



Characteristics of SARS-CoV-2 patients dying in Italy Report based on available data on March 1st, 2021

1. Sample

The present report describes the characteristics of 96,149 SARS-CoV-2 patients dying in Italy*, as reported by the Integrated Covid-19 Surveillance System coordinated by the National Institute of Health-ISS. Geographic distribution across the 19 regions and 2 autonomous provinces of Trento and Bozen is presented in *Table 1*. Absolute number and percentage of deaths are reported according to the 3 phases that characterized the pandemic from the beginning in 2020 to the 1st of March 2021: the first wave (March-May 2020), the low incidence phase (June-September 2020), and the second wave (October 2020 – March 2021), the latter is still ongoing.

The surveillance data on deaths are constantly updated and consolidated and both activities require time to be carried out. Each Region has its own organization for updating data and related execution times. Therefore, when reading the data by Region, it is necessary to take into account that the timing of notification, control, verification and updating of data varies from Region to Region and from period to period; this may involve variations (increasing and/or decreasing) and differences both with the data already published in the previous reports, and with the data published by the Civil Protection. It should also be considered that the regional differences in the percentage of deaths reported in the table should not be interpreted in terms of risk. In fact, case fatality depends on the number of infections occurring in each region over a period of time compatible with the possible observation of the fatal event. In this regard, it should also be taken into account that the difference between the number of infections and the notified cases may vary regionally and over time as a function of different test access strategies adopted during the epidemic, thus distorting the comparison of regional case fatality.

Table 1. Geographic distribution of deceased patients SARS-CoV-2 positive by period

REGION	March-May 20		June-Sept 20		Oct 20-March 21		Total	
	N	%	N	%	N	%	N	%
Lombardia	16,366	47.7	608	32.9	11,141	18.6	28,115	29.2
Emilia-Romagna	4,313	12.6	173	9.4	6,057	10.1	10,543	11.0
Veneto	1,950	5.7	249	13.5	7,636	12.7	9,835	10.2
Piemonte	3,992	11.6	123	6.7	4,114	6.9	8,229	8.6
Lazio	862	2.5	148	8.0	4,807	8.0	5,817	6.1
Toscana	1,046	3.0	96	5.2	3,400	5.7	4,542	4.7
Campania	479	1.4	62	3.4	3,857	6.4	4,398	4.6
Sicilia	301	0.9	58	3.1	3,884	6.5	4,243	4.4
Puglia	524	1.5	76	4.1	3,323	5.5	3,923	4.1
Liguria	1,518	4.4	136	7.4	1,808	3.0	3,462	3.6
Friuli-Venezia Giulia	350	1.0	21	1.1	2,356	3.9	2,727	2.8
Marche	978	2.9	8	0.4	1,450	2.4	2,436	2.5
Abruzzo	446	1.3	38	2.1	1,222	2.0	1,706	1.8
Trento	402	1.2	4	0.2	798	1.3	1,204	1.3
Sardegna	131	0.4	24	1.3	1,009	1.7	1,164	1.2
Bolzano	290	0.8	2	0.1	779	1.3	1,071	1.1

Umbria	75	0.2	9	0.5	934	1.6	1,018	1.1
Calabria	96	0.3	4	0.2	523	0.9	623	0.6
Valle d'Aosta	143	0.4	3	0.2	271	0.5	417	0.4
Molise	22	0.1	2	0.1	328	0.5	352	0.4
Basilicata	30	0.1	2	0.1	284	0.5	316	0.3
Total	34,314	100.0	1,846	100.0	59,981	100.0	96,141	100.0

Note: For 8 deceased persons, period was not possible to be evaluated; the number of deaths, relating to the period October 2020-March 2021, is in the consolidation phase due to the delay in notification.

* SARS-CoV-2 related deaths presented in this report are those occurring in patients who test positive for SARS-CoV-2RT by PCR, independently from pre-existing diseases.

2. Demographics

Mean age of patients dying for SARS-CoV-2 infection was 81 years (median 83, range 0-109, IQR 75-88). Women were 42,191 (43.9%). *Figure 1* shows that median age of patients dying for SARS-CoV-2 infection was more than 30 years higher as compared with the national sample diagnosed with SARS-CoV-2 infection (median age 48 years). *Figure 2* shows the absolute number of deaths by age group. Women dying for SARS-CoV-2 infection had an older age than men (median age women, 86 years - median age men, 80 years).

