Characteristics of SARS-CoV-2 patients dying in Italy
Report based on available data on December 16th, 2020

1. Sample

The present report describes the characteristics of 63,573 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 December the 16th 2020: the first wave (March-May), the low incidence phase (June-September), and the second wave (October-December), 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*

	March-May		June-September		October-16th December		Total	
REGION	**N**	***%***	**N**	***%***	**N**	***%***	**N**	***%***
Lombardia	16,359	*47.6*	607	*33.0*	7,104	*26.0*	24,070	*37.9*
Emilia Romagna	4,313	*12.5*	173	*9.4*	2,232	*8.2*	6,718	*10.6*
Piemonte	4,091	*11.9*	126	*6.9*	1,326	*4.8*	5,543	*8.7*
Veneto	1,950	*5.7*	248	*13.5*	2,884	*10.5*	5,082	*8.0*
Lazio	840	*2.4*	143	*7.8*	2,099	*7.7*	3,082	*4.8*
Toscana	1,045	*3.0*	96	*5.2*	1,764	*6.5*	2,905	*4.6*
Campania	477	*1.4*	58	*3.2*	2,102	*7.7*	2,637	*4.1*
Liguria	1,516	*4.4*	138	*7.5*	974	*3.6*	2,628	*4.1*
Puglia	524	*1.5*	75	*4.1*	1,460	*5.3*	2,059	*3.2*
Sicilia	300	*0.9*	57	*3.1*	1,654	*6.0*	2,011	*3.2*
Marche	981	*2.9*	7	*0.4*	223	*0.8*	1,211	*1.9*
Abruzzo	446	*1.3*	37	*2.0*	597	*2.2*	1,080	*1.7*
Friuli Venezia Giulia	346	*1.0*	21	*1.1*	632	*2.3*	999	*1.6*
Trento	402	*1.2*	4	*0.2*	389	*1.4*	795	*1.3*
Bolzano	290	*0.8*	2	*0.1*	380	*1.4*	672	*1.1*

Umbria	75	*0.2*	9	*0.5*	446	*1.6*	530	*0.8*
Sardegna	131	*0.4*	24	*1.3*	361	*1.3*	516	*0.8*
Valle d'Aosta	143	*0.4*	6	*0.3*	206	*0.8*	355	*0.6*
Calabria	96	*0.3*	4	*0.2*	225	*0.8*	325	*0.5*
Basilicata	29	*0.1*	2	*0.1*	143	*0.5*	174	*0.3*
Molise	22	*0.1*	2	*0.1*	146	*0.5*	170	*0.3*
Total	**34,376**	***100.0***	**1,839**	***100.0***	**27,347**	***100.0***	**63,562**	***100.0***

Note: *For 18 deceased persons, period was not possible to be evaluated*

* 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 80 years (median 82, range 0-109, IQR 75-88). Women were 27,132 (42.7%). *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 85 - median age men 80).

