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Factors associated with COVID-19 hospitalizations and deaths in French nursing homes

Running title: COVID-19 in nursing homes

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Brief summary:

Male gender, diabetes, an altered level of consciousness, and dyspnea were all associated with a greater risk of hospitalization. Male gender, thermal dysregulation, and being aged >85 years old were all associated with increased mortality risk.

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Tables/figures: 4

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Couderc, Correard and Daumas had full access to all of the data in the study, and take responsibility for the integrity of the data and the accuracy of the data analysis. Couderc and Correard are joint first authors; Villani and Daumas are joint last authors.

Study concept and design: Couderc, Correard, Villani and Daumas

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Availability of data and materials:

The data are available from the corresponding author upon reasonable request.

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Abstract

Objectives: To describe the clinical characteristics and management of residents in French nursing homes with suspected or confirmed coronavirus disease 2019 (COVID-19), and to determine the risk factors for COVID-19-related hospitalization and death in this population.

Design: A retrospective multicenter cohort study

Setting and Participants: Four hundred and eighty nursing home residents with suspected or confirmed COVID-19 between 1 March and 20 May 2020 were enrolled and followed until 2 June 2020 in 15 nursing homes in Marseille's greater metropolitan area.

Methods: Demographic, clinical, laboratory, treatment type, and clinical outcome data were collected from patients' medical records. Multivariable analyses were used to determine factors associated with COVID-19-related hospitalization and death. For the former, the competing risk analysis - based on Fine and Gray's model - took death into account.

Results: 480 residents were included. Median age was 88 years (IQR 80-93), and 330 residents were women. A total of 371 residents were symptomatic (77.3%), the most common symptoms being asthenia (47.9%), fever or hypothermia (48.1%), and dyspnea (35.6%). One hundred and twenty-three patients (25.6%) were hospitalized and 96 (20%) died. Male gender (sHR 1.63, 95% CI 1.12-2.35), diabetes (sHR 1.69, 95% CI 1.15-2.50), an altered level of consciousness (sHR 2.36, 95% CI 1.40-3.98), and dyspnea (sHR 1.69, 95% CI 1.09-2.62) were all associated with a greater risk of COVID-19-related hospitalization. Male gender (OR 6.63, 95% CI 1.04-42.39), thermal dysregulation (OR 2.64, 95% CI 1.60-4.38), falls (2.21 95% CI 1.02-4.75), and being aged >85 years old (OR 2.36 95% CI 1.32-4.24) were all associated with increased COVID-19-related mortality risk, whereas polymedication (OR 0.46, 95% CI 0.27-0.77) and preventive anticoagulation (OR 0.46, 95% CI 0.27-0.79) were protective prognostic factors.

Conclusions and Implications: Male gender, being aged >85 years old, diabetes, dyspnea, thermal dysregulation, an altered level of consciousness, and falls, must all be considered when identifying and protecting nursing home residents who are at greatest risk of COVID-19-related hospitalization and death.

INTRODUCTION

Since December 2019, the number of older, frailer patients infected with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has dramatically increased worldwide. Infection rates are higher in the elderly than in younger populations, and health outcomes are poorer .[1,2] The literature on novel coronavirus disease 2019 (COVID-19) - which is caused by SARS-CoV-2 - indicates that older adults are at particular risk of developing severe forms of the disease[3,4], particularly those with pre-existing comorbidities[5] and those who are frail (the result of cognitive[6] and functional[7] impairment). Early reports also suggested that older people may initially present more atypical COVID-19-related clinical manifestations and biological results than younger adults.[8,9]

In the context of the prevalence of COVID-19 in nursing home (NH) residents, research on clinical characteristics, care management, and disease-related outcomes is still scarce. A study in King county, Washington state, USA, reported that 54.5% of 101 NH residents infected over a period of three weeks were hospitalized for COVID-19, and that 33.7% subsequently died.[10] In a multicenter study in NH in Maryland, USA, residents with multiple symptoms had the highest risk of mortality and hospitalization. Interestingly, asymptomatic COVID-19 was also associated with higher mortality risk in that study (20.6%).[11] In France, between 1 March and 31 May 2020, of the 28 771 people who died from COVID-19, more than a third (10 327 persons) were living in nursing homes.[12] International comparisons of data are difficult because of intra- and inter-country differences in NH in terms of organization, COVID-19 testing policies, therapeutic management, and approaches to quantifying COVID-19-related deaths.[13] However, the general observation in NH literature is that COVID-19 increased mortality in NH residents in 2020.[13-15] Given the relatively small number of related studies to date, more research is needed on the clinical presentation and on risk factors for COVID-19-related hospitalization and death in this population. Accordingly, we implemented a

55 multicenter retrospective study to describe the clinical characteristics, biological
56 characteristics, and healthcare management of a relatively large cohort of residents with
57 suspected or confirmed COVID-19 living in NH located in the greater metropolitan area of
58 Marseille. The secondary objectives were to determine the factors associated with COVID-
59 19-related hospitalization and with death.