Figure 1. Median age of patients with SARS-CoV-2 infection and SARS-CoV-2 positive deceased patients

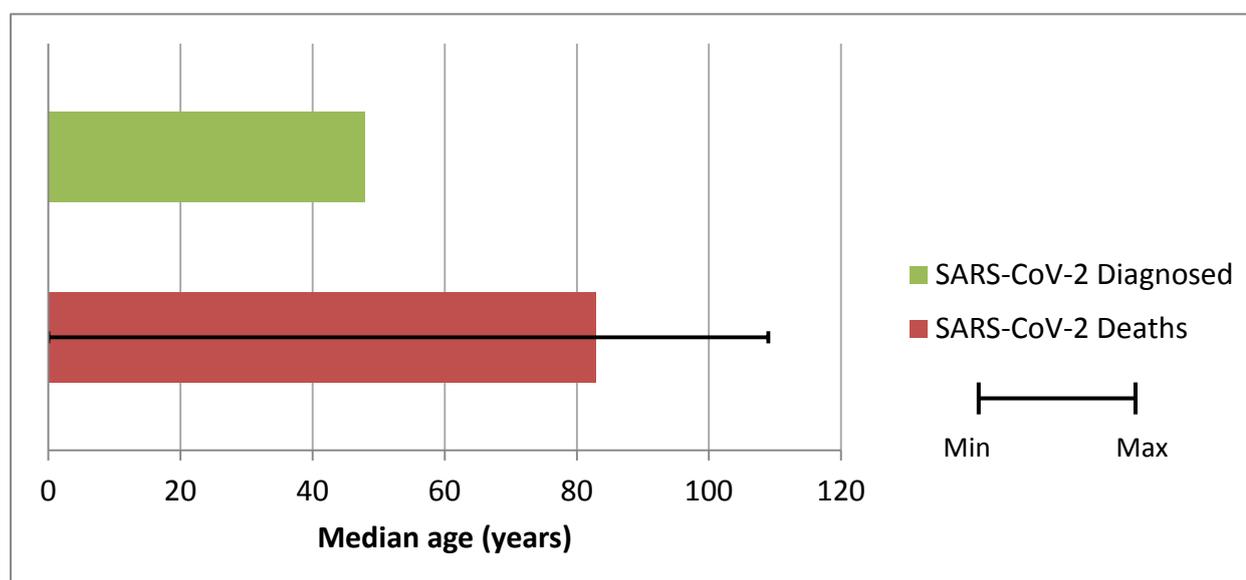


Figure 2. Absolute number of deaths by age group

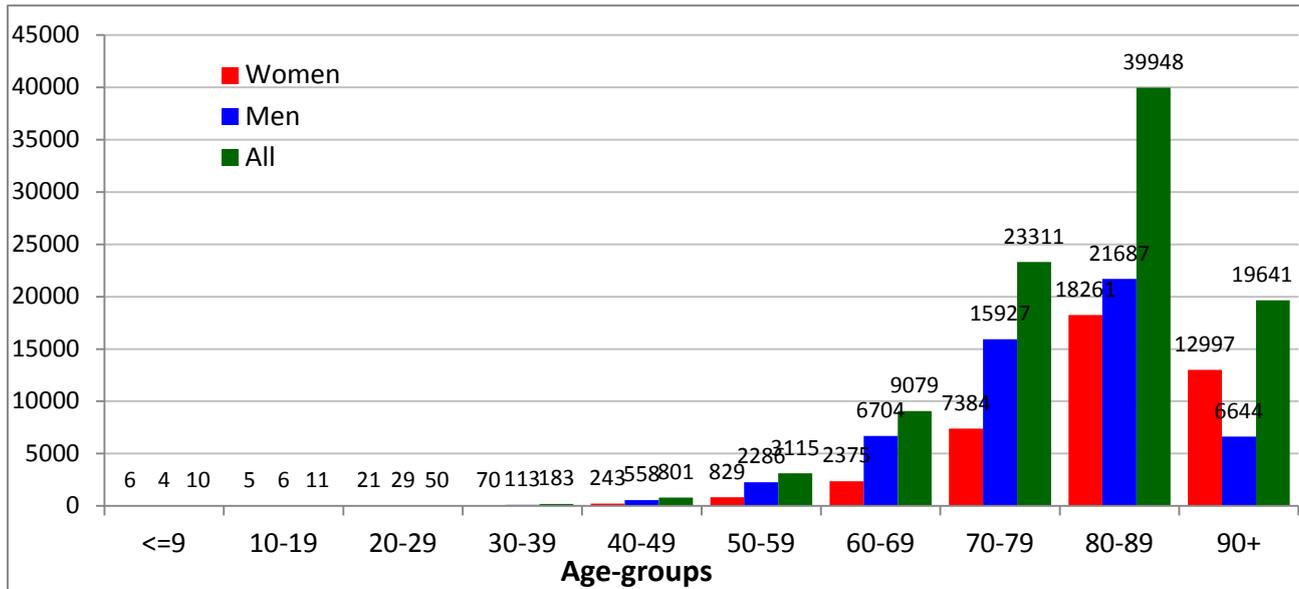
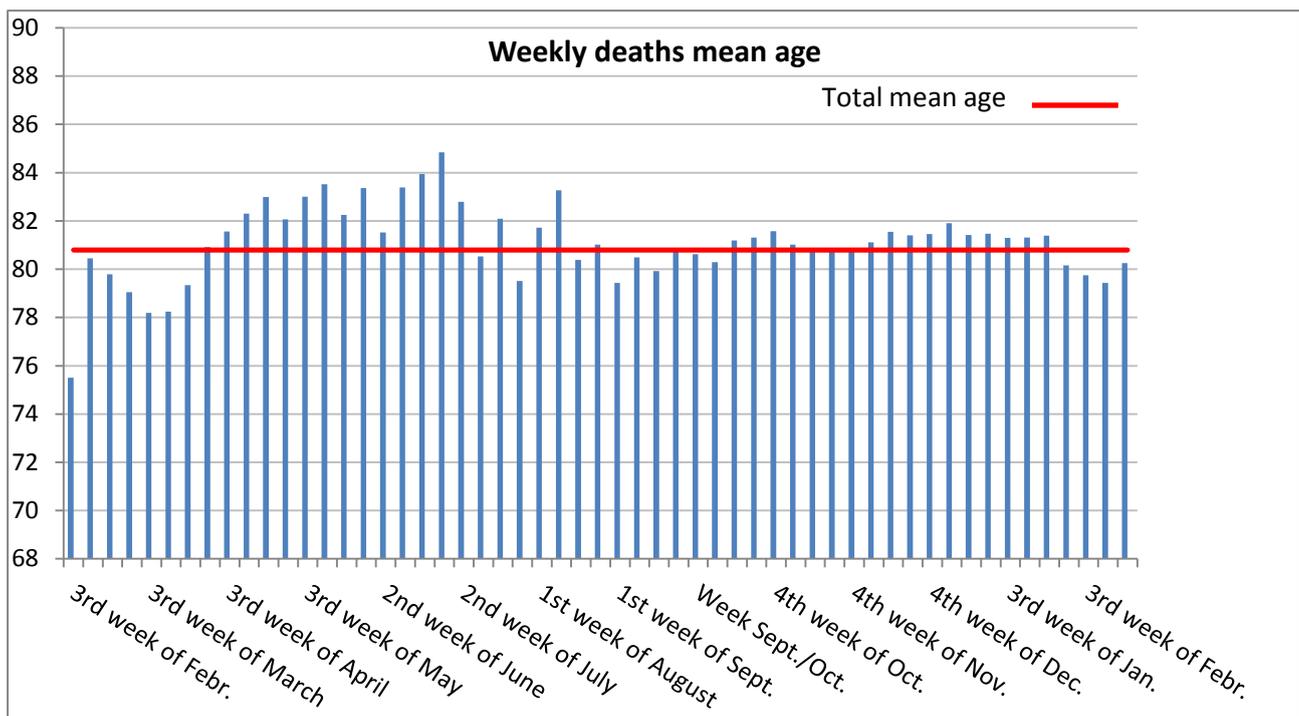


Figure 3 shows the trend in the average age of SARS-CoV-2 positive deceased patients per calendar week, starting from the 3rd week of February 2020 (the date of the first death dates back to 21st February 2020). The average age of weekly deceased persons has substantially increased up to 85 years (1st week of July) and then dropped slightly; a further reduction in the mean age of deaths was noted starting from the second week of February 2021.

Figure 3. Mean age of SARS-CoV-2 positive deceased patients by week of death



3. Deaths under the age of 50 years

As of March 1st 2021, 1,055 out of the 96,141 (1,1%), positive SARS-CoV-2 patients under the age of 50 died. In particular, 254 of these were less than 40 years (152 men and 102 women), age range between 0 and 39 years. For 62 patients under the age of 40 years no clinical information is available; out of the remaining ones, 156 had serious pre-existing pathologies (cardiovascular, renal, psychiatric pathologies, diabetes, obesity) and 36 had no major pathologies.

4. Pre-existing conditions

Table 2 presents most common comorbidities diagnosed before SARS-CoV-2 infection in a sample of SARS-CoV-2 positive deceased patients. Data on diseases were based on chart review and was available on 6,713 patients dying in-hospital for whom it was possible to analyse clinic charts. The medical records are sent to the ISS by the hospitals at different times, compatibly with the priorities of the activities carried out in the hospitals themselves. Therefore, the sample is opportunistic; it represents deaths in subjects who needed hospitalization only, and the regions are represented trying to maintain a proportionality with respect to the number of deaths. Mean number of diseases was 3.6 (median 3, SD 2.1). Overall, 3.1% of the sample presented with a no comorbidities, 11.9% with a single comorbidity, 18.5% with 2, and 66.6% with 3 or more.

