

A world apart: levels and determinants of excess mortality due to COVID-19 in care homes. The case of the Belgian region of Wallonia during the spring 2020 wave.

Olivier J Hardy¹, Dominique Dubourg², Mélanie Bourguignon², Simon Dellicour^{4,5}, Thierry Eggerickx², Marius Gilbert⁴, Jean-Paul Sanderson³, Aline Scohy⁶, Eline Vandael⁶, Jean-Michel Decroly⁷

Affiliations:

1 Evolutionary Biology and Ecology, Université Libre de Bruxelles, BE-1050 Brussels, Belgium

2 Direction de la recherche, de la statistique et de la veille des politiques, Agence pour une Vie de Qualité, BE- 6061 Charleroi, Belgium

3 Centre for Demographic Research, UCLouvain, BE-1348 Louvain-la-Neuve, Belgium

4 Spatial Epidemiology Lab (SpELL), Université Libre de Bruxelles, CP160/12, 50, av. FD Roosevelt, 1050 Bruxelles, Belgium

5 Department of Microbiology, Immunology and Transplantation, Rega Institute, KU Leuven, Herestraat 49, 3000 Leuven, Belgium

6 Department of Epidemiology and public health, Sciensano, BE-1050 Brussels, Belgium

7 Institut de Gestion de l'Environnement et d'Aménagement du Territoire (IGEAT), Université Libre de Bruxelles, CP130/03, 50, av. FD Roosevelt, BE-1050 Brussels, Belgium

Abstract

BACKGROUND: In Western countries, COVID-19 has been particularly deadly for care home residents.

OBJECTIVE: Understand the roles of the age and sex structures, health frailty and contamination dynamics on COVID-19 mortality in populations living inside and outside care homes.

METHODS: We compared COVID-19 death data recorded in March-June 2020 in Wallonia (southern Belgium) for populations living inside and outside care homes, using annual death data (2017) to assess the health condition of each population.

RESULTS: 64% of COVID-19 deaths were residents of care homes where the outbreak started after but at a faster pace than in the external population. Death rate varied from 0‰ to 340‰ (mean 43‰) per care home, increasing with both the number of residents and staff. Annual and COVID-19 mortality rates increased exponentially with age but were much higher in care homes. The ratio of M/F death rates was 1.6 for annual mortality and 2.0 for COVID-19 mortality (both confirmed and suspected). The COVID-19 mortality reached 24% (M) and 18% (F) of the annual mortality rate in care homes, for 5% (M) and 4% (F) outside care homes.

CONCLUSIONS: COVID-19 mortality rate was 130x higher inside than outside care homes due to the multiplicative effects of differences in the age and sex structure (11x), health frailty (3.8x), and infection risks (probably 3.5x) of its residents.

CONTRIBUTION: Care homes should be treated as a very specific population for epidemiological studies due to their extreme vulnerability to COVID-19.

Keywords: coronavirus, mortality rate, nursing homes, gender, age, Belgium

1. Introduction

Since its appearance in China by the end of 2019, the COVID-19 pandemic is known to cause higher mortality in males than females and among older people (Dudel et al. 2020, Medford & Trias-Llimós 2020, Wenham et al. 2020), as well as in people suffering from various comorbidity factors (Nepomuceno et al. 2020). In Europe and North America, COVID-19 has had a dramatic impact on people living in care homes (Comas-Herrera et al. 2020, ECDC 2020, Fisman et al. 2020, Ladhani et al. 2020, Petretto & Pili 2020), although one of the first policy applied to contain the outbreak was to ban family visits in care homes (Comas-Herrera, Ashcroft and Lorenz-Dant 2020, Verbeek et al. 2020). The high incidence of COVID-19 in care homes is likely related to the everyday contacts with the nursing personal, facilitating contagion (Arons et al. 2020, Ladhani et al. 2020), especially as many countries failed to provide sufficient personal protective equipment (PPE) for care homes at the beginning of the pandemic, usually concentrating the protections in limited supply (e.g. surgical masks and gloves) to hospitals (Logar 2020 for Italy, Rada 2020 for Spain, Quigley et al. 2020 for the United States, Szczerbińska 2020 for an international comparison). However, to assess if mortality rate due to COVID-19 was higher in care homes, it is important to factor out the age and sex effects, care homes being mostly populated by old people and also over-represented by women (Einiö et al. 2012). It is also important to take into account the health frailty of the population living in care homes (Falconer and O'Neill 2007), since people often enter care homes due to a deteriorating health status (Herm, Poulain and Anson, 2014) and that care home residents tend to have a lower social status than the rest of the population (Laferrère et al. 2013). Finally, distinguishing different categories of care homes according to their size or the types of health assistance they provide to their residents could be instructive to compare how COVID-19 affected populations differing by their general health frailty and/or by the risk of contamination through nursing services.

As PCR testing capacities were also strongly limited at the beginning of the outbreak, there was often a lack of test to assess whether deaths occurring within care homes resulted from COVID-19. In some countries like Belgium, the reporting of COVID-19 deaths by national authorities has been inclusive, including people suspected to have died from COVID-19 due to characteristic symptoms despite the absence of PCR testing (Comas-Herrera et al., 2020). The excess of deaths in spring 2020 compared to previous years according to national register data gave clear support to this inclusive approach (Sciensano 2020c; Bustos Sierra et al., 2020). From 8 March to 9 May 2020, during the most intense phase of the epidemic in terms of mortality, 8,735 COVID-19 deaths (confirmed and suspected) were recorded in Belgium, while over the same period an excess mortality of 8,280 deaths was recorded in the National Register (a difference of 455 deaths, barely 5% less) compared to the average mortality of 2015-19. However, it has been suggested that social isolation and the stress caused by anxiety could strongly affect elderly people during lockdown (Armitage & Nellums, 2020) and might also have been responsible for a substantial portion of excess mortality in nursing homes (Trabucchi and De Leo 2020). Although it is extremely hard to identify retrospectively the cause of death, we can expect that if COVID-19 mortality rate is affected by age and sex

following a particular pattern, COVID-19 suspected deaths should display the same pattern as COVID-19 confirmed deaths whenever the diagnose was correct.

Our objective is to characterize mortality resulting from COVID-19 in two different populations: residents of care homes for elderly people and the rest of the population, while accounting for age and sex effects as well as the general health status of each population. We focus on Wallonia, a region of southern Belgium, because we have good quality data on COVID-19 death as well as annual death data in care homes. First, we show the overall contrasts in mortality by COVID-19 between populations living in and out of care homes, as well as the variations in mortality between care home institutions according to the importance of medical assistance (distinguishing nursing homes from residential homes) and their size. We also compare the temporal dynamics of mortality in and out of care homes because we hypothesize (i) that the outbreak in care homes started after the one occurring outside care homes if infections originated from the nursing personal, and (ii) that the potentially high contagion within care homes might have caused a more rapid spread of the virus. To ensure that our results are not biased by strong geographic patterns, we assess the spatial autocorrelation of mortality rate per care home. Second, we seek to explain the mortality differential within and outside care homes through two factors: differences in structure by age and sex (structure effect) and differences in COVID-19 age and sex-specific death (health condition effect). We verify whether the age effect follows Gompertz exponential law, which can reflect vulnerability to external causes (Ricklefs & Scheuerlein 2002), and whether the sex effect deviates from the one observed for annual mortality. We attempt to explain the health condition effect, which results from (i) the unequal incidence of the disease in the populations being compared (infection effect) and (ii) the greater or lesser vulnerability of individuals once they have contracted the SARS-CoV2 (frailty effect). The latter can be approximated by the usual level of mortality, outside of the COVID-19 health crisis, in the populations studied. In the absence of systematic testing, it is not possible to measure the unequal incidence of the disease in the populations compared. However, we show that it is possible to estimate it by comparing mortality caused by COVID-19 and annual mortality because the two are tightly correlated in each population. Through these different analyses we provide a better understanding of the key factors at the origin of the high incidence of COVID-19 on the mortality in care homes.

2. Materials and Methods

2.1 Area of interest and institutional context related to care homes

Due to data availability of both COVID-19 and annual deaths, we focus on the French-speaking part of Wallonia in southern Belgium (i.e. the Walloon Region without the municipalities attached to the German-speaking community of eastern Wallonia). In this area, comprising c. 3.6 million inhabitants, all residential facilities for elderly people (FE)¹ are supervised by the

¹ The terms used here to designate different categories of care homes are those indicated on the Healthy Belgium website of the Belgian federal government (<https://www.healthybelgium.be/en/health-system-performance-assessment/specific-domains/care-for-the-elderly>)

regional administration AViQ (“Agence pour une Vie de Qualité”, <https://www.aviq.be>) which collected statistics regarding COVID-19 deaths, and performed recurrent systematic surveys on yearly mortality, the last one occurring in 2017. For some analyses, among FE we distinguish homes for elderly people (HEP), which host essentially old people who require assistance for daily meals, housekeeping and/or daily toilet but do not require substantial health care, and nursing homes (NH), which host essentially old people with the same needs as HEP residents but also people requiring additional health care due to more or less severe pathologies. According to the standards established by the *Code réglementaire wallon de l’Action sociale et de la Santé*, the number of nursing staff for 30 residents is 4.5 in HEP against 12.1 in NH. The latter must also have at least five nurses, one coordinating doctor and 0.1 full-time equivalent specialist in palliative care. NH also have written procedures for hand hygiene and the isolation of residents with an infection that carries a risk of contamination. On average, approximately half of the bed capacities of NH is devoted to host residents requiring health care services. In this paper, the residents in FE will be referred to as the FE population and the rest of the population living in the French-speaking part of Wallonia as the OUT-FE population.

