



Characteristics of SARS-CoV-2 patients dying in Italy Report based on available data on April 28th, 2021

1. Sample

The present report describes the characteristics of 118,592 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 28th of April 2021: the first wave (March-May 2020), the low incidence phase (June-September 2020), and the second wave (October 2020 – April 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 2020		June-September 2020		October 2020-April 2021		Total	
	N	%	N	%	N	%	N	%
Lombardia	16,362	47.7	607	28.9	15,515	18.9	32,484	27.4
Emilia Romagna	4,313	12.6	173	8.2	8,334	10.1	12,820	10.8
Veneto	1,950	5.7	249	11.9	9,076	11.0	11,275	9.5
Piemonte	4,006	11.7	368	17.5	6,513	7.9	10,887	9.2
Lazio	864	2.5	150	7.1	6,520	7.9	7,534	6.4
Campania	470	1.4	65	3.1	5,562	6.8	6,097	5.1
Toscana	1,046	3.0	96	4.6	4,783	5.8	5,925	5.0
Puglia	524	1.5	76	3.6	5,192	6.3	5,792	4.9
Sicilia	301	0.9	59	2.8	4,954	6.0	5,314	4.5
Liguria	1,521	4.4	136	6.5	2,377	2.9	4,034	3.4
Friuli Venezia Giulia	350	1.0	22	1.0	3,079	3.7	3,451	2.9
Marche	978	2.8	9	0.4	2,060	2.5	3,047	2.6
Abruzzo	447	1.3	39	1.9	1,904	2.3	2,390	2.0
Sardegna	131	0.4	24	1.1	1,201	1.5	1,356	1.1

Umbria	76	0.2	9	0.4	1,261	1.5	1,346	1.1
Trento	402	1.2	4	0.2	930	1.1	1,336	1.1
Bolzano	290	0.8	2	0.1	929	1.1	1,221	1.0
Calabria	96	0.3	4	0.2	789	1.0	889	0.7
Molise	22	0.1	2	0.1	452	0.6	476	0.4
Basilicata	30	0.1	2	0.1	426	0.5	458	0.4
Valle d'Aosta	143	0.4	3	0.1	303	0.4	449	0.4
Total	34,322	100.0	2,099	100.0	82,160	100.0	118,581	100.0

Note: For 11 deceased persons, period was not possible to be evaluated; the number of deaths, relating to the period October 2020-April 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 82 years (median 83, range 0-109, IQR 74-88). Women were 51,730 (43.6%). *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 47 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, 85 years - median age men, 80 years).