Before hospitalization, 21% of SARS-CoV-2 positive deceased patients followed ACE-inhibitor therapy and 13% angiotensin receptor blockers-ARBs therapy. This information can be underestimated because data on drug treatment before admission were not always described in the chart.

Table 2. Most common comorbidities observed in SARS-CoV-2 positive deceased patients

Diseases	N	%
<i>Ischemic heart disease</i>	1,876	27.9
<i>Atrial Fibrillation</i>	1,628	24.3
<i>Heart failure</i>	1,065	15.9
<i>Stroke</i>	780	11.6
<i>Hypertension</i>	4,408	65.7
<i>Type 2-Diabetes</i>	1,964	29.3
<i>Dementia</i>	1,585	23.6
<i>COPD (Chronic Obstructive Pulmonary Disease)</i>	1,161	17.3
<i>Active cancer in the past 5 years</i>	1,118	16.7
<i>Chronic liver disease</i>	333	5.0
<i>Chronic renal failure</i>	1,426	21.2
<i>Dialysis</i>	149	2.2
<i>Respiratory failure</i>	444	6.6
<i>HIV Infection</i>	16	0.2
<i>Autoimmune diseases</i>	285	4.2
<i>Obesity</i>	738	11.0
Number of comorbidities		
<i>0 comorbidities</i>	206	3.1
<i>1 comorbidity</i>	797	11.9
<i>2 comorbidities</i>	1,242	18.5
<i>3 comorbidities and over</i>	4,468	66.6

Table 3 presents the most common pre-existing chronic pathologies in patients who died, separately in men (n = 4,013) and women (n = 2,700). The average number of pathologies observed in women is 3.8 (median 4, Standard Deviation 2.0). In men the average number of pathologies observed is 3.5 (median 3, Standard Deviation 2.1).

Table 3. Most common comorbidities observed in SARS-CoV-2 positive deceased patients by gender

Diseases	Women		Men	
	N	%	N	%
<i>Ischemic heart disease</i>	629	23.3	1,247	31.1
<i>Atrial Fibrillation</i>	688	25.5	940	23.4
<i>Heart Failure</i>	486	17.6	579	14.2
<i>Stroke</i>	341	12.6	439	10.9
<i>Hypertension</i>	1,832	67.9	2,576	64.2
<i>Type 2-Diabetes</i>	728	27.0	1,236	30.8
<i>Dementia</i>	876	32.4	709	17.7
<i>COPD (Chronic Obstructive Pulmonary Disease)</i>	381	14.1	780	19.4
<i>Active cancer in the past 5 years</i>	407	15.1	711	17.7
<i>Chronic liver disease</i>	118	4.4	215	5.4
<i>Chronic renal failure</i>	535	19.8	891	22.2
<i>Dialysis</i>	49	1.8	100	2.5
<i>Respiratory failure</i>	188	7.0	256	6.4
<i>HIV Infection</i>	2	0.1	14	0.3
<i>Autoimmune diseases</i>	159	5.9	126	3.1
<i>Obesity</i>	293	10.9	445	11.1
Number of comorbidities				
<i>0 comorbidities</i>	55	2.0	151	3.8
<i>1 comorbidity</i>	283	10.5	514	12.8
<i>2 comorbidities</i>	469	17.4	773	19.3
<i>3 comorbidities and over</i>	1,893	70.1	2,575	64.2

Table 4 presents the most common pre-existing chronic diseases in deceased patients divided into 4 age groups (16-59, 60-69, 70-79, 80+ years). The prevalence of *ischemic heart disease*, *atrial fibrillation*, *heart failure*, *stroke*, *arterial hypertension*, *dementia*, *chronic renal failure*, *respiratory failure* increase with age. On the other hand, prevalence of *chronic liver disease*, diseases for which *dialysis* is required, *HIV infection*, and *obesity* decrease with age increasing; for *diabetes*, *COPD*, and *cancer* prevalence decreases only in the last age group in contrast to the growth with age; for *autoimmune diseases*, on the contrary, prevalence increases only in the last age group, in contrast to the decreasing with age. As for the number of pathologies, the prevalence of those with 3 or more pathologies increases with age, while the prevalence of those with less than 3 pathologies decreases with age. For all the considered pathologies, the *trend* is statistically significant

Table 4. Most common comorbidities observed in SARS-CoV-2 positive deceased patients by age-groups