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

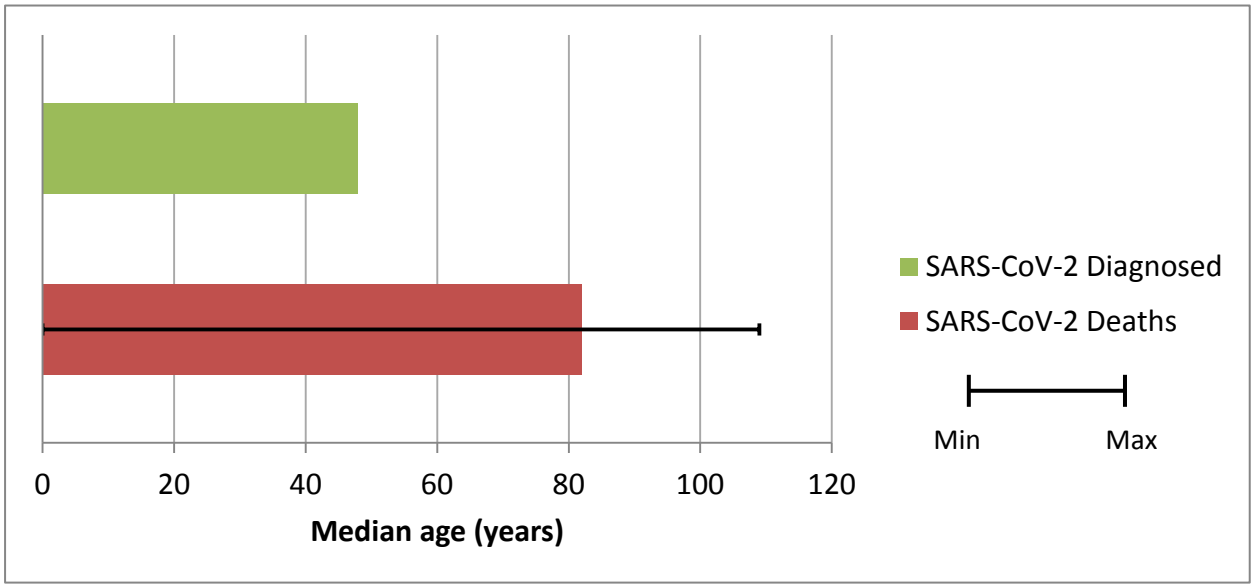


Figure 2. *Absolute number of deaths by age group*

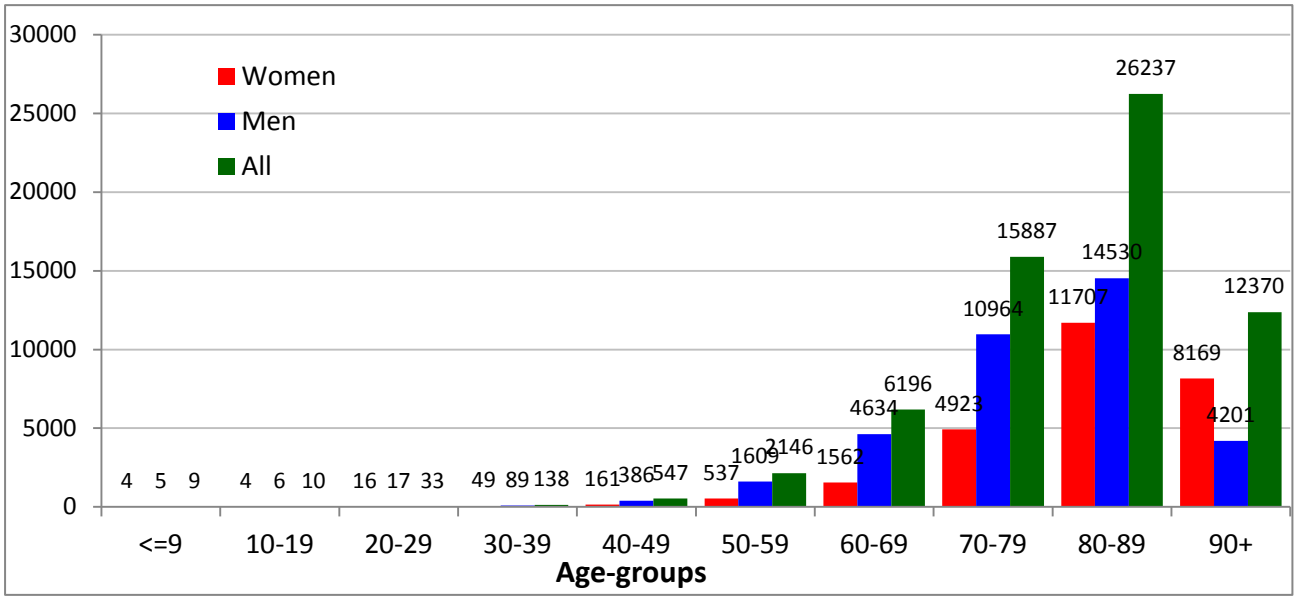
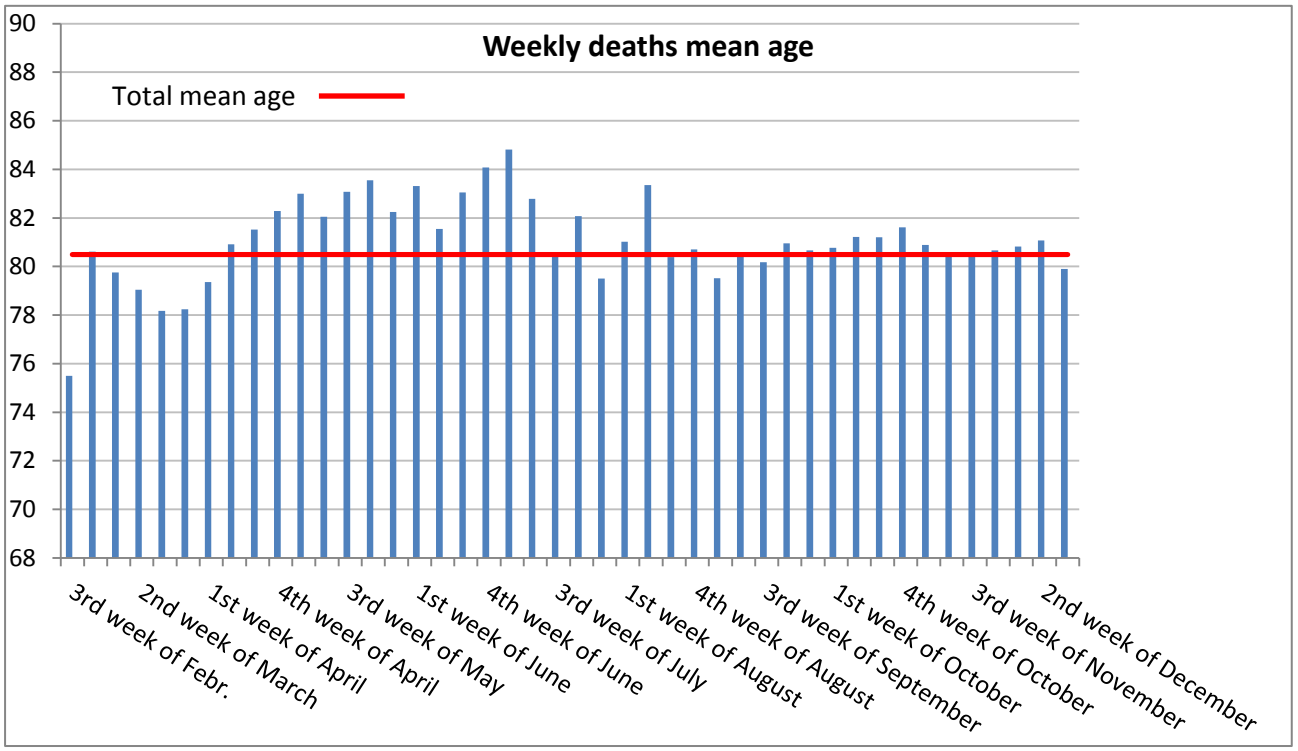