60

61 **METHODS**

62

63 ***Study design and participants***

64 We invited all 39 nursing homes located in the greater metropolitan area of Marseille to
65 participate in a 13-week retrospective observational cohort study. Of the 20 that agreed to
66 participate, 15 had at least one resident with suspected or confirmed COVID-19 at the time of
67 the study. The remaining five NH were therefore secondarily excluded. All residents with
68 suspected or confirmed COVID 19 between 1 March and 20 May 2020 were included. No
69 patient or patient legal representative opposed the use of their medical data when asked.
70 A suspected case was defined as a patient with acute respiratory illness who had been in
71 contact with a confirmed COVID-19 case in the 14 days prior to the onset of symptoms. A
72 confirmed case was defined as a suspected case who had tested positive for SARS-CoV-2
73 nucleic acid using a real-time reverse transcriptase-polymerase chain reaction (RT-PCR)
74 assay (nasal swabs). From the moment a first case was diagnosed in any given NH, screening
75 was performed for all residents approximately every 15 days. We monitored clinical
76 outcomes, including COVID-19-related hospitalization and death, until 2 June 2020, which
77 was the study end date. This end date was chosen as lockdown relaxation rules were
78 introduced facilitating greater NH access to relatives of residents.

79

With regard to investigating risk factors for hospitalization, residents who had the possibility to be hospitalized from 21 March 2020 onwards – the date when French Public Health Authorities facilitated hospital admissions for the country's NH residents - were included in the analysis. Prior to that date, only NH residents with few functional/cognitive impairments and no severe comorbidity who presented severe clinical symptoms could be hospitalized in France. With regard to investigating risk factors for death, all included residents (i.e., with suspected or confirmed COVID 19) for the enrollment period (i.e., 1 March and 20 May 2020) were included.

The study was authorized by The National Institute for Health Data (number INDS- MR 3109280520) and was conducted in accordance with the MR-004 study-type reference methodology approved by the National Commission for Information Technology and Civil Liberties (CNIL). In accordance with French legislation, formal approval from an ethics committee was not required for this type of retrospective non-interventional study based on the use of previously recorded data.

Data collection

Trained physicians (ALC, AD) used a standardized electronic form to collect COVID-19-specific data from clinical charts, laboratory findings, and chest computerized tomography (CT) scans, as well as data from NH records and treatments both for COVID-19 and for pre-existing comorbidities. They also collected the following data for each patient: demographic information (age, gender, body mass index (BMI), most recent iso-resource dependence group classification [16]), comorbidities, and flu and pneumococcus vaccination status.

To define their level of dependency, elderly people in France are divided into one of six iso-resource groups, which reflect different stages of loss of autonomy.[16] NH residents classified into iso-resource groups 1, 2 or 3 must be assisted in most or all their daily activities. We

105 defined cognitive impairment as a score of < 24 according to Mini-Mental State
106 Examination[17] (MMSE) test, or the presence of cognitive impairment symptoms (wandering,
107 hallucinations, hostility/aggressiveness or history of cognitive disorder). Undernutrition and
108 obesity were defined as a BMI of < 21 and ≥ 30, respectively.
109 The date of disease onset was defined as the day when COVID-19 symptoms were first
110 noticed or, for asymptomatic patients, the day a patient had a positive RT-PCR test. The
111 trained physicians collected data for the following symptoms suggestive of COVID-19 from
112 the patients' medical records: general symptoms (sudden deterioration in general health
113 condition or asthenia, anorexia, fever or hypothermia (thermal dysregulation), headaches,
114 myalgia and/or arthralgia), respiratory symptoms, ear nose and throat (ENT) symptoms,
115 gastrointestinal symptoms, worsening depression and geriatric-related syndromes (falls,
116 delirium (acute confusional state), and altered level of consciousness (defined as a Glasgow
117 coma score < 14)). Data on routine blood tests (blood count, renal and liver function, C-
118 reactive protein, creatine phosphokinase and D-dimers) and on chest CT scan results were
119 also collected. For all included patients, data on medications for pre-existing chronic
120 pathologies, polymedication (≥ 5 usual drugs per day), and management of COVID-19 were
121 also recorded. Some patients were 'home hospitalized', that is to say they were provided some
122 elements of hospital-type care for COVID-19 in their NH by an authorized external (i.e., not
123 NH-based) team of specialists. These elements included hydroxychloroquine treatment,
124 perfusions for hydration, and end-of-life care. Home hospitalization did not exclude potential
125 subsequent normal hospitalization if symptoms deteriorated. The numbers of home
126 hospitalized, hospitalized, and deceased patients were recorded. The reasons for home
127 hospitalization (which reflected the availability of each of the three hospital-type care
128 elements listed above), the reasons for hospitalization, and the causes of death were all

