Title: Life-years lost by COVID-19 patients in public hospitals of Marseille (APHM- South-Eastern France): a limited death toll

Authors Sylvie Arlotto[1,5], Alice Gares[1,5], Audrey Giraud-Gatineau[3,4], Jean-Christophe Lagier[2,5], Marie Thèrese Jimeno[5,7], Patrick Peretti-Watel [3,6], Matthieu Million[2.5],Philippe Parola[2.3], Philippe Brouqui[2,5], Didier Raoult [2.5], Stephanie Gentile[1,5]

Affiliations:

1-Aix Marseille Univ, School of medicine - La Timone Medical Campus, EA 3279: CEReSS - Health Service Research and Quality of life Center, Marseille, France

2- Aix-Marseille Univ, IRD, APHM, MEPHI, Marseille, France; IHU Méditerranée Infection, Marseille France;

3- Aix Marseille Univ, Institut de Recherche pour le Développement (IRD), Assistance Publique - Hôpitaux de Marseille (AP-HM), Service de Santé des Armées (SSA), Vecteurs - Infections Tropicales et Méditerranéennes (VITROME), Marseille, France;

4-French Armed Forces Center for Epidemiology and Public Health (CESPA), Service de Santé des Armées (SSA), Marseille, France;

5-Assistance Publique- Hôpitaux de Marseille (AP-HM), Marseille, France;

6-Southeastern Health Regional Observatory (ORS Paca), Marseille, France;

7 Service d'Information Médicale Public health Department La Timone Hospital

* Corresponding author: Stéphanie Gentile, StephanieMarie.GENTILE@ap-hm.fr, Aix Marseille Univ, School of medicine - La Timone Medical Campus, EA 3279: CEReSS - Health Service Research and Quality of life Center, Marseille, France

What is already know to is topic?

What is already known is that COVID-19 affects older patients as well as frail patients with co-morbidities, including those with obesity, diabetes, hypertension and cancer.

We also know that COVID-19 has a higher mortality rate in men.

What this study adds?

This study analyzes the profiles of patients who died at the Marseille University Hospital Center on the basis of medical records.

On the basis of their age and comorbidity we calculated a Carlson score which allowed us to adjust the YYL according to national statistics. Our results show that when the medical profile of deceased patients is taken into account, the number of years of life lost calculated solely on the basis of age is divided by three. This confirms that mortality due to COVID disease mainly affects elderly and frail subjects

Abstract

Objective

Between March 1 and June 15, France experienced the first wave of the COVID-19 pandemic, during which 29,549 deaths occurred among COVID-19 patients, 17,250 of whom died in hospital. Our hypothesis is that crude mortality rates are not sufficient to assess the impact of the epidemic on public health. The objective of this paper is to estimate the years of life lost (YLL) of patients who died from Covid 19.

Method

We realized a retrospective analysis of the exhaustive sample of COVID-19 PCR-positive patients who deceased in public hospitals of Marseille during this first wave. Data on demographic characteristics, co-morbidities and care pathways were collected from medical records. The Charlson Comorbidity Index (CCI) was used to assess what would have been the probability of dying within 1 year of these patients in the absence of COVID-19 and to estimate total YLL.

Results

Among the 1,631 patients who were hospitalized for COVID-19, 178 patients died, at an average age of 80 years.

According to CCI, 88.8% of the deceased patients had an 85% probability of dying within one year before COVID-19. Among the 11.2% who had a lower CCI probability, 18 out of 20 had at least one additional co-morbidity known to be a major risk factor of mortality in COVID-19 disease.

Cumulative total number of YLL was estimated to be 541 in this deceased population, i.e. an average of 3 years of life lost.

Conclusion

Although our results should be interpreted with caution, this analysis confirms that mortality due to COVID19 translates into a limited number of YLL due to both old age and preexisting comorbidities in the most vulnerable patients. This fact should be better taken into account in public health management of the pandemic both for risk communication and design of the most appropriate protective measures.

Strengths and limitations of this study

The strengths are:

1. The full analysis of clinical and comprehensive data of all patients who died from Covid19 in a health care facility and their degree of autonomy.
2. The use of the Charlson score, a validated indicator for predicting hospital mortality at one year.
3. Adjusting the calculation of the number of years of life lost based on national INED
4. data for each patient to comorbid status.

The weaknesses are:

1. These are only hospital data and only for one hospital in France.
2. We do not know the profile of patients who died at home. No clinical or even socio-demographic data is currently available in France.

1. Introduction

In France, as in most other European countries, the COVID-19 pandemic has gone through two phases: while the first cases of SARS-CoV-2 were recorded on January 24, 2020 the "first epidemic wave" officially took place between March 1 and June 15, 2020 ; a "second wave" has started in September and has been declining, although at a quite slow pace, since the end of October (1).

Detailed national statistics are already available about deaths attributable to COVID-19 during the first wave (2) and it has been argued that public health measures implemented by national authorities have been effective in reducing the death toll due to SARS-CoV-2 (3–5). Indeed, during this first wave, the French government, has implemented a national lockdown during 55 days lasting from March 17 to May 11, 2020, with a very significant impact both on the use of care (6) and economic activity (7,8). COVID-19 has had a major indirect impact on people that did not contract the virus. For example, people with emergency health needs have sometimes struggled to receive timely acute care, and those with chronic health conditions have faced disruptions to routine care. In addition, the pandemic and the subsequent economic crisis have led to a growing burden of mental ill-health, with emerging evidence of higher rates of stress, anxiety and depression; compounded by disruptions to health care for those with pre-existing mental health conditions (9,10).