Age-groups	16-59		60-69		70-79		80+		Total	
	(n=479)		(n=676)		(n=1,664)		(n=3,888)		(n=6,707)	
Diseases	N	%	N	%	N	%	N	%	N	%
Ischemic heart disease	32	6.7	138	20.4	493	29.6	1213	31.2	1,876	28.0
Atrial Fibrillation	12	2.5	71	10.5	320	19.2	1225	31.5	1,628	24.3
Heart Failure	22	4.6	68	10.1	223	13.4	751	19.3	1,064	15.9
Stroke	16	3.3	61	9.0	174	10.5	528	13.6	779	11.6
Hypertension	179	37.4	405	59.9	1,128	67.8	2,695	69.3	4,407	65.7
Type 2-Diabetes	114	23.8	228	33.7	594	35.7	1,028	26.4	1,964	29.3
Dementia	13	2.7	42	6.2	189	11.4	1,340	34.5	1,584	23.6
COPD (Chronic Obstructive Pulmonary Disease)	36	7.5	84	12.4	321	19.3	720	18.5	1,161	17.3
Active cancer in the past 5 years	79	16.5	131	19.4	344	20.7	563	14.5	1,117	16.7
Chronic liver disease	37	7.7	44	6.5	103	6.2	149	3.8	333	5.0
Chronic renal failure	53	11.1	100	14.8	331	19.9	942	24.2	1,426	21.3
Dialysis	20	4.2	18	2.7	51	3.1	60	1.5	149	2.2
Respiratory failure	21	4.4	27	4.0	99	5.9	296	7.6	443	6.6
HIV Infection	10	2.1	2	0.3	3	0.2	1	0.0	16	0.2
Autoimmune diseases	33	6.9	37	5.5	58	3.5	157	4.0	285	4.2
Obesity	144	30.1	148	21.9	222	13.3	224	5.8	738	11.0
Number of comorbidities										
0 comorbidities	49	10.2	42	6.2	51	3.1	64	1.6	206	3.1
1 comorbidity	118	24.6	124	18.3	225	13.5	329	8.5	796	11.9
2 comorbidities	118	24.6	156	23.1	328	19.7	639	16.4	1,241	18.5
3 comorbidities and over	194	40.5	354	52.4	1,060	63.7	2,856	73.5	4,464	66.6