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

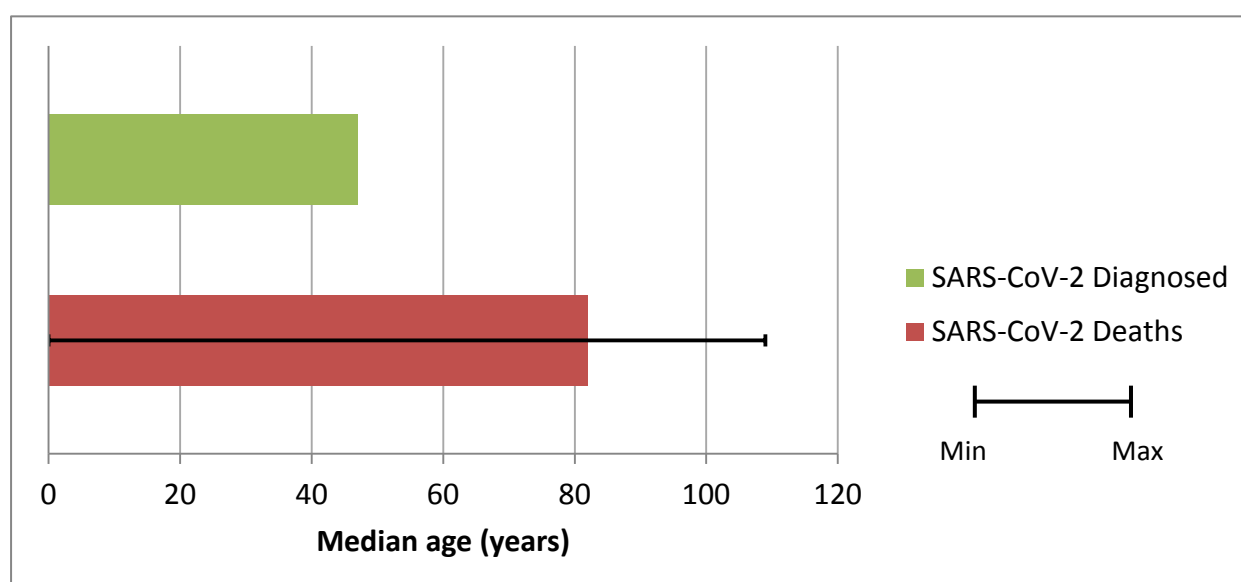
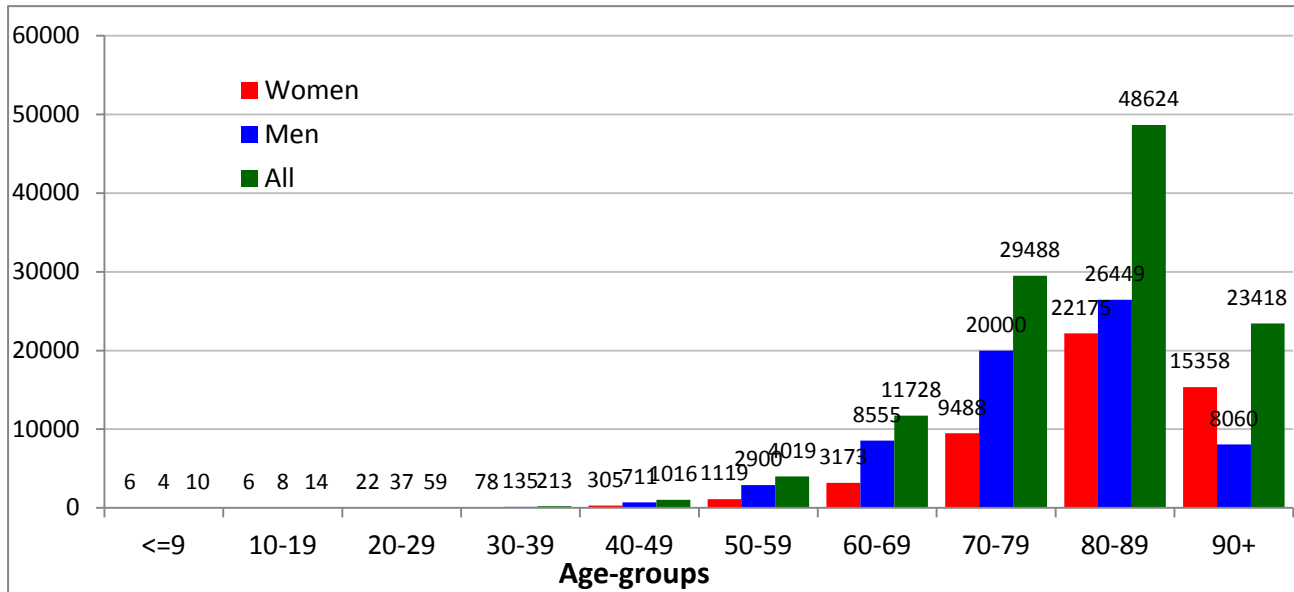


