COVID-19 in Dutch Intensive Care Units;

Patient characteristics and outcomes

compared with pneumonia patients in the ICU from 2017-2019

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Introduction

Despite the increased workload in patient care, all hospitals have put great effort in registering the data concerning COVID-19 patients. By using the online data entry system of the National Intensive Care Evaluation (NICE) foundation a limited amount of data (e.g. admission and discharge date and the age of the patient) on all COVID-19 patients has been recorded. By linking this data to more extensive clinical data, which are being collected regular by the NICE registration, it becomes possible to provide more clarity about the important characteristics and outcomes of COVID-19 patients. Because these extensive clinical data are subsequently supplied in batches from the electronic health record (EHR), these are not yet available for every COVID-19 patient. This means, when reading this report, make sure the results concern an overview of all COVID-19 patients or of COVID-19 patients who are linked to the extensive clinical data.

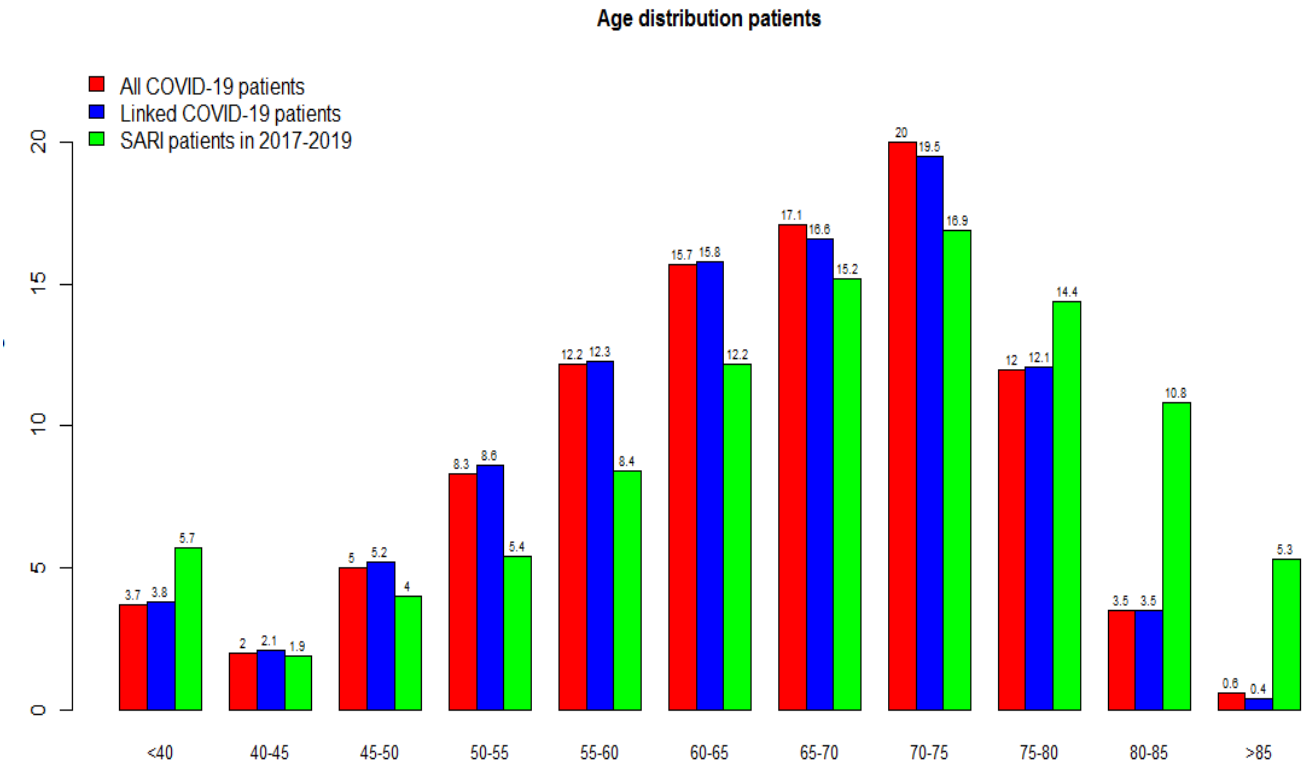
This report will be updated frequently in order to include more COVID-19 patients and more clinical data in the analyses. When only a limited amount of patients can be linked this could lead to bias: a distortion of the results can occur if the linked patients differ from the non-linked patients, for instance because the linked patients have been discharged relatively quickly, or because they died. If more data are available, there will be more certainty about the shown differences between patient groups and the associations between patient characteristics and their outcomes.In the table below the total number of admitted (confirmed) COVID-19 patients, the (confirmed) COVID-19 patients linked to the clinical data, and SARI patients are shown.