Figure 3 shows the trend in the average age of SARS-CoV-2 positive deceased patients per calendar week, starting from the 3rd week of February 2020 (the date of the first death dates back to 21st February 2020). The average age of weekly deceased persons has substantially increased up to 85 years (1st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

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 December 16th 2020, 737 out of the 63,573 (1.2%) positive SARS-CoV-2 patients under the age of 50 died. In particular, 190 of these were less than 40 years (117 men and 73 women), age range between 0 and 39 years. For 41 patients under the age of 40 years no clinical information is available; out of the remaining ones, 130 had serious pre-existing pathologies (cardiovascular, renal, psychiatric pathologies, diabetes, obesity) and 19 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 5,962 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, 12.4% with a single comorbidity, 18.4% with 2, and 66.2% with 3 or more.

Before hospitalization, 21% of SARS-CoV-2 positive deceased patients followed ACE-inhibitor therapy and 14% 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***	***%***
Ischemic heart disease	*1661*	*27.9*
Atrial Fibrillation	*1448*	*24.3*
Heart failure	*970*	*16.3*
Stroke	*691*	*11.6*
Hypertension	*3934*	*66.0*
Type 2-Diabetes	*1736*	*29.1*
Dementia	*1387*	*23.3*
COPD (Chronic Obstructive Pulmonary Disease)	*1036*	*17.4*
Active cancer in the past 5 years	*1011*	*17.0*
Chronic liver disease	*280*	*4.7*
Chronic renal failure	*1255*	*21.0*
Dialysis	*126*	*2.1*
Respiratory failure	*403*	*6.8*
HIV Infection	*15*	*0.3*
Autoimmune diseases	*257*	*4.3*
Obesity	*631*	*10.6*
Number of comorbidities		
0 comorbidities	*184*	*3.1*
1 comorbidity	*739*	*12.4*
2 comorbidities	*1095*	*18.4*
3 comorbidities and over	*3944*	*66.2*

