



Characteristics of SARS-CoV-2 patients dying in Italy Report based on available data on October 5th , 2021

1. Demographics

The present report describes the characteristics of 130,468 SARS-CoV-2 patients dying in Italy from the beginning of the surveillance to the 5th October 2021, 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 (1st quartile=74; 3rd quartile=88)). Women were 56,792 (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 45 years).

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

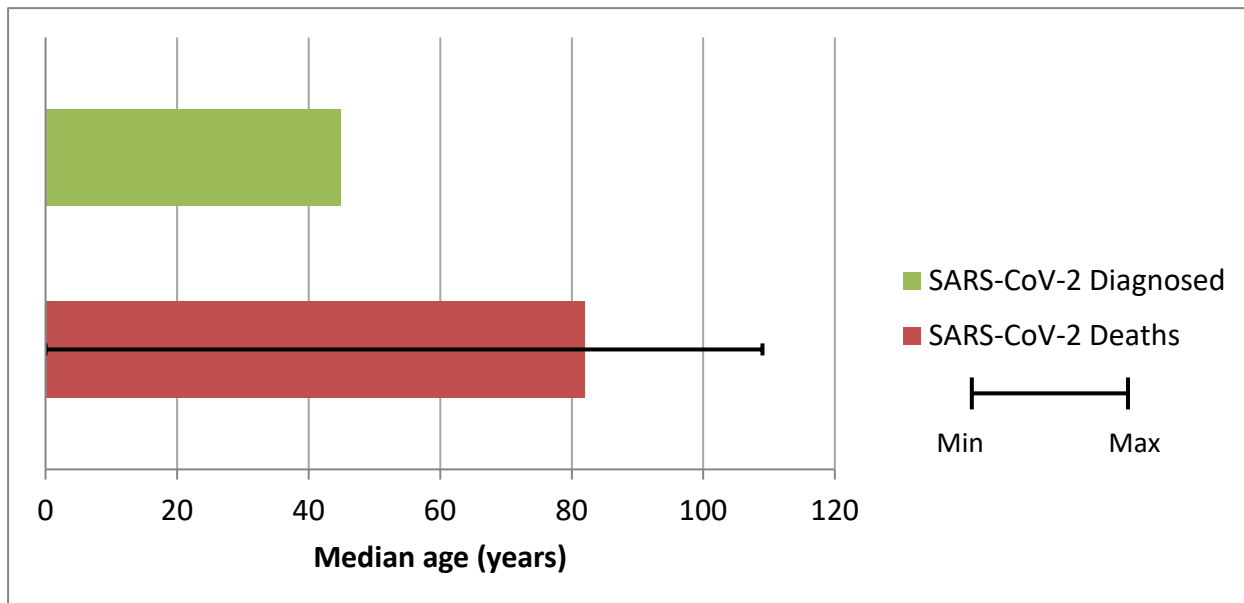
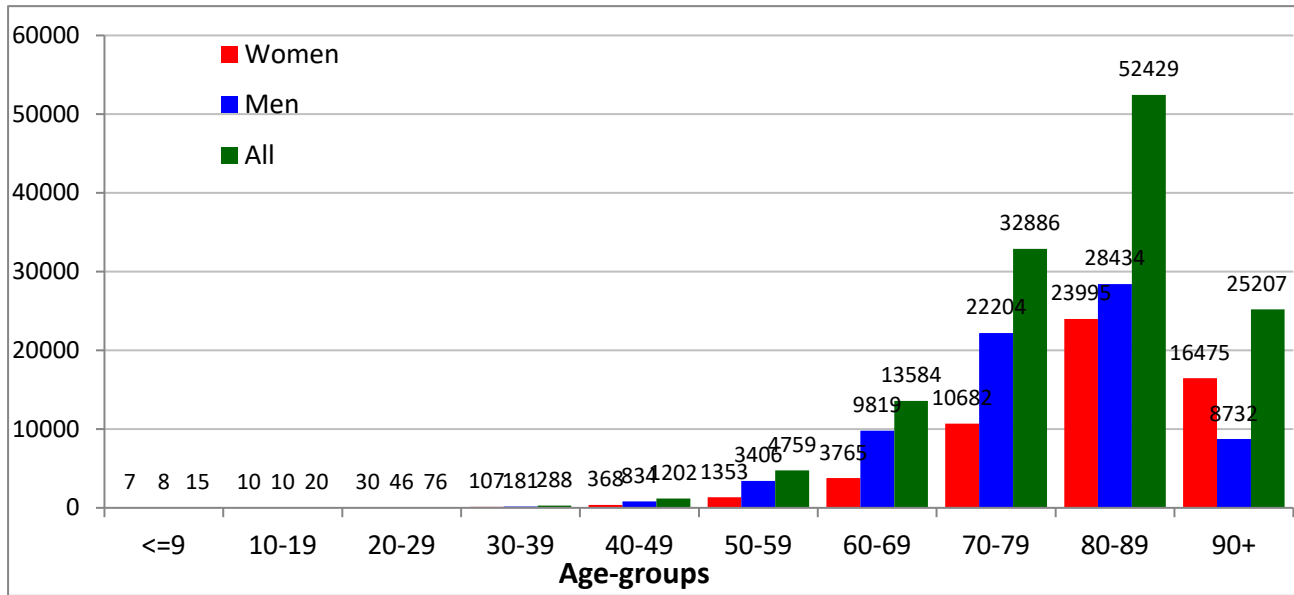