However, because COVID-19 frequently causes death in the old and frail, and those with underlying chronic conditions (11,12), the absolute death toll or excess mortality rates do not provide enough information to measure the actual impact of the epidemic. A more relevant measure of the relative public health impact of such epidemic is the measurement of potential years of life lost (13). Indeed, considering the age of death rather than the simple event of death allows a different weight to be assigned to deaths at different times of life. The presumption underlying the potential years of life lost is that a more "premature" death (i.e. at a younger age) will result in a greater loss of life and should be given a higher value from society’s standpoint. YLL is often used in comparing the health system performance of countries in addressing major killer diseases. Moreover, several studies suggest that YLL should be corrected for comorbidities of the deceased (14). Our study is based on data from the Assistance Publique - Hôpitaux de Marseille (AP-HM) which is the 3rd largest university hospital center in France. This CHU is made up of four public hospitals and has 3,400 beds, including 162 intensive care beds. In addition it includes a facility especially devoted to management of infectious diseases and related epidemic situations the University Hospital Institute of Mediterranean Infections (IHU) with 75 inpatient beds, a day hospital, an outpatient department with 14 consultation rooms and a travel clinic. The institute also includes five large NSB3 laboratories with diagnostic laboratories, research teams and technology platforms. Since the beginning of the COVID-19 epidemic, the IHU carried out early and massive PCR screening for both suspected COVID-19 individuals and confirmed case contacts and offered standardized treatment and follow-up for all persons over 18 years of age whose SARS-CoV-2

RNA was documented by PCR from a nasopharyngeal specimen. In total, more than 3,500 COVID-19 patients were followed by the IHU during the first wave of the epidemic (15).

Exhaustive availability of detailed medical files for patients hospitalized due to COVID-19 at the public hospitals of Marseilles (APHM) allowed us to perform a retrospective precise calculation of YLL related to deaths attributable to COVID-19 taking into account the age and sex profile of patients as well as co-morbidity data.

2. Materials & methods

Design and patient selection

We performed a retrospective analysis of PCR-positive patients hospitalized and deceased at the "Assistance Publique - Hôpitaux de Marseille" from March 1 to June 15, 2020.

Patient and Public Involvement: no patient involved

Data collection

During this period, data on all inpatient deaths (COVID-19 and non-COVID-19) and the number of hospitalizations of patients with COVID-19 were extracted from the hospital's information system which is linked to the French National Uniform Hospital Discharge Database (PMSI) (16).

For patients who were registered as having died from COVID-19, we collected data from their patients' medical records but in addition, these files were reviewed by an expert’s group of physicians to ultimately validate data on patient's demographics and lifestyle, pre-existing co-morbidities, care pathway and cause of death. In particular, for each patient, we checked that death was effectively due to COVID-19 and verified that it could not be attributed to another disease (e.g. cancer). In addition, co-morbidities diagnosed prior to hospital admission were collected based on anamnestic data.

In total, the data collected was as follows

Socio-demographic data: gender, age, date of death.

Data concerning in-hospital care pathway: the admission type (directly from home, from the emergency departments or transferred from another hospital), their transfer to the intensive care unit, the length of hospital stay and the number of patients in limitation and discontinuation of active therapies (LATA).

Lifestyle: Where the patient lived (institution or at home), the existence of a loss of autonomy and whether the patient was bedridden or not.

Patients' comorbidities: We used the Charlson Comorbidity Index (CCI) to assess what would have been the probability of death within 1 year of these patients in the absence of COVID-19 (17). This index is designed to predict 1-year mortality on the basis of a weighted composite score for the following categories: cardiovascular, endocrine (only diabetes), pulmonary, neurologic, renal, hepatic, gastrointestinal, and neoplastic diseases. It takes into account 19 comorbidities. Comorbidities are weighted from 1 to 6 for mortality risk and disease severity. The final score is obtained by summation of the weighted comorbidity scores adjusted on the patient's age (1 point for each decade from the age of 41 years). The higher the score, the higher the likelihood of mortality is within a one-year period according to the following algorithm: Score = 0 → Estimated 1-year mortality = 12%; Score = 1-2 → Estimated 1-year mortality = 26%; Score= 3-4 → Estimated 1-year mortality = 52%; Score ≥ 5 → Estimated 1-year mortality = 85% or more.

In addition, comorbidities that are not included in the CCI but are well-known for being risk factors of aggravated morbidity and mortality in COVID-19 patients (obesity, hypertension, sleep apnea, asthma, hypothyroidism, dyslipidemia, psychiatric disease and neurological pathology -excluding dementia) were also collected.

3. Statistical analysis

The dichotomous variables were described as whole integers and percentages, and the continuous variables as mean and standard deviation (or median and interquartile range in those with no criteria of normal distribution). The distribution of all variables was analyzed with the Kolmorogov-Smirnov test.

Age was grouped into the following classes: 0-40 years of age; 41-50 years of age; 51-60 years of age; 61-70 years of age; 71-80 years of age; 81-90 years of age; 90 years of age and over.

We estimated the number of years of life lost (YLL) by combining the CCI probabilities of dying within one year in each age and gender groups with average life expect according to national statistics (INED) (18)for those who would have survived in each of these groups.

We also established the crude mortality rate by calculating the ratio of number of deaths among the total number of hospitalized patients for COVID-19.

4. Results

Between March 1 and June 15, 2020, a total of 1,631 patients were hospitalized for COVID-19 at "Assistance Publique - Hôpitaux de Marseille" (APHM), including 702 at the IHU and 929 in other departments.

Among them 178 ultimately died with death being attributable to COVID-19 with certainty, a mortality rate of 10.9%.