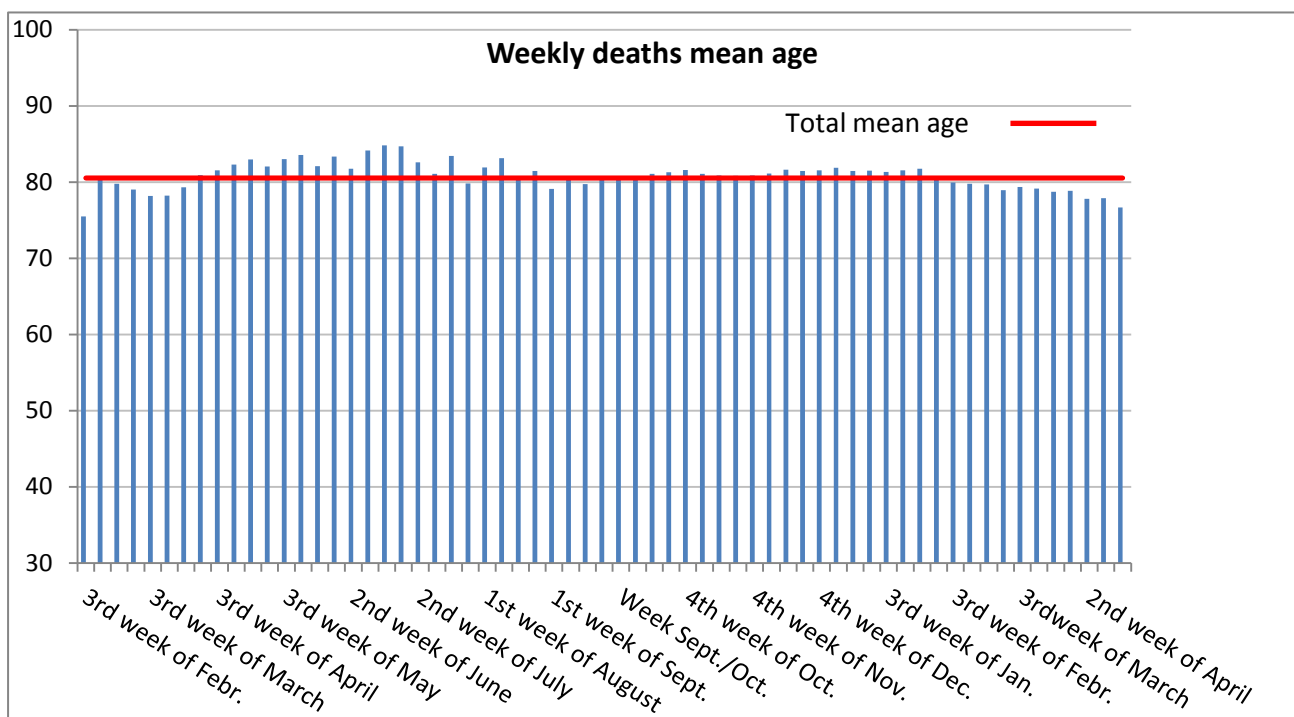
Figure 2. Absolute number of deaths by age group



Note: for 3 deaths age was not possible to be evaluated

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, and again, from the second week of April 2021 (probable protective effect of vaccinations carried out primarily on over-eighty-year-old persons).

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 April 28th 2021, 1,312 out of the 118,592 (1,1%), positive SARS-CoV-2 patients under the age of 50 died. In particular, 296 of these were less than 40 years (184 men and 112 women), age range between 0 and 39 years. For 81 patients under the age of 40 years no clinical information is available; out of the remaining ones, 174 had serious pre-existing pathologies (cardiovascular, renal, psychiatric pathologies, diabetes, obesity) and 41 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 7,199 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, 3.0% of the sample presented with a no comorbidities, 11.6% with a single comorbidity, 18.4% with 2, and 67.0% with 3 or more.

Before hospitalization, 20% 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>	2,019	28.0
<i>Atrial Fibrillation</i>	1,759	24.4
<i>Heart failure</i>	1,136	15.8
<i>Stroke</i>	829	11.5
<i>Hypertension</i>	4,729	65.7
<i>Type 2-Diabetes</i>	2,118	29.4
<i>Dementia</i>	1,677	23.3
<i>COPD (Chronic Obstructive Pulmonary Disease)</i>	1,232	17.1
<i>Active cancer in the past 5 years</i>	1,194	16.6
<i>Chronic liver disease</i>	360	5.0
<i>Chronic renal failure</i>	1,533	21.3
<i>Dialysis</i>	161	2.2
<i>Respiratory failure</i>	482	6.7
<i>HIV Infection</i>	18	0.3
<i>Autoimmune diseases</i>	317	4.4
<i>Obesity</i>	822	11.4
Number of comorbidities		
<i>0 comorbidities</i>	214	3.0
<i>1 comorbidity</i>	837	11.6
<i>2 comorbidities</i>	1,326	18.4
<i>3 comorbidities and over</i>	4,822	67.0