Figure 2 shows the absolute number of deaths by age group. In the age group ≥ 90 years only, the number of female deaths exceed those of males. This data is related to the fact that about 72% of the population over 90 years in Italy are women. Overall, women dying for SARS-CoV-2 infection had an older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

As of October the 5th 2021, 1,601 out of the 130,468 (1.2%), positive SARS-CoV-2 patients under the age of 50 died. In particular, 399 of these were less than 40 years (245 men and 154 women), age range between 0 and 39 years.

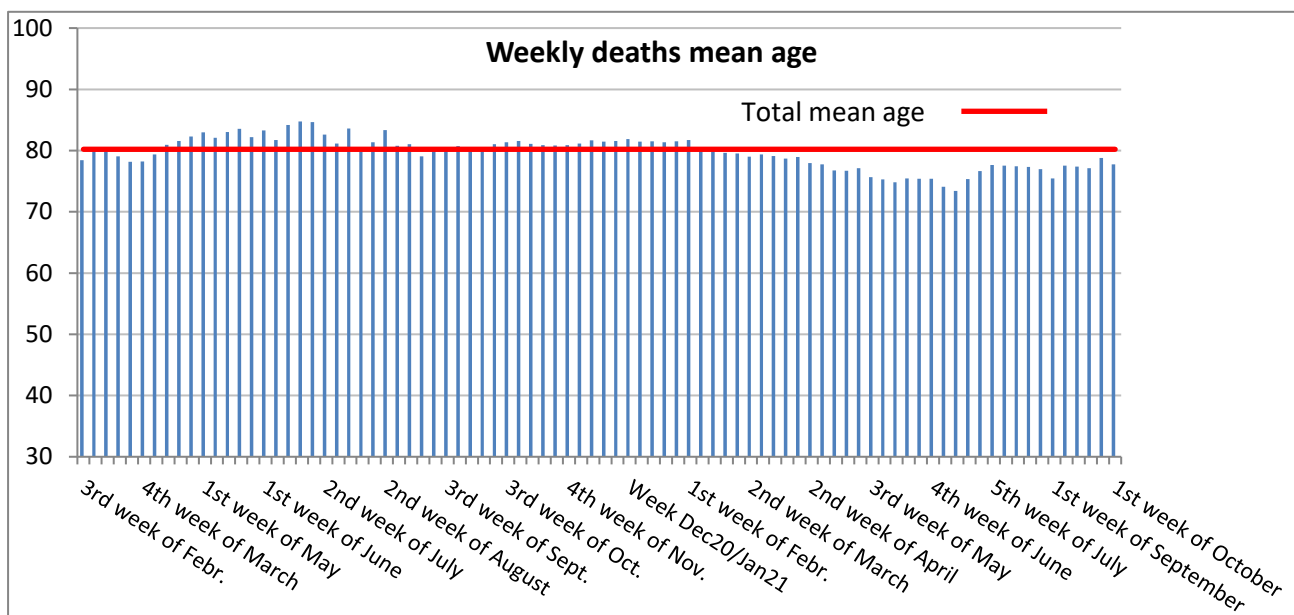
Figure 2. Absolute number of deaths by age group and sex