	Number of patients	**Number of hospitals**
All COVID-19 patients	7380	72
Linked COVID-19 patients	5326	68
SARI patients in 2017-2019	19835	80

Comparison COVID-19 with SARI

In this report, the data of the COVID-19 patients will be compared with a group of patients who was admitted to a Dutch ICU with severe pneumonia between the period of 1 January 2017 till 31 December 2019. This group is being called Severe Acute Respiratory Infection (SARI). In this report, SARIs will be defined based on the following (APACHE IV) reasons of admission: Pulmonary sepsis; Viral pneumonia; Aspiration pneumonia; Bacterial pneumonia; Fungal pneumonia; Parasitic pneumonia (i.e. Pneumocystis pneumonia); Other pneumonia.

The figure and table below show the age distribution of all COVID-19 patients, the linked COVID-19 patients and the SARI patients.

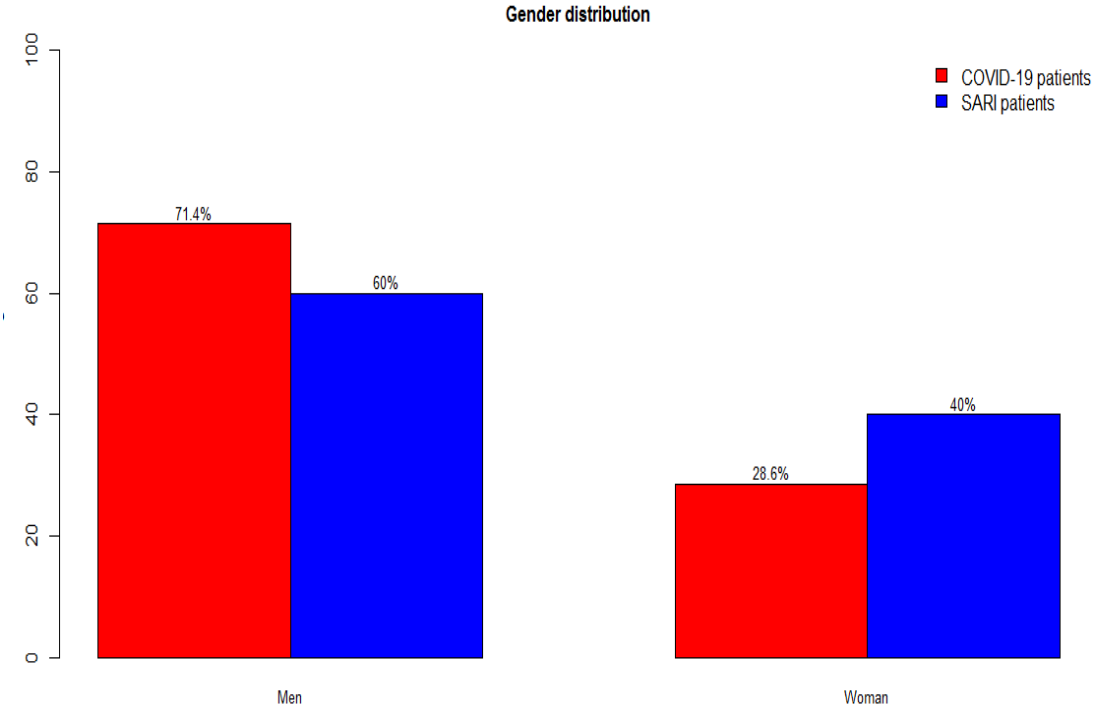


	Mean age (SD)
All COVID-19 patients	63.8 (11.4)
Linked COVID-19 patients	63.6 (11.5)
SARI patients in 2017-2019	66.3 (14.2)

