The impact of COVID-19 on deaths from dementia and Alzheimer's disease in Chile: an analysis of panel data for 16 regions, 2017–2022

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Summary

Background Although several studies have documented the detrimental impacts of global COVID-19 containment measures on individuals with Alzheimer's disease and dementia, a comprehensive analysis of mortality rates for these conditions within the Chilean population is notably lacking. This study aimed to analyze the impact of COVID-19 on mortality rates among individuals with dementia and Alzheimer's disease in Chile.

Methods A retrospective longitudinal cross-sectional study was conducted, considering mortality data for specific mental health conditions during the pre-pandemic and pandemic contexts of COVID-19 in Chile. Quantile regression techniques were employed to analyze the existence of differences between the two periods, while non-observable heterogeneity models for panel data methods were used to evaluate the effect of COVID-19 mortality on crude mortality rates.

Findings Statistically significant differences were observed in the number of deaths from dementia and Alzheimer's disease between the pre-pandemic and COVID-19 pandemic periods. Specifically, crude mortality rates decreased by 10% (–0.10 [95% CI: –0.16, –0.05]) during the pandemic period. Furthermore, the number of deaths from COVID-19 during the pandemic period has a very weak incidence of deaths from mental health conditions such as dementia and Alzheimer's. Specifically, a unit percentage increase in confirmed cases from COVID-19 would result in a 7% (–0.07 [95% CI: –0.13, –0.001]) decrease in the number of deaths from dementia and Alzheimer's. These findings are supported by the application of panel regression with one-way random effects models.

Interpretation The study findings indicate a reduction in mortality rates attributed to dementia and Alzheimer's disease during the COVID-19 pandemic in Chile. This decline could be attributed to the potential underreporting of mental illness as the cause of death during the pandemic period. Several studies have highlighted that approximately 30% of death certificates fail to document the presence of a dementia syndrome. Moreover, the cause of death recorded for individuals with mental health conditions may be influenced by the physician's familiarity with the patient or reflect the prevailing approach to managing end-stage dementia patients.

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Keywords: Alzheimer's disease; COVID-19; Chronic diseases; Dementia; Mental health; Mortality

Introduction

The COVID-19 pandemic, which originated in December 2019, has highlighted an increased vulnerability among the elderly and individuals with comorbidities associated with dementia.[1–3] This disease is emerging as a prominent contributor to morbidity and mortality within of this particular population. Dementia is characterized by a progressive decline in cognitive abilities, leading to

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Research in context

Evidence before this study

We conducted a comprehensive search across multiple databases, including Web of Science (WoS), PubMed/Medline, and Scopus, to identify studies addressing mortality rates related to dementia and AD in the context of the COVID-19 pandemic during the years 2020–2022. Our search criteria did not include restrictions on study design or language. We used the following search terms in English: Alzheimer's Disease, Dementia, Mortality, COVID-19. Our search retrieved one hundred seventy-eight citations (ninety-three from PubMed, sixty-one from Scopus, and twenty-four from WoS). After removing duplicates, fifty-three citations were identified, with twenty references from Scopus, and twenty from PubMed. The available evidence indicates a notable increase in deaths in 2021 related to AD and dementia in older female adults, coinciding with the start of the COVID-19 pandemic. Subsequently, in 2022, there was a decrease in mortality associated with these conditions. Various investigations have highlighted that AD and dementia played an important role as primary causes or comorbidities in COVID-19-related deaths, particularly among older people. Another factor that contributed to the high mortality rates among older adults with Alzheimer's and dementia during the COVID-19 pandemic was their place of residence, with a notably higher risk of death observed in nursing homes. Additionally, various experts have suggested personalised healthcare interventions for people with advanced cognitive impairment due to their increased susceptibility and vulnerability to the effects of COVID-19 control restrictions. Notably, from the available literature, there is a lack of articles documenting mortality rates from Dementia and AD in the context of the pandemic in Latin America during the COVID-19 pandemic.

Added value of this study

This research adds significant value by shedding light on the mortality patterns linked to Alzheimer's and Dementia during the COVID-19 pandemic in Chile. Furthermore, it delves into the bio-sociodemographic factors connected with mortality data. Chile has experienced remarkable economic growth in recent decades, yet over 30% of its population remains economically vulnerable. Consequently, this study holds paramount importance. It serves as a vital resource for informing decision-making processes and crafting public policies aimed at mitigating disparities in healthcare access for individuals with cognitive impairments. Additionally, it offers valuable insights to guide and support the families and caregivers of those affected.

Implications of all the available evidence

This study, complementing existing evidence, has the potential to guide government entities in gaining a deeper understanding of the trends and factors contributing to mortality among individuals with Alzheimer's and Dementia. In doing so, it serves as a valuable resource for the effective implementation of Chilean Law No. 21375, which supports Palliative Care and the Rights of individuals dealing with terminal or severe illnesses, in alignment with the technical guidance of palliative care. By leveraging this research, a more comprehensive approach can be developed to address the challenges faced by individuals with Alzheimer's and Dementia, as well as their families and caregivers. This approach underscores the importance of allocating resources in a manner that aligns with their unique bio-sociodemographic characteristics and evolving needs, not only in the current landscape but also in anticipation of potential future pandemics.

significant disruptions in daily functioning. Furthermore, it is crucial to acknowledge that the consequences of dementia extend beyond the affected individuals, impacting their caregivers as well. Types of dementia can be classified according to multiple criteria. In this regard, based on the area in which the lesion that causes it develops or is located, one of the types that represent the majority of cases of dementia is Alzheimer's disease (AD henceforth).[4] Individuals with dementia commonly have one or more chronic health conditions that further elevate their risk of experiencing severe cases of COVID-19 and increased mortality rates.[5] The prevalence of dementia cases is expected to increase in the coming years, which is likely to place an enormous burden on the health care system and society.[6]

The World Health Organization (WHO) introduced guidelines early in the pandemic aimed at limiting transmission and reducing the likelihood of contagion. These measures included quarantine, physical distancing, and confinement, which were implemented by various countries.[7,8] Although these measures were effective from an epidemiological standpoint, they had significant adverse effects on the elderly population, particularly those with dementia. In this aspect, various studies have demonstrated the substantial impact that COVID-19 has had on the well-being of this group of people and the difficulties they have had in receiving adequate care.[2,9,10] Additionally, there is an increased risk of disease among people with dementia, as their compromised cognitive functioning and judgment hinder their ability to voluntarily comply with various restrictions and protective measures.[11,12] In the hospital setting, in general, people with moderate or severe dementia are not admitted to intensive care units; due to the presence of other underlying chronic conditions that limit the feasibility of intensive therapeutic interventions.[13]