Note: for 2 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 20th 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 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. From the second week of July, the mean age of deaths increased slightly, remaining however below 80 years. 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. 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 7,910 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, 11.4% with a single comorbidity, 18.0% with 2, and 67.7% with 3 or more.

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

	All	Women	Men			
Diseases	N	%	N	%		
<i>Ischemic heart disease</i>	2,218	28.0	762	23.7	1,456	31.0
<i>Atrial Fibrillation</i>	1,958	24.8	835	25.9	1,123	23.9
<i>Heart failure</i>	1,245	15.7	578	17.6	667	14.0
<i>Stroke</i>	908	11.5	400	12.4	508	10.8
<i>Hypertension</i>	5,204	65.8	2,183	67.8	3,021	64.4
<i>Type 2-Diabetes</i>	2,317	29.3	882	27.4	1,435	30.6
<i>Dementia</i>	1,860	23.5	1,028	31.9	832	17.7
<i>COPD (Chronic Obstructive Pulmonary Disease)</i>	1,375	17.4	458	14.2	917	19.5
<i>Active cancer in the past 5 years</i>	1,291	16.3	469	14.6	822	17.5
<i>Chronic liver disease</i>	404	5.1	138	4.3	266	5.7
<i>Dialysis</i>	179	2.3	59	1.8	120	2.6
<i>HIV Infection</i>	18	0.2	2	0.1	16	0.3
<i>Autoimmune diseases</i>	366	4.6	202	6.3	164	3.5
<i>Obesity</i>	909	11.5	363	11.3	546	11.6
Number of comorbidities						
<i>0 comorbidities</i>	230	2.9	64	2.0	166	3.5
<i>1 comorbidity</i>	902	11.4	320	9.9	582	12.4
<i>2 comorbidities</i>	1,424	18.0	543	16.9	881	18.8
<i>3 comorbidities and over</i>	5,354	67.7	2,291	71.2	3,063	65.3
Complications from SARS-CoV-2 infection	N	%	N	%	N	%
<i>Acute respiratory distress syndrome</i>	7,264	93.6	2,906	91.7	4,358	94.9
<i>Acute renal injury</i>	1,929	24.9	674	21.3	1,255	27.3
<i>Acute cardiac injury</i>	792	10.2	292	8.9	500	10.5
<i>Co-infection</i>	1,562	20.1	602	19.0	960	20.9

In women (n=3,218) the average number of observed pathologies is 3.8 (median=4, range 0-12, Range InterQuartile-IQR (1st quartile=2; 3rd quartile=5)). In men (n=4,692) the average number of observed pathologies is 3.6 (median=3, range 0-12, Range InterQuartile-IQR (1st quartile=2; 3rd quartile=5)).

3. 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 (24.9%). Superinfection was observed in 20.1% and acute cardiac injury in 10.2% of cases.