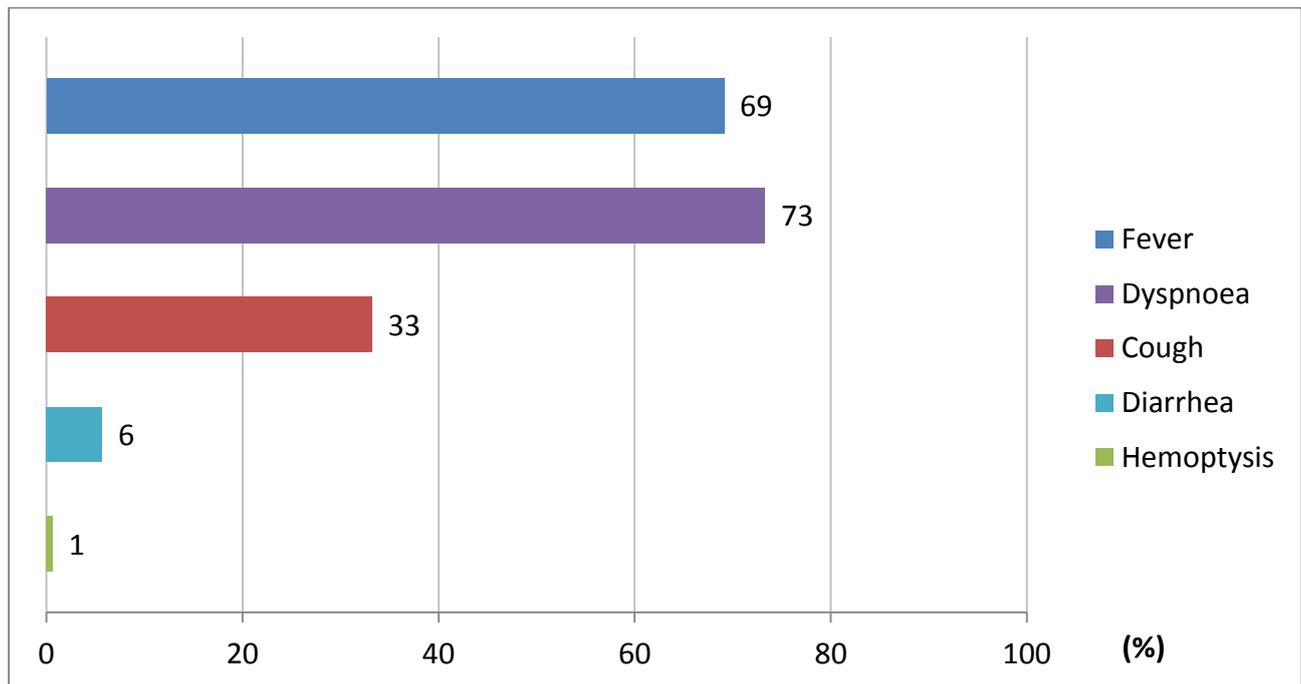
5. Diagnosis of hospitalization

In 90.4% of hospitalized persons who died and whose medical records were analysed (N=6,713; missing values=446), conditions (e.g. pneumonia, respiratory failure) or symptoms (e.g. fever, dyspnoea, cough) compatible with SARS-CoV-2 were mentioned. In 600 cases (9.6% of cases) the diagnosis of hospitalization was not related to the infection. In 83 cases the diagnosis of hospitalization concerned exclusively neoplastic pathologies, in 195 cases cardiovascular pathologies (for example Acute Myocardial Infarction-AMI, heart failure, stroke), in 75 cases gastrointestinal pathologies (for example cholecystitis, perforation of the intestine, intestinal obstruction, cirrhosis), in 247 cases other pathologies.

6. Symptoms

Figure 4 shows symptoms most commonly observed at hospital admission of hospitalized persons who died and whose medical records were analysed (N=6,713; missing values=184). Fever, dyspnoea and cough were the most commonly observed symptoms, while diarrhoea and haemoptysis were less commonly observed. Overall, 8.4% of patients did not present any symptoms at hospital admission.

Figure 4. Most common symptoms observed in SARS-CoV-2 positive deceased patients



7. Acute conditions

Between patients whose medical records were analysed, Acute Respiratory Distress syndrome was observed in the majority of patients (93.7% of cases), followed by acute renal failure (24.5%). Superinfection was observed in 19.7% and acute cardiac injury in 10.7% of cases (N=6713; missing values=149).

8. Treatments

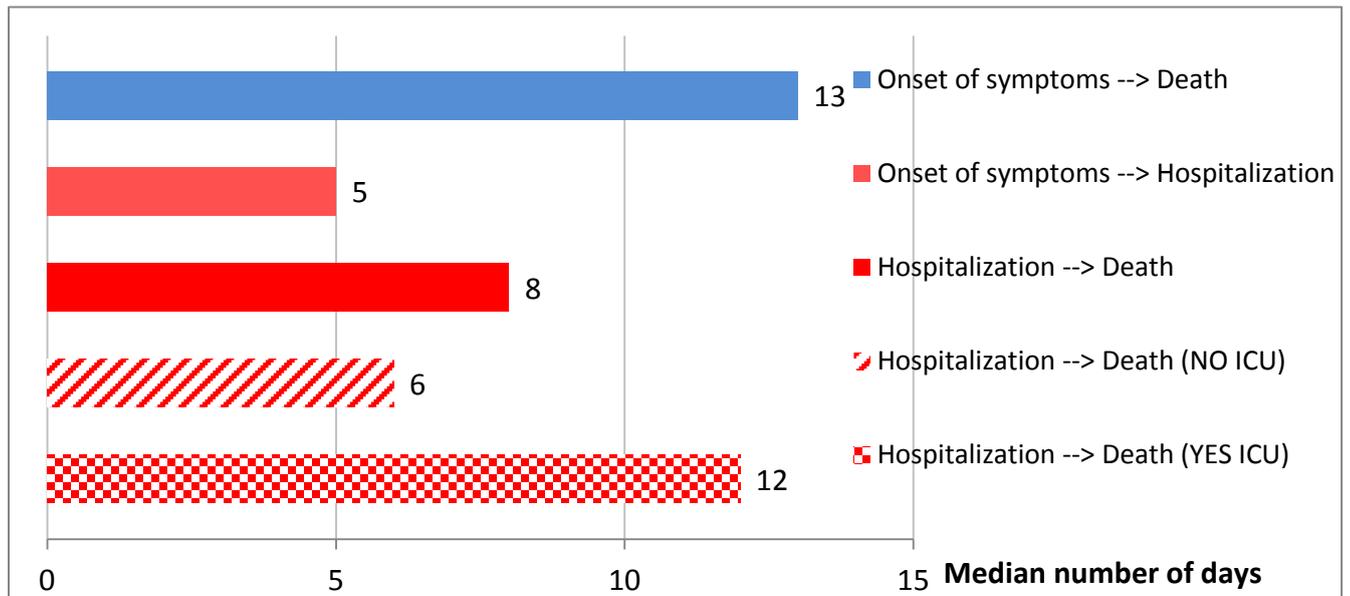
Antibiotics were used by 86.0% of patients during hospital stay, while less used were corticosteroids (55.0%) and antivirals (44.5%) (N=6713; missing values=112). Concomitant use of these 3 treatments was observed in 23.1% of cases.

Out of SARS-CoV-2 positive deceased patients, 3.8% were treated with Tocilizumab during hospitalization (N=6713; missing values=681).

