Characteristics of SARS-CoV-2 patients dying in Italy
Report based on available data on July 21st , 2021

1. Demographics

The present report describes the characteristics of 127,044 SARS-CoV-2 patients dying in Italy*, as reported by the Integrated Covid-19 Surveillance System coordinated by the National Institute of Health-ISS.

Mean age of patients dying for SARS-CoV-2 infection was 80 years (median 82, range 0-109, IQR 74-88). Women were 55,247 (43.5%). *Figure 1* shows that median age of patients dying for SARS-CoV-2 infection was more than 35 years higher as compared with the national sample diagnosed with SARS-CoV-2 infection (median age 46 years).

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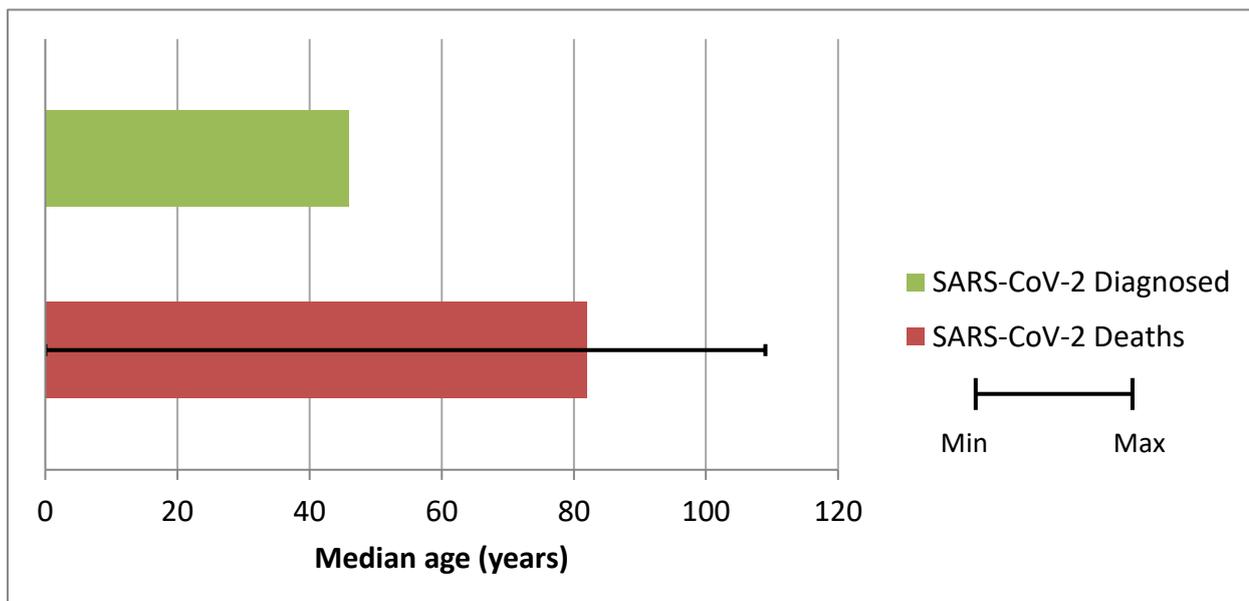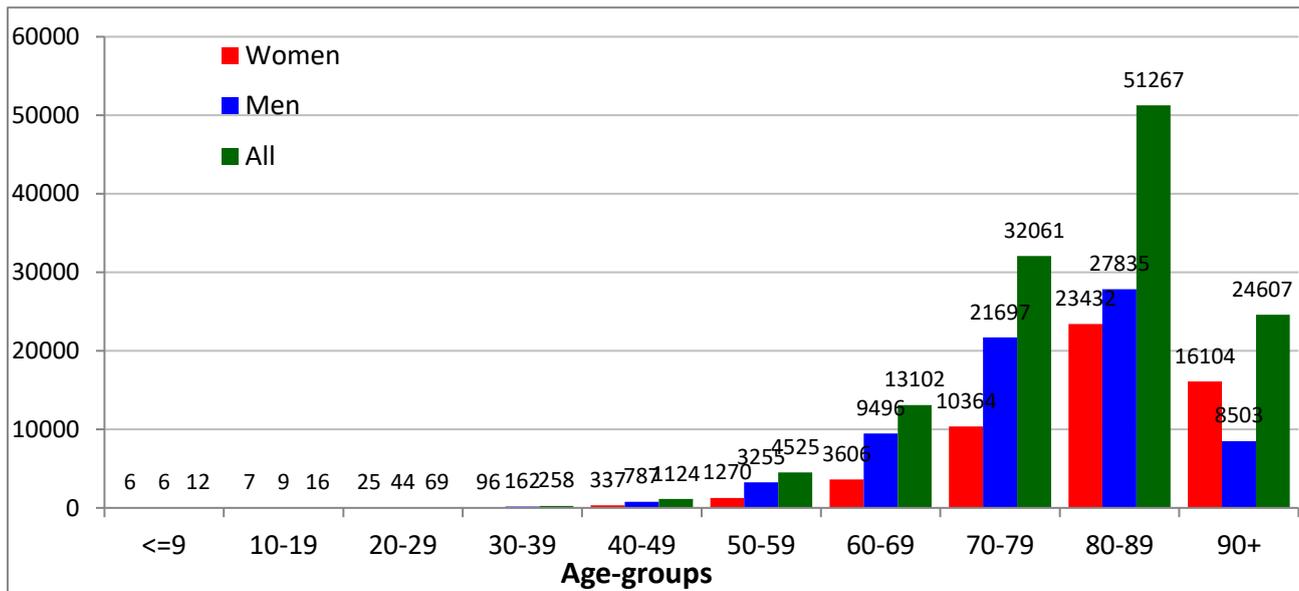