4. 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, 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

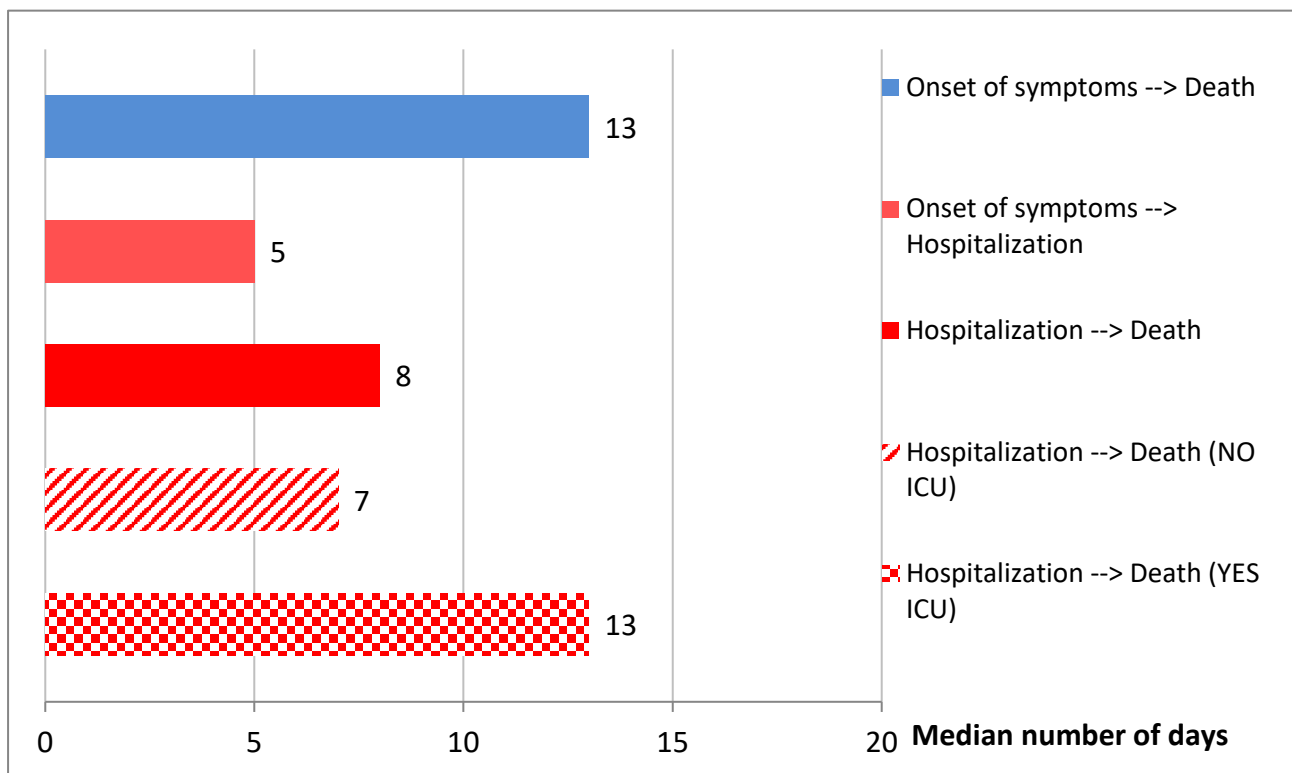
Age-groups	16-59 (n=565)		60-69 (n=781)		70-79 (n=1,895)		80+ (n=4,663)		Total (n=7,904)	
Diseases	N	%	N	%	N	%	N	%	N	%
Ischemic heart disease	37	6.5	159	20.4	546	28.8	1,475	31.6	2,217	28.0
Atrial Fibrillation	14	2.5	80	10.2	371	19.6	1,493	32.0	1,958	24.8
Heart Failure	27	4.8	72	9.2	244	12.9	901	19.3	1,244	15.7
Stroke	18	3.2	66	8.5	194	10.2	630	13.5	908	11.5
Hypertension	216	38.2	462	59.2	1,282	67.7	3,244	69.6	5,204	65.8
Type 2-Diabetes	140	24.8	259	33.2	683	36.0	1,235	26.5	2,317	29.3
Dementia	15	2.7	47	6.0	218	11.5	1,580	33.9	1,860	23.5
COPD (Chronic Obstructive Pulmonary Disease)	43	7.6	96	12.3	373	19.7	863	18.5	1,375	17.4
Active cancer in the past 5 years	98	17.3	144	18.4	379	20.0	669	14.3	1,290	16.3
Chronic liver disease	49	8.7	54	6.9	120	6.3	181	3.9	404	5.1
Dialysis	22	3.9	25	3.2	57	3.0	75	1.6	179	2.3
HIV Infection	11	1.9	2	0.3	4	0.2	1	0.0	18	0.2
Autoimmune diseases	41	7.3	46	5.9	76	4.0	203	4.4	366	4.6
Obesity	172	30.4	178	22.8	268	14.1	291	6.2	909	11.5
Number of comorbidities										
0 comorbidities	54	9.6	50	6.4	57	3.0	69	1.5	230	2.9
1 comorbidity	136	24.1	137	17.5	250	13.2	378	8.1	901	11.4
2 comorbidities	139	24.6	177	22.7	368	19.4	739	15.8	1,423	18.0
3 comorbidities and over	236	41.8	417	53.4	1,220	64.4	3,477	74.6	5,350	67.7