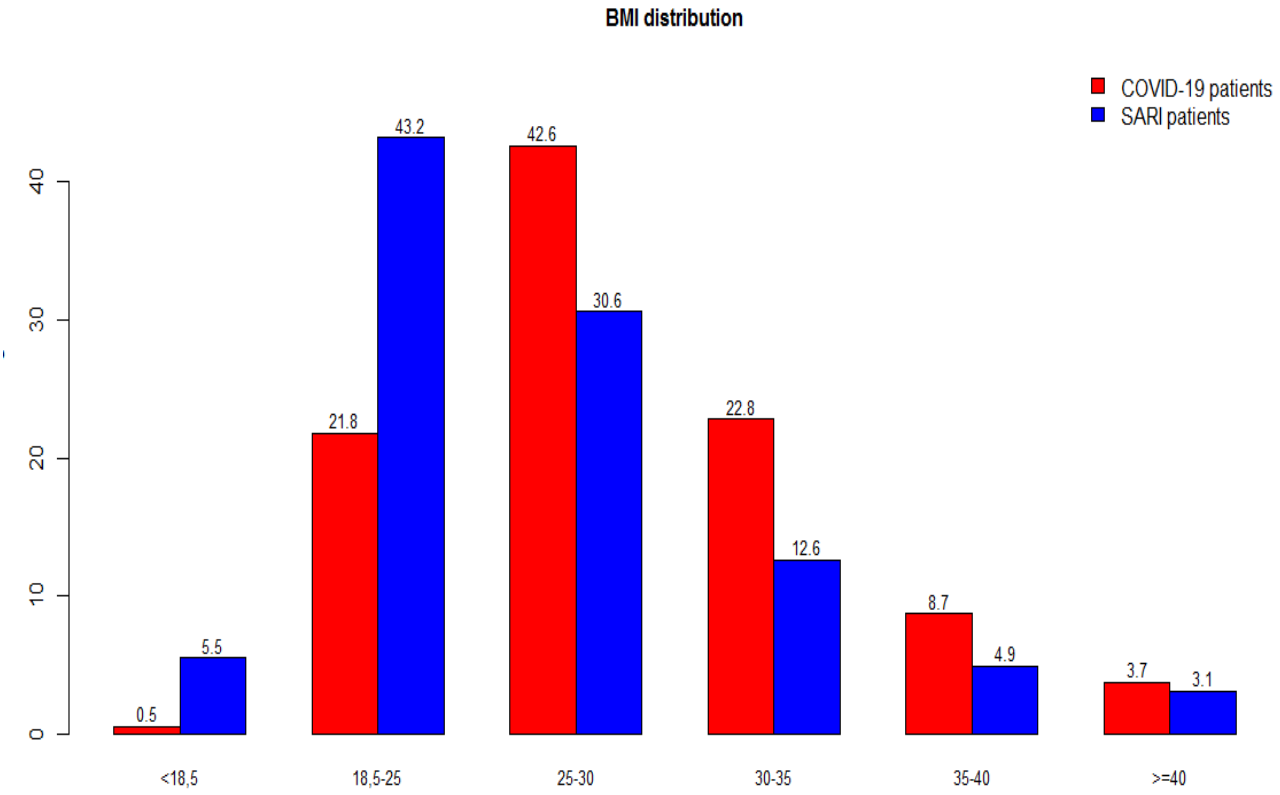
Patient characteristics

In the remainder of this report, the extensive data from the NICE registration will be used. Therefore, from here on, only the linked COVID-19 patients will be included. This group will continuously be compared with the SARI patients who have been admitted to the ICU in the previous three years (2017-2019).

In the figure below the distribution of men and women in the linked COVID-19 patients and the SARI patients is shown.



In the graph below, the BMI-distribution of the linked COVID-19 patients and the SARI patients is shown.