At the Marseille University Hospitals, in the last three years before 2020, there were an average of 246 deaths per month. In 2020, over the period studied, there were no more deaths per month, except in the month of April. The proportion of COVID-19 deaths for the four months averaged 16% of total number of deaths among patients being hospitalized at APHM (10% in March, 40% in April, 15% in May and 1% in June).

Table 1 presents descriptive statistics about demographic and clinical characteristics of COVID-19 deceased patients as well as comparison between the great majority (n=158) who had an a priori 85% probability or more of dying within one year according to CCI calculation versus those who did not (n=20). Mean age at death was 80 years old (25th percentile 72.8, Median 82, 75th percentile 89) and nearly two thirds of deceased patients were men. Nearly two thirds of patients were frail and 18% were already bedridden before their COVID-19 hospitalization. More than two-thirds (70.8%) of patients directly entered the hospital through the emergency departments. The most common care pathway was direct admission to the emergency department, followed by a conventional hospitalization (54.5%). One quarter of patients were transferred to intensive care (25.8%) during their hospitalization, and more than half of them were admitted in ICU within the first 24 hours after their admission. For 17.4% of patients, a limitation of active therapies had to be decided at some point of follow-up.

Table 1- Demographic, clinical characteristics and Charlson Comorbidity Index of COVID 19+ deceased patients in Marseilles (South Eastern France (public hospitals – March/June 2020 (n = 178)

		Probability of dying within one year		
	Total	**> 85%**	**< 85%**	**p**
Number of patients	**178**	**158**	**20**	
Men % (n)	60.7 (108)	59.5 (94)	70 (14)	0.365
Age Group % (n)				
0-40	0.6 (1)	0 (0)	5 (1)	
40-50	0.6 (1)	0 (0)	5 (1)	
51-60	5.6 (10)	3.2 (5)	25 (5)	<0.001
61-70	12.4 (22)	8.9 (14)	40 (8)	
71-80	27.5 (49)	27.8 (44)	25 (5)	
81-90	37.1 (66)	42 (66)	0 (0)	
> 90	16.6 (29)	18.5 (29)	0 (0)	

Quality of life style data				
Living in institutionalization % (n)	24.7 (44)	26.6 (42)	10 (2)	0.016
Bedridden & living in institutionalization % (n)	11.2 (20)	12 (19)	5 (1)	
Loss of autonomy & living at home % (n)	21.3 (38)	24.1 (38)	0 (0)	<0.001
Bedridden & living at home % (n)	6.7 (12)	7.6 (12)	0 (0)	0.210
Length hospital stays				
Average length of hospital stay (days)	10.4 ± 11.4 Median 7 Min 0 – Max 68	9.7 ± 10.7 Median 7 Min 0 – Max 68	15.5 ± 14.6 Median 10 Min 0 – Max 50	0.031
Length of hospital stay < 48 h	14 (25)	14.6 (23)	10 (2)	0.744
Patient healthcare trajectory				
Emergency department - Hospitalization conventionally % (n)	54.5 (97)	60.1 (95)	10 (2)	
Emergency department - Intensive care unit % (n)	9 (16)	7.6 (12)	20 (4)	
Emergency department - Hospitalization conventionally - Intensive care unit % (n)	7.3 (13)	5.1 (8)	25 (5)	
Home- Hospitalization conventionally % (n)	17.4 (31)	18.4 (29)	10 (2)	0.000
Home -Hospitalization conventionally - Intensive care unit % (n)	6.7 (12)	4.4 (7)	25 (5)	
Transfert - Hospitalization conventionally % (n)	1.7 (4)	2,5 (4)	0 (0)	
Transfert - Hospitalization conventionally - Intensive care unit % (n)	2.8 (5)	1,9 (3)	10 (2)	
Patient in limitation and discontinuation of active therapies (LATA) % (n)	17.4 (31)	19.6 (31)	0 (0)	0.028
Charlson comorbidity index				
Myocardial infarct % (n)	17.4 (31)	19.0 (30)	5 (1)	0.207
Congestive heart failure % (n)	14.6 (26)	16.5 (26)	0 (0)	0.048
Peripheral vascular disease % (n)	12.9 (23)	22 (13.9)	5 (1)	0.478

Cerebrovascular disease % (n)	11.8 (21)	13.3 (21)	0 (0)	0.136
Dementia % (n)	28.7 (51)	31 (49)	10 (2)	0.050
Chronic pulmonary disease % (n)	16.9 (30)	17.7 (28)	10 (2)	0.534
Connective tissue disease % (n)	1.7 (3)	1.9 (3)	0 (0)	1.000
Ulcer disease % (n)	5.1 (9)	5.7 (9)	0 (0)	0.600
Mild liver disease % (n)	1.7 (3)	1.9 (3)	0 (0)	1.000
Diabetes % (n)	27 (48)	27.2 (43)	25 (5)	0.833
Hemiplegia % (n)	1.7 (3)	1.9 (3)	0 (0)	1.000
Moderate or severe renal disease % (n)	12.4 (22)	13.9 (22)	0 (0)	0.075
Diabetes with end organ damage % (n)	2.2 (4)	2.5 (4)	0 (0)	1.000
Active tumor % (n)	10.1 (18)	11.4 (18)	0 (0)	0.111
Leukemia % (n)	0 (0)	0 (0)	0 (0)	
Lymphoma % (n)	3.4 (6)	3.8 (6)	0 (0)	1.000
Moderate or severe liver disease % (n)	1.7 (3)	1.9 (3)	0 (0)	1.000
Metastatic solid tumor % (n)	5.6 (10)	6.3 (10)	0 (0)	0.606
AIDS % (n)	0 (0)	0 (0)	0 (0)	
Other comorbidities				
• Obesity % (n)	11.8 (21)	8.9 (14)	35 (7)	0.003
• Asthma % (n)	5.6 (10)	5.1 (8)	10 (2)	0.312
• Hypertension % (n)	68.4 (117)	68.4 (108)	45 (9)	0.038
• Sleep Apnea % (n)	7.3 (13)	6.4 (10)	15 (3)	0.166
• Dyslipidemia % (n)	14.6 (26)	15.8 (25)	5 (1)	0.316
• Hypothyroidism % (n)	8.4 (15)	8.9 (14)	5 (1)	1.00
• Psychiatric disease	15.2 (27)	15.2 (24)	15 (3)	1.000
• Neurological pathology (excluding dementia)	15.2 (27)	16.5 (26)	5 (1)	0.318
All comorbidities	3.6 ± 1.8	3.8 ± 1.8	2.1 ± 1.2	0.001
	Median 3 Min 0 – Max 10	Median 4 Min 1 – Max 10	Median 2 Min 0 – Max 4	