Complications from SARS-CoV-2 infection	N	%	N	%	N	%	N	%	N	%
Acute respiratory distress syndrome	536	93.9	725	93.4	1,761	95.2	4,239	93.0	7,261	93.6
Acute renal injury	168	29.4	244	31.4	488	26.4	1,029	22.6	1,929	24.9
Acute cardiac injury	66	11.6	81	10.4	212	11.5	431	9.5	790	10.2
Co-infection	221	38.7	265	34.1	401	21.7	674	14.8	1,561	20.1

5. Time-line

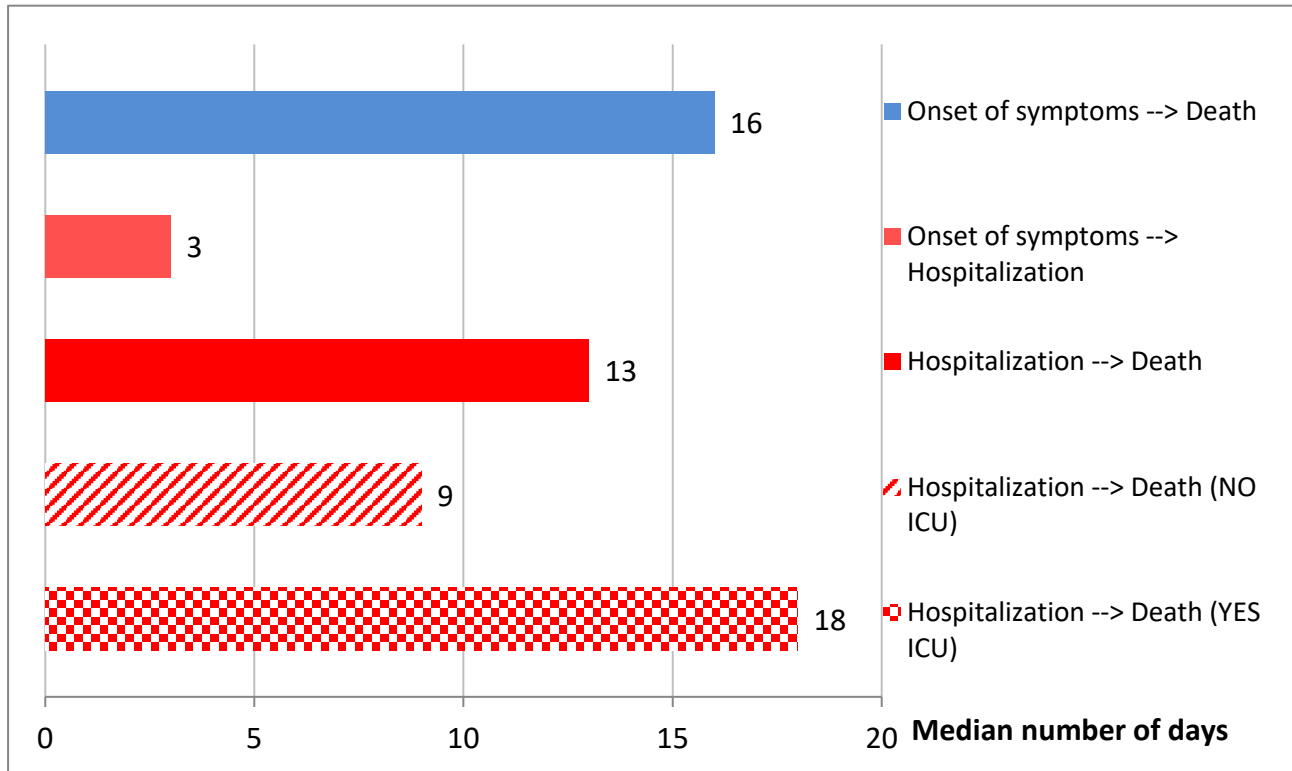
Figure 4 shows, for SARS-CoV-2 positive deceased patients whose medical records were analysed (N=7,910), the median times, in days, from the onset of symptoms to death (13 days), from the onset of symptoms to hospitalization (5 days) and from hospitalization to death (8 days). The time from hospitalization to death was 6 days longer in those who were transferred to intensive care than those who were not transferred (13 days vs. 7 days).