2.2 COVID-19 mortality data

Our analysis of mortality by COVID-19 in and out of FE covers the period between March 13 and June 30, 2020. Our data came from two sources. First, AViQ collected death data attributed to COVID-19 as reported by all 573 FE (446 NH and 127 HEP) existing in 2020 (data including death date, age and sex, which concerned only long-term residents). These deaths occurred essentially in hospitals (28% of cases), in which case a PCR and/or scanner test confirmed the COVID-19 diagnostic, or within NH or HEP institutions (72% of cases) where tests were available for only 27% of cases so that the majority of these cases are suspected to result from COVID-19, following the diagnosis of the attending physician and given the presence of characteristic symptoms (upper or lower respiratory tract infection, fever or chills, cough, shortness of breath or difficulty breathing, headache, new loss of taste or smell, etc; Dequeker et al. 2020). Second, Sciensano, the Federal Institution responsible for Health monitoring in Belgium (<https://www.sciensano.be>), collected COVID-19 related deaths data reported by hospitals and other settings, such as the monitoring care home agencies (including AViQ). We extracted from their dataset all COVID-19 related deaths (suspected and confirmed) reported in Wallonia (excluding the German-speaking municipalities). The Sciensano dataset considers the place of death, rather than the place of residence, to distribute deaths among Belgian regions. However, according to partial data on the place of residence of deaths, less than 1% of deaths occurring in the Brussels or Walloon regions concerned people residing in another region, so that we neglected these cases.

To assess the heterogeneity of COVID-19 mortality among institutions, the crude COVID-19 death rate per institution was computed by dividing the number of reported deaths by the total bed capacity of the institution. This ratio underestimates the actual mortality rate but should remain realistic given that >90% of the bed capacity was usually occupied at the

beginning of the outbreak. By institution, we here considered a physical site that received a particular approval number in the AViQ database, although some sites are managed by the same administrative entity. We tested if there was a spatial pattern in mortality by computing Moran's I statistic on crude death rate per FE institution, using binary weight matrices for institutions separated by the following distance intervals 0-10, 10-20, 20-50, 50-100 or >100 km.

To characterize the temporal dynamics of COVID-19 deaths from 13 March until 30 June 2020, we computed the cumulated number of deaths for FE residents and for the OUT-FE population (by subtracting the AViQ data from the Sciensano data for Wallonia). To assess the delay and pace of the outbreaks that occurred in each population, we also computed the median date at which people from each population died (i.e. when 50% of all deaths occurred) as well as the dates corresponding to the 0.05 and 0.95 quantiles.

To assess the age and sex effects, COVID-19 Sex-Age-Specific Death Rates (SASDR) were computed per sex and 5-years age classes, separately for the FE and OUT-FE populations, as the ratio of the number of COVID-19 deaths over the corresponding age and sex-specific population sizes estimated on January 1, 2020. For FE, these population sizes were derived from the population survey established on January 1, 2018, by AViQ (see below). This survey provides more reliable data on the FE population than the data on collective household² from the National Population Register because some residents in FE remain domiciled in their former place of residence, which leads to an underestimation of the FE population by the National Register. To estimate the population by age in FE on 1/1/20, a multiplication factor reflecting the change in total bed capacities between January 1, 2020, and January 1, 2018 was applied to the data for 1/1/18 (factor of $42103/40852 = 1.031$ for NH and $6249/6865 = 0.910$ for HEP). While this estimate may seem a bit tricky, since it keeps the age structure of the FE population constant and thus does not take into account possible cohort effects (e.g. the cohorts born in the early 1940s are smaller than the cohorts born in the late 1930s or late 1940), it does not alter the results. Indeed, National Population Register data on people living in collective households show that their age structure has remained almost constant between 2018 and 2020: for the age and sex groups 65 and older the difference in proportion between the two dates is still less than 1.3 percentage points. For the OUT-FE population, we used the StatBel data (<https://statbel.fgov.be>), based on the National Register, which provided the population size disaggregated by age and sex for our focal area on January 1, 2020, and subtracted the FE population.

2.3 Annual mortality data in 2017

We compared the overall health frailty of each population using their respective SASDR before the COVID-19 epidemic. AViQ conducted a survey in 2017 asking each of the 587 FE (440 NH and 147 HEP) existing that year to report deaths (including birth and death dates) throughout

² In Belgium, collective households are groups of more than two people living at the same address. They include the population residing in orphanages, prisons, religious communities and residences for elderly people.

the year, and to report their population on January 1, 2018. Here, we considered only deaths and population of long-term residents, excluding people that registered for revalidation short-stays (typically less than a month). Overall, in terms of bed capacities, 93.3% of NH and 84.8% of HEP provided their population statistics, and respectively 91.3% and 83.2% reported their 2017 deaths. Sex and age data were available for at least 98% of the people in each case. To correct raw numbers, they were divided by the proportion of responding institutions (in bed equivalents) and by the proportion of complete sex and age data, so that incomplete data were reported across all age by sex categories.

We extracted from StatBel population statistics the population on January 1, 2018, as well as the number of deaths during 2017, disaggregated by age and sex, for our focal area. From this overall population and death numbers, we subtracted the corresponding estimated numbers for FE (based on the AViQ 2017 survey) to estimate the population and associated deaths of people living outside of care homes, i.e. the OUT-FE population. In total, 37,131 deaths (17,978 men, 19,153 women) were recorded in 2017, which concerned FE residents for 22% of males (M) and 45% of females (F). Although the OUT-FE population parameters were obtained from residuals, subtracting approximated FE population parameters, bias is not expected given that FE residents constitute a minority of all deaths.

Annual SASDR were then computed for 5-years age categories by sex, separately for each population (OUT-FE and FE in which we also distinguished NH and HEP), by dividing the number of deaths occurring in 2017 by the population size on January 1, 2018.

2.4 Analytical strategy

The distribution of COVID-19 death rate per institution was established separately for NH and HEP, and within each type of institution separately for the smallest and largest institutions in terms of bed capacity. The criterion used to distinguish small and large institutions is where approximately half of the residents of a particular institution type (NH or HEP) live. We used Mann-Whitney U tests to assess whether the medians of these distributions differ.

As the FE and OUT-FE populations are expected to differ substantially in their age and sex composition, we established their age pyramids using population data on January 1, 2020, and used standardized mortality rates to compare them. For each population, COVID-19 SASDR per 5-years classes (m) were computed. Because the size of the HEP population is relatively small, COVID-19 SASDR often lack sufficient precision, so that we generally report them for FE (i.e. NH + HEP) only, and highlight differences between NH and HEP on overall mortality rates because the two populations have very similar age pyramids.

COVID-19 SASDR were represented on a log scale against the mid-age (a) of each class, and adjusted on an exponential function (i.e. Gompertz law) restricted to age classes between 65 and 99 years (to avoid classes with too small population sizes): $m = c.e^{b.a}$, where b and c are the adjusted coefficients. We estimated the number of years leading to a doubling of m as $\ln(2)/b$. We used Fisher distribution to compute 95% confidence intervals of mortality rates

following Ars et al. (1988) as the interval between $\frac{X}{(X+(n-X+1)F_{2(n-X+1),2X,0.975})}$ and $\frac{(X+1)F_{2(X+1),2(n-X),0.975}}{(n-X+(X-1)F_{2(X+1),2(n-X),0.975})}$, where X and n represent the age and sex-specific death number and population size, respectively, and $F_{d1,d2,\alpha}$ represents Fisher's distribution at level α with $d1$ and $d2$ degrees of freedom. The same procedure was applied on annual mortality rates.

To assess the (age and sex) structure and the health condition effects on the mortality differential by COVID-19 within an outside FE, a multiplicative decomposition of Crude COVID-19 Death Rate (CCDR) ratio was applied (Miettinen 1972, Keiding & Clayton 2014). According to this method, the ratio of the CCDR within FE and the CCDR outside FE is the product of the indirect Standardized Mortality Ratio in FE (SMR_FE) and a confounding risk ratio. The first one is obtained by dividing the CCDR within FE and the expected CCDR in FE if its population had experienced the COVID-19 SASDR of the population outside FE (ExpCCDR_FE). It can be interpreted as a factor that reflects differences in health conditions (frailty) between populations living in and out of care homes. The confounding risk ratio is obtained by dividing the ExpCCDR_FE and the CCDR observed outside FE. It measures the effect of differences in age and sex structure on the crude rate ratio. Finally, to attempt to factor out the effect of the general health condition of a particular population on COVID-19 mortality, we divided COVID-19 SASDR by the respective annual death rates. We then compared these ratios among populations to tentatively interpret them in terms of relative COVID-19 infection rates.

2.5 Interpretation of death rates

Computing classical demographic rates on mortality in FE is complicated due to the high turnover of people and the availability of death data for only a single year. However, with an increase of overall bed capacities of only 0.6% between 2017 and 2018 and the fact that c. 98.3% of beds are occupied, we can consider that the FE population is stable during a single year. Therefore, while the annual mortality rates computed overestimate the probability that a FE resident dies within a year, they can be interpreted as 365 times the probability that a FE resident dies within a day. They are thus proportional to the instantaneous rate of mortality (the so-called force of mortality) and as such represent adequate measures of the average health status of a particular age and sex category.

The situation is different for COVID-19 mortality rates because once the epidemic started in March 2020, FE institutions usually did not reintegrate new residents to replace their free beds until mid-June. We also ignore how many residents left their institution and were host in their family. Hence, COVID-19 death rates in FE must be somewhat underestimated.