Figure 2 shows the absolute number of deaths by age group. Women dying for SARS-CoV-2 infection had an older age than men (median age women, 85 years - median age men, 80 years). In the age group ≥ 90 years only, the number of female deaths exceed those of males. This data is related to the fact that about 72% of the population over 90 years in Italy are women.
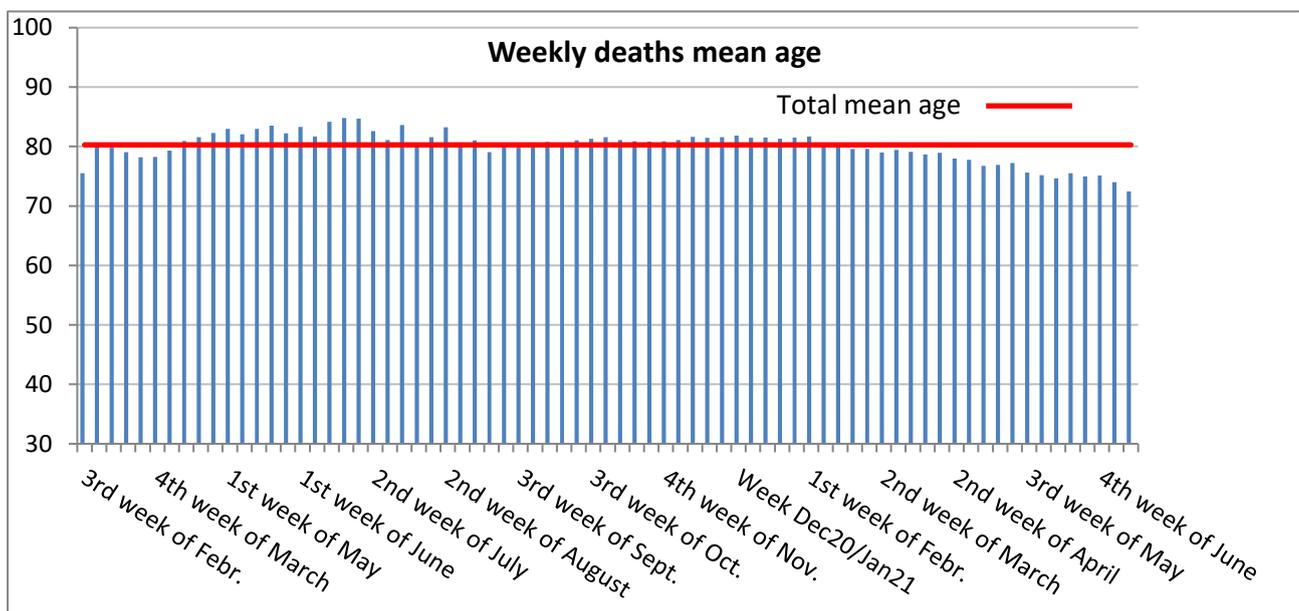
Figure 2. *Absolute number of deaths by age group*

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 2020) and then dropped slightly; a further reduction in the average age of deaths was detected starting from February-March 2021 (80 years in the 2nd week of February 2021), reaching 74 years in the 1st week of July 2021 and 72 years in the 2nd week of July 2021. This reduction in the average age of deaths is likely a consequence of the protective effect of vaccinations in the older population given priority to vaccination. It should be noted that the data of the last weeks of observation must be consolidated and therefore could undergo variations.