Table 3 presents the most common pre-existing chronic pathologies in patients who died, separately in men (n = 4,285) and women (n = 2,914). 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>	687	23.6	1,332	31.1
<i>Atrial Fibrillation</i>	751	25.8	1,008	23.5
<i>Heart Failure</i>	522	17.5	614	14.1
<i>Stroke</i>	362	12.4	467	10.9
<i>Hypertension</i>	1,982	68.0	2,747	64.1
<i>Type 2-Diabetes</i>	800	27.5	1,318	30.8
<i>Dementia</i>	928	31.8	749	17.5
<i>COPD (Chronic Obstructive Pulmonary Disease)</i>	405	13.9	827	19.3
<i>Active cancer in the past 5 years</i>	436	15.0	758	17.7
<i>Chronic liver disease</i>	125	4.3	235	5.5
<i>Chronic renal failure</i>	580	19.9	953	22.2
<i>Dialysis</i>	54	1.9	107	2.5
<i>Respiratory failure</i>	209	7.2	273	6.4
<i>HIV Infection</i>	2	0.1	16	0.4
<i>Autoimmune diseases</i>	174	6.0	143	3.3
<i>Obesity</i>	331	11.4	491	11.5
Number of comorbidities				
<i>0 comorbidities</i>	58	2.0	156	3.6
<i>1 comorbidity</i>	296	10.2	541	12.6
<i>2 comorbidities</i>	499	17.1	827	19.3
<i>3 comorbidities and over</i>	2,061	70.7	2,761	64.4

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=523)		(n=728)		(n=1,755)		(n=4,186)		(n=7,192)	
Diseases	N	%	N	%	N	%	N	%	N	%
Ischemic heart disease	35	6.7	151	20.7	515	29.3	1,317	31.5	2,018	28.1
Atrial Fibrillation	13	2.5	74	10.2	335	19.1	1,337	31.9	1,759	24.5
Heart Failure	24	4.6	69	9.5	232	13.2	810	19.4	1,135	15.8
Stroke	17	3.3	63	8.7	183	10.4	565	13.5	828	11.5
Hypertension	195	37.3	438	60.2	1,184	67.5	2,911	69.5	4,728	65.7
Type 2-Diabetes	125	23.9	243	33.4	641	36.5	1,109	26.5	2,118	29.4
Dementia	15	2.9	44	6.0	200	11.4	1,417	33.9	1,676	23.3
COPD (Chronic Obstructive Pulmonary Disease)	37	7.1	89	12.2	336	19.1	770	18.4	1,232	17.1
Active cancer in the past 5 years	92	17.6	138	19.0	357	20.3	606	14.5	1,193	16.6
Chronic liver disease	42	8.0	47	6.5	109	6.2	162	3.9	360	5.0
Chronic renal failure	57	10.9	112	15.4	350	19.9	1,014	24.2	1,533	21.3
Dialysis	21	4.0	20	2.7	53	3.0	67	1.6	161	2.2
Respiratory failure	25	4.8	30	4.1	106	6.0	320	7.6	481	6.7
HIV Infection	11	2.1	2	0.3	4	0.2	1	0.0	18	0.3
Autoimmune diseases	39	7.5	41	5.6	65	3.7	172	4.1	317	4.4
Obesity	159	30.4	165	22.7	241	13.7	257	6.1	822	11.4
Number of comorbidities										
0 comorbidities	51	9.8	45	6.2	54	3.1	64	1.5	214	3.0
1 comorbidity	126	24.1	130	17.9	234	13.3	346	8.3	836	11.6
2 comorbidities	132	25.2	168	23.1	342	19.5	683	16.3	1,325	18.4
3 comorbidities and over	214	40.9	385	52.9	1,125	64.1	3,093	73.9	4,817	67.0