3. Results

In the French-speaking part of Wallonia, between March 13 and June 30, 2020, COVID-19 caused a total of 2,126 deaths in FE (2010 in NH, 116 in HEP) and 1,195 deaths in the OUT-FE population (Table 1). Hence, 64% of the suspected and confirmed deaths of COVID-19 occurred in FE, even though the population living in these institutions constitutes barely 1.3%

of the Walloon population. Consequently, the crude COVID-19 death rates are extremely contrasted. They reach 44.2‰ in FE against 0.34‰ outside FE, i.e. a ratio of 1 to 130.

Table 1. Descriptive statistics about COVID-19 outbreak in Wallonia (excluding the German-speaking municipalities). (a) Population (January 1, 2020), (b) COVID-19 deaths from March 13 to June 30 2020, and (c) crude COVID-19 death rates (per 1,000 people), in residential facilities for elderly people (FE), including nursing homes (NH) and homes for elderly people (HEP), and in the rest of the population (OUT-FE). Statistics given for the whole population and the population aged 65 and more. Data sources: StatBel, AViQ.

a : Population (January 1, 2020, in thousands)								
	Total				65+			
	Both sexes		Females		Both sexes		Females	
	x 1,000 persons	%	x 1,000 persons	% both sexes population	x 1,000 persons	% total population	x 1,000 persons	% both sexes population
FE	48	1.3	36	74.6	46	95.1	35	76.2
NH	42	1.2	31	74.5	40	95.2	30	76.1
HEP	6	0.2	5	74.7	6	94.2	5	76.4
OUT-FE	3,519	98.7	1,788	50.8	626	17.8	349	55.7
Wallonia	3,567	100.0	1,824	51.1	672	18.8	384	57.1

b : COVID-19 deaths (March 13 to June 30, 2020)								
	Total				65+			
	Both sexes		Females		Both sexes		Females	
	persons	%	persons	% of both sexes deaths	persons	% of total deaths	persons	% of both sexes deaths
FE	2,126	64.0	1,354	63.7	2,090	98.3	1,339	64.1
NH	2,010	60.5	1,276	63.5	1,975	98.3	1,261	63.8
HEP	116	3.5	78	67.2	115	99.1	78	67.8
OUT-FE	1,195	36.0	478	40.0	1,001	83.8	416	41.6
Wallonia	3,321	100.0	1,832	55.2	3,091	93.1	1,755	56.8

c : Crude COVID-19 death rates (per 1,000 people)						
	Total			65+		
	Both sexes	Females	Males	Both sexes	Females	Males
FE	44.2	37.8	63.1	45.7	38.5	68.9
NH	48.1	40.9	69.0	49.6	41.6	75.1
HEP	18.5	16.7	24.0	19.5	17.3	26.6
OUT-FE	0.3	0.3	0.4	1.6	1.2	2.1
Wallonia	0.9	1.0	0.9	4.6	4.6	4.6

3.1 Distribution of COVID-19 death rate per institution

Mortality by COVID-19 varied according to the category of FE institutions: with 2,010 deaths out of 2,126 (95%), NH recorded a crude COVID-19 death rate (48‰) 2.6 times higher than HEP (19‰) (Table 1). COVID-19 death rate per institution varied widely from 0‰ to 340‰ and was affected by both the type of institution and their size (Fig. 1). About half of the residents of HEP lived in small-sized institutions ranging from 14 to 52 beds (mean = 37.8, N = 84) where 16‰ died from COVID-19, a lower rate than the 21‰ who died in medium-sized HEP institutions ranging from 54 to 148 beds (mean = 74.3, N = 43). Similarly, about half of the residents of NH lived in medium-sized institutions ranging from 29 to 104 beds (mean = 76.2, N = 284) where 40‰ died from COVID-19, a lower rate than the 53‰ who died in large-sized NH institutions ranging from 105 to 298 beds (mean = 134.1, N = 163).

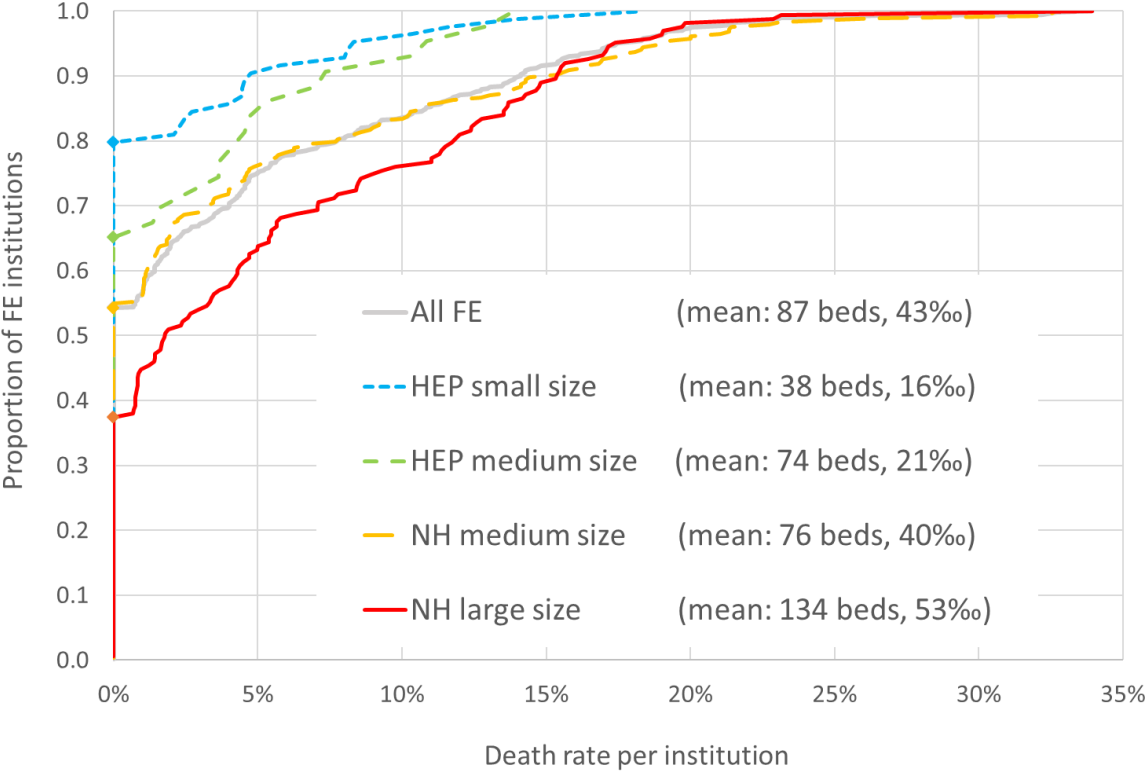


Figure 1. Cumulated distributions of COVID-19 death rate per FE institution (grey line) distinguishing nursing homes (NH) and homes for elderly people (HEP) and two size classes per FE category based on bed capacities (mean bed capacity indicated in the graph legend with the overall death rate). The symbols along the vertical axis highlight the proportions of institutions where no death was reported. Data source: AViQ.

Remarkably, a significant proportion of FE (55%) recorded no death, showing that the epidemic has affected care homes in a very variable manner. The proportion of institutions without COVID-19 death followed the trend shown above for death rates: 81% and 67% for small and medium-size HEP institutions, compared to 55% and 38% for medium-size and large

NH institutions, respectively (Fig. 1). Finally, while the crude COVID-19 death rate rarely exceeded 150‰ in HEP institutions, it exceeded this threshold in about 10% of NH institutions, regardless of size (Fig. 1). Mann-Whitney U tests on crude COVID-19 death rate per institution showed that globally NH and HEP differ significantly (z-score = 4.67, p-value < 0.00001) as well as medium NH versus large NH (z-score = -3.07, p-value = 0.001), while difference was only marginally significant between small HEP and medium HEP (z-score = -1.30, p-value = 0.097) and between medium HEP and medium NH (z-score = 1.20, p-value = 0.11).

The crude COVID-19 death rate per institution showed slight positive spatial autocorrelation between institutions separated by less than 10 km (Moran’s I = 0.058, p-value = 0.003) but no departure from spatial randomness at larger distances. Hence, there was no large-scale gradient of mortality rates across Wallonia.

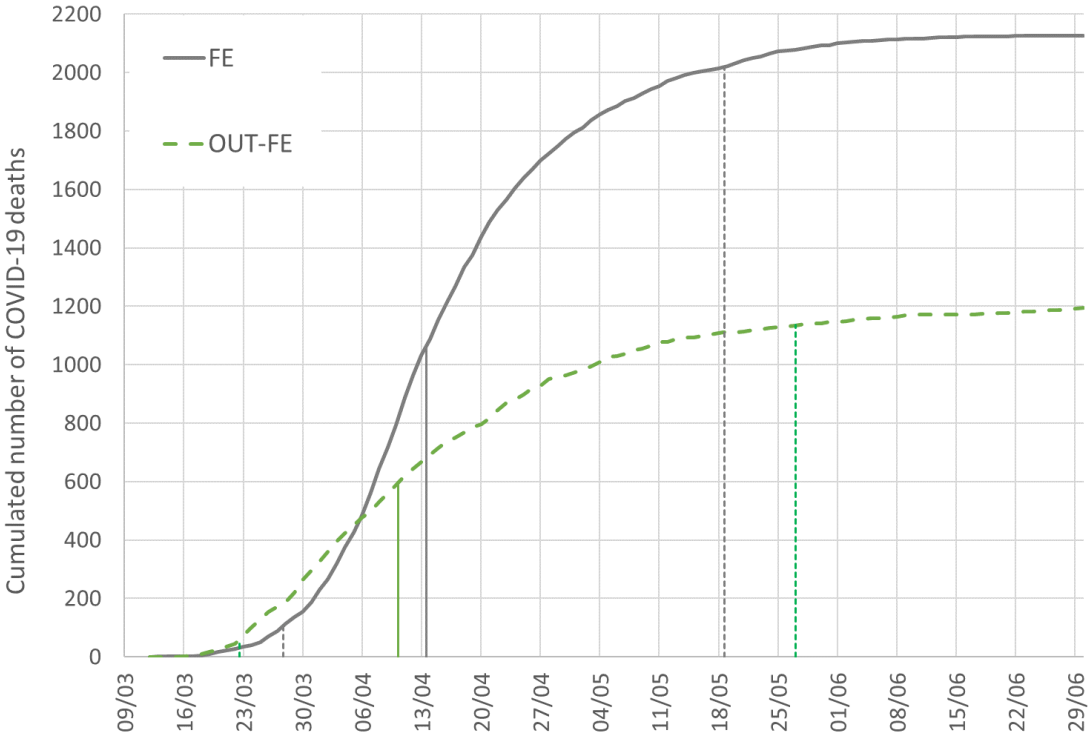


Figure 2. Cumulated number of deaths attributed to COVID-19 in Wallonia between March and June 2020, separately for persons living in residential facilities for elderly people (FE, grey plain line) and the rest of the population (OUT-FE, green stippled line). The dates at which 50% of the total deaths recorded in each population are indicated by vertical bars, while the 0.05 and 0.95 quantiles are indicated by vertical stippled lines. Data sources: Sciensano, AViQ.