Of the 178 patients, 25 died within the first 48 hours after admission, including 8 who died within the first 24 hours: two of these later patients had been transferred from the intensive care unit of another hospital, five came directly from their nursing home and one only from his personal home.

The most common co-morbidities included in the CCI were dementia (29%), uncomplicated diabetes (27%) and chronic pulmonary disease (17%). Hypertension was the most common co-morbidity among co-morbidities not included in the CCI (68.4%)

All deaths were clearly attributable to COVID-19 disease; three patients died as a result of arterial thrombotic disease: stroke, myocardial infarction and mesenteric ischemia; all others died as a result of acute respiratory syndrome.

<u>Estimation of probability of mortality at one year:</u>

According to CI 88.8% of patients had 85% probability of dying within one year, 10.1% a 52% probability (n = 18), one patient 26% and one 12%.

Analysis by age group shows that 34 patients were under 71 years. Of these, 19 had an 85% probability of dying within one year according to CCI. The profile of these 34 patients is presented in Table 2.

Table 2_ Clinical profile of deceased patients under 71 years of age.

Age group	% probability of dying within on years (Charlson)	Clinical description	No. of comorbidities	Life style
≤ 41 Years (1 patient)	12 (100%)	History of severe immune reaction to a viral infection	0	self-sufficient
41 - 50 Years (1 patient)	52 (100%)	Severe autism (syndrom of USHER), deaf, dumb, blind	4	bedridden / Institutionalised
51 - 60 Years (10 patients)	26 (10%)	None	0	
	52 (40%)	Dementia + Bundle branch block	2	Institutionalised
		High blood pressure + Asthma	2	self-sufficient
		Chronic pulmonary disease+ High blood pressure+ Sleep Apnea + hypothyroidism	4	self-sufficient
		Diabetes + High blood pressure + Congestive heart failure	3	self-sufficient
	85 (50%)	Metastatic solid tumor	1	Loss of independence
		Congestive heart failure + Renal disease + Diabetes + Dyslipidemia + Abdominal aortic aneurysm + Rheumatoid polyarthritis	6	bedridden
		Cerebrovascular disease + Chronic pulmonary disease (with home oxygen therapy) + Diabetes + High blood pressure + Asthma + Dyslipidemia + Sickle cell disease	7	self-sufficient
		Metastatic solid tumor + Cerebrovascular disease with Hemiplegia + High blood pressure	4	Loss of independence
		Metastatic solid tumor + Ulcer	2	Loss of independence

61 -70 Years (22 patients)	52 (36.4%)	Diabetes + High blood pressure + obesity	3	self-sufficient
		Diabetes + High blood pressure + obesity + Anxiety disorders + Rhythm disorder	5	self-sufficient
		Diabetes with chronic complications + obesity	2	self-sufficient
		Diabetes + Sleep Apnea + obesity+ mesenteric ischemia	3	self-sufficient
		High blood pressure + obesity + atrial fibrillation	3	self-sufficient
		High blood pressure	1	self-sufficient
		None	0	self-sufficient
		Schizophrenia + morbid obesity + hypothyroidism	3	Institutionalised
	85 (63.6%)	Dementia +Chronic pulmonary disease+ Anxio-depressive disorders	3	Institutionalised
		Chronic pulmonary disease + obesity + Diabetes + High blood pressure+ asthma	5	self-sufficient
		Malignancy (malignancy, including leukemia and lymphoma) + Chronic pulmonary disease + Speep Apnea + Polyarthrite rhumatoïde	4	self-sufficient
		Congestive heart failure+ obesity + pulmonary hypertension+ Diabetes + High blood pressure + dyslipidemia	7	self-sufficient
		Chronic pulmonary disease + asthma + Diabetes + High blood pressure	4	Loss of independence
		End stage Renal disease + High blood pressure + Congestive heart failure	3	self-sufficient
		Malignancy (malignancy, including leukemia and lymphoma)+ dysphagia or oro-esophageal ulcerations	2	self-sufficient
		Metastatic solid tumor+ Heart arrhythmia	2	Loss of independence
		Severe epilepsy + hepatitis B + mental retardation	3	Institutionalised
		Metastatic solid tumor	1	Loss of independence
		Dementia + Congestive heart failure + High blood pressure +amyloid angiopathy + Normal pressure hydrocephalus	5	bedridden / Institutionalised
		Dementia + obesity morbide + High blood pressure + hypothyroidism + Chronic pulmonary disease + venous insufficiency	7	bedridden / Institutionalised
		Dementia (Korsakoff) + Cerebrovascular disease with hemiplegia + Renal disease + Congestive heart failure+ High blood pressure + undernutrition	6	bedridden / Institutionalised
		Congestive heart failure + dyslipidemia + Diabetes + High blood pressure	4	self-sufficient