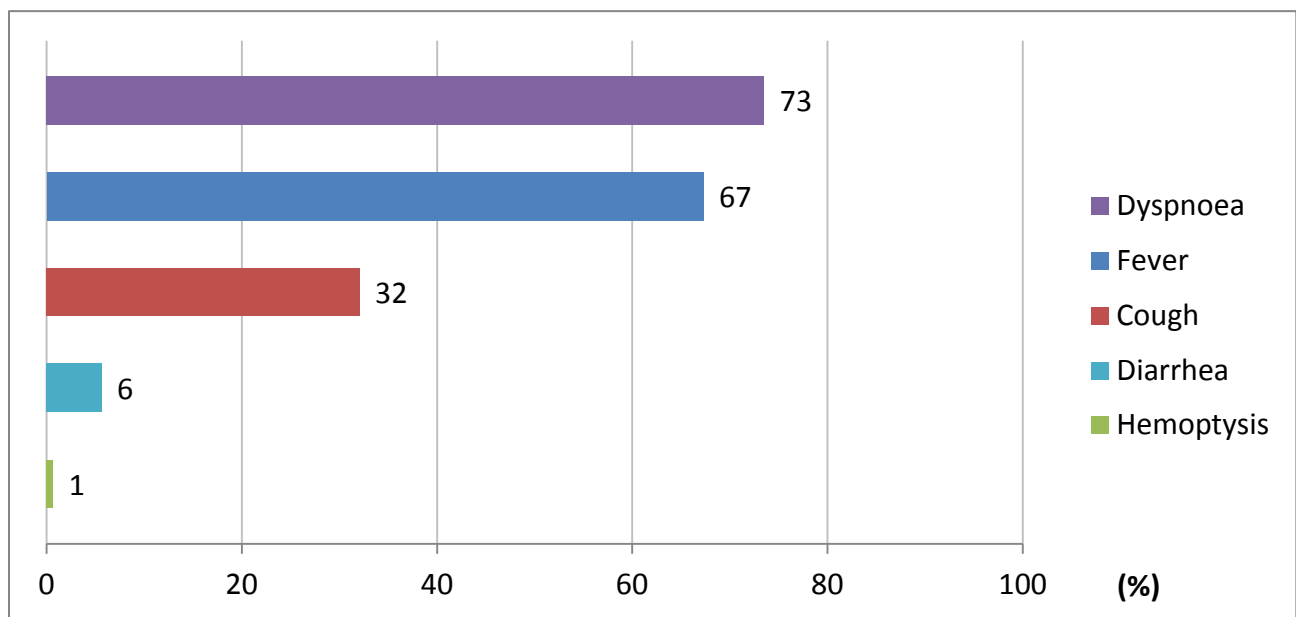
5. Diagnosis of hospitalization

In 90.3% of hospitalized persons who died and whose medical records were analysed (N=7,199; missing values=458), conditions (e.g. pneumonia, respiratory failure) or symptoms (e.g. fever, dyspnoea, cough) compatible with SARS-CoV-2 were mentioned. In 655 cases (9.7% of cases) the diagnosis of hospitalization was not related to the infection. In 91 cases the diagnosis of hospitalization concerned exclusively neoplastic pathologies, in 211 cases cardiovascular pathologies (for example Acute Myocardial Infarction-AMI, heart failure, stroke), in 77 cases gastrointestinal pathologies (for example cholecystitis, perforation of the intestine, intestinal obstruction, cirrhosis), in 276 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=7,199; missing values=212). Dyspnoea, fever, and cough were the most commonly observed symptoms, while diarrhoea and haemoptysis were less commonly observed. Overall, 8.6% 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 (24.6%). Superinfection was observed in 19.7% and acute cardiac injury in 10.5% of cases (N=7,199; missing values=150).