3.2 COVID-19 death temporal dynamics in and out of FE

While mortality levels by COVID-19 are much higher in FE than outside them, the temporal dynamics of mortality also differed in the two populations. Until April 5 the majority of deaths had occurred in the OUT-FE population while FE residents constituted the majority of cumulated deaths since April 6 (Fig. 2). The slight delay in the mortality dynamics of FE

residents can be quantified by the date at which 50% of the deaths reported in the observed period occurred: 3.5 days later in the FE population (April 13) than in the OUT-FE population (April 10). The wave of deaths was also more concentrated in FE, with 52 days between the dates for which 5% and 95% of the total deaths were reached (i.e. between 28/03 and 19/05), than in the OUT-FE population (65 days between 23/03 and 28/05). Hence, according to mortality data, the outbreak that occurred within the FE was delayed but then spread faster than the outbreak seen in the OUT-FE population.

3.3 Age and sex structure effect on COVID-19 death rate

The FE population, which makes 1.35% of the French-speaking part of Wallonia (3,567,294 inhabitants), has a peculiar age structure, with people aged 65 and over constituting 95% of the total population, compared to 18% in the OUT-FE population (Fig. 3). Moreover, among the people aged 65 and over, the oldest (85 and over) are over-represented in FE, accounting for 60% compared to only 11% in the OUT-FE population. As a result, the mean age reaches 84.2 years (SD = 9.6) in the FE and only 41.0 years (SD = 23.2) outside them. The gender structure is also very particular in the FE, characterized by a highly biased sex ratio, with 74.6% of females (51.1% in the overall population), a percentage increasing from 50.9% among the 60-64 years old to 91.2% in the ≥ 100 years old. Within the FE, the age pyramids of residents of NH and HEP are very similar, the main difference being a slightly higher proportion of males 60-74 years old in HEP (8.0%) compared to NH (6.3%), compensated by a lower proportion of males 80-94 years old in HEP (12.2%) compared to NH (13.8%).

Given the strong excess of females among FE residents, especially among the oldest and more vulnerable age classes, females constitute a majority (66%) of the COVID-19 deaths in FE. By contrast, in the OUT-FE population composed of 51% females, 40% of COVID-19 deaths were females. Overall, in Wallonia, females constituted 55% of COVID-19 deaths despite their lower vulnerability (see below) because among the people ≥ 65 years, the proportion of females living in FE (9.2%) is much larger than the proportion of males living in FE (3.9%).

The ExpCCDR_FE reaches 3.71‰, which is 10.9 times higher than CCDR outside FE (0.34‰). Hence, the difference of age pyramids between the populations, i.e. the (age and sex) structure effect, already predicts an 11-fold higher COVID-19 death rate inside than outside the FE population.

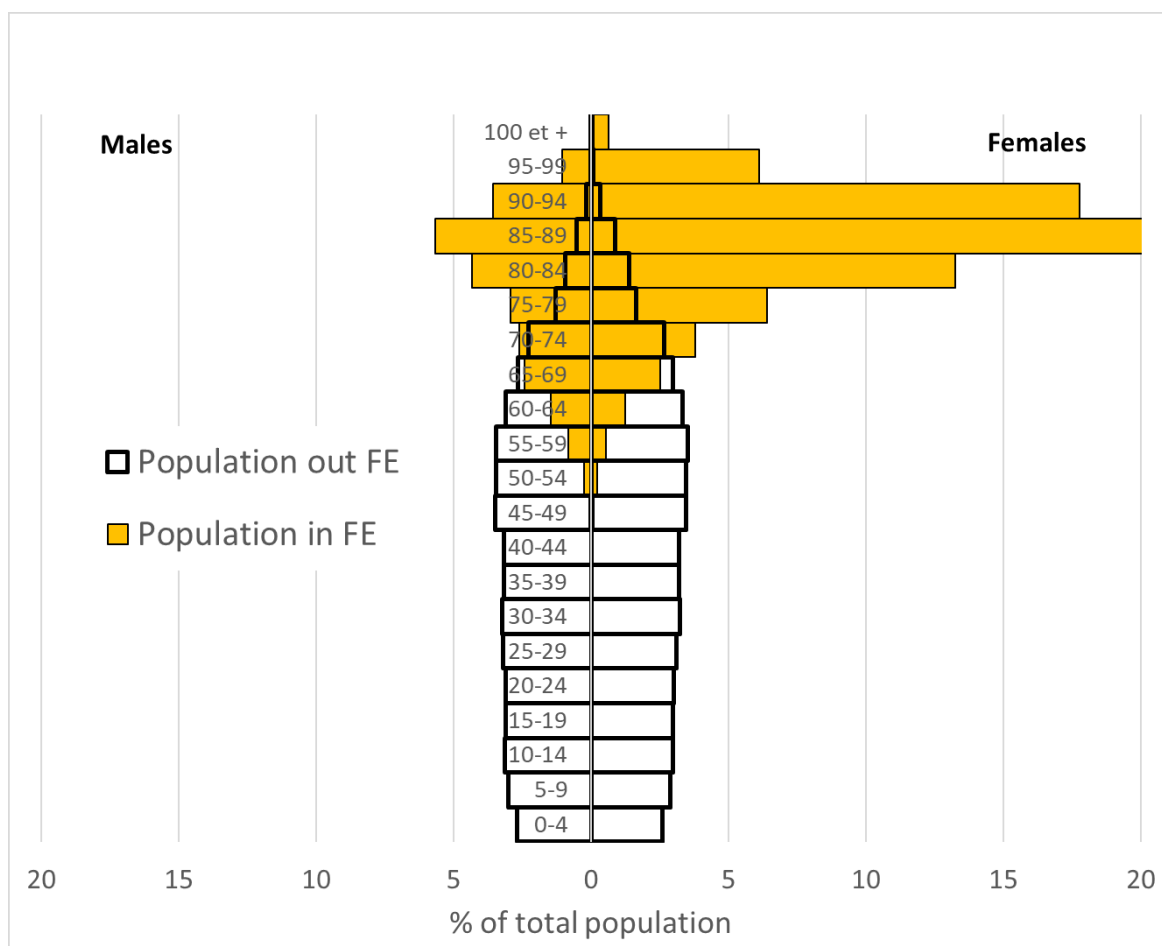


Figure 3. Age pyramids (in %) of the populations of the French-speaking part of Wallonia on January 1, 2020, for people living in residential facility for elderly people (FE, in orange) and the rest of the population (OUT-FE, white). The 65+ people made 95.1% of the FE population and 17.8% of the OUT-FE population. Data sources: StatBel, AViQ.

3.4 COVID-19 death rates by sex and age groups – health conditions effect

In both the FE and OUT-FE populations, COVID-19 SASDR (confirmed and suspected) closely followed Gompertz law (i.e. exponential increase with age), but with a lower slope in FE (mortality doubling every 24 years in M and 18 years in F) than OUT-FE (mortality doubling every 7.5 years in M and 6.6 years in F) (Fig. 4a). COVID-19 death rates were higher in males than in females of the same age class, by a factor of c. 2.0 among the 65-99 years old people, both inside and outside FE. As already shown with the distribution of death rates per institution (Fig. 1), there was also a sharp contrast between NH and HEP populations: across all ages, COVID-19 death rates in NH (6.9% in M, 4.1% in F) were approximately 2.9 (M) to 2.5 (F) times higher than in HEP (2.4% in M, 1.7% in F).

At all ages, COVID-19 death rates were much higher in FE than outside them (Fig. 4a), reflecting the health conditions effect. However, the ratio between FE over OUT-FE rates tends to decrease with age: while it exceeds 30 for people under 75, it reaches 10 for those aged 85-89 (the age group concentrating most COVID-19 deaths, both inside and outside FE), then 4

for people over 99 years. Thus, the mortality differential is most pronounced at the youngest ages.

The SMR_EF, which measures the contribution of differences in COVID-19 SASDR between FE and OUT-FE populations, i.e. the health conditions effect, equals 11.9 (44.2‰ / 3,71‰). Consequently, the excess mortality observed in FE results from the combination of a structure effect (x 10.9) and a health condition effect (x 11.9), their product giving the ratio between the CCDR of the two populations (10.9 x 11.9 ≈ 130).