A cross-sectional study in the United States compared excess deaths from AD and related dementias as an underlying or contributing cause, during the COVID-19 pandemic. Their results indicated a large increase in mortality in the first year of the pandemic, with excess deaths in long-stay health homes; and a decrease in mortality in the second year of the pandemic, with excess deaths at home and medical centres.[14]

Another systematic review study with meta-analysis evaluated the impact of the pandemic on the mortality of people with dementia without COVID-19. The results of this review indicated that there was a 25% increase in the risk of mortality among people living with dementia without COVID-19 during the pandemic. The authors noted that the reason for this increase is unclear, but mortality among people living with dementia is likely associated with modifiable factors, which could be mitigated by prevention strategies that limit the impact of the pandemic on social and health functions.[15]

In Chile, there is a knowledge gap regarding the impact on mortality rates among people with dementia during the pandemic period compared to the pre-pandemic period. Consequently, the objective of this study is to examine the impact of COVID-19 on mortality rates among individuals with dementia in Chile, comparing the pre-pandemic period (2017–2019) to the pandemic period (2020–2022). The hypothesis of this study considers that mortality due to AD and dementia among elderly people decreased during the COVID-19 pandemic. Furthermore, the study recognizes that once COVID-19 is effectively controlled in the population, there will be a resurgence of mental illnesses (MI) that may have been neglected during this period. Therefore, understanding the effect of COVID-19 on these chronic diseases is essential for effective planning and allocation of human and financial resources required for achieving universal health coverage. The proposed approach aligns with the World Health Organization's 2020 slogan in response to the pandemic, which emphasises "Health for all: let's protect everyone".[16] It is hoped that this study can provide valuable statistical information to government authorities on deaths attributed to MI in Chile during the COVID-19 pandemic.

Methods

Study design and target population

In this study with a cross-sectional descriptive design, data from death records were used, with free and anonymous access, obtained from the website of the Ministry of Health of Chile, at https://deis.minsal.cl/#datosabiertos.[17]

Data were collected from death records with clinical notification of cause of death due to AD, dementia and COVID-19 in Chile, during the pre-pandemic (2017–2019) and pandemic (2020–2022) period.

Deaths attributed to AD were determined based on the International Statistical Classification of Diseases and Related Health Problems (ICD-10),[18] specifically codes G30-G31. A total of 12,930 deaths were identified within this category. Deaths due to dementia were determined using the ICD-10 code F03, identifying a total of 10,859 deaths. Finally, deaths from COVID-19 considered ICD-10 code U07, identifying a total of 47,624 deaths.

In total, this study included a population of 71,413 registered people who died from causes of MI (dementia and AD) and COVID-19 between 2017 and 2022.

Data sources and the definition of variables

Mortality records of Chile from January 01, 2017 to December 31, 2022 in all regions of Chile were used, which are freely and openly accessible on the website of the Department of Statistics and Health Information (DEIS) of the Ministry of Health of Chile.[17] The selected and analyzed dataset provides information on age, sex, cause of death and place of death. Fig. 1 displays the spatial distribution of each region in the country.

To understand the real epidemiology of MI, this study considered the approach proposed by Calvache et al.,[19] who used the ICD-10 classification of

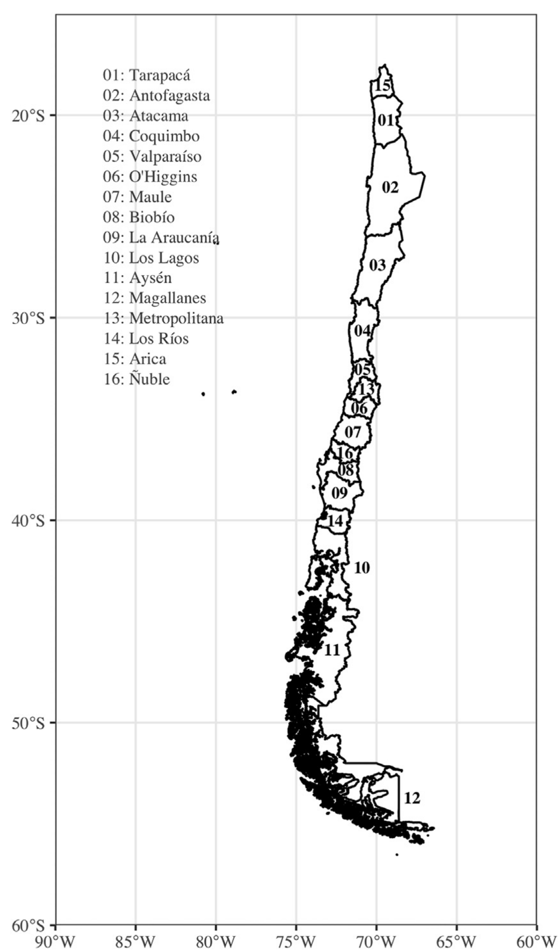

Fig. 1: Regions of Chile from north to south and the number of identifying regions.

chronic diseases requiring palliative care (PC). The ICD-10 is a standardized coding system used around the world to classify medical diagnoses and procedures. Also, it is used to record and report diagnoses, health-care statistics, disease tracking, and vital statistics; even to determine the cause of death. The specific code selected will depend on the clinical diagnosis and stage of the condition.

Table 1 shows the description of the causes of death due to AD, dementia and COVID-19.