129 collected, as were symptom duration, time between disease onset and hospital admission, and
130 the time between disease onset and death.
131
132 ***Statistical analysis***
133 As the study focused on all suspected or confirmed COVID-19 NH residents specifically
134 during the enrolment period, no a priori power calculation was needed. Continuous variables
135 were presented as the median and interquartile range (IQR) with 95% confidence intervals
136 (CI). Categorical variables were expressed as the number of patients (percentage) with 95%
137 CI.
138 Our analysis aimed to explore the association between epidemiological/clinical characteristics
139 and the risk of hospitalization/death in COVID-19 infected NH residents. Univariate and
140 multivariate logistic regression models were used to analyze all the variables studied as
141 potential factors of hospitalization/death (odds ratio; OR). Competing risk analysis based on
142 Fine and Gray's model was used to measure the time from disease onset to hospitalization, in
143 order to take into account the fact that patients who died could not have been hospitalized
144 after their death. Cox proportional hazard regression models were used to estimate cause-
145 specific hazard ratios (sHRs). The follow-up time was defined as the time between the date of
146 disease onset and the date of hospitalization.
147 All variables with a *p*-value of less than 0.05 in the univariate logistic regression or Cox
148 regression models were included in the multivariable analyses. Given the large number of
149 variables with $p<0.05$, we decided to select only those which were most clinically relevant
150 and which had few missing data for the multivariable analysis, in order to respect the
151 maximum authorized number of variables in each model (10 and 9 for the hospitalization and
152 death models, respectively)[18]. For correlated variables, the variable selected was the greatest
153 clinical relevance.

154 All statistical analyses were conducted using SPSS software. A p-value < 0.05 was chosen for

155 the statistical significance threshold.

156

RESULTS

Patients' demographic and clinical characteristics (Table 1)

Between 1 March and 20 May 2020, of the 1392 residents in the 15 participating nursing homes in the greater metropolitan area of Marseille, a total of 480 (34.5%) had suspected or confirmed COVID-19 and were included in the present study.

Median age of the study sample was 88 years (IQR 80-93, range 65-105), and 330 patients (68.8%) were women. All patients had at least one comorbidity. Neurocognitive disorders were the most common comorbidity, affecting 406 (84.6%) patients, followed by hypertension (257, 53.5%), and depression (216, 45.0%). Eighty-six patients (17.9%) had diabetes and 51 (10.6%) had chronic pulmonary disease. With regard to weight status, 186 (38.8%) were undernourished, and 43 (9.0%) were obese. The majority of residents (408, 85.0%) were classified in iso-resource groups 1, 2, or 3.

Of the 480 patients included, 371 (77.3%) were symptomatic, the most common symptoms being thermal dysregulation (48.1%) and asthenia (47.9%), followed by dyspnea (35.6%), dry cough (27.7%), and anorexia (21.0%). Gastrointestinal symptoms and delirium were observed in 17.7 and 12.3% of the patients, respectively. ENT symptoms, falls and an altered level of consciousness were uncommon. The median duration of symptoms was 17.0 days (IQR 8.0-28.5; N=110). ~~Of the 480 patients, 370 had incomplete clinical data.~~

Laboratory and imaging findings following COVID-19 diagnosis

Table 1 shows the biological characteristics of 339 patients with many missing laboratory data. One hundred and forty-one patients (29.4%) did not have a blood test at diagnosis of infection.

182 Lymphopenia, neutropenia and thrombocytopenia occurred in 109 (32.2%), 23 (6.8%) and 40
183 (11.8%) patients, respectively. The median C-reactive protein was 26 mg/L (IQR 7-67).
184 Of the 461 patients (96.0%) who had an RT-PCR test, 446 (92.9%) tested positive for
185 COVID-19. Only 42 patients had chest CT scans during hospitalization. All the scans showed
186 anomalies supporting the diagnosis of COVID-19.
187
188 ***Treatments and clinical outcomes***
189 The median number of medications for pre-existing chronic illnesses was 7 (IQR 4-9.2).
190 Polymedication was present for 348 patients (72.5%).
191 With regard to treatment for suspected or confirmed COVID-19, 375 patients (78.1%)
192 received azithromycin. Of these, 117 (24.4%) also received hydroxychloroquine, and 346
193 (72.1%) a second antibiotic (penicillin (7.9%) or ceftriaxone (59.4%)). No patient received
194 antivirals or anti-inflammatory agents. Preventive anticoagulation was initiated in 203 patients
195 (42.3%). Moreover, 163 patients (34.0%) received oxygen therapy, while 220 (45.8%)
196 received intravenous or subcutaneous hydration.
197
198 One hundred and thirty-four residents (27.9%) were home hospitalized (Supplementary Table
199 A1). The reasons for home hospitalization were to offer hydroxychloroquine treatment
200 (79.9%), perfusion for hydration (11.2%) and end-of-life care (6.0%), provided by an external
201 team of specialists in the 15 participating NH.
202 Between 21 March and 20 May 2020, of the 463 (26.6%) patients still alive, 123 were
203 hospitalized. Fifteen of the 134 residents who received home hospitalization were
204 subsequently admitted to a hospital during this same period. The main cause for
205 hospitalization was respiratory distress syndrome (45.5%). Median time from symptom onset
206 to hospitalization was 5.0 days (IQR 2.0-10.0).