Among the 5 patients aged between 51 and 60 years, who had an 85% probability of dying within one year, one was bedridden with 6 comorbidities, 3 had metastasized cancer and 1 had 7 comorbidities, including chronic respiratory failure requiring home oxygen therapy.
Among the 14 patients aged between 61 and 70 years, 8 already presented a loss of autonomy, including 3 bedridden patients. They all had numerous comorbidities such as dementia or the triad of diabetes, obesity and hypertension. The three patients who had less than 3 comorbidities, suffered from cancer including two metastatic ones.
Among the 4 patients aged between 51 and 60 years with a 52% probability of dying within a year according to CCI score, one was already institutionalized for severe dementia and the three others patients had cardiac and pulmonary significant comorbidities and had to be transferred to ICU during the first 24- hours after admission due to a severe clinical condition. Only one patient in this age group had no co-morbidities and a 26% probability of death according to CCI.
Among the 8 patients aged 61 to 70 years with a 52% probability of dying within a year according to CCI score, one was already institutionalized with serious pathologies and 5 patients had at least two of three major risk factors for COVID-19 mortality: obesity, diabetes and/or cardiovascular pathologies. Finally, two patients without significant comorbidities had been directly hospitalized through the emergency departments and were transferred to intensive care, one of them within the first 24 hours.
Finally, it must be mentioned that the two deceased patients younger than 51 years old already had poor prognosis before COVID-19: one of them was an institutionalized bedridden patient with multiple severe comorbidities, and the other one had a severe autoimmune disease with a history of myocarditis related to a viral infection (influenza).

Among the 49 deceased patients aged between 71 and 80 years, only five had an estimated 52% probability of dying within one year including 4 who presented at least one major risk of comorbidity for COVID-19 (cardiac pathology, diabetes or obesity). All five had been transferred to ICU. The remaining 44 deceased patients in this age group had an ex-ante 85% probability of dying within one year and, more than half (n=24, 54.5%) were already presenting some loss of autonomy, including 19 of them being bedridden and/or institutionalized. The majority of these 44 patients had been directly hospitalized through the emergency departments (n=37, 84%) and 13 (29%) were transferred to intensive care within the first 24 hours. The average number of co-morbidities in this group was 4.4, the most represented being hypertension (n=30, 68%), diabetes (n=18, 40%), always associated with hypertension or obesity, dementia (n=17, 38.6%), history of ischemic heart disease or heart failure (n=17, 38.6%), chronic respiratory pathologies (n=10, 22.7%) and neurological diseases other than dementia (n=10, 22.7%).

The profile of patients aged between 81 and 90 years, the most numerous among our population (n=66) was like that of patients in the decade 71-80 with an 85% probability of dying within a year.

More than half (n=49, 81%) were in loss of autonomy, 32 of whom were bedridden and/or institutionalized. Three-quarters (n=50, 75.7%) were admitted through the emergency room. The average number of co-morbidities was 3.5, the most represented being hypertension (n=45, 68%), diabetes (n=20, 30) always associated with hypertension or obesity, dementia (n=18, 27%), history of ischemic heart disease or heart failure (n=25, 37.8%), chronic respiratory pathologies (n=10, 15%) and neurological diseases other than dementia (n=12, 18%). Among this age group, only 9% had been transferred to intensive care versus 35% for patients aged between 71 and 80.

Finally, 29 patients were over 90 years old (16%). The vast majority were in loss of autonomy (n=26, 89%), 20 of whom were bedridden and/or institutionalized. Of these 29 patients, 17 had entered the hospital through the emergency departments and none had been admitted to intensive care. The mean number of co-morbidities was 3.4, the most common being hypertension (n=26, 89%), dementia (n=9, 34%), history of ischemic heart disease or heart failure (n=8, 27.5%).

If co-morbidities were not taken into account, the total number of YLL in the deceased population would have been estimated as 1776 years, i.e. an average of 10 years per patient. Taking into account the CCI to adjust for pre-existing comorbidities leads to a reduced more accurate estimation of 541 YLL, i.e. an average of 3 years of life lost (Table 3).

Table 3 – Years of life lost by COVID 19 + deceased patients in Marseilles hospitals (March-June 2020)

Age	No of patients	YLLs (using average life expectancy for age & gender)	YLLs (adjusted by Charlson Comorbidity Index)
0-40	1	57.7	50.8
40-50	1	33	15.8
51-60	10	264.3	76.75
61-70	22	437.5	133.5
71-80	49	583.6	147.2
81-90	66	399.8	117
> 90	29	0	0
Total		1775.9	541.05

5. Discussion

During the period studied that corresponds to the first wave of the COVID-9 pandemic in France, a total of 17 250 inpatients died from COVID-19 in France of which 870 in the Marseilles region. Our analysis of COVID-19 related deaths in public hospitals of Marseilles, the main city in this geographical area, represent 20.4% of the total death toll from COVID-19 in this region (19).

Surprisingly, we saw a decrease in the total number of deaths in CHU Marseille from all causes during this first epidemic phase, with excess mortality due to COVID-19 being only observed during the four weeks of the month of April ; a fact being corroborated by national statistics showing that 80% of COVID-19 related deaths occurred during this same month of April (19). This may be explained by the deprogramming of care for non-COVID-19 and non-urgent patients and the generalized lockdown that forced people to stay at home away from emergency care (6).