Analysis

Statistical modelling

Quantile regression. To observe the effect of the COVID-19 variants that have been dominant in Chile on dementia and AD deaths, in this study the analysis period was divided into quarterly windows, where quarter Q1 is defined with a start date of January 01, 2017 to March 31, 2017 and so on. According to reports from the Public Health Institute of Chile,[20] the dominant variants that have circulated in Chile during the times considered in this work were Delta, Gamma, and Omicron. In addition, the crude mortality rates (CDR) by region, represent the number of deaths in a given period per 1000 population. The calculation of CDR was carried out using the following formula:

$$CDR = \frac{k}{p} \times 1000,$$

where k is the number of deaths attributed to AD and dementia, and p is the population size. The CDR is affected by changes in the age-specific death rate and age structure.[21] However, this study specifically focused on the population of individuals aged 60 years and older, which helps mitigate any potential bias that may arise. This age group was chosen to ensure a more accurate analysis of the impact on mortality rates among older adults. The main objective was to assess whether the CDRs during specific quarters of the pandemic period (2020–2022) were higher than the CDRs in equivalent quarters of the pre-pandemic period (2017–2019). To achieve this, a quantile regression model, as described in previous studies,[22,23] was employed. The following quantile regression model was used in this study:

$$Q_{CDR}(\tau \mid X) = \beta_0 + \beta_1 X_1 + \beta_2 X_2, \quad (1)$$

where $Q_{CDR}(\tau|X)$ denotes the $\tau-$ th quantile of CDR conditional on X, $X_1 = COVID_{dummy}$ representing the pandemic effect is a dummy variable, which takes value 1 if region i has recorded a death due to COVID-19 and 0 otherwise, $X_2 = t$ relates to the temporal index across the quarters from 2017 to 2022. The dummy variable can be used to directly compare the differences between CDRs before and after COVID-19. The estimates of the model (1) are obtained by minimizing $\sum_{j=1}^{n} \varrho_\tau (y_j - \beta X_j)$ with respect to β, where $\tau \in (0, 1)$, ϱ_τ denotes a piece-wise linear function $\varrho_\tau(u) = u\{\tau - I(u < 0)\}$.

Panel data models. To quantify the impact that the number of deaths by COVID-19 has had on the number of deaths by AD and dementia in Chile, this study used regional panel data and random and/or fixed effects models. In this context, it is important to note that panel data models simultaneously consider both time and regions, while other models have the limitation of only expressing these heterogeneities across units or over time. Furthermore, panel data models are better at capturing the heterogeneity involved in both cross-sectional units and time dimensions to reduce estimation bias and multicollinearity and are better suited for studying the dynamics of change and complex behavioural models.[24,25] The two-way panel model is defined as:

$$\log(CDR)_{it} = \beta_0 + \beta_1 \log(COVIDd)_{it} + \beta_2 \log(IR)_{it} + \beta_3 \max T_{it} + \beta_4 \min T_{it} + \beta_5 MeT_{it} + u_{it} \quad (2)$$

$$u_{it} = \delta_i + \eta_t + \varepsilon_{it}, \; i = 1, \ldots, n \quad t = 1, \ldots, T$$

where $\log(COVIDd)$ is the number of monthly deaths from COVID-19, the $\log(\cdot)$ is with respect to the observations obtained at the beginning of the pandemic observed from March 2020, IR represents the COVID-19 incidence rate reported in the $i-$ th region, calculated by dividing the number of confirmed cases in a quarter by the total resident population (number confirmed/population (10,000 per unit)), $\max T$, $\min T$ and MeT denote maximum, minimum, and average temperatures (measured in Celsius) respectively, δ_i and η_t are the region and time fixed effects, respectively, and ε_{it} denotes the error term. This study differentiated between random effects models and fixed models by the relationship between δ_i and x_{it}, in particular, if $Cov(x_{it}, \delta_i) = 0$ the model (2) is considered as a random effect and if $Cov(x_{it}, \delta_i) \neq 0$ then the model (2) is a fixed model. In the case of considering a

Underlying cause of death	ICD-10 codes	Subcategory
Alzheimer's	G30	G30.1 G30.8 G30.9 G31.0 G31.1 G31.8 G31.9
Dementia	F03	F03
COVID-19	U07	U07.1 U07.2

Table 1: ICD-10 codes for conditions identified as potentially having palliative care needs.

two-way random effects model, the individual and temporal effects satisfy the following:

$$\delta_i \sim N\left(0, \sigma_\delta^2\right), \eta_t \sim N\left(0, \sigma_\eta^2\right), \varepsilon_{it} \sim N\left(0, \sigma_\varepsilon^2\right)$$

and

$$\mathrm{Cov}\left(\delta_i, \delta_j\right) = 0, \text{if} \quad i \neq j, \quad \mathrm{Cov}\left(\eta_t, \eta_s\right) = 0, \text{if}, s \neq t,$$
$$\mathrm{Cov}\left(\delta_i, \eta_t\right) = 0, \forall i, t.$$

In fixed effects models, parameter estimation can be performed through two methods: the within estimator and the dummy variable estimator, which is called least squares with dummy variables, as elaborated in the next section.[25]

For the random effects models, there are three estimation methodologies for the parameters, which are available in the free R statistical software,[26] through the plmtest command of the plm package. This command offers the following methods for random effects: swar (default),[27] amemiya,[28] and walhus.[29] In contrast, the within option provides an estimator for the fixed effects model. In the case that both δ_i as η_t are constant term, then ordinary leas squares (OLS) provide consistent and efficient estimates of β vector parameter. This simple version of the model (2) is known as Pooled model.[25]

Least squares dummy variables. To take into account the individual effect of each region of Chile and a possible time effect, the variables δ_i and η_t were considered as dummy variables. In a two-way model (2) with individual and time dummies, algebraic solutions are available for estimating all parameters of interest, including those associated with both sets of dummies.[30] These models are well known in the literature as fixed effects models or sometimes called the least squares dummy variables (LSDV for short) model. Specifically, in this study a dummy variable was generated for each region and each quarter of the year, as follow:

$$\begin{aligned} \log(\mathrm{CDR})_{it} = {} & \beta_1 \log(\mathrm{COVIDd})_{it} + \beta_2 \log(\mathrm{IR})_{it} \\ & + \beta_3 \max \mathrm{T}_{it} + \beta_4 \min \mathrm{T}_{it} + \beta_5 \mathrm{MeT}_{it} \\ & + \sum_{j=1}^{n} \psi_j \mathrm{R}_{it}^{j} + \sum_{j=1}^{T} \lambda_j \mathrm{Z}_{it}^{j} + \varepsilon_{it} \end{aligned} \tag{3}$$

where $R_{it}^j = I_{j(i,t)=j}, j = 1, \ldots, n$ with $I_{\{\}}$ is the dummy variable indicator function and the function $j(i,t) = j$ maps linker i at time t to region j and Z_{it}^j is defined for time dummies. It is important to acknowledge that Chile is characterized as one of the most centralized countries in Latin America and among the OECD nations.[31] This implies that there is a significant concentration of resources and development within the Metropolitan Region, which serves as the country's capital.

Model specification test. There are different tests available for fixed and/or random effect model, among which can be mentioned Hausman test, Breusch–Pagan test, F-test, and Bhargarva and Sargan Test. For a detailed formulation of these tests, we refer to Section 1 of the Supplementary Material.

