Risk factors for mortality of residents in nursing homes with Covid 19: a retrospective cohort study

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⁸

31 Abstract

32 Background and Objectives

33 Nursing homes have shown remarkably high Covid-19 incidence and mortality. We aimed to

- 34 explore the contribution of structural factors of nursing home facilities and the surrounding district
- 35 to all-cause and Covid-19-related deaths during a SARS-CoV-2 outbreak.
- 36 *Methods*

Retrospective cohort study of Covid-19 mortality at the facility level in nursing homes in Catalonia (North-East Spain). The investigated factors included characteristics of the residents (age, gender, comorbidities, and complexity and/or advanced disease), structural features of the nursing home (total number of residents, residents who return home during the pandemic, and capacity for pandemic response, based on an ad hoc score of availability of twelve essential items for implementing preventive measures), and sociodemographic profile of the catchment district

- 43 (household income, population density, and population incidence of Covid-19). Study endpoints
- 44 included all-cause death and Covid-19-related death (either PCR-confirmed or clinical suspicion).

45 Results

- 46 The analysis included 167 nursing homes that provide long-term care to 8,716 residents. Between
- 47 March 1 and June 1, 2020, 1,629 deaths were reported in these nursing homes; 1,089 (66.9%) of
- 48 them were Covid-19-confirmed. The multivariable regression showed a higher risk of death
- 49 associated with a higher percentage of complex patients (HR 1.09; 95%CI 1.05-1.12 per 10%
- 50 increase) or those with advanced diseases (1.13; 1.07-1.19), lower capacity for implementing
- 51 preventive measures (1.08; 1.05-1.10 per 1-point increase), and districts with a higher incidence
- 52 of Covid-19 (2.98; 2.53-3.50 per 1000 cases/100,000 population increase). A higher population
- 53 density of the catchment area was a protective factor (0.60; 0.50- 0.72 per log10 people/Km²
- 54 increase).

55 Conclusion

56 Presence of residents with complex/advance disease, low capacity for pandemic response and 57 location in areas with high incidence of Covid-19 are risk factors for Covid-19 mortality in nursing 58 homes and may help policymakers to prioritize preventative interventions for pandemic 59 containment.

60

61 Introduction

62 Six months after the first outbreak of the novel coronavirus disease (Covid-19), the global death

toll associated with the pandemic amounted to nearly half a million [1]. To date, various authors

have reported on the major role of long-term care (LTC) facilities, such as nursing homes, in

- 65 spreading SARS-CoV-2 to the most vulnerable populations during the Covid-19 pandemic [2].
- 66 This group has experienced an extremely high death toll and also has overwhelmed local health

67 systems. In some countries, LTC residents account for more than 50% of deaths attributed to

68 Covid-19. In Catalonia (North-East Spain), the government reported approximately 1,810 deaths 69 among residents of LTC facilities between March 15 and April 15 [3].

70 To date, large variations in Covid-19 death rates across LTC facilities have been observed.

71 Whether the high death rates are linked to the structural features of such settings or the poorer

health of individuals in these facilities compared to those living elsewhere is still unclear. Because

of the different policy implications of the relative influence of these features, there is a need to

deepen into the determinants of SARS-CoV-2 spread and mortality in LTC facilities [4,5].

75 Potential risk factors of the residential setting are a communal living area, multiple residents in a

single room, care provided by multiple caregivers – who may work across multiple different

77 facilities, shortage of healthcare resources (e.g., tests, and personal protective equipment), limited

access to skilled healthcare professionals, and the lack of specific guidance for managing the

79 outbreak in the residential setting [2,3,6]. In addition to these setting-specific risk factors, the

80 higher death rates are likely associated primarily with older age, high levels of multi-comorbidity,

disability, and immune senescence of old-age [5,7–9]. Finally, some authors have identified risk
 factors associated with the characteristics of the population in the catchment area, such as the mean

household income or the population density [10,11].

84 We aimed to assess whether living in a nursing homes for LTC is associated with an increased risk

85 of death from Covid-19 beyond the risk associated with age and chronic health conditions. We

86 used data from nursing homes, including residents' health characteristics, structural features, and

the demographic and epidemiological profile of the district where the nursing home is located, to

88 investigate the association between potential risk factors at the facility level and mortality in the

89 residential setting during the SARS-CoV-2 outbreak in Spain.