9. Time-line

Figure 5 shows, for SARS-CoV-2 positive deceased patients whose medical records were analysed (N=6,713), the median times, in days, from the onset of symptoms to death (13 days), from the onset of symptoms to hospitalization (5 days) and from hospitalization to death (8 days). The time from hospitalization to death was 6 days longer in those who were transferred to intensive care than those who were not transferred (12 days vs. 6 days).

Figure 5. Median hospitalization times (in days) in SARS-CoV-2 positive deceased patients



10. Comparison of death characteristics in the 3 quarters March-May 2020, June- September 2020, and October 2020 – March 2021

Table 5 summarizes the main characteristics of deaths with COVID-19 that occurred in 3 periods of time from the beginning of the pandemic in 2020: the initial quarter, March-May 2020, the second quarter, June-September 2020, and the third period October 2020 – March 2021. Overall, the sample represents 7.1% of all deaths from the beginning of the pandemic; in particular, the 13.5% of those who died between March and May 2020, 28.5% of those who died between June and September 2020, and 2.8% of those who died between October 2020 and March 2021.

Deaths of people with 3 or more pre-existing pathologies increase and those of persons with fewer pathologies or none decrease: this seems to indicate that in the second and third periods deaths concern older people and persons with a pre-existing health condition worse than those dying in the first quarter (table 5).

The use of drugs is also extremely different in the three periods, with a clear reduction in the use of antivirals and an increase in the use of steroids in the second and third periods.

Table 5. Mean age, prevalence of women, number of pre-existing diseases, complications and treatments in deaths with COVID-19 in the 3 periods March-May 2020, June-September 2020, and October 2020–March 2021

Sample of the evaluated clinical charts	All (n=6,713)	March-May 2020 (n=4,536)	June-Sept. 2020 (n=522)	Oct. 2020 – March 2021 (n=1,655)	p-value*
Mean age (years)	79.1	78.5	81.2	80.3	<0.001
	n (%)	n (%)	n (%)	n (%)	
Women	2,700 (40.2)	1,744 (38.4)	270 (51.7)	686 (41.5)	<0.001
N of comorbidities					
0	206 (3.1)	169 (3.7)	8 (1.5)	29 (1.8)	<0.001
1	797 (11.9)	608 (13.4)	44 (8.4)	145 (8.8)	
2	1,242 (18.5)	915 (20.2)	70 (13.4)	257 (15.5)	
3 or more	4,468 (66.6)	2,844 (62.7)	400 (76.6)	1,224 (74.0)	
Complications during hospitalization					
Acute Respiratory Distress Syndrome	6,149 (93.7)	4,165 (95.2)	428 (83.3)	1,556 (93.0)	<0.001
Acute renal failure	1,606 (24.5)	1,006 (23.0)	140 (27.2)	460 (27.5)	<0.001
Acute cardiac injury	704 (10.7)	472 (10.8)	52 (10.1)	180 (10.8)	0.897
Superinfection	1,294 (19.7)	729 (16.7)	217 (42.2)	348 (20.8)	<0.001
Treatments					
Antibiotics	5,674 (86.0)	3,835 (86.7)	442 (86.3)	1,397 (83.8)	0.013
Antivirals	2,937 (44.5)	2,609 (59.0)	163 (31.8)	165 (9.9)	<0.001
Steroids	3,629 (58.0)	1,912 (43.2)	336 (65.6)	1,381 (82.8)	<0.001
Tocilizumab	232 (3.8)	172 (4.4)	29 (5.9)	31 (1.9)	<0.001

* p-value for difference between the 3 periods

The distribution of the main pre-existing diseases in the different periods is presented in *figure 6*. The prevalence of *atrial fibrillation, stroke, dementia, cancer, renal failure, and obesity* varies significantly in the three periods. These pathologies are more frequently diagnosed in the deceased in the second and third period than in the first (*Figure 6*).