Role of the funding sources
The funding sources had no role in study design, data collection, data analysis, data interpretation, or writing of the manuscript.

Results

The findings from the study, as illustrated in Fig. 2, reveal an increase in mortality attributed to dementia from 2017 to 2022. More precisely, there was an increase of 580 deaths, resulting in a total of 2097 fatalities in 2022, compared to 1517 deaths reported in 2017. This represents a proportional increase of 16.94% over a span of six years. The formulas used for these calculations were obtained from the work of King M and colleagues[32] and Kane P and colleagues[33] (refer to Section 2.2.1 of the Supplementary Material). Regarding mortality related to AD, a similar trend is observed, with an increase of 640 deaths. In 2017, there were 1906 deaths, whereas in 2022, the number increased to 2546 deaths. This indicates a proportional increase of 18.70% in the absolute number of deaths.

In the annual progression of mortality rates, deaths due to dementia experienced a steady increase from 2017 to 2019. However, in the period spanning 2020–2021, there was a decline of 7.77% in deaths compared to the pre-pandemic period. Subsequently, there was a 3.28% increase in deaths from 2021 to 2022. Conversely, deaths attributed to AD exhibited a continuous upward trend, with the exception of 2020.

Fig. 3, presents a comparative analysis of causes of death according to the ICD-10 classification in 2017 and 2022 for people aged 65 years and older. The highest number of deaths was observed among individuals aged 80 years and older during the study period.

Specifically, within the age group of individuals aged 80 years and older, there was a significant increase of 33.86% (9570 deaths, $p < 0.0001$) in deaths attributed to dementia compared to other age groups, where the number of deaths was 1289 for individuals younger than 80 years.

The same trend is observed in deaths from AD in individuals aged 80 years and older, with a total of 10,786 deaths recorded during the study period, where deaths in this demographic group demonstrate a significant increase of 35.33% ($p < 0.0001$) compared to AD deaths in individuals under 80 years of age, which were a total of 2144 deaths during the same period. Additionally, deaths attributed to COVID-19 in the age group of 80 years and older represented 50.27% of the total deaths within that age group.

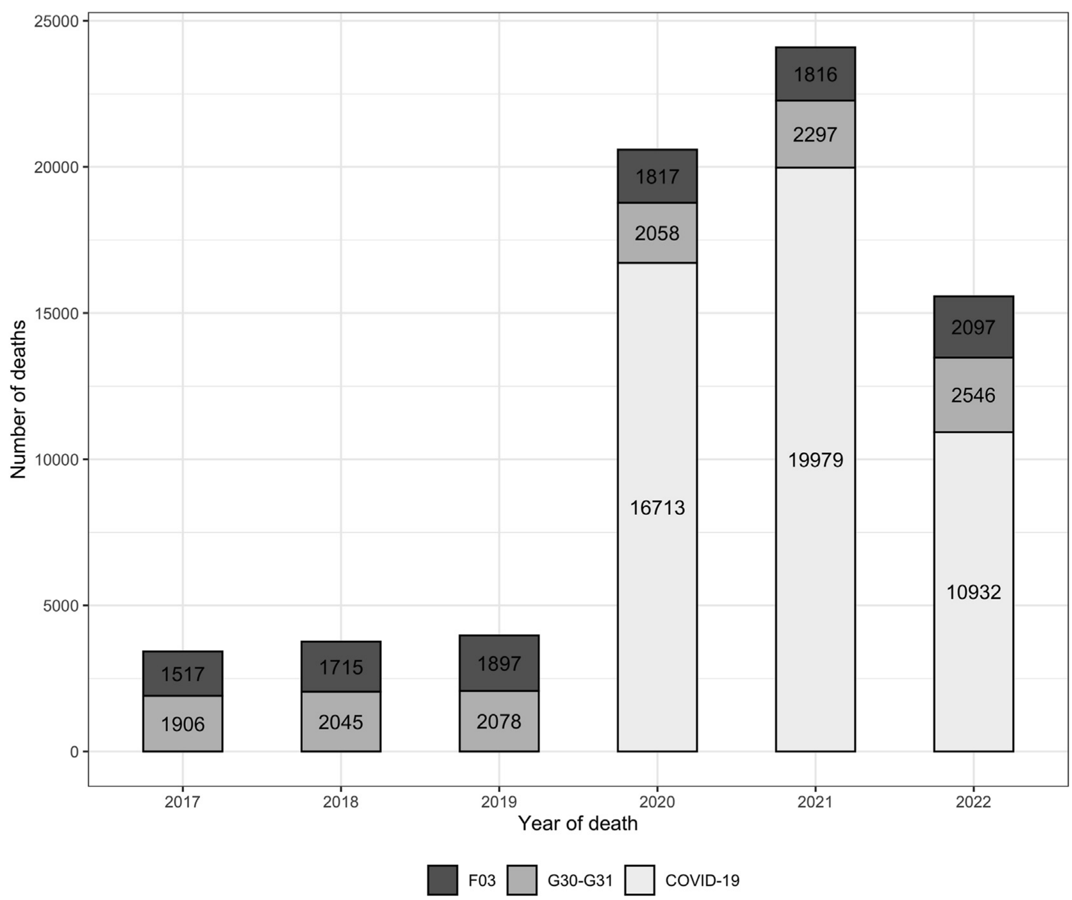

Fig. 2: Deaths in Chile by conditions according to ICD-10 grouping 2017–2022. In each bar, black indicates deaths from dementia (F03), gray represents deaths from Alzheimer's disease (G30-G31), and light indicates deaths from COVID-19 (U07).

As shown in Supplementary Table S1 of the Supplementary Material, dementia deaths among individuals aged over 80 account for 40,16% and 40,29% in the pre-pandemic and post-pandemic periods, respectively. A similar pattern is observed in deaths attributed to AD among those aged over 80, with percentages of 44.77% and 45.85% in both periods. This indicates a notably high mortality rate from these diseases within this age range.

Table 2 reports the frequencies and percentages for each age group and place of death during the pre-pandemic and pandemic contexts. When combining dementia and AD mortality rates before the pandemic, 66.15% of deaths occurred among women, while 33.85% were among men. On the other hand, during the pandemic period, there was an increase in female deaths (67.42%) and a decrease in male deaths (32.58%). According to the place of death, during the pre-pandemic period, 67.44% of deaths (including dementia and AD) occurred at home. However, this percentage increased to 77.84% during the pandemic, indicating a notable increase in deaths occurring at home.