Table 3 presents the most common pre-existing chronic pathologies in patients who died, separately in men (n = 3,589) and women (n = 2,379). 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*

	Women		**Men**	
Diseases	***N***	***%***	***N***	***%***
Ischemic heart disease	556	*23.4*	1105	*30.8*
Atrial Fibrillation	608	*25.6*	840	*23.4*
Heart Failure	444	*18.2*	526	*14.4*
Stroke	299	*12.6*	392	*10.9*
Hypertension	1630	*68.7*	2304	*64.2*
Type 2-Diabetes	633	*26.7*	1103	*30.7*
Dementia	761	*32.1*	626	*17.4*
COPD (Chronic Obstructive Pulmonary Disease)	328	*13.8*	708	*19.7*
Active cancer in the past 5 years	369	*15.5*	642	*17.9*
Chronic liver disease	97	*4.1*	183	*5.1*
Chronic renal failure	460	*19.4*	795	*22.2*
Dialysis	39	*1.6*	87	*2.4*
Respiratory failure	167	*7.0*	236	*6.6*
HIV Infection	2	*0.1*	13	*0.4*
Autoimmune diseases	145	*6.1*	112	*3.1*
Obesity	244	*10.3*	387	*10.8*
Number of comorbidities				
0 comorbidities	48	*2.0*	136	*3.8*
1 comorbidity	258	*10.9*	481	*13.4*
2 comorbidities	400	*16.9*	695	*19.4*
3 comorbidities and over	1667	*70.2*	2277	*63.4*