90 Methods

91 Study setting and participants

92 This was a retrospective cohort study of Covid-19 mortality risk factors in the residential setting 93 in Catalonia (North-East Spain). The study included clinical, mortality, and structural information 94 corresponding to all public and private nursing homes in the administrative health region 95 *Metropolitana Nord* (population 1,986,032 people) in Barcelona, Spain between March 1 and June 96 1, 2020, during the Covid-19 outbreak. Skilled nursing facilities (i.e., intermediate care) and 97 mental health facilities were excluded from the analysis.

98 On March 1, 2020, the Department of Health of Catalonia launched a comprehensive disease 99 control program to minimize Covid-19 spread and mortality among residents in nursing homes.

The containment strategy was implemented in all LTC facilities in the study area and involved 64

primary care teams that reported daily information regarding the epidemiological status of each

102 nursing home. The primary care teams provided preventive epidemiological recommendations, 103 including the partition of communal living areas, isolation of suspected cases and contacts, 104 guidance on personal protective measures to nursing home workers. In the advent of a confirmed 105 or suspected case of Covid-19, the teams also conducted systematic screening of close 106 contacts—or all residents, in centers with high incidence—using real-time reverse transcription— 107 melawarase sheir measures (rf DCD) form measures have a series.

107 polymerase chain reaction (rt-PCR) from nasopharyngeal swabs.

108 The study protocol was approved by the institutional review board of Hospital Germans Trias109 Pujol.

110 Data collection

111 Demographic and clinical data of residents were extracted from electronic medical records using 112 a standardized data collection form [12]. The structural and organizational features of each nursing 113 home were gathered at facility assessment visits by the study team. The demographic and 114 epidemiological profile of the nursing home district was retrieved from the Statistical Institute of 115 Catalonia. Deaths were identified from the Mortality Registry of the Department of Health of 116 Catalonia. All data were handled according to the General Data Protection Regulation 2016/679 117 on data protection and privacy for all individuals within the European Union and the local 118 regulatory framework regarding data protection.

119 Definitions

120 Variables regarding the residents' health characteristics in each nursing home included 121 demographic characteristics (i.e., age and gender), and clinical characteristics (i.e., number of 122 comorbidities and percentage of residents with high dependence in activities of daily living, 123 defined as a Barthel score < 50 [13]). We also recorded the percentage of residents identified on 124 electronic medical records as complex chronic patients (CCP) and patients with advanced chronic 125 disease (ACD) by their primary care teams, according to clinical guidelines of the Catalan Health 126 Department [14]. These guidelines define CCP based on their clinical condition (e.g. 127 multimorbidity, disability, difficult symptom control) and/or social environment (e.g., lack of 128 support from family or caregivers, isolated household). Patients with ACD are those with advanced 129 and irreversible chronic conditions that limit their life expectancy to approximately 12 months. 130 Comorbidities were codified according to the ICD-10 system and included dementia, asthma or 131 chronic obstructive pulmonary disease, hypertension, type-1 diabetes mellitus, type-2 diabetes 132 mellitus, chronic kidney disease, cerebrovascular disease, cardiovascular disease.

Structural features of nursing homes were characterized according to their capacity for pandemic preparedness and response (SNQ12 score) and other relevant organizational variables such as current number of residents and percentage of residents who return home to live with their relatives due to the pandemic. The capacity of the nursing home for pandemic preparedness and response was assessed using an *ad hoc* set of 12 essential items that yields a score, called SNQ12 (*sine qua* 138 non conditions for implementing the measures) [15]. The score indicates the number of unmet 139 requirements, which ranges from 0 (all requirements are met) to 12 (all requirements are unmet). 140 The requirements are related to three areas: 1) personal protective equipment (PPEs) (adequate 141 supply, routine use, and use for waste management and cleaning/disinfection), 2) surveillance and 142 communication (routine monitoring of symptom onset by non-healthcare professionals and 143 communication of symptoms to occupational health services), and 3) cleaning and waste 144 management (regular hand washing before and after contact with Covid-19 patients or their 145 contacts, adequate laundry procedures, cleaning and disinfection of surfaces, use of an adequate 146 disinfectant, adequate disposal of used PPEs) (Appendix Figure 1).