The findings from Table 2 suggest discernible discrepancies in the results between the pre-pandemic and pandemic periods, particularly in the place of death and among certain age groups. We tested for differences in proportions and found variations in mortality proportions by the place of death and age groups, with specifically significant distinctions within the 75–79 age group in dementia deaths, and the 70–74 age group in AD deaths (refer to Section 2.2.2 Supplementary Table S1 of the Supplementary Material).

Results from quantile regression model

The CDRs in each of the 16 Regions of Chile were calculated using the observed number of deaths attributed to dementia and AD, in the population of adults over 65 years of age with data obtained from the Census.[34]

The estimated values obtained from the quantile regression model, as described in equation (1), are presented in Table 3. To evaluate the assumptions of the quantile regression model, such as linearity in the regressors, null correlation and normality in the residuals

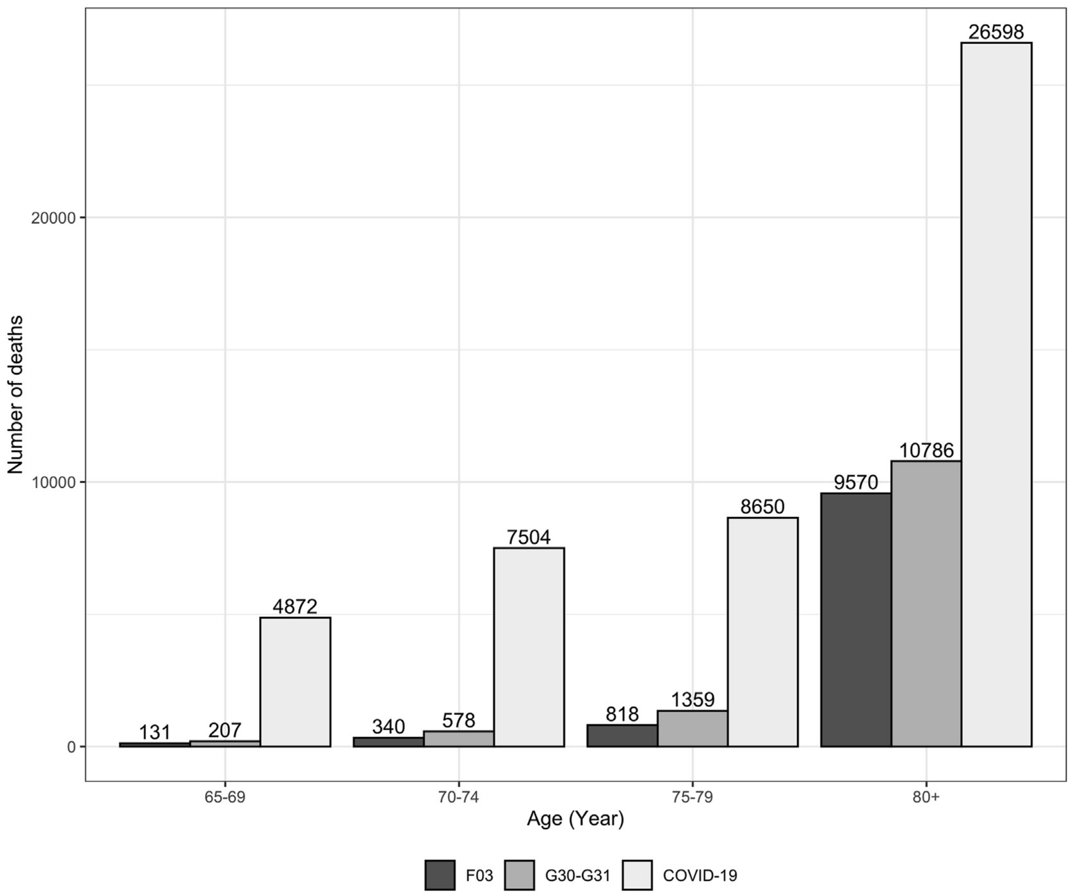

Fig. 3: Deaths in Chile by age groups and causes according to ICD-10 grouping 2017–2022. In each bar, black indicates deaths from dementia (F03), gray represents deaths from Alzheimer's disease (G30–G31), and light indicates deaths from COVID-19 (U07).

of the Model, the tests corresponding to this analysis are presented in section 2.3.1, Supplementary Fig. S1 of the Supplementary Material. From these results it can be inferred that the model satisfies the hypothesis of linearity and non-correlation. However, it does not meet the assumption of normality in the residuals.

Table 3 shows that the COVID-19 pandemic period there was a significant 10% reduction in the number of CDRs.

Supplementary Fig. S2 of the Supplementary Material provides a detailed description of the outlier data related to the CDRs in different time periods. Close examination of this figure reveals that Region 2 displays the lowest CDRs, while Regions 11, 12, 14, and 15 exhibit the highest levels of CDRs. Additionally, the figure includes information about the number of COVID-19 deaths in Chile during the initial phase of the pandemic until the end of the study period.

Fig. 4 visually represents the fitted values of the quantile regression model. Specifically, the black line represents the fitted values, while each boxplot represents the CDRs observed in the 16 regions from the first quarter of 2017 to the fourth quarter of 2022. It also highlights three distinct waves of infection, represented by light gray bands. The first wave, designated (a), peaked on June 15, 2020, with the Delta variant as the dominant strain. The second wave, designated (b), occurred between April and June 2021, exhibiting two peaks on April 9 and June 5, respectively; with the Gamma variant as the dominant strain. The gray block (c) illustrates a significant increase in cases associated with the Omicron variant, beginning in January 2022.

Finally, Fig. 4 illustrates the estimated trend of the quantile regression model, revealing a discernible 10% decrease during the pandemic period. This suggests that if the pandemic had not occurred, the trend in CDRs would likely have been higher. Furthermore, within this framework, analysis of the peaks of COVID-19-related deaths and the prevalence of various dominant variants indicates an observable increase in the CDR medians during these periods.