207 Ninety-six residents (20%) died over the study period: 42 in hospital and 54 in NH; 57
208 (11.9%) received end-of-life care. Median time from symptom onset to death was 12.0 days
209 (IQR 8.0-24.3). Death was attributed to COVID-19 in most cases (90.5%).
210
211 ***Factors associated with hospitalization and death***
212 Sixteen factors were associated with an increased risk of COVID-19-related hospitalization in
213 the univariate analysis (Table 2 and supplementary Table A2). In multivariable and competing
214 risk analyses, male gender (sHR 1.63, 95% CI 1.12-2.35; *p*=0.010), diabetes (sHR 1.69, 95%
215 CI 1.15-2.50; *p*=0,008), an altered level of consciousness (sHR 2.36, 95% CI 1.40-3.98;
216 *p*=0.001), and dyspnea (sHR 1.69, 95% CI 1.09-2.62; *p*=0.018) all remained associated with
217 an increased risk of hospitalization (Figure 1).
218 Twenty-two factors were associated with increased risk of mortality in univariate analysis
219 (Table 3 and see Supplementary Table A3). In the multivariable model, male gender (OR
220 6.63, 95% CI 1.04-42.39; *p*=0.001), thermal dysregulation (OR 2.64, 95% CI 1.60-4.38;
221 *p*=0.0001), falls (2.21 95% CI 1.02-4.75; p=0.043), and being aged >85 years old (OR 2.36
222 95% CI 1.32-4.24; p=0.004) were all independently associated with an increased risk of
223 mortality. Conversely, polymedication (OR 0.46, 95% CI 0.27-0.77) and preventive
224 anticoagulation (OR 0.46, 95% CI 0.27-0.79) were protective prognostic factors (Figure 1).
225
226

227 **DISCUSSION**

228 To our knowledge, this is the first multicenter study in France to describe a relatively large
229 cohort of older residents (mean age of 88 years) with suspected or confirmed COVID-19 in a
230 large number of nursing homes. Among the 480 residents included, 77.3% were symptomatic,
231 and 26.6% were hospitalized. Male gender, diabetes, an altered level of consciousness, and
232 dyspnea, were all associated with an increased risk of hospitalization. The overall mortality
233 was 20% during the study period. Being >85 years old, male gender, thermal dysregulation
234 and falls, were all associated with an increased risk of mortality.

235

236 In the literature, the number of deaths linked to COVID-19 in NH is unclear. In France, as of
237 1 June 2020, the mortality among NH residents with diagnosed COVID-19 was 27.4%. [19]
238 Sacco et al. [14] also found a 27% COVID-19 mortality diagnosed residents in their study of a
239 middle-sized nursing home in Maine-et-Loire, in the west of France. In the USA, McMichael
240 et al. found a mortality percentage of 33.7% in 101 residents in an NH in Washington,[10] while
241 more recently, Tang et al. [11] reported 20.6% COVID-19 mortality - which is closer to that in
242 our study- in 1970 residents in an NH in Maryland. With regard to hospitalization, 26.6% of
243 our study sample were admitted to hospital. In the literature, this percentage varies between
244 16 and 54.5%.[10,11,14,20]

245

246 To our knowledge, our cohort is the oldest (in terms of patients' age) described in the
247 literature.[7,8,11,21,22] Unsurprisingly, all studies have shown that older patients have a poorer
248 COVID-19 prognosis.[1,8,23,24–27] Furthermore, the present study is one of the first to investigate
249 prognostic factors associated with the risk of hospitalization and death in NH residents.
250 Unlike other French and international studies[10,14], we did not consider staff members' or
251 visitors' infectious status.

252 With regard to the factors listed above which were associated with hospitalization and death,
253 different studies on COVID-19 have found that men are significantly more likely to get the
254 disease than women[9,28], and that male gender is significantly associated with COVID-19-
255 related mortality.[8,21] Comorbidities including hypertension, diabetes, and
256 cardiovascular/respiratory diseases affect COVID-19 patient prognosis. In particular, diabetes
257 is associated with a higher risk of developing a severe form of the disease and admission to an
258 intensive care unit.[29,30] In Tang et al.'s study in Maryland, renal disease, diabetes and
259 depression were associated with an increased risk of hospitalization.[11] In line with the
260 literature [8,23,30], older age and comorbidities were significantly associated with death in our
261 study. Falls are an atypical symptom of COVID-19[14,31], and our study is the first to show an
262 association between falls and hospitalization of NH residents with confirmed or suspected
263 COVID-19. Unlike the literature[32], we found that polymedication was a protective factor
264 against death.
265
266 Most patients in our study sample were symptomatic, which reflects findings in the literature.
267 [8,21] Having said that, some studies have reported a substantial proportion of asymptomatic
268 patients.[11,33] We may have overestimated the proportion of symptomatic patients because we
269 took into account symptomatic residents who tested negative for a RT-PCR test after being in
270 contact with a confirmed COVID-19 case. Furthermore, the fact that France conducted
271 systematic screening campaigns in NH, limited the number of asymptomatic people not
272 screened. The most common COVID-19 symptoms in our study sample were thermal
273 dysregulation and asthenia, followed by respiratory symptoms. These symptoms are
274 consistent with previously reports. Anorexia, a common digestive symptom of many illnesses
275 in older patients[34], was present in 21% of residents in our study. ENT symptoms were present
276 in less than 10% of the residents, which reflects findings in the literature that anosmia and