147 The district demographic and epidemiological profile was assessed and defined using the 148 household income and density of population in the municipality, and the population incidence of 149 Covid-19 in the post code district (lowest administrative division) where the nursing home is 150 located.

Deaths were classified as Covid-19-related when individuals had a positive rt-PCR or a clinical suspicion of Covid-19. Clinical suspicion of Covid-19 was defined based on the national guidelines available at the time as individuals with clinical features of acute respiratory disease of sudden onset and any severity, primarily characterized by fever, cough, and shortness of breath. Other symptoms such as odynophagia, anosmia, dysgeusia, muscular pain, diarrhea, chest pain, or headache could also be considered suggestive of SARS-CoV-2 at the physician's discretion.

157 Statistical Analysis

158 Continuous and categorical variables were presented as the mean and standard deviation (SD) (or median and interquartile range [IQR], defined by 25th and 75th percentiles) and number (%), 159 respectively. The excess deaths were defined as the difference between deaths reported in 2020 160 161 and the median of 2016-2019 for the same months of the year; the Covid-19 contribution to the 162 excess deaths was computed by the difference between confirmed or suspected Covid-19 deaths 163 and all-cause mortality. In our primary analysis to determine the risk factors associated with 164 mortality, we used univariate and multivariate Poisson regression models at facility level. 165 Variables for the multivariate model were treated as linear, and were chosen using an Akaike Information Criteria (AIC)-based backward stepwise procedure. Results were presented as the 166 167 hazard ratio (HR) and the 95% confidence interval (CI). In a secondary analysis, we grouped the 168 nursing homes according to their characteristics using cluster analysis based on k-nearest neighbor 169 classifier [16,17]. The resulting clusters (phenogroups) were described in a heatmap that represents 170 the intensity of each characteristic based on the difference (below or above) between the average 171 of the given cluster and that of the overall sample. We used a random forest classifier and the Gini 172 measure of importance [18] to determine the weight of each variable in each cluster. The 173 significance threshold was set at a two-sided alpha value of 0.05. All analyses and plots were 174 performed using R version 3.6 [19].

175 **Results**

176 Characteristics of the nursing homes

The analysis included 167 nursing homes providing long-term care to 8,716 residents. Table 1 summarizes the characteristics of the nursing homes included in the analysis. The mean age was 87.1 years, 56.6% of them were classified as CCPs and/or ACD patients, and 82.1% were identified as highly dependent. The median SNQ12 score was 1.4 unmet preventative items, reflecting an overall high level of pandemic preparedness. The individual demographic, clinical, and epidemiological characteristics of included residents are summarized in the Appendix Table 1.

183 Mortality

184 Between March 1 and June 1, 2020, a total of 1,629 deaths were reported in the nursing homes 185 included in the analysis. Of these, 1,089 (66.9%) were registered as Covid-19 deaths in the 186 mortality registry of the Department of Health. The cause of the death of the remaining 671 deaths 187 could not be confirmed. Overall, the excess deaths in the analyzed nursing homes compared with 188 the same period in the four previous years were estimated to be 971 deaths; Covid-19-confirmed 189 deaths accounted for 89.2% of all excess mortality (Figure 1). At the nursing home level, the 190 median (IQR) mortality rate was 14.3 (7.6 - 26.1) deaths/100 residents/3-month study period for 191 all-cause death, and 3.9 (0.0 - 18.4) for Covid-19 confirmed deaths.

192 Risk factors for mortality

193 According to the multivariate analysis, the risk of Covid-19 related deaths was higher in nursing 194 homes with a higher percentage of CCP patients (hazard ratio 1.09; 95%CI 1.05-1.12 per 10 units 195 increase) or ACD patients (1.13; 1.07-1.19 per 10 units increase), lower capacity for pandemic 196 preparedness and response (1.08, 1.05-1.10 per unit increase) and located in areas with high 197 incidence of Covid-19 (2.98; 2.53-3.50 per 1000 cases/100,000 population increase) (Table 2). 198 The risk factors of all-cause death were the same as those of Covid-19 related death. For Covid-199 19-related deaths, the univariate analysis revealed a higher risk of death in nursing homes with a 200 high percentage of residents who returned home to live with their relatives. This variable was 201 selected in the stepwise method, but it was not significantly associated with Covid-19-related 202 deaths in the multivariate analysis. The only variable associated with lower all-cause deaths was 203 living in high-density population areas (0.60; 0.50- 0.72 per log 10 people/km2). The risk factors 204 significantly associated to all-cause death were the same as those of Covid-19 related death (Table 205 2).