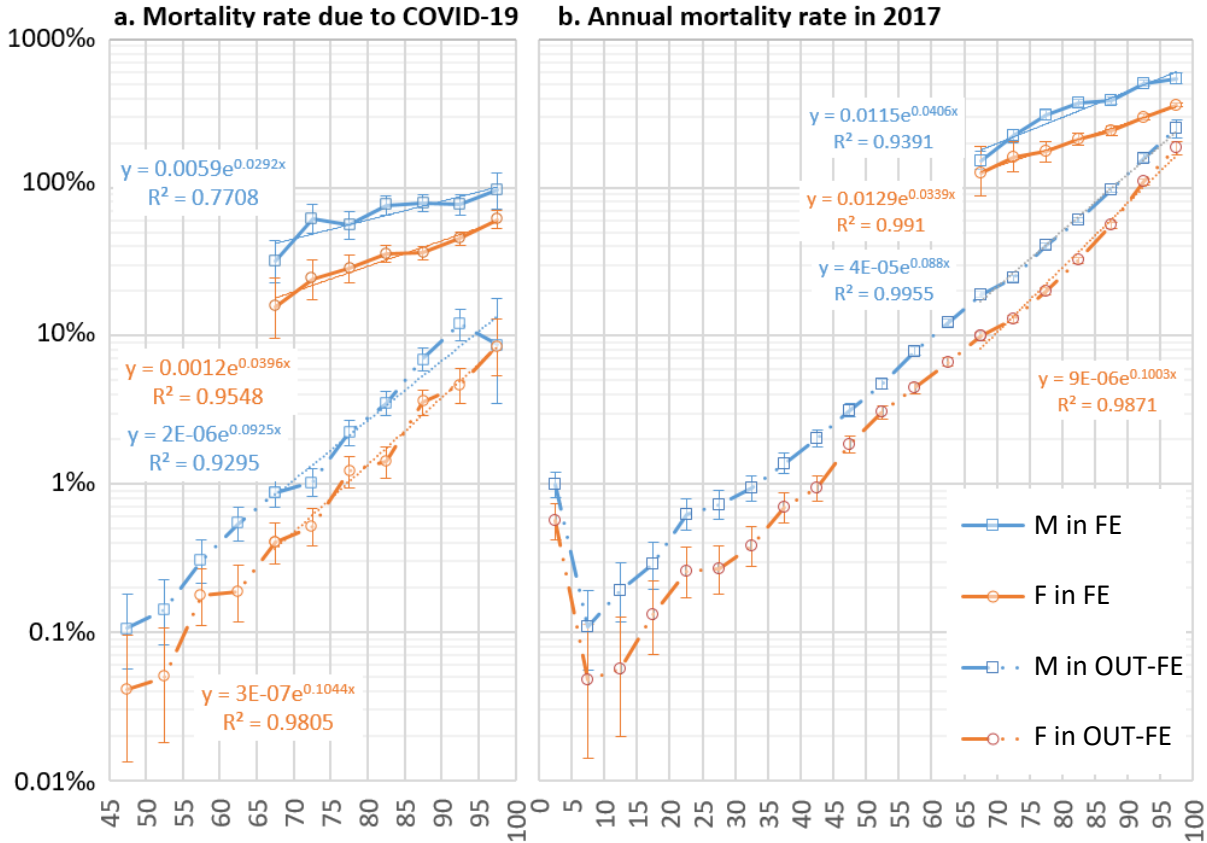


Figure 4. Age and sex-specific death rates due to (a) COVID-19 during spring 2020 and (b) all causes during 2017 in Wallonia, separately for residential facilities for elderly people (FE, plain lines) and the rest of the population (OUT-FE, stippled-dotted lines), and for males (blue) and females (red). Death rates are represented on a logarithmic scale. Equations and thin straight lines represent the best-fitting exponential curves adjusted to the 65-99 age classes. Data sources: Sciansano, AViQ, StatBel.

3.5 Annual overall death rates by sex and age groups – a proxy of overall health frailty

When excluding child mortality (0-4 years class), SASDR based on 2017 mortality data also closely followed Gompertz’s laws, both in the FE and OUT-FE populations, but were overall 5 (in FE) to 20 (OUT-FE) times higher than the COVID-19 death rates (Fig. 4b). Age-specific death rates were higher in males (M) than in females (F) of the same age class, by a factor of c.1.6 in FE and 1.7 OUT-FE among the 65-99 years old people. However, mortality rates were much

higher in FE than outside for the same age class and they increased with age less rapidly in FE (mortality doubling every 17 years in M and 20 years in F) than OUT-FE (mortality doubling every 8 years in M and 7 years in F). Therefore, while annual death rates were c. 10 times higher in FE than OUT-FE for the 65-69 class, they remained only c. 2 times higher for the 95-99 class (Fig. 4b), indicating that the morbidity of care home residents tends to be stronger among the youngest residents when their age is taken into account.

In 2017, annual CDR reached 266.7‰ in FE against 7.0‰ in the OUT-FE populations, a 38-fold difference. Using the SASDR observed outside FE weighed by the population sizes of the FE population predicts a crude death rate of 70.7‰ in the FE population if it was as healthy as the OUT-FE population under a same age pyramid. Hence, the health frailty of the FE population can explain a $266.7/70.7 = 3.77$ -fold increase in mortality compared to the OUT-FE population. Across all age classes, annual death rates in NH (34.1% in M, 25.2% in F) were approximately 1.2 times higher than in HEP (27.6% in M, 20.1% in F), reflecting that NH institutions host a higher proportion of residents in poor health condition than HEP institutions.

3.6 Comparison of COVID-19 and annual SASDR to infer differences in contamination rates between populations

While mortality levels by age and sex of COVID-19 are lower than those of 2017, within each population and sex, the COVID-19 SASDR is nearly proportional to the annual SASDR (Fig. 4a,b). However, there are two major differences between COVID-19 and annual mortality. First, the gap between mortality by COVID-19 and annual mortality is lower in care homes than in the rest of the population (Fig 4a). Second, the excess mortality in males, already present in the annual overall mortality, is even higher in the case of COVID-19 mortality. In and out FE, while the male-to-female mortality ratio for those aged 65+ reached c. 1.6 in 2017, it exceeded 2.0 for COVID-19 mortality.

The fact that within and outside FE COVID-19 SASDR is near proportional to the annual SASDR suggests that the latter might be a good proxy of the average effect of comorbidity factors (or health frailty) conditioning the risk of dying from COVID-19 when one is infected. Under this assumption, we can tentatively factor out the impact of comorbidity factors using the ratio of COVID-19 over annual death rates for each age class and sex (Fig. 5). Although these ratios are slightly higher for males than females in both the FE and OUT-FE populations, and a little higher before age 75 than at later ages for men in FE, the main difference is between populations: while COVID-19 death rates are around 16% (F) to 20% (M) of the annual death rates in FE, they reached only 4.6% (F) to 5.3% (M) of the annual death rates outside FE. If we assume that this difference results from different levels of exposure to the SARS-CoV-2 virus causing COVID-19, FE residents would have been c. 3.5 times more contaminated than the OUT-FE population of similar age. Moreover, average ratios over the 65-99 old people distinguishing NH from HEP populations indicate that the contamination was probably 1.6 (HEP) to 3.8 (NH) times higher than in the OUT-FE population, and thus that NH institutions would have been at least twice more contaminated than HEP institutions.

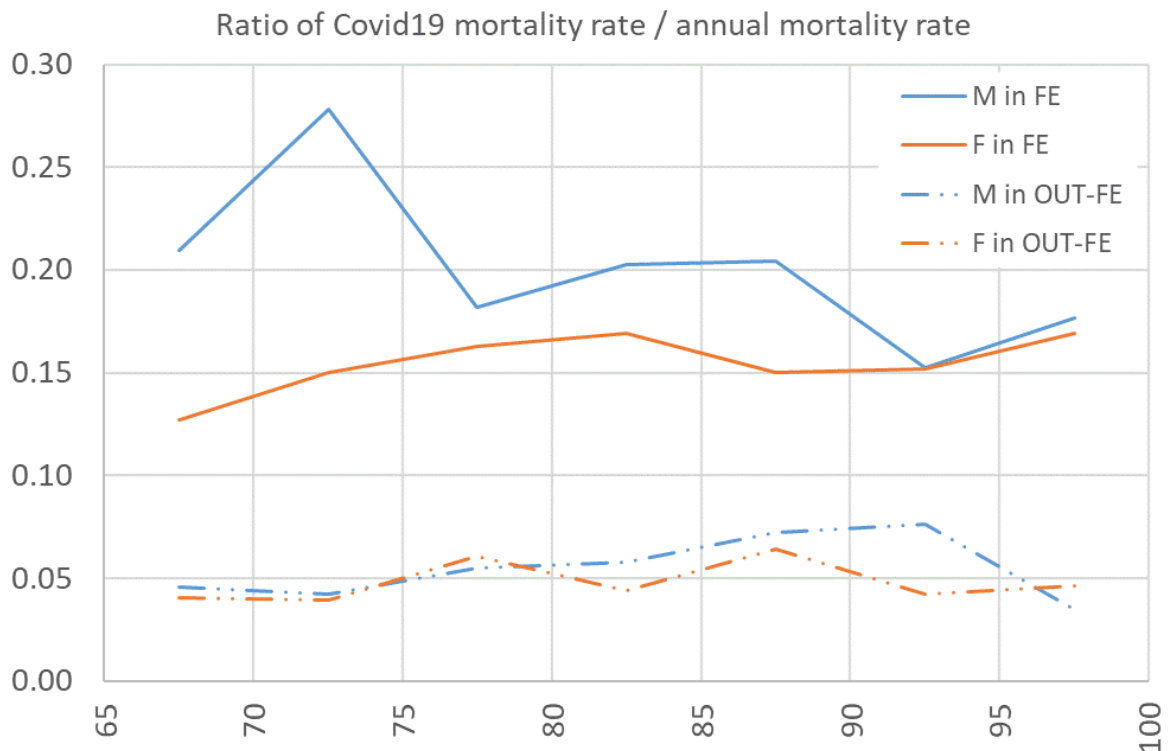


Figure 5. Ratio of COVID-19 over annual death rates in males (M, blue) and females (F, red) separately for residential facilities for elderly people (FE, plain lines) and the rest of the population (OUT-FE, dotted-stippled lines). Data sources: AViQ, Sciensano, StatBel.