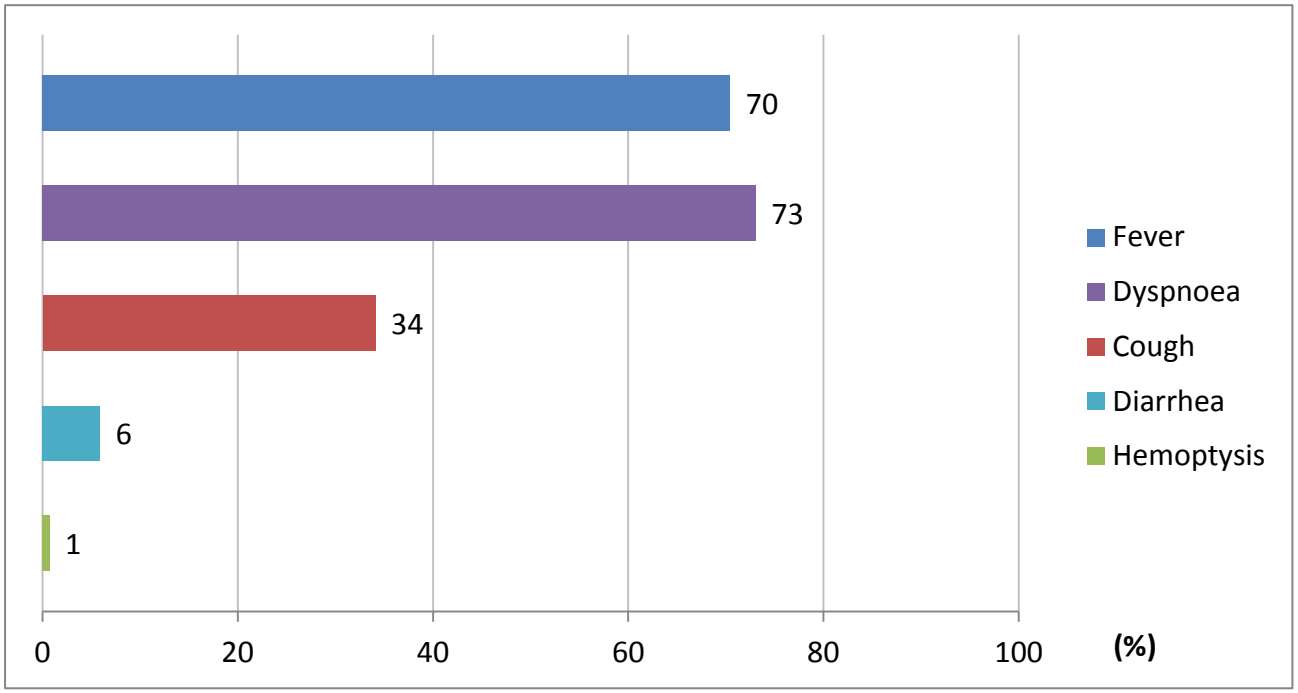
5. Diagnosis of hospitalization

In 90.6% of hospitalized persons who died and whose medical records were analysed (N=5962), conditions (e.g. pneumonia, respiratory failure) or symptoms (e.g. fever, dyspnoea, cough) compatible with SARS-CoV-2 were mentioned. In 522 cases (9.4% of cases) the diagnosis of hospitalization was not related to the infection. In 76 cases the diagnosis of hospitalization concerned exclusively neoplastic pathologies, in 176 cases cardiovascular pathologies (for example Acute Myocardial Infarction-AMI, heart failure, stroke), in 73 cases gastrointestinal pathologies (for example cholecystitis, perforation of the intestine, intestinal obstruction, cirrhosis), in 197 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=5962). Fever, dyspnoea and cough were the most commonly observed symptoms, while diarrhoea and haemoptysis were less commonly observed. Overall, 8.0% 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** (**94.0% of cases**), followed by acute renal failure (23.8%). Superinfection was observed in 19.4% and acute cardiac injury in 10.8% of cases.

8. Treatments

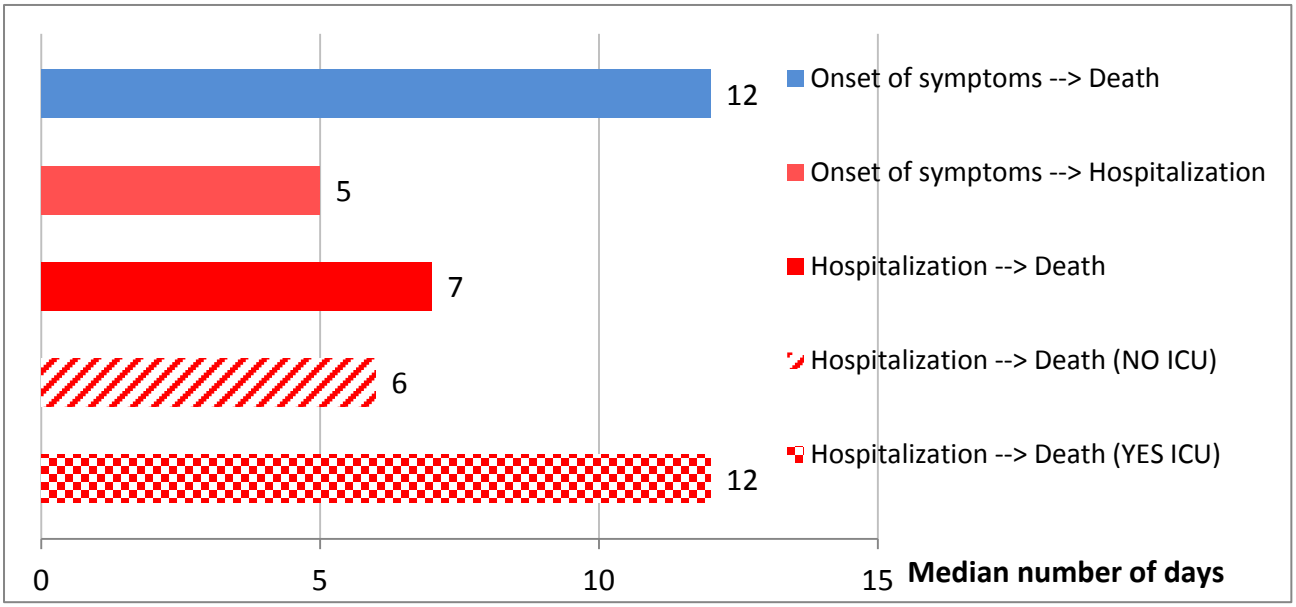
Antibiotics were used by 85.8% of patients during hospital stay, while less used were corticosteroids (51.3%) and antivirals (48.7%). Concomitant use of these 3 treatments was observed in 23.9% of cases.

Out of SARS-CoV-2 positive deceased patients, 4.1% were treated with Tocilizumab during hospitalization.

9. *Time-line*

Figure 5 shows, for SARS-CoV-2 positive deceased patients whose medical records were analysed (N=5962), the median times, in days, from the onset of symptoms to death (12 days), from the onset of symptoms to hospitalization (5 days) and from hospitalization to death (7 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, June- September, and October-16th December 2020*

Table 4 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, the second quarter, June-September, and the third period October-December. Overall, the sample represents 9.6% of all deaths from the beginning of the pandemic; in particular, the 13.3% of those who died between March and May, 27.5% of those who died between June and September, and 3.7% of those who died between October and December.