206 Comparison of characteristics among nursing home clusters

The cluster analysis based on the k-nearest neighbor classifier identified eight groups of nursing
 homes that were significantly different from each other. Resident health characteristics, structural

features, and sociodemographic factors were stratified according to each cluster. Figure 2 illustrates the intensity of each characteristic (i.e., the extent of the difference between the mean

- of a given cluster and that of the entire sample) in the resulting clusters and the contribution of
- 212 each characteristic to their definition. Key characteristics of each cluster were as follows:

213 Nursing homes in **cluster 1** were placed in low densely populated areas with high population 214 incidence of Covid-19, and high household income; cluster 2 were facilities with a high proportion 215 of CCP and ACD patients, and located in areas with low population incidence of Covid-19; cluster 216 **3** had low proportion of CCPs and highly dependent residents; **cluster 4** had higher number of 217 residents than the median, although with a very low proportion of CCPs; nursing homes in this 218 cluster were placed in areas with low household income; cluster 5 had low proportion of ACD 219 patients and dependent residents, and had higher number of residents that returned home with their 220 relatives; cluster 6 were placed in areas with high household income and low population incidence 221 of Covid-19; cluster 7 had high proportion of CCP and ACD patients; nursing homes in this cluster 222 were located in densely populated areas; cluster 8 had a high SNQ12 score—indicating very 223 limited capacity for pandemic preparedness and response-and high proportion of CCPs and older 224 residents than the median.

- 225 Association of nursing home clusters with mortality

226 The mortality rate in each cluster is shown in Figure 3. During the study period, the median (IQR)

proportion of all-cause deaths and Covid-19-related deaths in the eight nursing home clusters was

- 228 12.3% (7.6 26.1) and 3.9% (0.0 18.4), respectively. Clusters 1, 4, and 8 had a greater all-cause
- mortality rate than the median. Correspondingly, clusters 1, 7, and 8 had a greater Covid-19-related
- 230 mortality rate than the median.
- 231

232 Discussion

233 To our knowledge this is the first study on risk of mortality at a facility level of residents with 234 Covid-19 in nursing homes. Our analysis revealed that a ten percent increase in the proportion of 235 residents with complex or advanced diseases increased the mortality risk by 9% and 13%, 236 respectively; a 1-point increase in the 12-points score of unmeet measures for containing SARS-237 CoV-2 spread increases the mortality risk by 8%, and an increase in population incidence of 1000 238 Covid-19 cases per 100,000 population increases the mortality risk by 198%. Location in a highly 239 densely populated area was the only factor associated with a reduced mortality rate, which might 240 be related to improved access to hospitals with intensive care units in urban areas, as previously 241 suggested [20].

The clustering of nursing homes according to their residents' profile and structural capacities provided a global perspective of the type of nursing homes that might be more susceptible to

Covid-19 mortality in the advent of future outbreaks. Consistently with our regression analysis, 244 245 clusters with greater mortality than the median (cluster numbers 1,4,7, and 8) were all located in 246 neighborhoods with high incidence of Covid-19. These results align with previous studies that 247 reported a significant relationship between LTC mortality and Covid-19 incidence in the 248 catchment area [5,10,11]. The increasing evidence on the influence of the local incidence of Covid-249 19 on mortality underscores the paramount importance of early detection-and response 250 to—SARS-CoV-2 entry into facilities—often with new residents, staff, or visitors—for preventing 251 uncontrolled outbreaks in this setting [5,21]. These finding also suggests that population efforts to 252 contain Covid-19 incidence may also contribute to reducing Covid-19 deaths at their local nursing 253 homes