Results from panel data model

To evaluate the impact of COVID-19 deaths on the CDRs for the 16 Regions of Chile throughout the study period, a bidirectional model was used. The results

Prior to the Pandemic 2017–2019 (N = 11, 158)	Dementia		Alzheimer's	
	N	(%)	N	(%)
Deaths	5129	45.97%	6029	54.03%
Sex				
Female	3353	30.05%	4028	36.10%
Male	1776	15.92%	2001	17.93%
Place of death				
House	3401	30.48%	4124	36.96%
Hospital or Clinic	1435	12.86%	1572	14.09%
Other	293	2.63%	333	2.98%
Posterior to the Pandemic 2020–2022 (N = 12, 631)				
Deaths	5730	45.37%	6901	54.64%
Sex				
Female	3822	30.34%	4684	37.08%
Male	1898	15.03%	2217	17.55%
Place of death				
House	4433	35.10%	5398	42.74%
Hospital or Clinic	1046	8.28%	1199	9.49%
Other	251	1.99%	304	2.41%

Table 2: Demographic characteristics of the sample.

obtained from estimating Model (2)–(3) on the panel data are presented in Table 4, where it was observed that COVID-19 had a significant effect on the reduction in the number of CDRs. For instance, a one percent increase in new cases of COVID-19 corresponded to a 7% decrease in the number of CDRs. Furthermore, this study considered the temperature variable as a potential explanatory factor for the number of CDRs. However, the results indicated that temperature did not have a significant impact on the CDRs.

Another crucial aspect was the estimation of regional and temporal covariate dummies in the LSDV model (3) presented in Supplementary Table S2 of the Supplementary Material, where the results show a significant regional effect, with a p value of <0.001 and a high adjusted R^2 value of 0.947. Finally, a significant decline in the number of CDRs was observed in all Regions of Chile (p < 0.0001). It is important to mention that the regions of the extreme north (Antofagasta, Atacama, and Coquimbo), the central regions (O'Higgins, Maule, Ñuble, and Santiago), as well as the regions of the extreme south (Los Lagos and Aysén), experienced a particularly substantial decrease compared to other regions.

Parameter	Quantil regression model	p-value	CI
β_0	0.33	<0.0001	(0.32; 0.38)
β_1	−0.10	0.03	(−0.16; −0.05)
β_2	0.01	<0.0001	(0.01; 0.014)
Num. Obs.	384		
Percentile	0.50		

Table 3: Quantile regression model: The estimated parameters, along with their corresponding p-values, and the confidence intervals (CI) for model (1).

Additionally, model selection tests were performed, and p-values obtained are shown in Supplementary Table S3 of the Supplementary Material. These results confirm that the fixed effects model is the most appropriate approach to analyze the panel data in question. For this model, goodness-of-fit tests of the residuals were conducted performed. Specifically, the Shapiro–Wilk test was used to evaluate the normality assumption, yielding a p-value of <0.001, indicating that the residuals do not follow a normal distribution. Additionally, the Durbin–Watson independence test was applied, resulting in a p-value of 0.89 which confirms the independence of the residuals.

Discussion

A retrospective longitudinal cross-sectional analysis was conducted to examine how COVID-19 has affected mortality rates among elderly individuals with dementia and AD in Chile. This study compared the pre-pandemic period from 2017 to 2019 with the pandemic period from 2020 to 2022. The results indicated that the number of deaths related to dementia and AD in all regions shows significant differences between the pre-pandemic and post-pandemic periods. Although fluctuations in trends are evident, the general trajectory of mortality rates from dementia and AD among Chilean older adults has shown a constant upward trend between 2017 and 2022, with respective increases of 16.94% and 18.70%.

Dementia-related deaths displayed a consistent upward trend from 2017 to 2019, which might derive from social determinants and poorer healthcare assistance, mainly associated with delaying in establishing a dementia diagnosis.[35] However, a 7.77% drop occurs during 2020–2021 compared to pre-pandemic levels, followed by a 3.28% increase in 2022 compared to 2021, which might suggest that the impact of the COVID-19 pandemic on dementia mortality rates was not sustained. In contrast, AD related deaths displayed a consistent annual increase, with exception of 2020. Additionally, the results of the quantile regression model showed that the COVID-19 pandemic significantly reduced the number of observed deaths from dementia and AD among population aged 65 years and older for each region by 10%. This trend could be attributed to various factors, such as the impact of the COVID-19 pandemic on healthcare services, population demographics, and differences in the diagnosis and treatment of dementia and AD.[36]

It is important to note that during periods of peak dominance of certain variants, there was an increase in the CDRs. However, when considering the entire study

