in the social determinants of health: social determinants of health play an important role on COVID-19 outcomes [48–50]. The magnitude of these differences is relevant to policy and decision makers, not only for the risk of mortality during pandemic, but also during no pandemic periods. More analysis is needed to shed light on this matter.

A debate exists on the feasibility of strategies aimed at protecting high-risk groups [51], and since this work covers all dependent persons —with the legal recognition of dependency by the regional public administration— in Castilla-La Mancha, it provides information that may be key in designing policies to help the most vulnerable population.

5. Limitations

The authors of this work are unaware of whether the cause of death of the individuals included in the analysis is COVID-19. This work does, however, allow us to study the factors associated with death between the dates analysed (March and June 2020) in terms of overall mortality, but should not be interpreted as factors associated with death due to COVID-19; they are factors associated with death during the first wave of the COVID-19 pandemic and during a temporally equivalent non-pandemic period. Notwithstanding, our findings appear to be consistent with the literature: the age cohort that suffered most from the disease and its associated mortality is that of older adults, and residents of nursing homes and long-term care users had higher mortality rates, as they belong to groups considered to be fragile and which tend to present higher levels of dependence [9,14,44].

Another limitation of this study lies in the total number of users. Due to the pandemic situation, the lockdown, or the fact that those responsible for dependence assessments decided not to carry these out in order to guarantee the protection of users and their workers, the rate at which the administrations recognize the level of dependency of potential users may have been reduced, affecting the total number of dependent persons. To show the magnitude of this problem, we analysed the average number of monthly registrations per year based on the information available (see Table A1 and Fig. A1 in the Appendix). This question does not have a simple solution and the research team will have to wait for future databases to determine whether the problem detected is ongoing or whether the cause of the decrease in the average number of monthly registrations per year is the result of circumstances unrelated to the pandemic.

Moreover, although the database informs us of the situation of all the dependent persons in Castilla-La Mancha and not only the group of older adults residing in nursing homes, but there is also no data on socioeconomic status or medical records —we cannot know whether people have comorbidities or not, for example—. This information is important given that low socioeconomic status is associated with a lower level of health and both impact in mortality. Furthermore, knowledge of socioeconomic disparities is important for understanding and mitigating COVID-19-related health inequalities [48].

6. Conclusions

COVID-19 pandemic had impacted our societies in many dimensions. In terms of mortality and cases, people aged over 65 years old and dependent persons were one of the most affected groups. The understanding of mortality risk factors in a pandemic and non-pandemic period is important to establish appropriated public policies to protect these vulnerable group. According to our results, the risk of mortality on dependent persons have risen because pandemic, and second, that sex, age, level of dependence, being a resident of nursing home and geographic location —which affect healthcare, population density or ageing index— are associated with mortality in both pandemic and non-pandemic periods. Being male, present a higher level of dependence and living in a nursing home and in a place with a higher population density had an extra increase in the risk of mortality during the first wave of the pandemic, and living in some health area also increased that risk —while decreased in others—. These results agree with the literature on the mortality of vulnerable groups during the pandemic period. Public policy makers should consider the results of this study to guarantee the wellbeing of dependent persons and to contribute to avoid intraregional differences in both pandemic and non-pandemic periods.

Ethics approval

Informed consent was not necessary according to current legislation (see point number (54), and article 9.2.h in Regulation (EU) 2016/679. This research was conducted according to the guidelines laid down in the Declaration of Helsinki. Our work does not have direct participation of people and it has been developed through a proper treatment of personal information, according to Regulation (EU) 2016/679. In addition, the study is approved by the Social Research Ethics Committee (SREC) of the University of Castilla-La Mancha under the case number CEIS-694401-F3R2 in order to confirm externally the ethics in the elaboration of this research.

Data availability

The authors do not have permission to share the data. The data has been provided by a third party through a formal agreement, the Consejería de Bienestar Social de la Junta de Comunidades de Castilla-La Mancha (Spain) —regional government— which is the owner of the intellectual property of the data. The research team has signed an agreement of collaboration with the Consejería de Bienestar Social de la Junta de Comunidades de Castilla-La Mancha (Spain) and for this reason they can exploit this database. The database is private and cannot be shared. If researchers want to access the database, they should contact to Consejería de Bienestar Social.

Funding

This work has been funded by the Universidad de Castilla-La Mancha (grant No. 2022-GRIN-34431) and by the project SBPLY/21/180501/000066 of the Regional Government of Castilla-La Mancha.

CRediT authorship contribution statement

Isabel Pardo-Garcia: Writing – review & editing, Writing – original draft, Validation, Supervision, Resources, Project administration, Investigation, Funding acquisition, Formal analysis, Conceptualization. **Roberto Martinez-Lacoba:** Writing – review & editing, Writing – original draft, Validation, Supervision, Software, Methodology, Investigation, Formal analysis, Data curation, Conceptualization. **Pablo Moya-Martínez:** Writing – review & editing, Validation, Software, Resources, Methodology, Investigation, Formal analysis, Data curation. **Elisa Amo-Saus:** Writing – review & editing, Writing – original draft, Supervision, Software, Methodology, Investigation, Formal analysis, Conceptualization. **Raúl del Pozo-Rubio:** Writing – review & editing, Validation, Software, Investigation. **Francisco Escribano-Sotos:** Writing – review & editing, Writing – original draft, Validation, Supervision, Resources, Project administration, Methodology, Investigation, Funding acquisition, Formal analysis, Data curation, Conceptualization.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Acknowledgement

The authors would like to express their gratitude to the Consejería de Bienestar Social de la Junta de Comunidades de Castilla-La Mancha (Spain) for providing the database and for placing their trust in the research team.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.heliyon.2024.e28931.

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