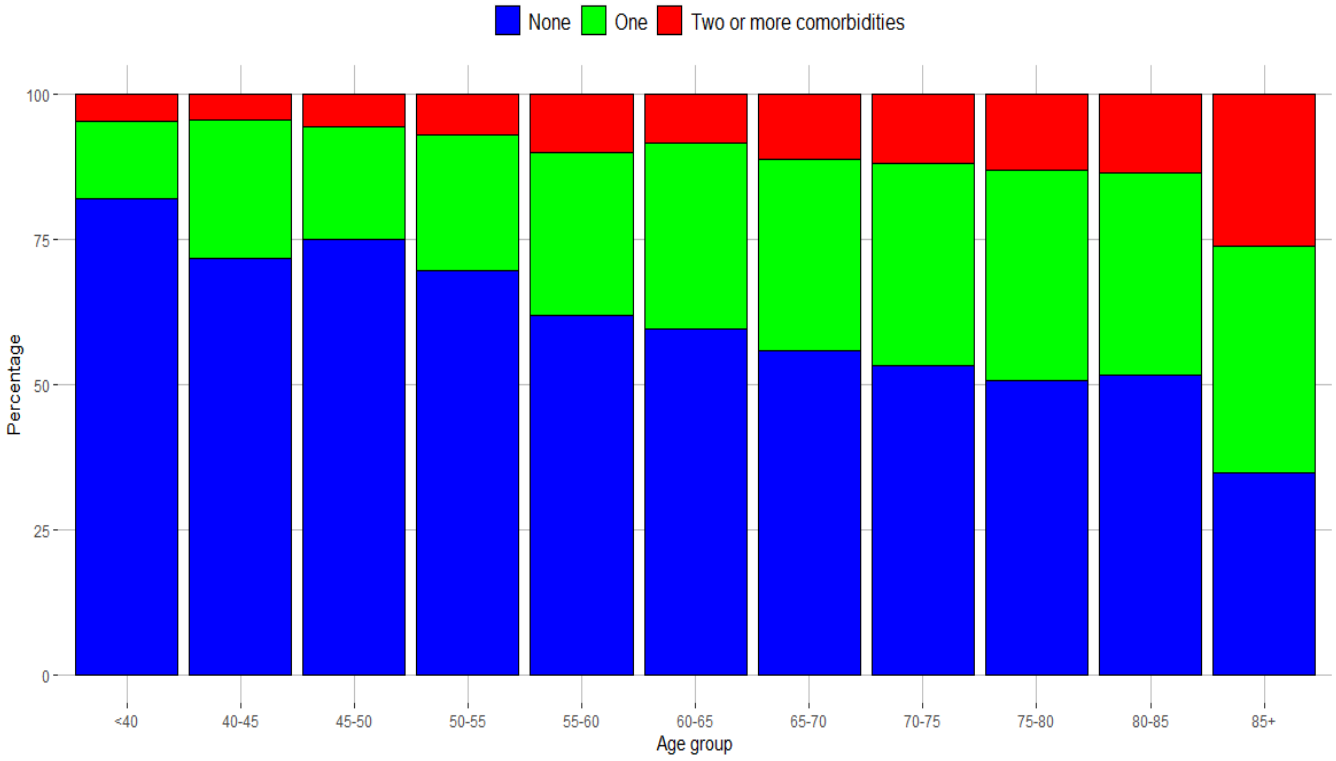


	Mean BMI (SD)
Linked COVID-19 patients	29.0 (5.2)
SARI patients in 2017-2019	26.2 (6)

The table below shows for several different comorbidities (secondary diagnoses) the number and percentage of patients who had the concerning comorbidity. Additionally, this table shows the number and percentage of the patients that were mechanically ventilated at ICU admission, and that were mechanically ventilated within the first 24 hours of ICU admission.

	COVID-19 patients N(%)	**SARI patients N(%)**
COPD/Respiratory insufficiency	661 (12.4)	7549 (38.1)
Renal failure	236 (4.4)	1717 (8.7)
Cirrhosis	19 (0.4)	239 (1.2)
Cardiovascular insufficiency	77 (1.4)	760 (3.8)
Malignancy/Haematological insufficiency	142 (2.7)	1960 (9.9)
Immunological insufficiency	459 (8.6)	3807 (19.2)
Diabetes	1211 (22.7)	4006 (20.2)
Mechanically ventilated at ICU admission	2106 (39.5)	7941 (40)
Mechanically ventilated within the 1st 24 hours	3648 (68.5)	11153 (56.2)

In the graph below, the percentage of COVID-19 patients without, with one or with two or more comorbidities are given for different age groups.



**Note since the report of 2020-12-10 diabetes is also counted as a comorbidity, as a result of this the percentage of patients with one or more comorbidities may have increased compared to previous reports.*

Patient outcomes and determinants

In the table below important characteristics of COVID-19 patients who died are compared with COVID-19 patients who have been discharged alive from the hospital.
N.B. This analysis excludes the patients who are still in the Intensive Care. However, the number of these patients are being shown in the last column of the table. The listed percentages should be read horizontally.