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

2. Deaths under the age of 50 years

As of July 21st 2021, 1,479 out of the 127,044 (1,2%), positive SARS-CoV-2 patients under the age of 50 died. In particular, 355 of these were less than 40 years (221 men and 134 women), age range between 0 and 39 years. For 105 patients under the age of 40 years no clinical information is available; out of the remaining ones, 206 had serious pre-existing pathologies (cardiovascular, renal, psychiatric pathologies, diabetes, obesity) and 44 had no major pathologies.

3. Pre-existing conditions

Table 1 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 7,681 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 3.7 (median 3, SD 2.1). Overall, 2.9% of the sample presented with a no comorbidities, 11.5% with a single comorbidity, 18.1% with 2, and 67.4% with 3 or more.

Table 1. Most common comorbidities observed in SARS-CoV-2 positive deceased patients

Diseases	All N	All %	Women N	Women %	Men N	Men %
Ischemic heart disease	2158	28.1	741	23.7	1417	31.1
Atrial Fibrillation	1884	24.5	806	25.8	1078	23.6
Heart failure	1209	15.7	562	17.6	647	13.9
Stroke	883	11.5	388	12.4	495	10.9
Hypertension	5051	65.8	2121	67.9	2930	64.3
Type 2-Diabetes	2253	29.3	854	27.4	1399	30.7
Dementia	1810	23.6	1002	32.1	808	17.7
COPD (Chronic Obstructive Pulmonary Disease)	1320	17.2	438	14.0	882	19.3
Active cancer in the past 5 years	1252	16.3	455	14.6	797	17.5
Chronic liver disease	387	5.0	134	4.3	253	5.5
Chronic renal failure	1630	21.2	617	19.8	1013	22.2
Dialysis	168	2.2	56	1.8	112	2.5
Respiratory failure	523	6.8	219	7.0	304	6.7
HIV Infection	18	0.2	2	0.1	16	0.4
Autoimmune diseases	351	4.6	193	6.2	158	3.5
Obesity	870	11.3	350	11.2	520	11.4
Number of comorbidities						
0 comorbidities	226	2.9	61	2.0	165	3.6
1 comorbidity	884	11.5	311	10.0	573	12.6
2 comorbidities	1393	18.1	530	17.0	863	18.9
3 comorbidities and over	5178	67.4	2220	71.1	2958	64.9

In women (n = 3,122) the average number of observed pathologies is 3.8 (median 4, Standard Deviation 2.0). In men (n = 4,559) the average number of observed pathologies is 3.6 (median 3, Standard Deviation 2.1).

4. Acute conditions

Between patients whose medical records were analysed, Acute Respiratory Distress syndrome was observed in the majority of patients (93.6% of cases), followed by acute renal failure (24.7%). Superinfection was observed in 19.9% and acute cardiac injury in 10.2% of cases (N=7,681; missing values=148).

5. Characteristics of deaths by age group

Table 2 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 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.

As for the complications related to SARS-CoV-2 infection, it is possible to observe how, with the exception of respiratory complications that are present in a homogeneous way in all age groups, non-respiratory complications are more commonly observed in the deceased of age < 70 years. This data indicate that, if in the very elderly deaths SARS-CoV-2 positive are linked to a greater vulnerability caused by pre-existing diseases, in the younger population, which has fewer chronic diseases, death is often associated with the coexistence of respiratory and non-respiratory complications of the infection.