4. Discussion

In Wallonia, care home residents constitute only 1.33% of the population but 64% of the COVID-19 deaths reported during spring 2020, so that the CCDR was c. 130 times higher than for the population living outside of care homes. According to our analyses, this seemingly dramatic ratio results from the combination of three main factors. First, the peculiar age pyramid of the care homes population predicts a CCDR 11 times higher than for the external population, because COVID-19 is much more deadly for older people (structure effect). Second, the low average health condition of care home residents increases their annual death rate by c. 3.8 times compared to the external population after accounting for age and sex effects, while COVID-19 mortality appears highly correlated to the presence of other comorbidity factors (health frailty effect). Finally, care home residents have probably been on average 3.5 times more exposed to the SARS-CoV-2 virus than the external population of similar age (1.6 times more in HEP, 3.8 times more in NH), and tended to be more exposed when living in larger institutions (higher SARS-CoV-2 prevalence). All these effects worked nearly multiplicatively to generate such a high death toll on care homes. These inferences are based on a number of assumptions that merit to be discussed.

The higher mortality of COVID-19 on older people has been reported since the beginning of the epidemics (Verity et al. 2020). Our analyses using 5-years age classes allow us to better characterize this relationship, showing that the death rate doubles approximately every 6 years of age increment for people living outside of care homes, and every 20 years for care home residents, a result similar to that observed by Guilmoto (2020) in a comparison of COVID-19 SASDR in Western Europe and the United States. This type of mortality-age relationship is known as Gompertz law (Gompertz 1825), which is sometimes interpreted as reflecting an increase in the vulnerability of individuals to extrinsic causes (Ricklefs & Scheuerlein 2002). Gompertz law often fits well mortality data for a wide range of causes (Riggs 1991 for ischemic heart disease in the US; Imaizumi 1996 for breast cancer in Japan), as well as total mortality rates at national level (all causes confounded, Horiuchi *et al.*, 2003; Dolejs 2015), as confirmed in our analyses of the annual mortality rate (if we exclude child mortality). What is remarkable here is that the exponents of the Gompertz law adjusted to our data were very similar for COVID-19 mortality and overall annual mortality (Fig. 4a, b) while they differed strongly between populations living inside or outside care homes. This strong correlation between COVID-19 and annual mortality rates suggests that the risk of dying from COVID-19 largely depends on the person's initial health condition, as supported by numerous clinical observations showing the strong impact of multiple comorbidity factors (Williamson *et al.* 2020) or of a frailty index (Hewitt *et al.* 2020).

The higher mortality of COVID-19 on males than females has also been reported since the beginning of the epidemics (Verity et al. 2020; Wenham *et al.* 2020; Williamson *et al.* 2020). In Wallonia, COVID-19 death rate was approximately double in males than in females of the same age, and appears higher than the male mortality excess observed for annual mortality rates unrelated to COVID-19 (M/F mortality ratio from 1.6 to 1.7). Interestingly, this excess mortality in males was identical when considering suspected and confirmed cases of COVID-19 deaths in care homes (results not shown), suggesting that most suspected cases were correctly diagnosed. This is also supported by the very good quantitative correspondence between the daily deaths attributed to COVID-19 (including suspected cases) and the daily deaths excess occurring in spring 2020 compared to previous years (Molenberghs *et al.* 2020; Wu *et al.* 2020). Despite their higher vulnerability, males constituted only 44.8% of COVID-19 deaths in Wallonia, a paradox resulting from the much lower proportion of males (3.9%) than females (9.2%) ≥ 65 years old living in care homes, while the care homes population has been more infected.

We tentatively interpreted the higher ratio of COVID-19 over annual death rates in care homes compared to the outside population as reflecting a higher contamination in care homes, due to the potentially rapid spread of the virus in such an environment (Arons *et al.* 2020). However, other factors may also play a role, in particular the quality of care treatments, given that a minority of care home residents who died from COVID-19 were hospitalized (28%) whereas nearly all the victims of the OUT-FE population were hospitalized. Moreover, during the peak of the COVID-19 infection wave of spring 2020, in particular between April to early May, the proportion of deaths of care home residents in hospital was lower (26%) than just

before and after (41%), possibly because the risk of saturating hospitals' intensive care facilities influenced the decision to hospitalize or not COVID-19 patients. Nevertheless, in hospitals, the proportion of patients of whatever origin who died from COVID-19 was very high among the ≥ 80 years old (39%) compared to the < 60 years old (4%) (Van Beckhoven *et al.*, 2020), so that even if a higher proportion of care home residents were hospitalized, it may not have changed much their survival chance, as suggested by the absence of correlation between the COVID-19 death rates per care home and the proportion of deaths that occurred in hospitals (results not shown). Moreover, differences in care quality cannot explain why HEP, in which 40% of the residents who died from COVID-19 were hospitalized, were 2.4 times less affected than NH institutions, even after factoring out the difference in health condition of their respective populations. The lower level of close contacts with caregivers in HEP compared to NH is a more parsimonious explanation of this contrast.

We currently lack serological tests data allowing to compare the level of presumed infection in the different populations but for the general population in Belgium, seroprevalence reached 6.0% (95% CI 5.1 to 7.1; Herzog *et al.* 2020) in the week of 20-26 April 2020, a value similar to that reported in other well-hit countries (Eckerle & Meyer 2020). If we assume that the contamination by the SARS-CoV-2 virus has been 3.5 more prevalent in care homes than outside them, we could expect a seroprevalence of c. 20% in care homes.

Other lines of evidence of the importance of viral transmission in care homes come from (i) the temporal dynamics of deaths and (ii) the distribution of COVID-19 deaths and cases per institution. First, the delayed but then faster increase of deaths in care homes compared to the external population (Fig. 2) is consistent with primary infections originating from the care home staff or possibly visitors (explaining the delay), followed by a more rapid viral contamination within each institution contaminated due to the difficulty to limit interpersonal contacts and/or to the lack of PPE (explaining the faster increase). Second, the crude COVID-19 death rate was very heterogeneous among care home institutions, with 54% of them having no COVID-19 death to deplore, while 17% of them lost at least 100‰ of their residents, and 2.6% lost between 200‰ and up to 340‰ of their residents. There was only a weak spatial autocorrelation of these mortality rates, limited to a radius of 10 km, possibly reflecting the impact of local clusters and/or the movement of staff between related care homes but we lack data to test the later hypothesis. If we assume that in the most hit institutions virtually all the residents had been infected and led to an average mortality rate of 250‰, a mean mortality rate of 44.2‰ over all institutions would correspond to a mean prevalence of $44.2/250 \approx 18\%$. Hence, a different reasoning suggest again that about a fifth of the residents of care homes had been contaminated by SARS-CoV-2.

The absence of COVID-19 deaths mostly occurred in HEP (without care facilities) and in small institutions, while high mortality rates mostly occurred in NH and tended to increase with the bed capacity of the institution (Fig. 1). Hence, the risk that the SARS-CoV-2 virus entered and spread through a care home clearly increased with the presence of a health care staff and with the size of the institution, as expected from the potential number of interpersonal contacts, during a period where PPE and possibly adequate staff formation for such epidemic were in

deficit. It is worth noting that the nearly two-fold lower mortality rate observed in medium-sized HEP (2.1%) compared to NH (4.0%) is very consistent with the distribution of positive COVID-19 tests performed from end April to May 2020 (Hoxha *et al.* 2020). Among institutions where at least 50% of the residents and staff were tested, the rate of positive tests reached 2.5% for residents and 1.6% for staff in HEP (7,402 persons tested in 100 institutions), against 5.9% for residents and 4.2% for staff in NH (60,667 persons tested in 370 institutions; unpublished results). The importance of transmission by staff was also highlighted in six care homes of London, where SARS-CoV-2 genome sequencing showed that there were often multiple introductions of the virus per institution and that staff working across different care homes had a 3-fold higher risk of being contaminated than staff working in single care homes (Ladhani *et al.* 2020). Conversely, in France, 17 nursing homes where the staff decided to self-confine voluntarily with the residents at the beginning of the pandemic recorded 4 to 8-times less cases and deaths than the national averages (Belmin *et al.* 2020).

5. Conclusion

In Wallonia, as in other countries where care homes have been heavily impacted by COVID-19, the epidemics that occurred in care homes and outside them showed distinct dynamics (see Humblet 2020 for Belgium; Logar 2020 for Italy; Rada 2020 for Spain). Care homes represent a very specific context as a result of the particular vulnerability of its population and the difficulty to contain the SARS-CoV-2 transmission once it has infected an institution. Given the high death toll that care homes underwent in many Western countries, care homes should be given special attention to understand how to avoid primary infection and how to limit contamination of its residents and staff. Our global analyses of death rates revealed that the size of the institution and the importance of nursing services provided (higher in NH than in HEP) were important factors determining the relative death toll. Nevertheless, our analyses do not reveal why nearly half of the institutions have not recorded any death while nearly one in six lost at least a tenth of their residents. These contrasts may result from (i) the stochastic nature of a primary infection (as suggested by the institution size effect), (ii) differences in mean health status of residents among institutions (e.g. HEP *versus* NH), or (iii) differences in the organisation and/or specific measures taken by each institution in response to the COVID-19 epidemic. Further research investigating the history of infections within representative institutions could clarify these questions. A comparison of serologic tests conducted inside and outside care homes would also be helpful to confirm our interpretation that the prevalence of SARS-CoV-2 was much higher within care homes than outside them. Finally, we recommend that epidemiological models integrate care home populations as a specific entity in their forecast.