Per patient characteristic, the number and percentage of deceased and survived COVID-19 patients has been displayed. The column containing the P-value shows whether the differences between the deceased and the survived COVID-19 patients are statistically significant. A P-value smaller than 0.05 shows that the presented differences are statistically significant (cannot be explained based on coincidence). A P-value of 0.05 or bigger means that the discovered differences are a coincidence.

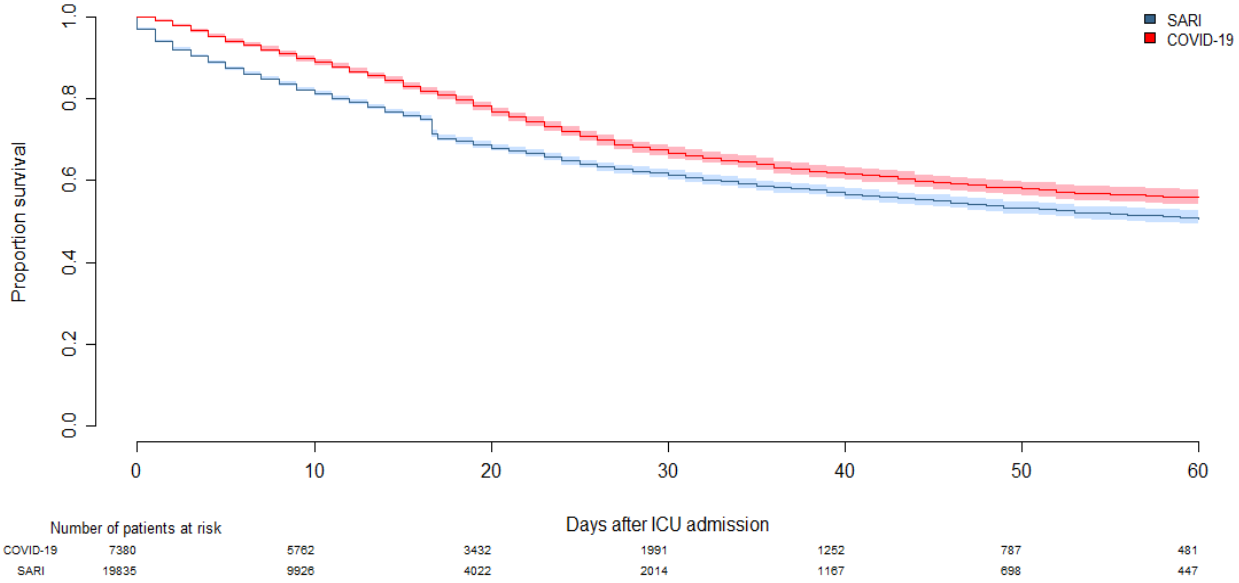
Finally, the association between the patient characteristic and mortality is shown with Odds Ratio's (OR). An OR shows approximately how much the risk of dying is increased in relation to the comparison category, also known as the reference population. Regarding age: due to the small numbers, the three youngest age categories have been combined into one reference population. Therefore, in the remaining age categories the OR indicate how much more the risk of dying is increased in comparison to this reference population. The 95%-confidence interval (CI) of the OR is displayed in the second last column and indicates whether the association found between the patient characteristics and mortality is statistically significant (confidence interval does NOT include 1) or not significant (confidence interval DOES include1).