277 ageusia are more frequently found in young patients.[5,35] Atypical presentation in older adults
278 may include gastrointestinal symptoms and geriatric syndromes complicating the diagnostic
279 pathway. Surprisingly, delirium was less frequent in our study than in previous studies on NH
280 adults[7,36], perhaps due to the fact that 84.6% of our study sample were diagnosed with
281 neurocognitive disorders and consequently, it may have been difficult to accurately attribute
282 symptoms to delirium or to underlying dementia.
283
284 With regard to COVID-19 management and treatment, 78.1% of our study sample received
285 azithromycin while 72.1% also received another antibiotic. Less than a quarter were
286 prescribed hydroxychloroquine. We found that azithromycin was independently associated
287 with a reduced risk of death in univariate analysis. However, larger studies have shown no
288 such benefit, and as of June 2020, this treatment was no longer recommended.[37,38] We found
289 no association between hydroxychloroquine and hospitalization or mortality. Recent clinical
290 data documented no benefit in patients treated with hydroxychloroquine, whether alone or in
291 combination with azithromycin, and warned about potential adverse effects.[37,39]
292 Almost half of our patients received preventive anticoagulation. It is very likely that many of
293 the others had previously had anticoagulation treatment. Preventive anticoagulation was
294 recommended because of frequent thromboembolic events in cases of COVID-19.[40]
295 Preventive anticoagulation was associated in our multivariable analysis with a reduced risk of
296 death, which reflects previous findings .[22]
297
298 Our study has limitations. First, despite its multicenter design, it only included residents in the
299 greater metropolitan area of one city - Marseille - and only from 15 out of 20 nursing homes
300 which agreed to participate (as the other five had no suspected or confirmed COVID-19 case).
301 Although relatively large, the size of the cohort might have prevented some specific clinical

302 symptoms from being highlighted and limited the identification of all prognostic factors.
303 Furthermore, because of its retrospective design, the study had missing data. The missing data
304 were primarily laboratory data, limiting the study's ability to draw conclusions about
305 laboratory-base predictors of outcomes. We selected only variables which were most relevant,
306 and which had few missing data for the multivariable analysis. In addition, only hospitalized
307 patients had chest CT scans. With regard to the investigation of risk factors of hospitalization,
308 we included only residents hospitalized from 21 March 2020 onwards (i.e., three weeks after
309 the study start date), as this was the date that French Public Health Authorities facilitated
310 hospitalization for NH residents throughout the country. Before this date, the advice given
311 was to provide residents with care in their NH (NH-staff based care, and, when possible,
312 home hospitalization), and to only transfer those with severe and critical forms of COVID-9
313 to hospital. Home hospitalization in NH continued even after 21 March 2020.
314 Finally, it is important to underline that our results reflect the specific French healthcare and
315 NH context regarding COVID-19 management, and cannot be extrapolated to other countries.
316

317 **Conclusions and Implications**

318 This is the largest retrospective multicenter cohort study of NH residents with suspected or
319 confirmed COVID-19 to date in France. Furthermore, our cohort is the oldest (in terms of
320 residents' age) in the literature. A minority of older residents had uncommon, atypical
321 symptoms of COVID-19. These were not associated with poor prognosis. Male gender,
322 diabetes, an altered level of consciousness, and dyspnea were all associated with an increased
323 risk of hospitalization in this frail population. Multivariable regression also showed that male
324 gender, thermal dysregulation, falls and being aged > 85 years old, were all associated with an
325 increased risk of death. Anticoagulation was a protective factor against death.
326 While dyspnea is a precursor to hospitalization, in NH residents, the risk of COVID-19-
327 related mortality was linked to demographic data and the occurrence of falls, and these factors

should be considered when caring for COVID-19-diagnosed NH residents in order to improve prognosis.

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Appendix 1

Table A1: Characteristics of the 134 residents who benefited from 'home hospitalization'

Appendix 2

Table A2: Variables not associated with an increased risk of hospitalization: univariate analysis of the 123/463 persons hospitalized

Appendix 3

Table A3: Variables not associated with an increased risk of hospitalization: univariate analysis of the 96/480 persons who died

Figure 1: Multivariable analysis of hospitalizations with competing risk (463 residents) and deaths (480 residents)

496 **Table 1**. Characteristics of the study sample (n=480)