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 4*).

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 4. *Mean age, prevalence of women, number of pre-existing diseases, complications and treatments in deaths with COVID-19 in the 3 periods March-May, June- September, and October-16th December 2020*

Sample of the evaluated clinical charts	**All (n=5,962)**	**March-May 2020 (n=4,470)**	**June-Sept 2020 (n=501)**	**Oct-16th Dec 2020 (n=991)**	***p-value****
N of comorbidities					
0	184 (3.1)	169 (3.8)	6 (1.2)	9 (0.9)	*<0.001*
1	739 (12.4)	606 (13.6)	44 (8.8)	89 (9.0)	
2	1095 (18.4)	895 (20.0)	66 (13.2)	134 (13.5)	
3 or more	3944 (66.2)	2800 (62.6)	385 (76.8)	759 (76.6)	
Complications during hospitalization					
Acute Respiratory Distress Syndrome	5499 (94.0)	4142 (95.2)	412 (83.2)	945 (94.6)	*<0.001*
Acute renal failure	1389 (23.8)	1001 (23.0)	134 (27.1)	254 (25.4)	*0.052*
Acute cardiac injury	632 (10.8)	471 (10.8)	49 (9.9)	112 (11.2)	*0.743*
Superinfection	1134 (19.4)	722 (16.6)	203 (41.0)	209 (20.9)	*<0.001*
Treatments					
Antibiotics	5052 (85.8)	3813 (86.7)	424 (86.0)	815 (81.7)	*<0.001*
Antivirals	2865 (48.7)	2599 (59.1)	157 (31.8)	109 (10.9)	*<0.001*
Steroids	3022 (51.3)	1903 (43.3)	321 (65.1)	798 (80.0)	*<0.001*
Tocilizumab	218 (4.1)	170 (4.3)	28 (5.9)	20 (2.1)	*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, COPD, cancer, renal insufficiency, 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*