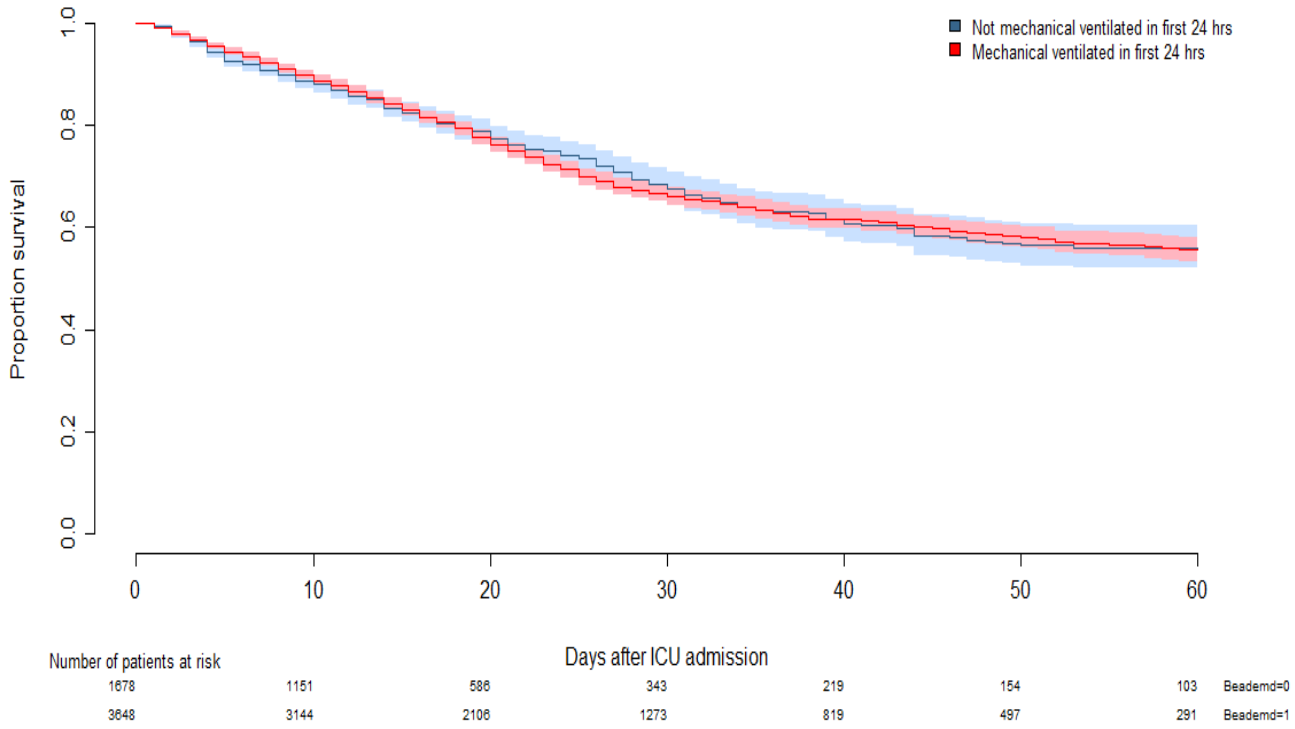
	COVID-19 survivors N (%)	**COVID-19 deceased N (%)**	**P-value**	**Odds ratio (95% CI)**	**COVID-19 still in hospital N**
All patients	3494 (69)	1569 (31)			263
Age groups			<0.001		
<40	178 (92.7)	14 (7.3)		reference	9
40-45	101 (91)	10 (9)		reference	2
45-50	238 (89.5)	28 (10.5)		reference	11
50-55	383 (87.8)	53 (12.2)		1.38 (0.92-2.06)	19
55-60	520 (84)	99 (16)		1.9 (1.33-2.7)	35
60-65	596 (75.3)	195 (24.7)		3.26 (2.35-4.51)	50
65-70	549 (65.7)	287 (34.3)		5.21 (3.8-7.15)	48
70-75	557 (56.8)	423 (43.2)		7.57 (5.55-10.31)	54
75-80	290 (46.9)	328 (53.1)		11.27 (8.15-15.57)	27
80-85	65 (36.3)	114 (63.7)		17.47 (11.53-26.47)	7
>85	6 (26.1)	17 (73.9)		28.23 (10.67-74.65)	0
Gender			<0.001		
Men	2419 (67.2)	1181 (32.8)		reference	204
Woman	1075 (73.5)	388 (26.5)		0.74 (0.65-0.85)	59