Characteristics	N or Median (IQR)	% or [min-max]	Missing data
Age (years)	88 (80-93)	[65-105]	-
65-74	67	14.0	
75-84	112	23.3	
85-94	213	44.4	
95-105	88	18.3	
Gender Male	150	31.3	-
Female	330	68.8	
Nutrition*Undernutrition	186	38.8	-
Status Obesity	43	9.0	-
Polymedication≥5 drugs for pre-existing conditions	348	72.5	-
Vaccinated for Flu	379	79.0	-
Pneumococcus	188	39.2	-
Comorbidities			
Cognitive impairment**	406	84.6	-
Hypertension	257	53.5	-
Dyslipidemia	31	6.5	-
Type 2 diabetes	86	17.9	-
Cerebrovascular disease	95	19.8	-
Coronaropathy	70	14.6	-
Congestive heart failure	71	14.8	1
Atrial fibrillation	91	19.0	-
Asthma	11	2.3	-
Chronic obstructive pulmonary disease	51	10.6	-
Chronic respiratory insufficiency	16	3.3	-
Depression	216	45.0	-
Psychiatric disorders	51	10.6	-
Chronic kidney disease	69	14.4	-
Cancer history	31	6.5	-
Iso-resource groups 1	102	21.3	3
2	228	47.5	
3	78	16.3	
4	61	12.7	
5 and 6	8	1.7	
Hospitalization*** In COVID-19 unit	123	26.6	-
Home hospitalization	134	27.9	-
End-of-life care	57	11.9	-
Death In COVID-19 unit	42	8.5	-

Characteristics	N or Median (IQR)	% or [min-max]	Missing data
Symptoms	371	77.3	-
Dyspnea	171	35.6	-
Dry cough	133	27.7	-
Thermal dysregulation	231	48.1	-
Fever	217	45.2	-
Asthenia	230	47.9	-
Anorexia	101	21.0	-
Gastrointestinal symptoms	85	17.7	-
Myalgia or arthralgia	14	2.9	-
Headaches	8	1.7	-
ENT symptoms	40	8.3	-
Falls	39	8.1	-
Delirium	59	12.3	-
Worsening depression	27	5.6	-
Altered level of consciousness	32	6.7	-
Positive RT-PCR test result	446	92.9	-
Laboratory findings	339	70.6	-
Red blood cells (G/L)[1]	4 (4-5)	[2-6]	164
White blood cells (G/L)[2]	6 (4-7)	[2-20]	162
Neutrophils (G/L)[3]	4 (3-5)	[1-21]	165
Neutropenia****	23	6.8	165
Lymphocytes (G/L)[4]	1 (1-2)	[0-7]	164
Lymphopenia****	109	32.2	164
Thrombocytopenia****	40	11.8	443
AST (UI/L)[6]	25 (20-36)	[11-147]	344
ALT (UI/L)[7]	14 (10-21)	[5-68]	344
AP (UI/L)[8]	76 (66-86)	[35-338]	410
GGT (UI/L)[9]	27 (15-39)	[6-313]	353
Bilirubin (µmol/L)[10]	6 (4-8)	[2-20]	413
Creatinine (µmol/L)[11]	77 (64-107)	[64-107]	175
GFR (ml/min)[12]	41.1 (29.8-57.5)	[5.2-174.4]	178
Potassium (mmol/L)[14]	4 (4-4)	[2-7]	166
Sodium (mmol/L)[13]	140 (138-143)	[125-173]	168
D dimer (µg/L)[15]	911 (680-1476)	[215-32463]	381
CPK (UI/L)[16]	74 (42.3-225.3)	[13-4036]	398

In nursing home	54	11.3		CRP (mg/L)[5]	26 (7-67)	[0-350]	169

[1] (normal range: 4.4-5.7), [2] (normal range: 3.9-10.9), [3] (normal range: 1.7-7.1), [4] (normal range: 1.1-3.2), [5] (normal range: 0-10), [6] (normal range: 0-50), [7] (normal range: 0-50), [8] (normal range: 35-130), [9] (normal range: 0-60), [10] (normal range: 0-21), [11] (normal range: 60-104), [12] (normal range: >60), [13] (normal range: 136-145), [14] (normal range : 3.4-4.5), [15] (normal range: 0-500), [16] (normal range: 10-200)

N = number, IQR = interquartile range

- = no missing data

*Undernutrition was defined as body mass index < 21; obesity was defined as body mass index ≥ 30
**Cognitive impairment was defined as a score of <24 for the Mini-Mental State Examination (MMSE) test or the presence of cognitive impairment symptoms (wandering, hallucination, hostility/aggressiveness or cognitive disorder history)
***of the 463 residents still alive on 21 March, 2020 (17 patients died between 1 March and 21 March 2020)
**** Neutropenia was defined as a neutrophil level <1.5 G/L; lymphopenia was defined as a lymphocyte level <1.0 G/L, and thrombocytopenia was defined as a platelet level < 150 G/L
ENT = ear, nose and throat; CRP = C-reactive protein; AST = aspartate aminotransferase; ALT = alanine aminotransferase; AP = alkaline phosphatase; GGT = gamma glutamyl transferase; GFR = glomerular filtration rate; CPK = creatine phosphokinase; RT-PCR = reverse transcriptase-polymerase chain reaction