Three-quarters of COVID-19 deceased patients included in our analysis were admitted to hospital through emergency departments, and of the patients admitted to intensive care, more than half were transferred during the first 24 hours after hospitalization. These results showing that many patients who ultimately died were admitted in hospitals with an already highly critical condition, suggest that medical care pathways prior to hospitalization had not been optimal. They raise concerns about the appropriateness of the French national recommendations in place during the first lockdown that encouraged COVID-19 patients to stay isolated at home with no medical follow-up and to wait for clinical symptoms of a worsening condition, mainly based on the appearance of dyspnea, to call medical emergency services (Centre SAMU 15) (20). Such recommendations may have led to delays in medical consultations for a significant proportion of patients requiring emergency care, since numerous publications have subsequently shown that dyspnea is not an essential criterion of initial severity for COVID-19 related disease. Indeed, in Marseilles hospitals, about one third of COVID-19 patients feeling well and without dyspnea, had hypoxemia (happy or silent hypoxemia) at time of first admission, which is strongly associated with a poor prognosis (21–23).

In our analysis, 88.8% of COVID-19 deceased patients had 85% probability of dying within one year, according to the Charlson Comorbidity Index (CCI). Among the various methods used to predict hospital mortality by weighting comorbidities, CCI has been widely applied since many studies have consistently demonstrated that it is a valid prognostic indicator for mortality. This index has been validated for its ability to predict mortality in various disease subgroups, including cancer, renal disease, stroke, intensive care, and liver disease (17,24–28). Only 20 of the deceased patients had a lower probability of death within one year (< 85%) according to CCI but nearly all of them (18 out of 20) exhibited at least two co-morbidities (obesity, hypertension, diabetes, etc.) that are not included in the CCI but are well-known for being major risk factors of severity and mortality in the case of COVID-19 infection. Overall, we estimated an average of 3 years of life lost per deceased individual. Indeed, our analysis has tended to overestimate total number of YLL since the Charlson's score does not include some comorbidities that are major risk factors in the context of COVID-19. Of the 178 deceased patients, only two died without a diagnosed co-morbidity. In the Italian study, similar to ours, only 4% of the patients had no co-morbidities. Overall, as in the Italian study on the death profiles of COVID-19 patients, we found a quarter (27%) of all our deceased patients with at least 2 of the 3 co-morbidities (diabetes, obesity or hypertension) that are the main risk factors for COVID-19 disease (29).

The main result of our study is that the largest share of COVID-19 mortality occurs among individuals who already had an ex-ante high probability of death within one year due to old age and/or pre-existing morbidity. This finding is in line with all previous studies demonstrating that presence of comorbidities is associated with a higher risk of mortality and negative outcomes in COVID-19 patients pre-existing diseases (30–32).

Generalizability of our findings based on COVID-19 patients followed in the main public hospitals of Marseilles during the first wave of the pandemic must be interpreted with some limitations in mind. First, our analysis focused only on patients dying in hospital and did not include deaths at home or in institutions for managed care of the elderly. It must however be noted that on average individuals living in institutions caring for the elderly are 85 years old or more (33) ;YLL due to COVID-19 is likely to have been also limited in this population, although reduction of care and social activities, and disruption of family visits that resulted from the lockdown, may have accelerated death of these individuals and has certainly decreased their quality of life and well-being. The exact causes of death at home during the study period are not yet available, but in any case attributing these deaths to COVID-19 disease will not be easy, as it is now established that during the national first lockdown in France, access to care has been significantly reduced for non COVID-19 patients especially for cardiovascular pathologies, vascular accidents and cancer surgery (34,35). Second, although the age and gender distribution of patients who died in our sample is similar to that observed at the national level and the time profile of mortality due to COVID-19 is also similar between the public hospitals in Marseille and the national statistics, we cannot claim that our results are fully representative of the overall situation in France. Indeed, mortality among Marseilles hospitalized patients due to COVID-19 has been significantly lower (11 %) than the national (19%) and even regional (14.5%) mortality rates. In Marseilles, the presence of the IHU has enabled the early implementation of standardized mass screening and treatment protocols, which may have significantly contributed to quality and safety of care (19).

Despite these limitations, our results could be useful to inform two dimensions of public health policies dealing with the COVID-19 pandemic in France and elsewhere.

The first-dimension deals with risk communication in the context of an infectious disease pandemic. The management of the COVID-19 epidemic led to a quite unprecedented situation, in which mortality was highlighted almost constantly, with daily updates of death statistics in social media and news. The wearing of face masks, the use of antibacterial sprays and wipes, as well as social distancing and public health campaigns were also visible and may have been interpreted by some sectors of the population as ubiquitous indicators of death (36). It is now well established that daily reporting of the number of deaths, combined with widespread lockdown, has been very prejudicial to the mental health of the general population, in France as in other countries (37,38). The absolute number of deaths is an imperfect measure of mortality and is not a good representation of the severity of the epidemic, as it does not provide insight into the age distribution of deaths or how risk levels vary by age, and consequently does offer enough information as to how many years of life were lost due to the disease. Our study suggests that the number of deaths should not be communicated to the population without contextualizing it, i.e. without comparing it to the previous years, and without describing the patient profile (at least age).

The second dimension deals with the complex trade-offs involved in public decision-making between saving lives from a major infectious threat such as Sars-Cov-2 on the one hand, while maintaining adequate health care for other diseases and limiting the social and economic consequences of restrictive public health measures to contain the spread of the virus on the other hand. The choice of public authorities to save lives "whatever the cost is", according to the words of French president, Emmanuel Macron (39), is highly respectable on ethical grounds. However, the limited number of YLL observed in our study when confronted to the social and economic loss due to lockdown (an estimated 9 to 11% reduction of national GDP in 2020) suggest that the cost of saving life-years from COVID-19 has been above the thresholds usually deemed acceptable in medical care (40–43). Moreover, the fact that COVID-19 mortality tends to concentrate among individuals with a high probability of dying from other causes in the short term raises questions about intergenerational equity (44,45) that should be a matter of a more transparent public debate in order to maintain a large consensus in the whole population around the fight against the pandemic.