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

Age-groups	16-59 (n=551)		60-69 (n=761)		70-79 (n=1,848)		80+ (n=4,515)		Total (n=7,675)	
Diseases	N	%	N	%	N	%	N	%	N	%
Ischemic heart disease	36	*6.5*	154	*20.2*	538	*29.1*	1429	*31.7*	2157	*28.1*
Atrial Fibrillation	13	*2.4*	79	*10.4*	355	*19.2*	1437	*31.8*	1884	*24.5*
Heart Failure	26	*4.7*	70	*9.2*	241	*13.0*	871	*19.3*	1208	*15.7*
Stroke	17	*3.1*	64	*8.4*	190	*10.3*	612	*13.6*	883	*11.5*
Hypertension	207	*37.6*	453	*59.5*	1245	*67.4*	3146	*69.7*	5051	*65.8*
Type 2-Diabetes	135	*24.5*	255	*33.5*	669	*36.2*	1194	*26.4*	2253	*29.4*
Dementia	15	*2.7*	45	*5.9*	215	*11.6*	1535	*34.0*	1810	*23.6*
COPD (Chronic Obstructive Pulmonary Disease)	41	*7.4*	92	*12.1*	358	*19.4*	829	*18.4*	1320	*17.2*
Active cancer in the past 5 years	94	*17.1*	142	*18.7*	368	*19.9*	647	*14.3*	1251	*16.3*
Chronic liver disease	46	*8.3*	52	*6.8*	114	*6.2*	175	*3.9*	387	*5.0*
Dialysis	22	*4.0*	20	*2.6*	55	*3.0*	71	*1.6*	168	*2.2*
HIV Infection	11	*2.0*	2	*0.3*	4	*0.2*	1	*0.0*	18	*0.2*
Autoimmune diseases	40	*7.3*	44	*5.8*	71	*3.8*	196	*4.3*	351	*4.6*
Obesity	169	*30.7*	174	*22.9*	254	*13.7*	273	*6.0*	870	*11.3*

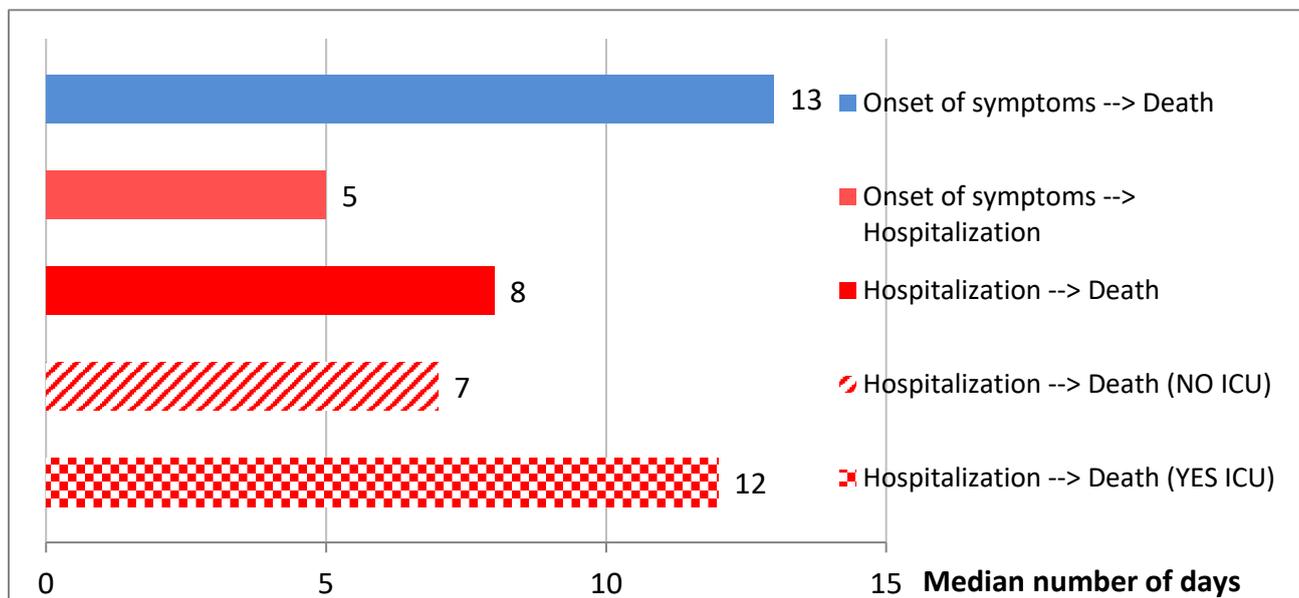| Number of comorbidities										
0 comorbidities	53	9.6	49	6.4	56	3.0	68	1.5	226	2.9
1 comorbidity	133	24.1	135	17.7	246	13.3	369	8.2	883	11.5
2 comorbidities	136	24.7	172	22.6	360	19.5	724	16.0	1392	18.1
3 comorbidities and over	229	41.6	405	53.2	1186	64.2	3354	74.3	5174	67.4
Complications from SARS-CoV-2 infection	**N**	**%**	**N**	**%**	**N**	**%**	**N**	**%**	**N**	**%**
Acute respiratory distress syndrome	522	93.7	707	93.4	1716	95.2	4103	93.0	7048	93.6
Acute renal injury	160	28.7	239	31.6	474	26.3	984	22.3	1857	24.7
Acute cardiac injury	64	11.5	80	10.6	210	11.7	414	9.4	768	10.2
Co-infection	212	38.1	259	34.2	378	21.0	647	14.7	1496	19.9
Shock	254	45.6	302	39.9	438	24.3	621	14.1	1615	21.5