547 **Table 2.** Variables associated with an increased risk of hospitalization: univariate analysis of 123
548 hospitalizations in 463 residents
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Variables	Total N=463 (%)	Not hospitalized N=340 (%)	Hospitalized N=123 (%)	sHR	CI 95%	*p*
Gender (male)	318 (68.7)	248 (72.9)	70 (56.9)	1.77	[1.25-2.52]	0.001
Comorbidities						
Cognitive impairment *	391 (84.4)	280 (82.4)	111 (90.2)	1.81	[1.00-3.29]	0.050
Type 2 diabetes	84 (18.1)	48 (14.1)	36 (29.3)	2.03	[1.39-2.95]	<0.0001
Congestive heart failure	70 (15.1)	42 (12.4)	28 (22.8)	1.88	[1.23-2.87]	0.003
Atrial fibrillation	88 (19.0)	57 (16.8)	31 (25.2)	1.55	[1.03-2.32]	0.034
Symptoms	365 (78.8)	252 (74.1)	113 (91.9)	3.38	[1.77-6.43]	<0.0001
Dyspnea	163 (35.2)	96 (28.2)	67 (54.5)	2.51	[1.77-3.57]	<0.0001
Thermal dysregulation	222 (47.9)	147 (43.2)	75 (61.0)	1.83	[1.28-2.62]	0.001
Gastrointestinal symptoms	82 (17.7)	52 (15.3)	30 (24.4)	1.61	[1.07-2.42]	0.021
Altered level of consciousness	32 (10.9)	12 (3.5)	20 (16.3)	3.34	[2.12-5.26]	<0.0001
Biology						
CRP (IQR)	26.0 (7.0-68.0)	18.0 (5.0-56.8)	35.0 (13.0-120.0)	1.01	[1.00-1.01]	<0.0001
High CPK level	21 (4.5)	8 (2.4)	13 (10.6)	1.98	[1.00-3.88]	0.050
AST (IQR)	25.0 (20.0-36.0)	22.0 (18.0-29.0)	30.0 (23.0-55.8)	1.03	[1.02-1.03]	<0.0001
Treatment						
Antibiotics (except azithromycin)	329 (71.1)	227 (66.8)	102 (82.9)	2.09	[1.30-3.37]	0.002
Hydration	210 (45.4)	140 (11.8)	70 (56.9)	1.67	[1.17-2.38]	0.004
Oxygen therapy	153 (33.0)	83 (24.4)	70 (56.9)	3.13	[2.20-4.46]	<0.0001
Aerosol	11 (2.4)	5 (1.5)	6 (4.9)	2.03	[1.07-3.83]	0.029
Contraindications	46 (9.9)	27 (7.9)	19 (15.4)	1.81	[1.12-2.92]	0.014

550
551 sHR = specific hazard ratio
552 *Cognitive impairment was defined as a score < 24 according to the Mini-Mental State Examination (MMSE) test, or the presence of
553 cognitive impairment symptoms (wandering, hallucination, hostility/aggressiveness or cognitive disorder history)
554 N = number, IQR = interquartile range
555 High CPK level was defined as CPK > 200 UI/L
556 CRP = C-reactive protein; AST = aspartate aminotransferase; CPK = creatine phosphokinase
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570 **Table 3.** Variables associated with an increased risk of mortality: univariate analysis of 96 deaths in
571 480 residents
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Variables	Total N=480 (%)	Survived N=384 (%)	Deceased N=96 (%)	OR	CI 95%	*p*
Age > 85 years	301 (62.7)	228 (59.4)	73 (76.0)	2,17	[1.30-3.62]	0.003
Gender (male)	145 (31.3)	92 (27.1)	53 (43.1)	2.04	[1.33-3.14]	0.001
Polymedication ≥5 drugs for pre-existing comorbidities	348 (72.5)	291(75.8)	57 (59.4)	0.47	[0.29-0.75]	0.001
Comorbidities						
Dyslipidemia	31 (6.5)	19 (4.9)	12 (12.5)	2.74	[1.28-5.87]	0.009
Atrial fibrillation	91 (19.0)	66 (17.2)	25 (26.0)	1.70	[1.00-2.88]	0.049
Psychiatric disorders	51 (10.6)	47 (12.2)	4 (4.2)	0.31	[0.11-0.89]	0.029
Chronic kidney disease	69 (14.4)	48 (12.5)	21 (21.9)	1.96	[1.11-3.47]	0.021
Symptoms	371 (77.3)	280 (72.7)	91 (95.8)	15.89	[3.84-65.68]	<0.0001
Dyspnea	171 (35.6)	110 (28.4)	62 (64.6)	4.60	[2.87-7.9]	<0.0001
Thermal dysregulation	231 (48.1)	167 (43.5)	64 (66.7)	2.6	[1.62-4.16]	<0.0001
Falls	39 (8.1)	26 (6.8)	13 (13.5)	2.16	[1.06-4.38]	0.033
Altered level of consciousness	32 (6.7)	20 (5.2)	12 (12.5)	2.60	[1.22-5.53]	0.013
Biology						
GFR (IQR)	41.1 (29.8-57.5)	43.2 (32.2-58.9)	32.0 (17.5-49.3)	0.98	[0.97-0.99]	0.004
CRP (IQR)	26.0 (7.0-67.0)	18 (5.0-53.3)	80 (31.0-150.0)	1.02	[1.01-1.02]	<0.0001
High CPK level	22 (26.8)	8 (14.8)	14 (50.0)	5.75	[2.00-16.51]	0.001
AST (IQR)	25.0 (20.0-36.0)	23.0 (18.5-32.0)	35.0 (24.0-60.0)	1.03	[1.01-1.05]	0.002
Treatment						
Azithromycin	375 (78.1)	308 (80.2)	67 (69.8)	0.57	[0.35-0.94]	0.028
Hydration	220 (45.8)	154 (40.1)	66 (68.8)	3.29	[2.04-5.30]	<0.0001
Preventive anticoagulation	203 (42.3)	175 (45.6)	28 (29.2)	0.49	[0.30-0.80]	0.004
Oxygen therapy	163 (34.0)	94 (24.5)	69 (71.9)	7.88	[4.77-13.03]	<0.0001
Hospitalization	128 (26.7)	84 (21.9)	44 (45.8)	3.02	[1.89-4.83]	<0.0001