Contributors Author: SG, SA, DR conceived the research and participated in the study design. SA, SG, AG, AGG and MTJ assisted in collecting the data. SA, AG and SG analyzed the data. SG, SA drafted the manuscript. All authors read and approved the final manuscript.

Competing interests: None declared.

Funding: The authors have not declared a specific grant for this research from any funding agency in the public, commercial or not-for-profit sectors

Patient consent for publication: Not required.

Ethics approval: Data presented were collected retrospectively using the electronic health recording system of the hospital in accordance with the European Regulation n°2016/679 General Data Protection Regulation (GDPR) and registered in the hospital's GDPR registry n°2019-74.

Data sharing statements: Data are available upon reasonable request.

6. References

1. Santé Publique France. COVID-19 : point épidémiologique du 3 décembre 2020 [Internet]. Santé Publique France. Available from: /maladies-et-traumatismes/maladies-et-infections-respiratoires/infection-a-coronavirus/documents/bulletin-national/covid-19-point-epidemiologique-du-3-decembre-2020

2. Fouillet A, Pontais I, Caserio-Schönemann C. Excess all-cause mortality during the first wave of the COVID-19 epidemic in France, March to May 2020. Euro Surveill Bull Eur Sur Mal Transm Eur Commun Dis Bull. 2020;25(34).

3. Di Domenico L, Pullano G, Sabbatini CE, Boëlle P-Y, Colizza V. Impact of lockdown on COVID-19 epidemic in Île-de-France and possible exit strategies. BMC Med. 2020 Jul 30;18(1):240.

4. De Figueiredo AM, Codina AD, Cristina D, Figueiredo MM, Saez M, León AC. Impact of lockdown on COVID-19 incidence and mortality in China: an interrupted time series study. :19.

5. Siqueira CA dos S, de Freitas YNL, Cancela M de C, Carvalho M, Oliveras-Fabregas A, de Souza DLB. The effect of lockdown on the outcomes of COVID-19 in Spain: An ecological study. PLoS ONE. 2020 Jul 29;15(7).

6. Pullano G, Valdano E, Scarpa N, Rubrichi S, Colizza V. Evaluating the effect of demographic factors, socioeconomic factors, and risk aversion on mobility during the COVID-19 epidemic in France under lockdown: a population-based study. Lancet Digit Health. 2020 Dec;2(12):e638–49.

7. Chen S, Igan D, Pierri N, Presbitero A. Tracking the Economic Impact of COVID-19 and Mitigation Policies in Europe and the United States. IMF Work Pap. 2020 Jul 10;20.

8. Malliet P, Reynès F, Landa G, Hamdi-Cherif M, Saussay A. Assessing Short-Term and Long-Term Economic and Environmental Effects of the COVID-19 Crisis in France. Environ Resour Econ. 2020 Aug 1;76(4):867–83.

9. Beck F, Léger D, Fressard L, Peretti-Watel P, Verger P. Covid-19 health crisis and lockdown associated with high level of sleep complaints and hypnotic uptake at the population level. J Sleep Res. 2020 Jun 28;

10. OECD/European Union (2020). How resilient have European health systems been to the COVID-19 crisis? In: Health at a Glance: Europe 2020: State of Health in the EU Cycle [Internet]. Paris; Available from: https://doi.org/10.1787/85e4b6a1-en.

11. Zhou F, Yu T, Du R, Fan G, Liu Y, Liu Z, et al. Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: a retrospective cohort study. The Lancet. 2020 Mar 28;395(10229):1054–62.

12. Weiss P, Murdoch DR. Clinical course and mortality risk of severe COVID-19. The Lancet. 2020 Mar 28;395(10229):1014–5.

13. Maximova K, Rozen S, Springett J, Stachenko S. The use of potential years of life lost for monitoring premature mortality from chronic diseases: Canadian perspectives. Can J Public Health Rev Can Sante Publique. 2016 15;107(2):e202–4.

14. Cassini A, Högberg LD, Plachouras D, Quattrocchi A, Hoxha A, Simonsen GS, et al. Attributable deaths and disability-adjusted life-years caused by infections with antibiotic-resistant bacteria in the EU and the European Economic Area in 2015: a population-level modelling analysis. Lancet Infect Dis. 2019;19(1):56–66.

15. VITROME – IHU [Internet]. [cited 2020 Dec 17]. Available from: https://www.mediterranee-infection.com/recherche/vitrome/

16. Boudemaghe T, Belhadj I. Data Resource Profile: The French National Uniform Hospital Discharge Data Set Database (PMSI) . Int J Epidemiol. 2017 Apr;46(2):392-392d.

17. Charlson ME, Pompei P, Ales KL, MacKenzie CR. A new method of classifying prognostic comorbidity in longitudinal studies: development and validation. J Chronic Dis. 1987;40(5):373–83.

18. Tables de mortalité par sexe, âge et niveau de vie − Tables de mortalité par niveau de vie | Insee [Internet]. [cited 2020 Dec 17]. Available from: https://www.insee.fr/fr/statistiques/3311422?sommaire=3311425&q=table+mortalit%C3%A9

19. Courtejoie N, Dubost C-L. Parcours hospitalier des patients atteints de la Covid-19 lors de la première vague de l’épidémie. DREES. 2020 Oct;(67):39.

20. Ministère des Solidarités et de la Santé: Que faire si la maladie s’aggrave ? [Internet]. Available from: https://solidarites-sante.gouv.fr/

21. Brouqui P, Amrane S, Million M, Cortaredona S, Parola P, Lagier J-C, et al. Asymptomatic hypoxia in COVID-19 is associated with poor outcome. Int J Infect Dis. 2021 Jan;102:233–8.