- The multiple regression and cluster analysis were also consistent regarding the importance of the capacity of the nursing home for pandemic preparedness and response. Although most nursing homes showed low SNQ12 scores—indicating few unmet needs for applying containment measures—facilities in cluster 8, characterized by higher SNQ12 scores (mean of 5 unmet items over a total of 12 essential requirements) than the median, experienced high mortality levels.
- 259 Finally, our multivariate analysis revealed a significant relationship between higher percentages 260 of CCP and/or ACD patients and increased mortality risk. According to local clinical guidelines, CCP and ACD patients are characterized by high clinical complexity and the presence of an 261 262 advanced—often terminal—disease, respectively [14], suggesting an increased likelihood of death 263 in the advent of any infection or acquired disease. Interestingly, cluster no. 2, characterized by the 264 higher health risk of its residents, had similar mortality than clusters 4, 5, and 6, with a more 265 favorable resident health profile. These conflicting results suggest that the mechanisms driving 266 mortality risk in nursing homes are complex and may depend on the conjunction of various factors.
- 267 Our analysis had the intrinsic limitations of retrospective studies, particularly regarding data 268 completeness. Owing to the overload of the healthcare system during the investigated period, a 269 large number of deaths could not be tested for SARS-CoV-2 PCR and remained unconfirmed. We 270 were unable to gather information regarding the worker profiles in each nursing home. Unlike 271 skilled nursing homes aimed at intermediate care or mental health resources, which tend to be 272 coordinated by the healthcare authorities, non-specialized nursing homes aimed at long-term stay 273 are a case-mix of organizational models. Hence, the inclusion of the characteristics of the work 274 team profile (e.g., skills, resident/worker ratio, and presence of physicians) might have provided 275 interesting insights regarding the capacity of the residence to cope with the outbreak [22].
- Our results raise important policy implications by suggesting structural factors of the nursing homes and their surrounding districts that are important drivers of Covid-19-related mortality in
- this setting. Identification of facilities with low capacity for pandemic response, located in areas
- with high incidence of Covid-19 and low density of population (e.g., rural areas) could help public
- 280 health officers to identify facilities where preventative interventions need to be prioritized. The

- 281 presence of complex patients and those with advanced chronic diseases also increased mortality
- risk, though these factors alone seem not to explain mortality trends at facility level. Efforts should
 be geared to protecting older adults living in the highest risk facilities.

285 **Disclosures**

- 286 *Contributors*
- 287 CS, DO, MAM, RLA and OM designed the study. DO, MAM, RLA, EN, MMM, NPG, JMB-S,
- 288 MEI, IGS, SRN, RM, MTC, JVP, NH, JA collected the data. CS, DO, MM, OM analyzed the data.
- 289 CS, DO, OM interpreted the data. CS, DO, OM wrote the manuscript. All authors reviewed and
- approved the final version of the manuscript.
- 291
- 292 Declaration of interests
- 293 We declare no competing interests.
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364 Tables

365 Table 1. Characteristics of nursing homes

	Total
	(N = 167)
Average resident profile	
Age of residents, in years	87.1 (2.1)
Percentage of male residents	26.4 (9.6)
Number of comorbidities	1.5 (0.6)
Percentage of CCPs	46.1 (17.3)
Percentage of ACD patients	10.5 (8.9)
Percentage of dependent residents*	82.1 (9.5)
Structural features	
SNQ12 score	1.4 (1.7)
Current number of residents	46.2 (29.8)
Percentage of residents who return home	1.4 (3.0)
District demographic and epidemiological profile	
Mean household income, in Euro	36099.6 (5527.5)
Density of population per km ² , in log ₁₀	17.9 (9.5)
Population incidence of Covid-19	0.9 (0.3)

366

367 Data are mean (SD). CCP=complex chronic patient. ACD=advanced chronic disease. SNQ12=number of unmet

368 epidemic and infection control preparedness requirements (0-12). *Barthel score < 50.