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574 OR = odds ratio
575 N = number, IQR = interquartile range
576 High CPK level was defined as CPK > 200 UI/
577 CRP = C-reactive protein; AST = aspartate aminotransferase; GFR = glomerular filtration rate
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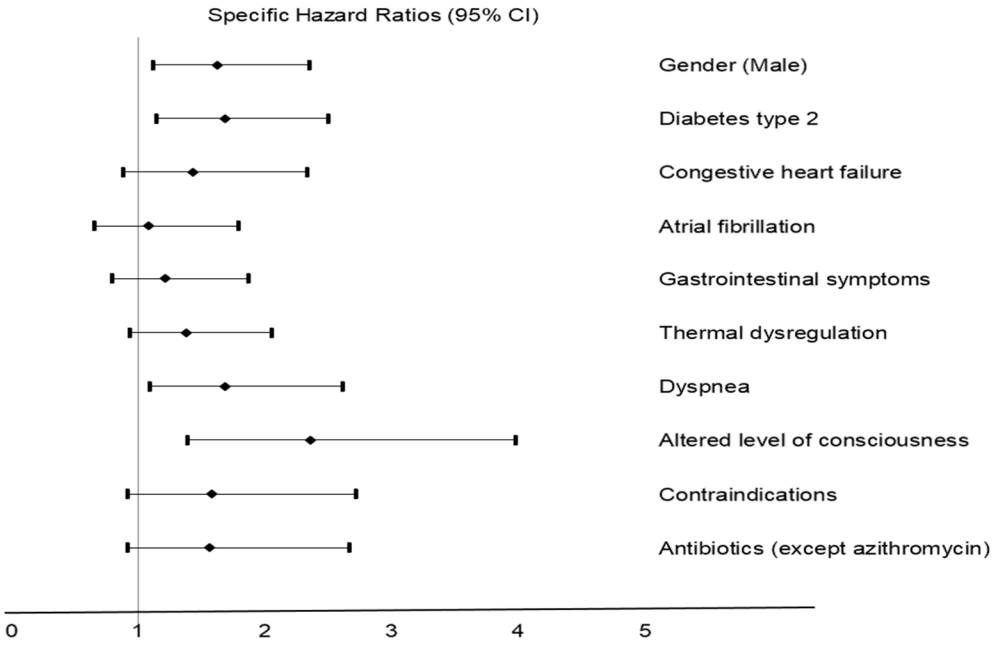
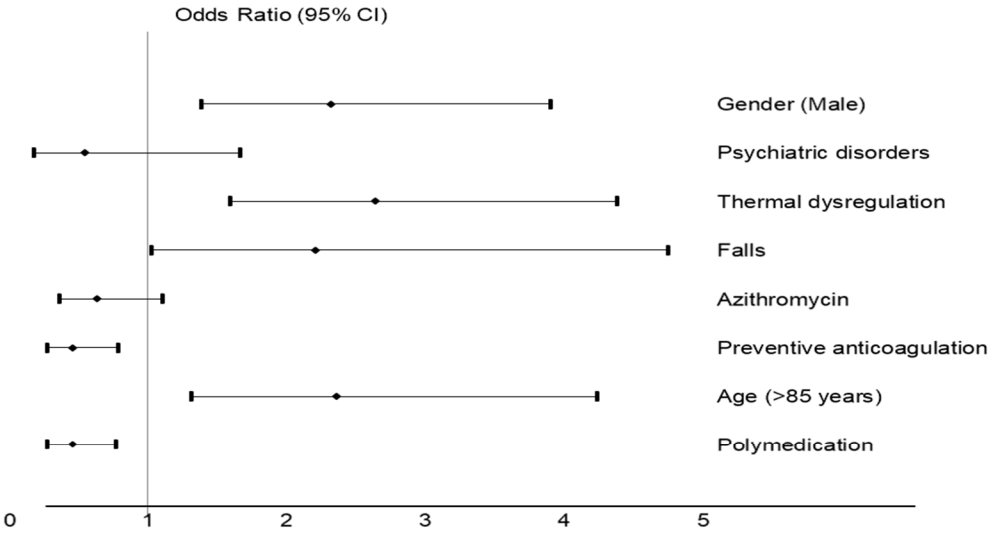
Multivariate analysis of factors associated with time to hospitalization with death as competitive risk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