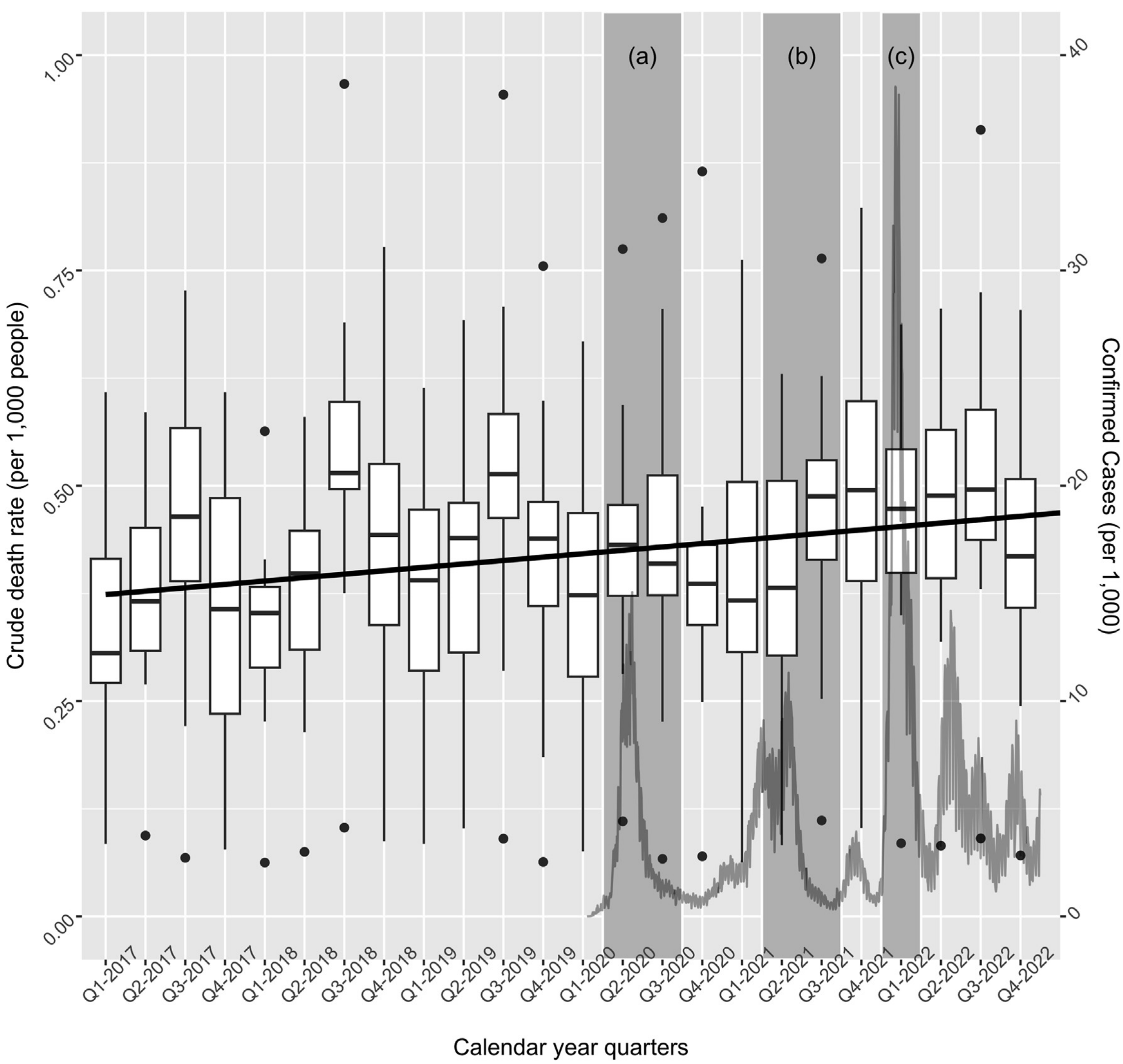

Fig. 4: Crude deaths ratios (CDRs) by dementia and Alzheimer's diagnoses with deaths from 2017 to 2022. Boxplots represent the CDRs values of all regions of Chile across every quarter from 2017 to 2022. The solid black line illustrates the quantile regression model's fit, while the gray curve depicts the COVID-19 death number from March 2020 to December 2022. Panels (a), (b), and (c) correspond to the peaks in COVID-19 deaths associated with the Delta, Gamma, and Omicron variants, respectively.

period, there was a downward trend in CDRs attributable to COVID-19.

Thus, the number of confirmed cases of COVID-19 had an impact on dementia and AD mortality. On the other hand, this negative trend could be attributed to various factors. For instance, there was an underreporting of deaths of people with underlying mental illness conditions who were infected with COVID-19 and had this pathology registered as the cause of death. The implementation of stringent health measures in Chile, following the declaration of a state of emergency on March 18, 2020, might serve as another potential cause. This encompassed a nighttime curfew, national lockdown, and regional quarantines that lasted until September 2021.[37] The first positive case of COVID-19 in Chile was registered on February 29, 2020. With more than five million diagnosed cases and over 60 thousand deaths reported as of May 3, 2023, Chile was one of the most affected Latin American countries by the coronavirus pandemic.[38,39]

The results presented here for Chile are consistent with the findings report by the APS Group Scotland,[40] where they indicate that the reduction in excess deaths involving dementia during the course of the pandemic may relate to improved measures to reduce infection in care homes and the prioritization of the vaccination program. This reduction is also likely to be related to the peak in excess deaths caused by dementia at the start of

Parameter	OLS	CI	Fixed effect	CI	Within	CI	Random effect	CI
	Pooled		LSDV				Swar	
β_1	0.06 (0.04)	(0.01; 0.12)	0.002 (0.93)	(−0.04; 0.04)	0.002 (0.93)	(−0.04; 0.04)	−0.014 (0.47)	(−0.05; 0.02)
β_2	0.003 (0.78)	(−0.02; 0.03)	−0.07 (0.05)	(−0.13; −0.001)	−0.07 (0.05)	(−0.13; −0.001)	0.01 (0.38)	(−0.01; 0.02)
β_3	0.04 (0.20)	(−0.02; 0.10)	0.03 (0.23)	(−0.02; 0.07)	0.03 (0.23)	(−0.02; 0.07)	0.05 (0.02)	(0.01; 0.10)
β_4	−0.013 (0.68)	(−0.08; 0.05)	0.02 (0.52)	(−0.04; 0.07)	0.02 (0.52)	(−0.04; 0.07)	0.02 (0.47)	(−0.03; 0.07)
β_5	−0.07 (0.31)	(−0.19; 0.06)	−0.05 (0.28)	(−0.14; 0.04)	−0.05 (0.28)	(−0.14; 0.04)	−0.10 (0.02)	(−0.19; −0.02)
R^2	0.15		0.95		0.02		0.08	
Adj. R^2	0.14		0.95		−0.11		0.06	
Num. Obs.	384		384		384		384	
σ_ε	0.47		0.25		0.25		0.25	
σ_δ							0.34	
σ_η							0.05	

Table 4: **Time effect model: Coefficient estimates, their p-values (in parentheses), and confidence intervals of model (2)–(3) on the panel data.**

the pandemic. Although these strategies effectively curbed the spread of COVID-19, as various studies have indicated, they also had significant implications for the mental health of individuals and families.[41–43] A notable study conducted across three South American countries,[42] including Chile, reported significant declines in memory function among 53% of individuals living with dementia. It also found increased levels of sadness (31%) and anxiety (37%). Another study in the United Kingdom[43] revealed that family caregivers were experiencing increased feelings of exhaustion and overwhelm. These findings support what was mentioned by the World Health Organization (WHO) that individuals with dementia were more vulnerable during the pandemic period.[44]

The findings of this study highlighted a significant regional effect. Specifically, we noted a reduction in the number of observed deaths from dementia and AD among the population 65 and older in the southernmost (Regions 9, 10, 11), as well as in the extreme north (Regions 2, 3, 4) and the zone central (Regions 6, 7, 8, 16) in contrast with other regions of the country. This pattern could be attributed to several potential factors. One of the most immediate considerations is the lower population density in these extreme regions, as well as limited access to health services, and the lack of integration of indigenous peoples in public health programs. While seemingly counterintuitive, it is possible that the lack of medical intervention leads to fewer diagnosed cases of dementia and AD, and thus fewer recorded deaths from these causes. However, this also suggests that many cases may go undiagnosed and untreated, which presents a significant public health concern. Another aspect worth considering is the potential lack of integration of indigenous populations into public health programs. If these communities are not receiving adequate healthcare or are underrepresented in health data, this could contribute to the decreased number of recorded deaths from dementia and AD in regions where they represent significant parts of the population, like Regions 8, 9 and 10. Previous work has shown that socioeconomic inequality and the structure and dynamics of the Chile's healthcare system prevent delivery of quality care to the majority of those affected by dementia.[45,46] However, more research is needed to fully understand the complexities of these regional disparities and to develop strategies that ensure equitable healthcare services across all regions of the country. Understanding these regional differences is crucial for creating informed public health strategies and ensuring that healthcare resources are allocated where they are most needed.