Figure 4. Median hospitalization times (in days) in SARS-CoV-2 positive deceased patients



If we restrict the assessment to the last 6 months (*Figure 4-bis*), we note how the median time from the onset of symptoms to death has increased, especially for those who are hospitalized in intensive care; the median time from the onset of symptoms to hospital admission was reduced. These positive data may be the combined result of a greater timing in hospitalization, which means earlier initiation of treatment in an organism where the disease has not yet had its devastating effect, and improved care, even in intensive care.

Figure 4-bis. Median hospitalization times (in days) in SARS-CoV-2 positive deceased patients during the last 6 months



6. Comparison of the characteristics of SARS-COV-2 positive deaths in 'unvaccinated-no dose', in 'vaccinated with early contagion', and in those with 'full vaccination course'

From 01/02/2021 to 05/10/2021 there are 38,096 SARS-COV-2 positive deaths. Out of these, 1,440 are the SARS-COV-2 positive deaths in vaccinated with 'complete vaccination course' (3.7% of all SARS-COV-2 positive deaths in the period under review).

Table 3 presents the most common clinical features in SARS-COV-2 positive deceased patients 'not vaccinated-any dose', 'vaccinated with early contagion', and in those with 'full vaccination course': pre-existing chronic diseases and complications.

In this analysis, the deceased with a documented SARS-CoV2 positive swab who had not yet received any vaccine dose of any kind are classified as 'unvaccinated-no dose'. These are subjects who contracted the infection before vaccination.

The deceased with a positive swab for SARS-CoV2 documented within 14 days after the start of the vaccination course (therefore within 14 days immediately following the first dose of Pfizer-Biontech, Moderna and AstraZeneca vaccines or in 14 days immediately following the single dose for the Janssen/Johnson & Johnson vaccine) are classified as 'vaccinated with early contagion'. These are subjects who contracted the infection before completing vaccination or in a period in which this had not yet stimulated a specific immune response sufficient to reduce the susceptibility to infection.

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 vaccination course'. 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

88 and 97% (“COVID-19 epidemic. 29 September 2021 national update” (in Italian, pdf); <https://www.epicentro.iss.it/en/coronavirus/sars-cov-2-integrated-surveillance-data>).