6. Acknowledgments

We thank Patrick Lusyne from StatBel for helping us obtain the adequate population and annual deaths data, and for interesting discussions to interpret our results. We also warmly thank the staff of the hospitals and care homes for their conscientious reporting of COVID-19

deaths despite the difficult times. We are grateful to two anonymous reviewers for their constructive comments. OJH, SD and TE are supported by the *Fonds de la Recherche Scientifique* (F.R.S. - FNRS, Belgium).

References

- Armitage, R., & Nellums, L. B. (2020). COVID-19 and the consequences of isolating the elderly. *The Lancet Public Health*, 5(5), e256. [https://doi.org/10.1016/S2468-2667\(20\)30061-X](https://doi.org/10.1016/S2468-2667(20)30061-X)
- Arons, M. M., Hatfield, K. M., Reddy, S. C., Kimball, A., James, A., Jacobs, J. R., Taylor, J., Spicer, K., Bardossy, A. C., Oakley, L. P., Tanwar, S., Dyal, J. W., Harney, J., Chisty, Z., Bell, J. M., Methner, M., Paul, P., Carlson, C. M., McLaughlin, H. P., ... Public Health—Seattle and King County and CDC COVID-19 Investigation Team. (2020). Presymptomatic SARS-CoV-2 Infections and Transmission in a Skilled Nursing Facility. *The New England Journal of Medicine*, 382(22), 2081–2090. <https://doi.org/10.1056/NEJMoa2008457>
- Ars P., Dal L., Poulain M. (1988) Comment appréhender le problème statistique des petits nombres en démographie ?, in *Les migrations internationales* (Actes du colloque de l'AIDELF de Calabre, 1986), pp. 156-170
- Belmin, J., Um-Din, N., Donadio, C., Magri, M., Nghiem, Q. D., Oquendo, B., Pariel, S., Lafuente-Lafuente, C. (2020). Coronavirus Disease 2019 Outcomes in French Nursing Homes That Implemented Staff Confinement With Residents. *JAMA Network Open*, 3(8), e2017533–e2017533. <https://doi.org/10.1001/jamanetworkopen.2020.17533>
- Bustos Sierra, N., Bossuyt, N., Braeye, T., Leroy, M., Moyersoeyn, I., Peeters, I., Scohy, A., Van der Heyden, J., Van Oyen, H., & Renard, F. (2020). All-cause mortality supports the COVID-19 mortality in Belgium and comparison with major fatal events of the last century. *Archives of Public Health*, 78(1), 117. <https://doi.org/10.1186/s13690-020-00496-x>
- Comas-Herrera A, Ashcroft E and Lorenz-Dant K. (2020) *International examples of measures to prevent and manage COVID-19 outbreaks in residential care and nursing home settings*. Report in LTCcovid.org, International Long-Term Care Policy Network, CPEC-LSE, 11 May 2020. <https://ltccovid.org/wp-content/uploads/2020/05/International-measures-to-prevent-and-manage-COVID19-infections-in-care-homes-2-May-1.pdf>
- Comas-Herrera A, Zalakaín J, Litwin C, Hsu AT, Lemmon E, Henderson D and Fernández J-L (2020) *Mortality associated with COVID-19 outbreaks in care homes: early international evidence*. Article in LTCcovid.org, International Long-Term Care Policy Network, CPEC-LSE, 26 June 2020. <https://ltccovid.org/wp-content/uploads/2020/06/Mortality-associated-with-COVID-among-people-who-use-long-term-care-26-June-1.pdf>
- Dequeker, S., Latour, K., Vandaele E., Islamaj, E., Int Panis, L. (2020). COVID-19 surveillance in residential institutions. Version 3.3–01/07/2020. https://www.sciensano.be/sites/default/files/protocol_covid-19_surveillance_in_residential_institutions_20200701_version_3.3.pdf
- Dolejs, J. (2015). Age Trajectories of Mortality from All Diseases in Five Countries of Central Europe During the Last Decades. *Biodemography and Social Biology*, 61(1), 40-64. <https://doi.org/10.1080/19485565.2014.936999>
- Dudel, C., Riffe, T., Acosta, E., Raalte, A. van, Strozza, C., & Myrskylä, M. (2020). Monitoring trends and differences in COVID-19 case-fatality rates using decomposition methods: Contributions of age structure and age-specific fatality. *PLOS ONE*, 15(9), e0238904. <https://doi.org/10.1371/journal.pone.0238904>
- Eckerle, I., & Meyer, B. (2020). SARS-CoV-2 seroprevalence in COVID-19 hotspots. *The Lancet*, 396(10250), 514–515. [https://doi.org/10.1016/S0140-6736\(20\)31482-3](https://doi.org/10.1016/S0140-6736(20)31482-3)

- ECDC Public Health Emergency Team, Danis Kostas, Fonteneau Laure, Georges Scarlett, Daniau Côme, Bernard-Stoeklin Sibylle, Domegan Lisa, O'Donnell Joan, Hauge Siri Helene, Dequeker Sara, Vandael Eline, Van der Heyden Johan, Renard Françoise, Sierra Natalia Bustos, Ricchizzi Enrico, Schweickert Birgitta, Schmidt Nicole, Abu Sin Muna, Eckmanns Tim, Paiva José-Artur, Schneider Elke. High impact of COVID-19 in long-term care facilities, suggestion for monitoring in the EU/EEA, May 2020. *Euro Surveill.* 2020;25(22):pii=2000956. <https://doi.org/10.2807/1560-7917.ES.2020.25.22.2000956>
- Einiö, E., Guilbault, C., Martikainen, P. & Poulain, M. (2012). Gender Differences in Care Home Use among Older Finns and Belgians. *Population*, vol. 67(1), 71-95. <https://doi.org/10.3917/popu.1201.0075>
- Falconer, M., & O'Neill, D. (2007). Profiling disability within nursing homes: a census-based approach. *Age Ageing*, 36(2), 209-213. <https://doi.org/10.1093/ageing/afl185>
- Fisman, D. N., Bogoch, I., Lapointe-Shaw, L., McCready, J., & Tuite, A. R. (2020). Risk Factors Associated With Mortality Among Residents With Coronavirus Disease 2019 (COVID-19) in Long-term Care Facilities in Ontario, Canada. *JAMA Network Open*, 3(7), e2015957–e2015957. <https://doi.org/10.1001/jamanetworkopen.2020.15957>
- Flaxman, S., Mishra, S., Gandy, A., Unwin, H. J. T., Mellan, T. A., Coupland, H., Whittaker, C., Zhu, H., Berah, T., Eaton, J. W., Monod, M., Ghani, A. C., Donnelly, C. A., Riley, S., Vollmer, M. A. C., Ferguson, N. M., Okell, L. C., & Bhatt, S. (2020). Estimating the effects of non-pharmaceutical interventions on COVID-19 in Europe. *Nature*, 584(7820), 257–261. <https://doi.org/10.1038/s41586-020-2405-7>
- Gompertz, B. (1825). XXIV. On the nature of the function expressive of the law of human mortality, and on a new mode of determining the value of life contingencies. In a letter to Francis Bailly, Esq. F. R. S. &c. *Philosophical Transactions of the Royal Society of London*, 115, 513–583. <https://doi.org/10.1098/rstl.1825.0026>
- Herm, A., Poulain, M., & Anson, J. (2014). Excess mortality risks in institutions: The influence of health and disability status. In *Mortality in an International Perspective* (pp. 245-263). Springer, Cham.
- Herzog, S., Bie, J. D., Abrams, S., Wouters, I., Ekinci, E., Patteet, L., Coppens, A., Spiegeleer, S. D., Beutels, P., Damme, P. V., Hens, N., & Theeten, H. (2020). Seroprevalence of IgG antibodies against SARS coronavirus 2 in Belgium: A prospective cross-sectional study of residual samples. *MedRxiv*, <https://doi.org/10.1101/2020.06.08.20125179>
- Hewitt, J., Carter, B., Vilches-Moraga, A., Quinn, T. J., Braude, P., Verduri, A., Pearce, L., Stechman, M., Short, R., Price, A., Collins, J. T., Bruce, E., Einarsson, A., Rickard, F., Mitchell, E., Holloway, M., Hesford, J., Barlow-Pay, F., Clini, E., ... Guaraldi, G. (2020). The effect of frailty on survival in patients with COVID-19 (COPE): A multicentre, European, observational cohort study. *The Lancet Public Health*, 5(8), e444–e451. [https://doi.org/10.1016/S2468-2667\(20\)30146-8](https://doi.org/10.1016/S2468-2667(20)30146-8)
- Horiuchi, S., Finch, C. E., Meslé, F., & Vallin, J. (2003). Differential patterns of age-related mortality increase in middle age and old age. *The Journals of Gerontology Series A: Biological Sciences and Medical Sciences*, 58(6), B495-B507. <https://doi.org/10.1093/gerona/58.6.B495>
- Hoxha, A., Wyndham-Thomas, C., Klamer, S., Dubourg, D., Vermeulen, M., Hammami, N., & Cornelissen, L. (2020). Asymptomatic SARS-CoV-2 infection in Belgian long-term care facilities. *The Lancet Infectious Diseases*. [https://doi.org/10.1016/S1473-3099\(20\)30560-0](https://doi.org/10.1016/S1473-3099(20)30560-0)
- Humblet, P. (2020). Inégalités sociales de santé: Tout a changé ? *Politique*, 112, 99-102
- Imaizumi, Y. (1996). Longitudinal analysis of mortality from breast cancer in Japan, 1950–1993: fitting Gompertz and Weibull functions. *Mechanisms of ageing and development*, 88(3), 169-183. [https://doi.org/10.1016/0047-6374\(96\)01735-6](https://doi.org/10.1016/0047-6374(96)01735-6)
- Keiding, N., & Clayton, D. (2014). Standardization and control for confounding in observational studies: a historical perspective. *Statistical Science*, 29 (4), 529-558. <https://doi.org/10.1214/13-STS453>