8. Treatments

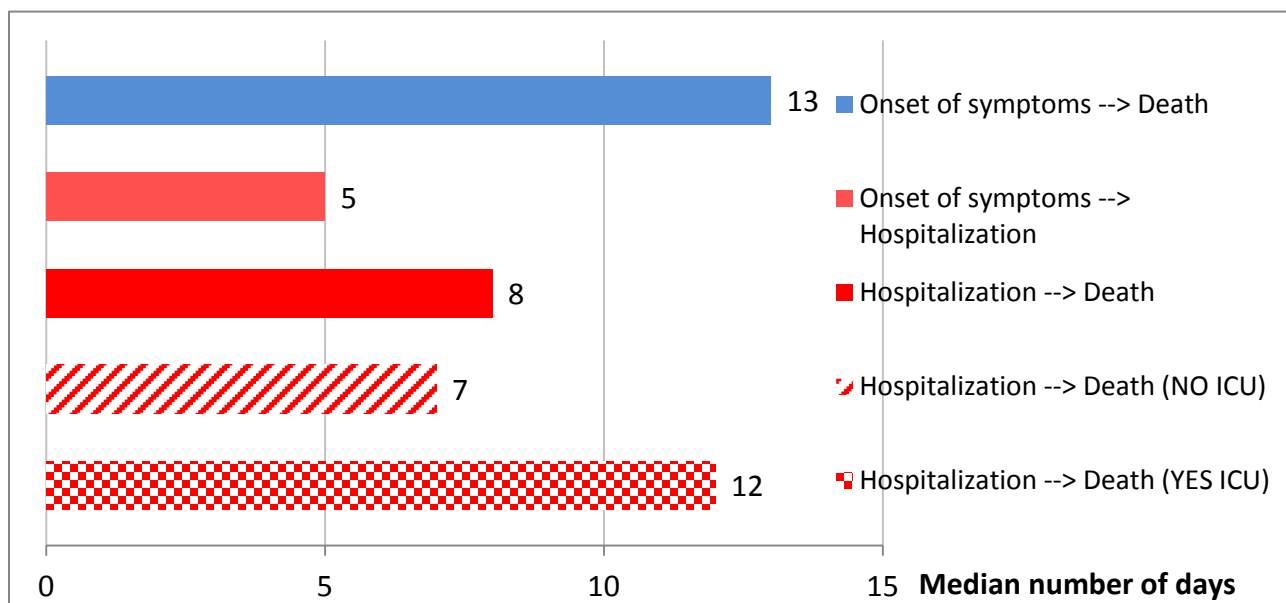
Antibiotics were used by 86.1% of patients during hospital stay, while less used were corticosteroids (57.4%) and antivirals (42.4%) (N=7,199; missing values=114). Concomitant use of these 3 treatments was observed in 21.6% of cases.

Out of SARS-CoV-2 positive deceased patients, 3.9% were treated with Tocilizumab during hospitalization (N=7,199; missing values=701).

9. Time-line

Figure 5 shows, for SARS-CoV-2 positive deceased patients whose medical records were analysed (N=7,199), 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 5 days longer in those who were transferred to intensive care than those who were not transferred (12 days vs. 7 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 – April 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–April 2021. Overall, the sample represents 6.2% of all deaths from the beginning of the pandemic; in particular, the 13.5% of those who died between March and May 2020, 26.2% of those who died between June and September 2020, and 2.6% of those who died between October 2020 and April 2021.

Compared to the period of the first epidemic wave (March-May 2020), in the period of the second epidemic wave (October 2020-April 2021) deceased persons have a greater clinical complexity, as demonstrated by the higher number of comorbidities and the higher presence of complications (especially chronic renal failure and superinfection). The use of drugs also appears different between the two epidemic waves, with a lower use of antivirals and tocilizumab and a greater use of steroids in patients who died in the second wave (table 5).

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=7,199)	March-May 2020 (n=4,537)	June-Sept. 2020 (n=544)	Oct. 2020–March 2021 (n=2,118)	p-value*
	n (%**)	n (%**)	n (%**)	n (%**)	
N of comorbidities					
0	214 (2.9)	169 (3.5)	8 (1.7)	37 (1.8)	<0.001
1	837 (11.5)	608 (12.9)	46 (8.7)	183 (8.9)	
2	1,326 (18.3)	916 (19.9)	71 (13.7)	339 (16.2)	
3 or more	4,822 (67.2)	2,844 (63.7)	419 (76.0)	1,559 (73.1)	