	All-cause deaths			Covid-19-related deaths		
	Univariate analysis Multivariate analysis		Univariate analysis	Multivariate analysis		
	Hazard Ratio (95% CI)	Hazard Ratio (95% CI)	p-value	Hazard Ratio (95% CI)	Hazard Ratio (95% CI)	p-value
Average resident profile						
Age of residents in each facility †	0.99 (0.83-1.18)			0.99 (0.97-1.01)		
Percentage of male residents	1.01 (1.03-1.05)			1.00 (0.95-1.05)		
Number of comorbidities †	1.15 (1.08-1.22)*			1.35 (1.25-1.46)*		
Percentage of CCPs	1.04 (1.02-1.06)*	1.04 (1.02-1.06)	0.0015	1.10 (1.06-1.11)*	1.09 (1.05-1.12)	< 0.0001
Percentage of ACD patients	1.09 (1.05-1.13)*	1.09 (1.04-1.13)	0.0002	1.15 (1.10-1.20)*	1.13 (1.07-1.19)	< 0.0001
Percentage of dependent residents	1.03 (1.01-1.07)			1.00 (0.95-1.05)		
Structural features						
SNQ12 §	1.06 (1.04-1.08)*	1.04 (1.03-1.07)	< 0.0001	1.11 (1.09-1.14)*	1.08 (1.05-1.10)	< 0.0001
Current number of residents†	1.00 (0.99-1.01)			1.00 (0.98-1.02)		
Percentage of residents who return home	1.03 (0.91-1.14)			1.17 (1.01-1.31)*		
Sociodemographic profile						
Mean household income, in Euro‡	0.95 (0.90-1.02)			0.95 (0.86-1.04)		
Density of population, log10 people/km ² §	0.84 (0.74-0.95)*	0.67 (0.59-0.77)	< 0.0001	0.91 (0.77-1.08)	0.60 (0.50-0.72)	< 0.0001
Population incidence of Covid-19	1.67 (1.48-1.87)*	1.79 (1.59-2.03)*	< 0.0001	2.72 (2.33-3.18)*	2.98 (2.53-3.50)*	< 0.0001

370 Table 2. Estimated effect of long-term care facilities' features in all deaths and Covid-19 related deaths.

371

372 CCP= complex chronic patient; ACD= advanced chronic disease; Dependent resident=Barthel score < 50; SNQ12=

373 number of unmet essential items for implementing preventive measures (0-12).

Hazar ratios and 95% CI are shown.

- 374 375 376 HR represents the estimated effect for an increase of 10 units, unless otherwise indicated.
- 377 † HR for an increase in 1 unit.
- 378 ‡ HR for an increase of 10,000€/annum in mean household income.

379 § HR for an increase in 1 log10 people/km².

380 || HR for an increase in incidence of Covid-19 of 1,000 cases/100,000 population.

381 *p-value for univariate analysis <0.05

383 Figure Legends

384 [Figures are presented herein in low resolution for rapid assessment; it will be formatted385 adequately before submission]



Figure 1. Excess mortality of 2020 relative to the average of the past four years (2016-2019). Bars show the number of weekly deaths reported in 2020 in all nursing homes included in the analysis over the study period. Deaths reported in 2020 have been classified as Covid-19 confirmed and unconfirmed, which include deaths of individuals with suspected Covid-19 diagnosis. The median number of deaths for the same weeks in the previous 4 years (2016-2019) is shown in grey. The continuous line shows the death toll attributed to Covid-19 in the general population of the catchment area.















Figure 3. Mortality at the cluster level for all-cause deaths and Covid-19 related deaths. The dotted line shows the median mortality rate for the entire sample. Bars show the mean mortality rate of each cluster; error lines represent the standard error of the mean (SEM). Red and green indicate mean cluster mortality higher and lower than the total median, respectively. For both colors, light tones indicate that the SD of the cluster encompasses the overall median, whereas intense tones indicate that the whole SD range is above (red) or below (green) the total median.



416 Appendix Figure 1. Characteristics among nursing home clusters. For each cluster (x-axis), barplots show the 417 mean (SD) of a given characteristic. The median of the entire sample is shown with a green line. The extent of the 418 difference between the mean of a given cluster and the median of the entire sample is illustrated with the following 419 color code: green tones indicate a mean of the cluster below the median of the entire sample, whereas purple tones 420 indicate a mean of the cluster above the median of the entire sample. In both cases, more intense colors represent 421 greater differences between the cluster and the whole sample.