During the study period between 2017 and 2022, the majority of dementia related deaths, as per the ICD-10 classification, occurred among individuals aged 80 and older. In this age group, there was a significant increase of 34.19% (9750 deaths) compared to those under 80 years old. In contrast, AD mortality decreased in the same age group (80 and older), with a total of 10,786 deaths. This result is consistent with the finding of a prospective cohort carried out in low- and middle-income countries, which revealed that in older people the main cause of disability is dementia and that mortality rates from this cause increase with age.[46] In this sense, an observational study[35] indicates that older people with dementia who become infected with COVID-19 have a higher risk of short-term mortality. In our study, 88.12% of dementia deaths occurred in people aged 80 years or older (Fig. 3). Therefore, it is necessary to provide focused care for this group of people.

A systematic review with meta-analysis examining the association between dementia and mortality in older adults with COVID-19 concluded that older adults with dementia with COVID-19 infection have a higher risk of mortality compared to older adults without dementia.[47] This is consistent with the results of a cohort study[48] in older people, where they concluded that dementia is an important risk factor for death in people over 85 years of age, and that dementia shortens life, especially among women. Particularly, the study carried out by Agüero-Torres et al.,[48] considered the combined mortality rates from dementia and AD in the pre-pandemic period, where women accounted for 66.15% of deaths versus men, who accounted for 33.85% of deaths. They also highlighted that in the pandemic period, there was an increase in the percentage of deaths of women (67.42%), at the same time as a decrease in deaths of men (32.58%). These findings align with the conclusions of other studies, indicating that women, individuals aged 80 or older, and non-Hispanic black and Hispanic populations vs non-Hispanic whites face an elevated risk of mortality associated with AD and dementia.[49]

Our study is consistent in that the mortality rates of dementia and AD are higher in women than in men, with percentages of dementia in women ranging from 30.05% to 30.34% from the pre-pandemic period to the post-pandemic period respectively. In turn, the AD percentages varied from 36.10% to 37.08% between the pre-pandemic and pandemic periods (Supplementary Table S1, Supplementary Material).

Regarding the place of death in the pre-pandemic period, 67.44% of deaths (dementia and AD) occurred at home, increasing to 77.84% of deaths at home during the pandemic period. Our findings align with similar trends reported by Chen et al.,[14] who observed a significant increase in deaths that occurred at home among older people with AD and dementia, compared to those that occurred in nursing homes. This change can be attributed to the unique circumstances of the COVID-19 pandemic, where due to fear of transmission, many home care clients canceled in-person visits. At the same time, healthcare providers faced significant barriers to providing care, such as shortages of personal protective equipment and safe transportation options.[50–52] Given the unique needs of this demographic, the demand for home-based palliative care and resources is crucial. In particular, this group tends to receive palliative care less frequently and carries a high burden of disease.[53] As such, a palliative care approach that includes advanced care planning and involves patients with dementia in decision-making processes could be vital in mitigating the risks that lead to unfavorable outcomes, thereby reducing the overall burden of care.[35] Therefore, it is strongly recommended to integrate palliative care interventions as a standard part of care for people with dementia living at home.[54] When designing these interventions, it is essential to consider strategies that address the unique needs of this population. This could include predicting the course of the disease, avoiding overly aggressive treatments, and planning advanced care.[55] Incorporating these personalized palliative care strategies into future pandemic preparedness plans could significantly improve the quality of care and outcomes for patients with dementia. This is particularly relevant given the observed shift toward an increase in home deaths of these patients during the pandemic. By developing more robust, patient-centered models of care, we could better maintain the health and dignity of people with dementia in the face of any future public health crisis.

Strengths and limitations

An important strength of this study is the method used to assess the possible relationships between the COVID-19 pandemic and mental illness mortality. By incorporating geographic location into the model as an explanatory variable, the magnitude and statistical significance of the observed results increased considerably.

The findings of this study have several limitations. First, this study employed a longitudinal design. Therefore, this type of study requires variables recorded both over time and by location, which can be challenging to acquire. In this context, monthly records of several sociodemographic variables were not available by region; therefore, they could not be utilized in analyzing the association between COVID-19 and social determinants of health (SDH), such as race/ethnicity, socioeconomic level, rural/urban residence, and housing status, in relation to avoiding mental illness. Therefore, our results should be interpreted in light of the absence of controlling for any SDH, which might have impacted our results, especially on a regional level. Another limitation is the absence of declaration of comorbidities in the death records used, thus it was not possible to verify whether the cause of death was actually due to COVID-19 or due to a comorbidity. Finally, it is important to consider underreporting in the pandemic context, declared in various investigations across the entire spectrum of health care, which generates limitations in the results.[56,57]

A subsequent study is proposed that not only considers the geographical differences that affect self-protection habits against mental health diseases and COVID-19 but also incorporates the SDH. Further investigation is needed to understand the underlying causes for these contrasting patterns and to inform future healthcare policies and interventions targeting dementia and AD among Chilean older adults.

Conclusions

Our study indicates a reduction in reported mortality rates attributed to dementia and AD during the COVID-19 pandemic in Chile, which might be affected by potential underreporting of mental illness as a cause of death. Additionally, the recorded cause of death for patients with mental health conditions can vary based on the physician's relationship with the patient and the typical management strategies for end-stage dementia. This highlights the need for improved documentation and reporting methods in the context of mental health conditions, particularly during crisis situations like pandemics. Such insights are crucial for future health policy and research to better address the needs of those with dementia and AD.

Contributors

GF, CB-S, JN, and MF conceptualized this study and contributed to its design. GF and CB-S acquired the data. GF and JN conducted the statistical analysis. GF, CB-S and JN, formatted tables, figures and wrote the first draft. GF, CB-S, JN, and MF performed literature review and contributed to the result analysis and interpretation. JN and MF have accessed and verified the underlying data. GF, CB-S, JN, and MF were responsible for the decision to submit the manuscript. All authors approved of the final version.

Data sharing statement

All data used in these analyses are publicly available from the domain: https://deis.minsal.cl/#datosabiertos. Additionally, all data collected for the study and posterior results are available from the corresponding author upon reasonable request.

Editor note

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Declaration of interests

We declare no competing interests.

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Appendix A. Supplementary data

Supplementary data related to this article can be found at https://doi.org/10.1016/j.lana.2024.100726.

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