6. Treatments

Antibiotics were used by 86.3% of patients during hospital stay, while less used were corticosteroids (59.2%) and antivirals (40.6%) (N=7,681; missing values=113). The common use of antibiotic therapy can be explained by the presence of superinfections or is compatible with the initiation of empiric therapy in patients with pneumonia, awaiting laboratory confirmation of SARS-CoV-2 infection. Concomitant use of these 3 treatments was observed in 21.0% of cases.

Out of SARS-CoV-2 positive deceased patients, 3.8% were treated with Tocilizumab during hospitalization (N=7,681; missing values=722).

7. Time-line

Figure 4 shows, for SARS-CoV-2 positive deceased patients whose medical records were analysed (N=7,681), 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*

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

Table 3 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– July 2021. Overall, the sample represents 6.2% of all deaths from the beginning of the pandemic.

Compared to the period of the first epidemic wave (March-May 2020), in the period of the second epidemic wave (October 2020- July 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 3*).

Table 3. *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– July 2021*
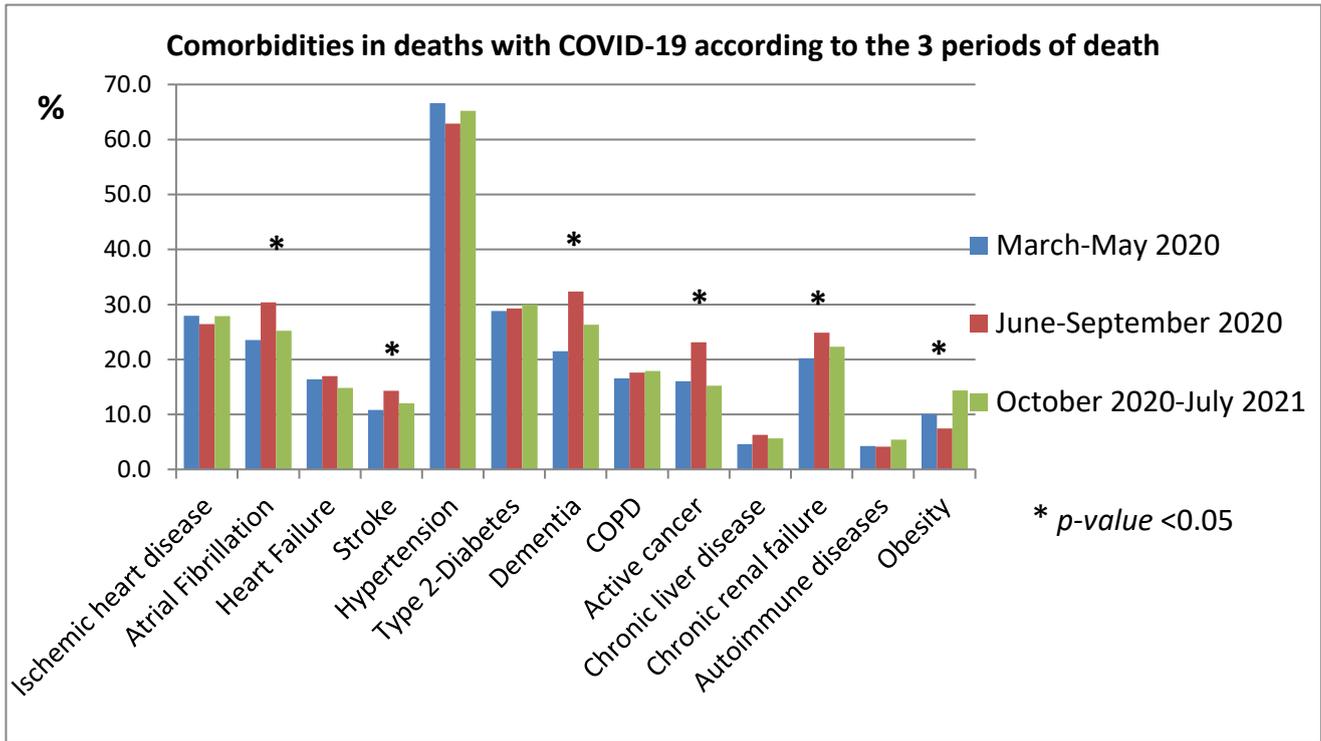
Sample of the evaluated clinical charts	All (n=7,681)	March-May 2020 (n=4,538)	June-Sept. 2020 (n=545)	Oct. 2020–July 2021 (n=2,598)	p-value*
	n (%**)	n (%**)	n (%**)	n (%**)	
N of comorbidities					
0	226 (2.9)	169 (3.5)	8 (1.7)	49 (2.0)	<0.001
1	884 (11.4)	608 (13.0)	46 (8.7)	230 (9.1)	
2	1,393 (18.1)	916 (20.0)	71 (13.8)	406 (15.8)	
3 or more	5,178 (67.6)	2,845 (63.6)	420 (75.8)	1,913 (73.1)	
Complications during hospitalization					
Acute Respiratory Distress Syndrome	7,051 (93.5)	4,167 (95.0)	443 (82.9)	2,441 (93.2)	<0.001
Acute renal failure	1,857 (24.4)	1,007 (22.6)	146 (27.7)	704 (27.1)	<0.001
Acute cardiac injury	770 (10.2)	472 (10.6)	57 (10.5)	241 (9.2)	0.181
Superinfection	1,497 (19.7)	729 (16.2)	225 (43.4)	543 (21.3)	<0.001
Treatments					
Antibiotics	6,529 (86.2)	3,837 (86.5)	460 (86.3)	2,232 (85.7)	0.589
Antivirals	3,070 (40.2)	2,610 (57.8)	171 (32.6)	289 (11.4)	<0.001
Steroids	4,483 (59.2)	1,914 (43.1)	352 (66.9)	2,217 (85.2)	<0.001
Tocilizumab	266 (3.7)	173 (4.0)	30 (6.3)	63 (2.6)	<0.001