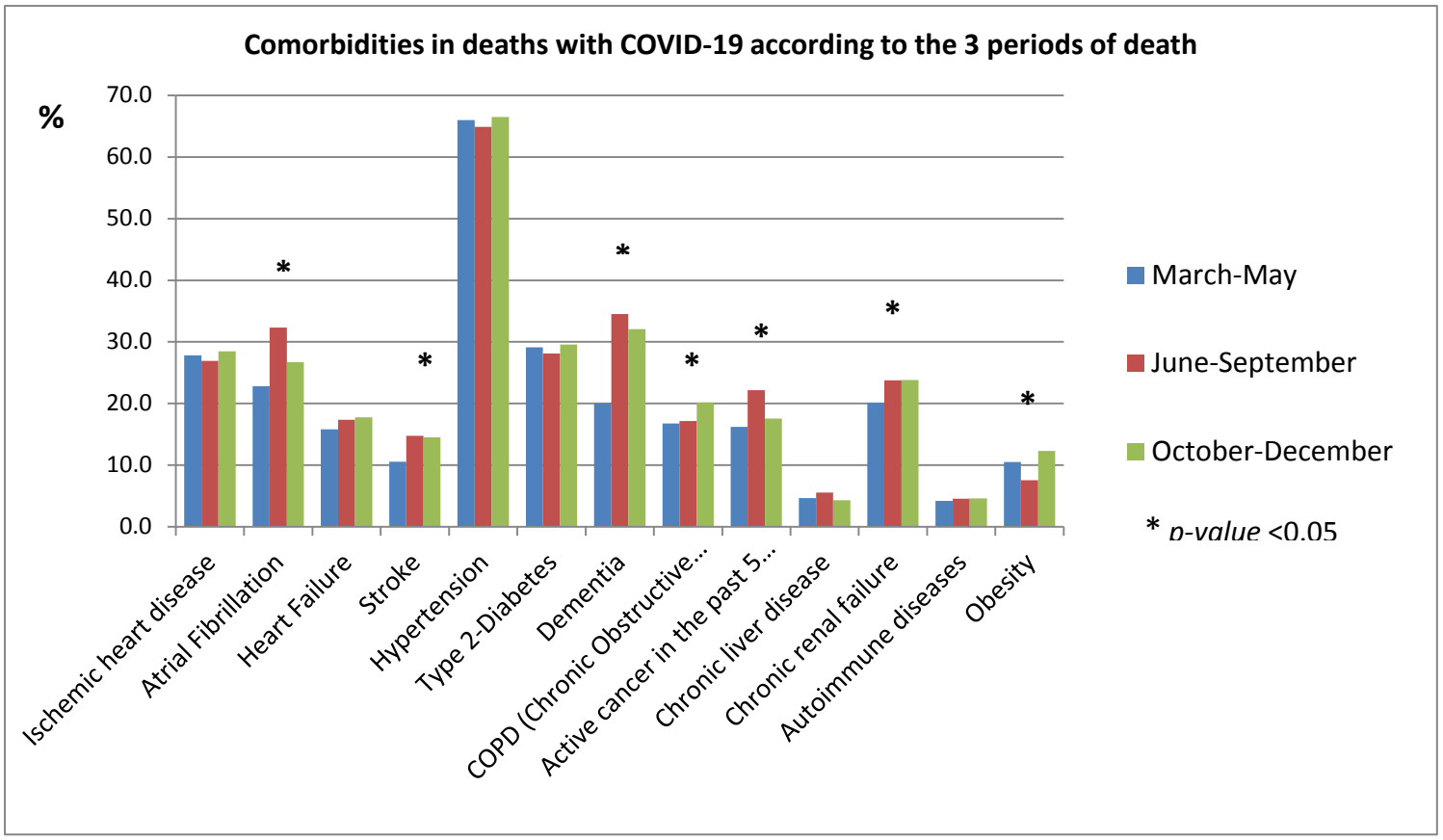


Table 5 shows the durations, as median times (in days), from the symptoms onset to death, SARS-CoV-2 testing, and hospitalization, and from the hospitalization to death, in the 3 periods considered. Between the first and second period doubles the time that passes from the onset of symptoms to death, 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 5. *Median times (in days) between symptoms onset, PCR test, hospitalization and death in the 3 periods*

	All (n=5,962)		**March-May 2020 (n=4,470)**		**June-September 2020 (n=501)**		**Oct-16th Dec 2020 (n=991)**		***p-value****
Times(in days)	**Median**	***IQR***	**Median**	***IQR***	**Median**	***IQR***	**Median**	***IQR***	
From symptoms onset to death	12	*7-20*	12	*7-19*	22	*9-55*	11	*7-18*	*<0.001*
From symptoms onset to SARS-CoV-2 testing	5	*2-8*	5	*2-9*	3	*1-7*	3	*1-6*	*<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	*3-14*	7	*3-13*	15	*5-43*	7	*3-12*	*<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

Members of the SARS-CoV-2 Surveillance Group

Luigi Palmieri, Elvira Agazio, Xanthi Andrianou, Pierfrancesco Barbariol, Antonino Bella, Eva Benelli, Luigi Bertinato, Matilde Bocci, Stefano Boros, Giovanni Calcagnini, Marco Canevelli, Federica Censi, Alessandra Ciervo, Elisa Colaizzo, Martina Del Manso, Corrado Di Benedetto, Chiara Donfrancesco, Massimo Fabiani, Francesco Facchiano, Marco Floridia, Fabio Galati, Marina Giuliano, Tiziana Grisetti, Cecilia Guastadisegni, Yllka Kodra, Ilaria Lega, Cinzia Lo Noce, Pietro Maiozzi, Valerio Manno, Margherita Martini, Alberto Mateo Urdiales, Eugenio Mattei, Claudia Meduri, Paola Meli, Giada Minelli, Lorenza Nisticò, Graziano Onder, Lucia Palmisano, Daniele Petrone, Patrizio Pezzotti, Flavia Pricci, Ornella Punzo, Vincenzo Puro, Federica Quarata, Valeria Raparelli, Flavia Riccardo, Simone Rocchetto, Paolo Salerno, Giulia Sarti, Debora Serra, Matteo Spuri, Paola Stefanelli, Marco Tallon, Manuela Tamburo De Bella, Dorina Tiple, Marco Toccaceli Blasi, Federica Trentin, Brigid Unim, Luana Vaianella, Nicola Vanacore, Maria Fenicia Vescio, Emanuele Rocco Villani, Silvio Brusaferro.