22. Shenoy N, Luchtel R, Gulani P. Considerations for target oxygen saturation in COVID-19 patients: are we under-shooting? BMC Med. 2020 Aug 19;18(1):260.

23. Tobin MJ, Laghi F, Jubran A. Why COVID-19 Silent Hypoxemia Is Baffling to Physicians. Am J Respir Crit Care Med. 2020 Aug 1;202(3):356–60.

24. Singh B, Bhaya M, Stern J, Roland JT, Zimbler M, Rosenfeld RM, et al. Validation of the Charlson comorbidity index in patients with head and neck cancer: a multi-institutional study. The Laryngoscope. 1997 Nov;107(11 Pt 1):1469–75.

25. Fried L, Bernardini J, Piraino B. Charlson comorbidity index as a predictor of outcomes in incident peritoneal dialysis patients. Am J Kidney Dis Off J Natl Kidney Found. 2001 Feb;37(2):337–42.

26. Tessier A, Finch L, Daskalopoulou SS, Mayo NE. Validation of the Charlson Comorbidity Index for predicting functional outcome of stroke. Arch Phys Med Rehabil. 2008 Jul;89(7):1276–83.

27. Christensen S, Johansen MB, Christiansen CF, Jensen R, Lemeshow S. Comparison of Charlson comorbidity index with SAPS and APACHE scores for prediction of mortality following intensive care. Clin Epidemiol. 2011 Jun 17;3:203–11.

28. Quan H, Li B, Couris CM, Fushimi K, Graham P, Hider P, et al. Updating and validating the Charlson comorbidity index and score for risk adjustment in hospital discharge abstracts using data from 6 countries. Am J Epidemiol. 2011 Mar 15;173(6):676–82.

29. Iaccarino G, Grassi G, Borghi C, Ferri C, Salvetti M, Volpe M, et al. Age and Multimorbidity Predict Death Among COVID-19 Patients: Results of the SARS-RAS Study of the Italian Society of Hypertension. Hypertens Dallas Tex 1979. 2020;76(2):366–72.

30. Kuswardhani RAT, Henrina J, Pranata R, Lim MA, Lawrensia S, Suastika K. Charlson comorbidity index and a composite of poor outcomes in COVID-19 patients: A systematic review and meta-analysis. Diabetes Metab Syndr Clin Res Rev. 2020 Nov 1;14(6).

31. Christensen DM, Strange JE, Gislason G, Torp-Pedersen C, Gerds T, Fosbol E, et al. Charlson Comorbidity Index Score and Risk of Severe Outcome and Death in Danish COVID-19 Patients. J Gen Intern Med. 2020 Jun 24;1–3.

32. Bezzio C, Saibeni S, Variola A, Allocca M, Massari A, Gerardi V, et al. Outcomes of COVID-19 in 79 patients with IBD in Italy: An IG-IBD study. Gut. 2020 Jul 1;69(7).

33. Ministère des Solidarités et de la Santé. 728 000 résidents en établissements d'hébergement pour personnes âgées en 2015 [Internet]. Available from: https://drees.solidarites-sante.gouv.fr/etudes-et-statistiques/publications/etudes-et-resultats/article/728-000-residents-en-etablissements-d-hebergement-pour-personnes-agees-en-2015

34. Bulletin de l'Académie Nationale de Médecine. The resumption of surgical activities: A health emergency and a contribution to the economic recovery. 2020 May.

35. Bersano A, Kraemer M, Touzé E, Weber R, Alamowitch S, Sibon I, et al. Stroke care during the COVID-19 pandemic: experience from three large European countries. Eur J Neurol. 2020 Sep;27(9):1794–800.

36. Menzies RE, Menzies RG. Death anxiety in the time of COVID-19: theoretical explanations and clinical implications. Cogn Behav Ther. 2020 Jun 11;13.

37. Chan-Chee C, Léon C, Lasbeur L, Lecrique J-M, Raude J, Arwidson P, et al. The mental health of the French facing the COVID-19 crisis: prevalence, evolution and determinants of anxiety disorders during the first two weeks of lockdown (coviprev study, march 23-25 and march 30 – april 1st, 2020). (Santé Publique France).

38. Peretti-Watel P, Alleaume C, Léger D, Beck F, Verger P. Anxiety, depression and sleep problems: a second wave of COVID-19. Gen Psychiatry. 2020 Sep 22;33(5).

39. Adresse aux Français, 12 mars 2020 [Internet]. elysee.fr. [cited 2020 Dec 17]. Available from: https://www.elysee.fr/emmanuel-macron/2020/03/12/adresse-aux-francais

40. McCabe C, Claxton K, Culyer AJ. The NICE Cost-Effectiveness Threshold. PharmacoEconomics. 2008 Sep 1;26(9):733–44.

41. Devlin N, Parkin D. Does NICE have a cost-effectiveness threshold and what other factors influence its decisions? A binary choice analysis. Health Econ. 2004;13(5):437–52.

42. Dubois RW. Cost–effectiveness thresholds in the USA: are they coming? Are they already here? J Comp Eff Res. 2015 Dec 21;5(1):9–12.

43. Moatti JP, Marlink R, Luchini S, Kazatchkine M. Universal access to HIV treatment in developing countries: going beyond the misinterpretations of the 'cost-effectiveness' algorithm. AIDS Lond Engl. 2008 Jul;22 Suppl 1:S59-66.

44. Williams A. Intergenerational Equity: An Exploration of the 'Fair Innings' Argument. Health Econ. 1997;6(2):117–32.

45. Asheim GB. Intergenerational Equity. Annu Rev Econ. 2010;2:197–222.