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

** Sex- and age-standardized prevalence using the total population of COVID-19 deaths on July 21, 2021 as the standard population

The distribution of the main pre-existing diseases in the different periods is presented in *figure 5*. 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 5*).

Comorbidities in deaths with COVID-19 according to the 3 periods of death

■ March-May 2020
■ June-September 2020
■ October 2020-July 2021

* *p-value* <0.05

^ Sex- and age-standardized prevalence using the total population of COVID-19 deaths on July 21, 2021 as the standard population

Table 4 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 4. *Median times (in days) between symptoms onset, PCR test, hospitalization and death in the 3 periods*

	All				All				*p-value**
Times(in days)	**Median**	*IQR*	**Median**	*IQR*	**Median**	*IQR*	**Median**	*IQR*	
From symptoms onset to death	13	8-21	12	7-19	24	10-55	14	8-22	*<0.001*
From symptoms onset to SARS-CoV-2 testing	4	2-8	5	2-9	3	0-7	2	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	8	4-15	7	3-13	15	6-45	9	4-16	*<0.001*

* *p-value* for difference between the 3 periods
IQR = Inter-Quartile Range

9. Characteristics of SARS-COV-2 positive deaths with "complete vaccination course"

Table 5 presents the most common clinical features in SARS-COV-2 positive deceased patients with "complete vaccination course": pre-existing chronic diseases, complications, treatments.

All deaths with a confirmed diagnosis of SARS-CoV2 virus infection documented 14 days after completion of the vaccination course (i.e. 14 days after completion of the second dose for Pfizer-BioNtech, Moderna and Astra Zeneca vaccines or 14 days after the single dose for the Janssen/Johnson & Johnson vaccine) are classified as full course vaccinated. This definition is in line with the recommendations of the Center for Disease Control (CDC) in the United States (https://www.cdc.gov/coronavirus/2019-ncov/vaccines/fully-vaccinated.html). However, a complete vaccination cycle does not guarantee 100% vaccination efficacy. In fact, controlled clinical studies have shown a vaccine efficacy of vaccines in use in Italy with values between ~~70~~ 88 and ~~95~~97% ("COVID-19 epidemic. 21 July 2021 national update" (in Italian, pdf); https://www.epicentro.iss.it/en/coronavirus/sars-cov-2-integrated-surveillance-data).