This type of analysis is proposed with the aim of comparing the SARS-COV-2 positive deceased at 'full vaccination course' with two samples of SARS-COV-2 positive deceased persons: those who had not received any vaccine dose and those who, despite having received a dose of vaccine, could not enjoy the benefits, having contracted the infection before completing the vaccination or in a period in which the vaccination had not yet stimulated a specific immune response sufficient to reduce the susceptibility to infection. This last group, defined as 'vaccinated with early contagion', is therefore similar from a biological point of view to the non-vaccinated population. By a biological point of view, this last group is therefore similar to the non-vaccinated population. By comparing the deceased 'vaccinated with early contagion' and with a 'complete vaccination cycle', the possible bias linked to the fact that vaccination priority was initially given to very elderly and frail people is reduced.

For this analysis, the date of 02/01/2021 was chosen as the index date because it corresponds to the five weeks necessary for the completion of the vaccination cycle starting from the start of the vaccination campaign which took place on 12/27/2020.

Up to 05/10/2021 there are 33,620 SARS-COV-2 positive deaths in those who had not yet received any vaccination dose ('unvaccinated-no dose'), 2,130 SARS-COV-2 positive deaths in 'vaccinated with early contagion' and 1,440 SARS-COV-2 positive deaths in vaccinated with a 'full vaccination course' (3.7% of the SARS-COV-2 positive deaths that occurred in the period from 01/02/2021 to 05/10/2021). It should be noted that these data cannot provide information about the effectiveness of the vaccination but are 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 on the 05/10/2021 there were 42,835,902 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 here presented is based on a sample of 671 clinical charts related to deaths 'unvaccinated-no dose' (2.0% of 33,620 SARS-COV-2 positive deaths 'unvaccinated-no dose'), 239 clinical charts related to deaths 'vaccinated with early contagion' (11.2% of 2,130 SARS-COV-2 positive deaths in 'vaccinated with early contagion') and 171 clinical charts of deaths with 'complete vaccination course' (11.9% of the 1,440 SARS-COV-2 positive deaths in vaccinated with 'complete vaccination course') which occurred up to 05/10/2021.

Compared to the deceased 'unvaccinated-no dose', those with a 'full vaccination course' had a significantly higher average age (85.5 vs 78.3). The average number of observed pathologies is significantly higher in the group of vaccinated with 'full vaccination course' (5.0 vs 3.9 pre-existing pathologies) and in particular, the presence of heart disease (ischemic heart disease atrial fibrillation, and heart failure) dementia and cancer proved to be higher in this sample; the opposite happens with obesity. In addition, in the 'full vaccination course' population death occurs more frequently as a result of extra-respiratory complications (acute myocardial damage) and less frequently due to respiratory failure.

Compared to the deceased 'vaccinated with early contagion', those with a 'full vaccination course' were slightly older (85.5 vs 83.9). The average number of observed pathologies is however higher in the group of vaccinated with 'full vaccination course' (5.0 vs 4.1 pre-existing pathologies); ischemic heart disease, heart failure and cancer are even more present in this sample; obesity is less present. Similarly to the previous comparison, in the 'full vaccination course' population death occurs more frequently as a result of extra-respiratory complications (especially acute myocardial damage) and less frequently due to respiratory failure. Also in this case, as for the analysis of deaths presented in paragraphs 2 to 6, it should be noted that the sample is opportunistic; it represents only deaths that occurred in subjects who needed hospitalization and refers to the sample of clinical charts sent to the ISS by hospitals. In this context, it should be noted that the mean age in the sample of clinical charts of 'unvaccinated-no dose' deaths is 78.3 against an average age of all deaths belonging to this group of 77.9; the mean age of deaths 'vaccinated with early contagion' is 83.9 years against a mean age of all deaths belonging to this group of 82.4 years and the mean

age in the sample of clinical charts of deaths with 'full vaccination course' is 85.5 years against a mean age of 84.0 for people who died under the same vaccination conditions in the population. The proportion of women in the sample of clinical charts analyzed in the 'unvaccinated-no dose' death group is 42.3% against 42.0% in the population; that of deaths 'vaccinated with early contagion' is 39.7% against 41.8% in the population, and that of deaths with 'full vaccination course' is 43.3% compared to 44.2% in the population.