Figure 6. Pre-existing pathologies in deaths with COVID-19 in the 3 periods

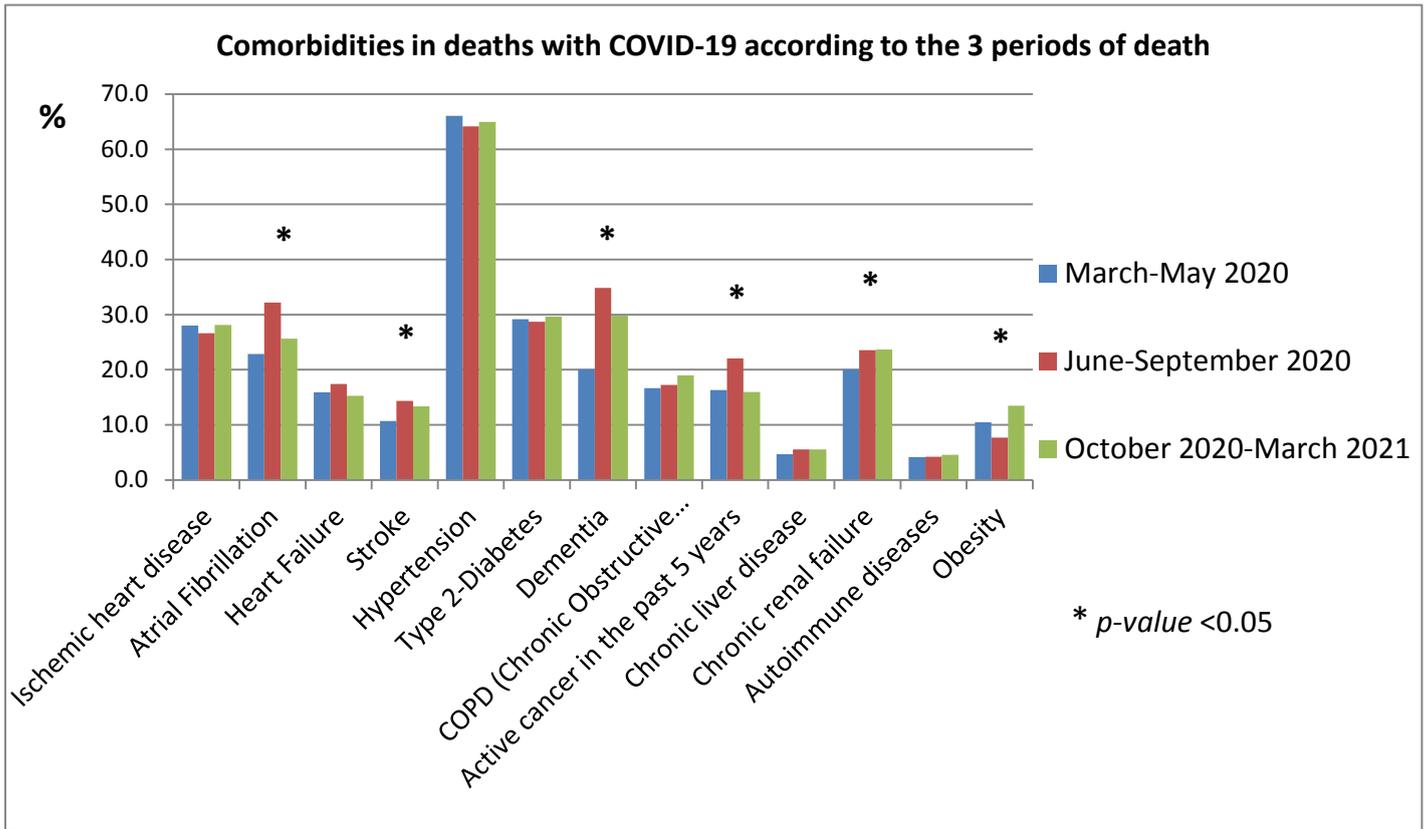


Table 6 shows the durations, as median times (in days), from the symptoms onset to death, SARS-CoV-2 testing, and hospitalization, and from the hospitalization to death, in the 3 periods considered. Between the first and second period doubles the time that passes from the onset of symptoms to death, while it returns to the initial levels in the third period; the time from the onset of symptoms to the swab for the detection of SARS-CoV-2 infection decreases in the second period and remain stable in the third, as well as the time between the onset of symptoms and hospitalization; the median duration in days from hospitalization to death doubles between the first and second period; it decreases again in the third period. These results seem to suggest a greater reactivity of the Health System evidenced by the greater speed in carrying out diagnostic tests and hospitalization.

Table 6. Median times (in days) between symptoms onset, PCR test, hospitalization and death in the 3 periods

Times(in days)	All (n=6,713)		March-May 2020 (n=4,536)		June-Sept. 2020 (n=522)		Oct. 2020 – March 2021 (n=1,655)		p- value*
	Median	IQR	Median	IQR	Median	IQR	Median	IQR	
From symptoms onset to death	13	8-21	12	7-19	23	9-57	13	8-21	<0.001
From symptoms onset to SARS-CoV-2 testing	4	2-8	5	2-9	3	1-7	3	0-6	<0.001
From symptoms onset to hospitalization	4	2-7	4	2-7	3	1-7	3	1-7	<0.001
From hospitalization to death	7	3-15	7	3-13	15	6-44	8	4-15	<0.001

* p-value for difference between the 3 periods

IQR = Inter-Quartile Range

The data here presented can be explained by a greater knowledge about the infection and a greater ability and timeliness of treatment in the period June-August in comparison to the previous quarter. In addition, it is likely that in the months of March and April SARS-CoV-2 infection was under-diagnosed in many frail elderly who died (such as those living in RSA). This may have led to an underestimation of the burden of the diseases in persons dying in that period

This report was produced by SARS-CoV-2 Surveillance Group

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