Up to 21/07/2021 there are 423 SARS-COV-2 positive deaths in vaccinated with "complete vaccination cycle" and represent 1.2% out of 35,776 ~~all~~ SARS-COV-2 positive deaths occurred in the period from 01/02/2021 to 21/07/2021. It should be noted that this data cannot provide information about the effectiveness of the vaccination but is provided for purely descriptive purposes. The date of 01/02/2021 was chosen as the index date because it corresponds to the five weeks period necessary for the completion of the vaccination cycle starting from the start of the vaccination campaign which took place on 27/12/2020. It should also be noted that as of 21/07/2021 there were 22,129,193 people vaccinated with a full course (14 days from the completion of the second dose for the Pfizer-BioNtech, Moderna and AstraZeneca vaccines or 14 days from the administration of the single dose for the vaccine Janssen/Johnson & Johnson).

The analysis is based on a sample of 70 medical records out of 423 SARS-COV-2 positive deaths that occurred up to 21/07/2021 in vaccinated people with a "complete vaccination course" (16.5%). Compared to the totality of deaths for which medical records were analyzed (see paragraph 1), in the sample of deceased with "complete vaccination cycle" the mean age is very high (88.6 vs. 80 years, see paragraph 1). Furthermore, the mean number of pathologies observed in this group of deaths is 5.0 (median 5, SD 2.2), much higher than in deaths of the general population (3.7, paragraph 3). After acute respiratory failure, superinfections are the most common complications in people who died with a full vaccination course. Antibiotic and steroid treatments are the most used therapies on these patients.

Also in this case, as for the analysis of deaths presented in paragraphs 3 to 7, it should be noted that the sample is of an opportunistic type; it represents only deaths that occurred in subjects who needed hospitalization and refers to the sample of medical records sent to the ISS by hospitals. In this context, it should be noted that the mean age in the sample of medical records here presented (n=70) is 88.6 years, against 86.3 of deaths with a complete vaccination cycle in the population (n=423); the proportion of women is 51.4% and 52.0% respectively.

The results here presented may have two possible explanations. First of all, very elderly patients with numerous comorbidities may have a reduced immune response and therefore may be susceptible to SARS-CoV-2 infection and its complications, despite having been vaccinated. Secondly, this result can be explained by the fact that priority for vaccination was given to older and more vulnerable people, which represent the population with the highest prevalence of full-cycle vaccination at the date in which this analysis was carried out.

Table 5. *Clinical characteristics observed in SARS-COV-2 positive deceased patients with "full vaccination course"*

Cases in deceased persons with "full vaccination course"

	Mean	std. dev.
Age	88.6	7.7

	N	%
Women	36	_51.4_
Diseases	**N**	**%**
Ischemic heart disease	35	_50.0_
Atrial Fibrillation	23	_32.9_
Heart failure	21	_30.0_
Stroke	7	_10.0_
Hypertension	47	_67.1_
Type 2-Diabetes	19	_27.1_
Dementia	27	_38.6_
COPD (Chronic Obstructive Pulmonary Disease)	16	_22.9_
Active cancer in the past 5 years	13	_18.6_
Chronic liver disease	3	_4.3_
Chronic renal failure	12	_17.1_
Dialysis	1	_1.4_
Respiratory failure	9	_12.9_
HIV Infection	0	_0.0_
Autoimmune diseases	7	_10.0_
Obesity	2	_2.9_
N of comorbidities		
_0_	3	_4.3_
_1_	5	_7.1_
_2_	15	_21.4_
3 or more	47	_67.1_
Complications during hospitalization	**N**	**%**
Acute Respiratory Distress Syndrome	60	_89.6_
Acute renal failure	12	_17.9_
Acute cardiac injury	5	_7.5_
Superinfection	16	_23.9_
Treatments	**N**	**%**
Antibiotics	_64_	_94.1_
Antivirals	_1_	_1.5_
Steroids	_53_	_77.9_
Tocilizumab	_1_	_1.5_

Quarata, Valeria Raparelli, Flavia Riccardo, Simone Rocchetto, Chiara Sacco, Paolo Salerno, Giulia Sarti, Debora Serra, Stefania Spila Alegiani, Matteo Spuri, 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.