- Ladhani, S. N., Chow, J. Y., Janarthanan, R., Fok, J., Crawley-Boevey, E., Vusirikala, A., Fernandez, E., Perez, M. S., Tang, S., Dun-Campbell, K., Evans, E. W., Bell, A., Patel, B., Amin-Chowdhury, Z., Aiano, F., Paranthaman, K., Ma, T., Saavedra-Campos, M., Myers, R., ... Ramsay, M. E. (2020). Increased risk of SARS-CoV-2 infection in staff working across different care homes: Enhanced CoVID-19 outbreak investigations in London care Homes. *The Journal of Infection*, 81(4), 621–624. <https://doi.org/10.1016/j.jinf.2020.07.027>
- Laferrière, A., Van den Heede, A., Van den Bosch, K., & Geerts, J. (2013). 22 Entry into institutional care: predictors and alternatives. In *Active ageing and solidarity between generations in Europe: First results from SHARE after the economic crisis*, (pp. 253-264). DeGruyter.
- Liu, T., Wu, S., Tao, H., Zeng, G., Zhou, F., Guo, F., & Wang, X. (2020). Prevalence of IgG antibodies to SARS-CoV-2 in Wuhan—Implications for the ability to produce long-lasting protective antibodies against SARS-CoV-2. *MedRxiv*, 2020.06.13.20130252. <https://doi.org/10.1101/2020.06.13.20130252>
- Logar, S. (2020). Care home facilities as new COVID-19 hotspots: Lombardy Region (Italy) case study. *Arch Gerontol Geriatr*. 89:104087. <https://doi:10.1016/j.archger.2020.104087>
- Medford, A., & Trias-Llimós, S. (2020). Population age structure only partially explains the large number of COVID-19 deaths at the oldest ages. *Demographic Research*, 43, 533–544. <https://doi.org/10.4054/DemRes.2020.43.19>
- Miettinen, O. S. (1972). Components of the crude risk ratio. *American Journal of Epidemiology*, 96(2), 168-172. <https://doi.org/10.1093/oxfordjournals.aje.a121443>
- Molenberghs, G., Faes, C., Aerts, J., Theeten, H., Devleeschauwer, B., Bustos Sierra, N., Braeye, T., Renard, F., Herzog, S., Lusyne, P., Van der Heyden, J., Van Oyen, H., Van Damme, P., & Hens, N. (2020). *Belgian COVID-19 Mortality, Excess Deaths, Number of Deaths per Million, and Infection Fatality Rates (8 March—9 May 2020)* [Preprint]. *Epidemiology*. <https://doi.org/10.1101/2020.06.20.20136234>
- Nepomuceno, M. R., Acosta, E., Alburez-Gutierrez, D., Aburto, J. M., Gagnon, A., & Turra, C. M. (2020). Besides population age structure, health and other demographic factors can contribute to understanding the COVID-19 burden. *Proceedings of the National Academy of Sciences*, 117(25), 13881–13883. <https://doi.org/10.1073/pnas.2008760117>
- Petretto, D.R.; Pili, R. (2020). Ageing and COVID-19: What Is the Role for Elderly People? *Geriatrics*, 5, 25.
- Quigley, D. D., Dick, A., Agarwal, M., Jones, K. M., Mody, L., & Stone, P. W. (2020). COVID-19 Preparedness in Nursing Homes in the Midst of the Pandemic. *Journal of the American Geriatrics Society*, 68(6), 1164–1166. <https://doi: 10.1111/jgs.16520>
- Rada, A. G. (2020). Covid-19: the precarious position of Spain's nursing homes. *BMJ*, 369:m1586. doi: <https://doi.org/10.1136/bmj.m1586>
- Ricklefs, R. E., & Scheuerlein, A. (2002). Biological implications of the Weibull and Gompertz models of aging. *Journals of Gerontology - Series A Biological Sciences and Medical Sciences*, 57(2), B69–B76. Scopus. <https://doi.org/10.1093/gerona/57.2.B69>
- Riggs, J. E. (1991b). Longitudinal Gompertzian analysis of ischemic heart disease mortality in the US, 1962–1986: a method of demonstrating the deterministic dynamics describing its decline. *Mechanisms of ageing and development*, 57(1), 1-14. [https://doi.org/10.1016/0047-6374\(91\)90020-Z](https://doi.org/10.1016/0047-6374(91)90020-Z)
- Robbiani, D. F., Gaebler, C., Muecksch, F., Lorenzi, J. C. C., Wang, Z., Cho, A., Agudelo, M., Barnes, C. O., Gazumyan, A., Finkin, S., Hägglöf, T., Oliveira, T. Y., Viant, C., Hurley, A., Hoffmann, H.-H., Millard, K. G., Kost, R. G., Cipolla, M., Gordon, K., ... Nussenzweig, M. C. (2020). Convergent antibody responses to SARS-CoV-2 in convalescent individuals. *Nature*, 584, 437–442. <https://doi.org/10.1038/s41586-020-2456-9>

- Sciensano (2020a). COVID-19 Bulletin Epidémiologique Hebdomadaire du 30 avril 2020, Bruxelles, Belgique. https://covid-19.sciensano.be/sites/default/files/Covid19/COVID-19_Weekly%20report_20200430%20-%20FR_0.pdf
- Sciensano (2020b). COVID-19 Bulletin Epidémiologique Hebdomadaire du 22 mai 2020, Bruxelles, Belgique. https://covid-19.sciensano.be/sites/default/files/Covid19/COVID-19_Weekly%20report_20200522%20-%20FR.pdf
- Sciensano (2020c). COVID-19 Bulletin Epidémiologique Hebdomadaire du 19 juin 2020, Bruxelles, Belgique. https://covid-19.sciensano.be/sites/default/files/Covid19/COVID-19_Weekly%20report_20200619%20-%20FR.pdf
- Szczerbińska, K. (2020). Could we have done better with COVID-19 in nursing homes? *European Geriatric Medicine* volume, 11, 639–643. <https://doi.org/10.1007/s41999-020-00362-7>
- Trabucchi, M., & De Leo, D. (2020). Nursing homes or besieged castles: COVID-19 in northern Italy. *The Lancet Psychiatry*, 7(5), 387-388. [https://doi.org/10.1016/S2215-0366\(20\)30149-8](https://doi.org/10.1016/S2215-0366(20)30149-8)
- Van Beckhoven D., Duysburgh E., Montourcy M., De Rouck M., Vilain A. Catteau L. Deblonde J., Wyndham-Thomas C., Van Goethem N. (2020). Points clés de la surveillance des patients hospitalisés atteints d’une infection COVID-19 confirmée: Résultats jusqu’au 14 juin 2020. Bruxelles, Belgique: Sciensano. Numéro de dépôt légal : D/2020/14.440/65. https://covid-19.sciensano.be/sites/default/files/Covid19/COVID-19_THEMATIC%20REPORT_COVID-19%20HOSPITALISED%20PATIENTS_FR.pdf
- Verbeek, H., Gerritsen, D. L., Backhaus, R., de Boer, B. S., Koopmans, R. T., & Hamers, J. P. (2020). Allowing visitors back in the nursing home during the COVID-19 crisis—A Dutch national study into first experiences and impact on well-being. *Journal of the American Medical Directors Association*. 21(7), 900-904. <https://doi.org/10.1016/j.jamda.2020.06.020>
- Verity, R., Okell, L. C., Dorigatti, I., Winskill, P., Whittaker, C., Imai, N., Cuomo-Dannenburg, G., Thompson, H., Walker, P. G. T., Fu, H., Dighe, A., Griffin, J. T., Baguelin, M., Bhatia, S., Boonyasiri, A., Cori, A., Cucunubá, Z., FitzJohn, R., Gaythorpe, K., ... Ferguson, N. M. (2020). Estimates of the severity of coronavirus disease 2019: A model-based analysis. *The Lancet Infectious Diseases*, 20(6), 669–677. [https://doi.org/10.1016/S1473-3099\(20\)30243-7](https://doi.org/10.1016/S1473-3099(20)30243-7)
- Wenham, C., Smith, J., & Morgan, R. (2020). COVID-19: The gendered impacts of the outbreak. *The Lancet*, 395(10227), 846–848. [https://doi.org/10.1016/S0140-6736\(20\)30526-2](https://doi.org/10.1016/S0140-6736(20)30526-2)
- Williamson, E. J., Walker, A. J., Bhaskaran, K., Bacon, S., Bates, C., Morton, C. E., Curtis, H. J., Mehrkar, A., Evans, D., Inglesby, P., Cockburn, J., McDonald, H. I., MacKenna, B., Tomlinson, L., Douglas, I. J., Rentsch, C. T., Mathur, R., Wong, A. Y. S., Grieve, R., ... Goldacre, B. (2020). Factors associated with COVID-19-related death using OpenSAFELY. *Nature*, 584(7821), 430–436. <https://doi.org/10.1038/s41586-020-2521-4>
- Wu, J., McCann, A., Katz, J., & Peltier, E. (2020). 153,000 Missing Deaths: Tracking the True Toll of the Coronavirus Outbreak. *The New York Times*. Retrieved 22 July 2020, from <https://www.nytimes.com/interactive/2020/04/21/world/coronavirus-missing-deaths.html>