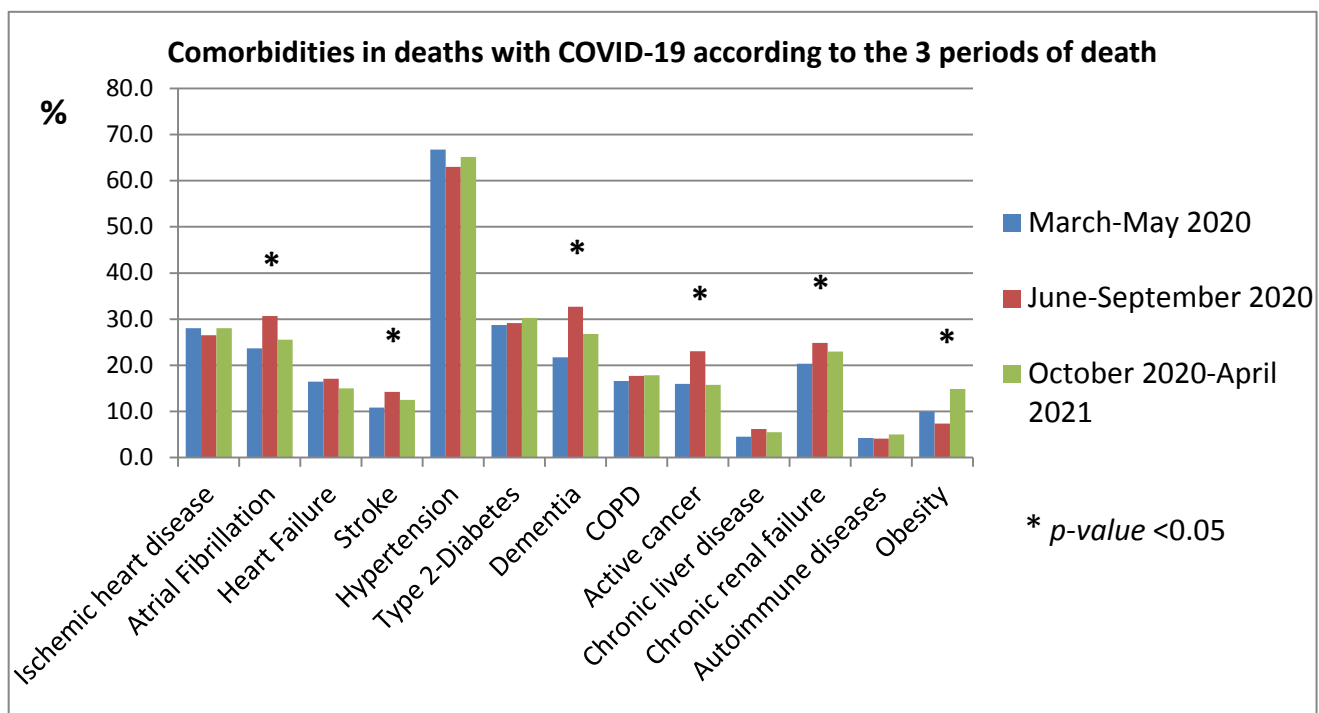
Complications during hospitalization					
Acute Respiratory Distress Syndrome	6,602 (93.6)	4,166 (95.0)	442 (82.9)	1,994 (93.4)	<0.001
Acute renal failure	1,732 (24.3)	1,006 (22.5)	145 (27.6)	581 (27.3)	<0.001
Acute cardiac injury	743 (10.4)	472 (10.5)	57 (10.5)	214 (10.0)	0.797
Superinfection	1,390 (19.4)	729 (16.1)	225 (43.2)	436 (20.7)	<0.001
Treatments					
Antibiotics	6,098 (85.9)	3,836 (86.5)	459 (86.3)	1,803 (84.8)	0.180
Antivirals	3,002 (41.7)	2,609 (57.6)	171 (32.5)	222 (10.6)	<0.001
Steroids	4,065 (57.3)	1,914 (43.0)	351 (66.7)	1,800 (84.6)	<0.001
Tocilizumab	251 (3.7)	172 (4.0)	30 (6.3)	49 (2.4)	<0.001

* *p*-value for difference between the 3 periods

** Sex- and age-standardized prevalence using the total population of COVID-19 deaths on April 28, 2021 as the standard population

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 (sex- and age-standardized prevalence ^)



^ Sex- and age-standardized prevalence using the total population of COVID-19 deaths on April 28, 2021 as the standard population

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=7,199)		March-May 2020 (n=4,537)		June-Sept. 2020 (n=544)		Oct. 2020– March 2021 (n=2,118)		p- value*
	Median	IQR	Median	IQR	Median	IQR	Median	IQR	
From symptoms onset to death	13	8-21	12	7-19	24	10-56	13	8-21	<0.001
From symptoms onset to SARS-CoV-2 testing	4	2-8	5	2-9	3	0-7	3	0-6	<0.001
From symptoms onset to hospitalization	4	2-7	4	2-7	3	1-7	4	1-7	<0.001
From hospitalization to death	7	3-15	7	3-13	16	6-45	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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