The results here presented clearly indicate that people who died after completing the vaccination course have a high level of clinical complexity, significantly higher than people who could not benefit from the effect of the vaccine due to early contagion or because they haven't even started the vaccination course. It is possible to hypothesize that very elderly patients with numerous diseases may have a reduced immune response and therefore be susceptible to SARS-CoV-2 infection and its complications despite having been vaccinated. These very fragile persons with a reduced immune response are those who can benefit most from a broad vaccination coverage of the entire population as this would further reduce the risk of infection.

Table 3. Clinical characteristics observed in SARS-COV-2 positive deceased patients 'unvaccinated-no dose', 'vaccinated with early contagion' and with 'full vaccination course'

	Unvaccinated (no dose)		Vaccinated with early contagion (Diagnosis <= 14 days from the 1 st dose or unique dose)		Full vaccination course (Diagnosis > 14 days from the 2 nd dose or unique dose)		p-value
	Mean	std. dev.	Mean	std. dev.	Mean	std. dev.	
Age	78.3	12.8	83.9	8.4	85.5	9.3	<0.001
	N	%	N	%	N	%	
Women	284	42.3	95	39.7	74	43.3	0.727
Diseases	N	%	N	%	N	%	
<i>Ischemic heart disease</i>	181	27.4	60	25.3	65	38.2	0.009
<i>Atrial Fibrillation</i>	170	25.7	75	31.6	56	32.9	0.071
<i>Heart failure</i>	95	14.4	29	12.2	37	21.8	0.021
<i>Stroke</i>	65	9.8	23	9.7	21	12.4	0.600
<i>Hypertension</i>	441	66.7	164	69.2	117	68.8	0.731
<i>Type 2-Diabetes</i>	196	29.7	67	28.3	46	27.1	0.776
<i>Dementia</i>	119	18.0	58	24.5	57	33.5	<0.001
<i>COPD (Chronic Obstructive Pulmonary Disease)</i>	105	15.9	48	20.3	40	23.5	0.042
<i>Active cancer in the past 5 years</i>	93	14.1	27	11.4	35	20.6	0.030
<i>Chronic liver disease</i>	33	5.0	14	5.9	13	7.6	0.397
<i>Dialysis</i>	17	2.6	10	4.2	5	2.9	0.442
<i>HIV Infection</i>	1	0.2	0	0.0	0	0.0	0.735
<i>Autoimmune diseases</i>	47	7.1	11	4.6	14	8.2	0.300
<i>Obesity</i>	103	15.6	38	16.0	13	7.6	0.023
Number of comorbidities							
<i>0 comorbidities</i>	20	3.0	3	1.3	0	0.0	0.002
<i>1 comorbidity</i>	61	9.2	26	11.0	9	5.3	

<i>2 comorbidities</i>	110	16.6	31	13.1	15	8.8	
<i>3 comorbidities and over</i>	470	71.1	177	74.7	146	85.9	
Number of comorbidities	Mean	std. dev.	Mean	std. dev.	Mean	std. dev.	
	3.9	2.2	4.1	2.2	5.0	2.5	<0.001
Complications from SARS-CoV-2 infection	N	N	N	%	N	%	
<i>Acute respiratory distress syndrome</i>	624	94.0	232	97.5	151	89.9	0.006
<i>Acute renal injury</i>	188	28.3	70	29.4	45	26.8	0.846
<i>Acute cardiac injury</i>	52	7.8	9	3.8	19	11.3	0.015
<i>Co-infection</i>	170	25.6	45	18.9	39	23.2	0.113

This report was produced by SARS-CoV-2 positive deaths surveillance Group

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