	COVID-19 survivors N (%)	COVID-19 deceased N (%)	P-value	Odds ratio (95% CI)	COVID-19 still in hospital N
BMI groups			<0.001		
<18.5	14 (53.8)	12 (46.2)		1.58 (0.72-3.44)	2
18.5-25	694 (65.2)	371 (34.8)		reference	61
25-30	1446 (68.6)	663 (31.4)		0.84 (0.73-0.98)	95
30-35	824 (73.5)	297 (26.5)		0.66 (0.56-0.79)	58
35-40	293 (69.8)	127 (30.2)		0.8 (0.63-1.01)	29
>40	135 (75)	45 (25)		0.61 (0.43-0.88)	11
Comorbidities					
COPD & respiratory insufficiency No	3123 (70.3)	1317 (29.7)	<0.001	reference	225
COPD & respiratory insufficiency Yes	371 (59.6)	252 (40.4)		1.61 (1.36-1.91)	38
Renal failure No	3405 (70.3)	1441 (29.7)	<0.001	reference	244
Renal failure Yes	89 (41)	128 (59)		3.4 (2.58-4.48)	19
Cardiovascular insufficiency No	3464 (69.4)	1528 (30.6)	<0.001	reference	257
Cardiovascular insufficiency Yes	30 (42.3)	41 (57.7)		3.1 (1.93-4.98)	6
Malignancy No	3433 (69.7)	1495 (30.3)	<0.001	reference	256
Malignancy Yes	61 (45.2)	74 (54.8)		2.79 (1.97-3.93)	7
Immunological insufficiency No	3247 (70.1)	1385 (29.9)	<0.001	reference	235
Immunological insufficiency Yes	247 (57.3)	184 (42.7)		1.75 (1.43-2.14)	28
Number of comorbidities			<0.001		
None	2261 (75.1)	750 (24.9)		reference	149
1	990 (63.8)	562 (36.2)		1.7 (1.49-1.94)	80
>1	243 (48.6)	257 (51.4)		3.18 (2.61-3.86)	34
Diagnoses at ICU-admission					
Cardiopulmonary resuscitation No	3481 (69.6)	1523 (30.4)	<0.001	reference	261
Cardiopulmonary resuscitation Yes	13 (22)	46 (78)		8.09 (4.36-15.01)	2
Mechanical ventilation at admission No	2196 (71.8)	861 (28.2)	<0.001	reference	163
Mechanical ventilation at admission Yes	1298 (64.7)	708 (35.3)		1.39 (1.23-1.57)	100
Gastrointestinal bleeding No	3485 (69)	1565 (31)	1	reference	262
Gastrointestinal bleeding Yes	9 (69.2)	4 (30.8)		0.99 (0.3-3.22)	1
Diabetes No	2783 (71.3)	1122 (28.7)	<0.001	reference	210
Diabetes Yes	711 (61.4)	447 (38.6)		1.56 (1.36-1.79)	53
Diagnoses in 1st 24 hours of ICU-admission					
Acute renal failure No	3294 (71.1)	1342 (28.9)	<0.001	reference	241
Acute renal failure Yes	200 (46.8)	227 (53.2)		2.79 (2.28-3.4)	22
Mechanical ventilation within the 1st 24 hours No	1194 (75)	399 (25)	<0.001	reference	85
Mechanical ventilation within the 1st 24 hours Yes	2300 (66.3)	1170 (33.7)		1.52 (1.33-1.74)	178
Confirmed infection No	766 (70.7)	318 (29.3)	0.197	reference	58
Confirmed infection Yes	2728 (68.6)	1251 (31.4)		1.1 (0.95-1.28)	205
Vasoactive medication No	1611 (75)	538 (25)	<0.001	reference	116
Vasoactive medication Yes	1883 (64.6)	1031 (35.4)		1.64 (1.45-1.86)	147

Kaplan Meier survival curve

In the figure below, one can see a first estimate of the percentage of COVID-19 patients (the vertical axis) who have survived the hospitalisation, including a period in ICU, since the day of ICU admission until a certain moment in time (the horizontal axis). In the first figure a distinction has been made between all COVID-19 patients who were admitted to the ICU (black line), the linked COVID-19 patients (the red line) and the SARI patients from the years 2017-2019 (blue line). The second figure shows the linked COVID-19 patients who have (dotted) or have not (solid) been mechanically ventilated at the first day of admission.
These estimations have to be interpreted with care, because the patients who are currently being treated have been included in these analyses too and consequently their outcome is not yet known. Therefore, based on this figure we cannot conclude that COVID-19 patients have a better prognosis compared to the SARIs. The current group of COVID-19 patients and the previous SARI patients possibly differ regarding important clinical characteristics such as age and secondary diseases such as diabetes or COPD. Further research could prove whether the survival chance differs between the COVID-19 and SARI population. What can be concluded from the first analysis, however, is that the death rate for COVID-19 patients in an ICU does not seems to be higher than for patients with another type of pneumonia.





Variations over time

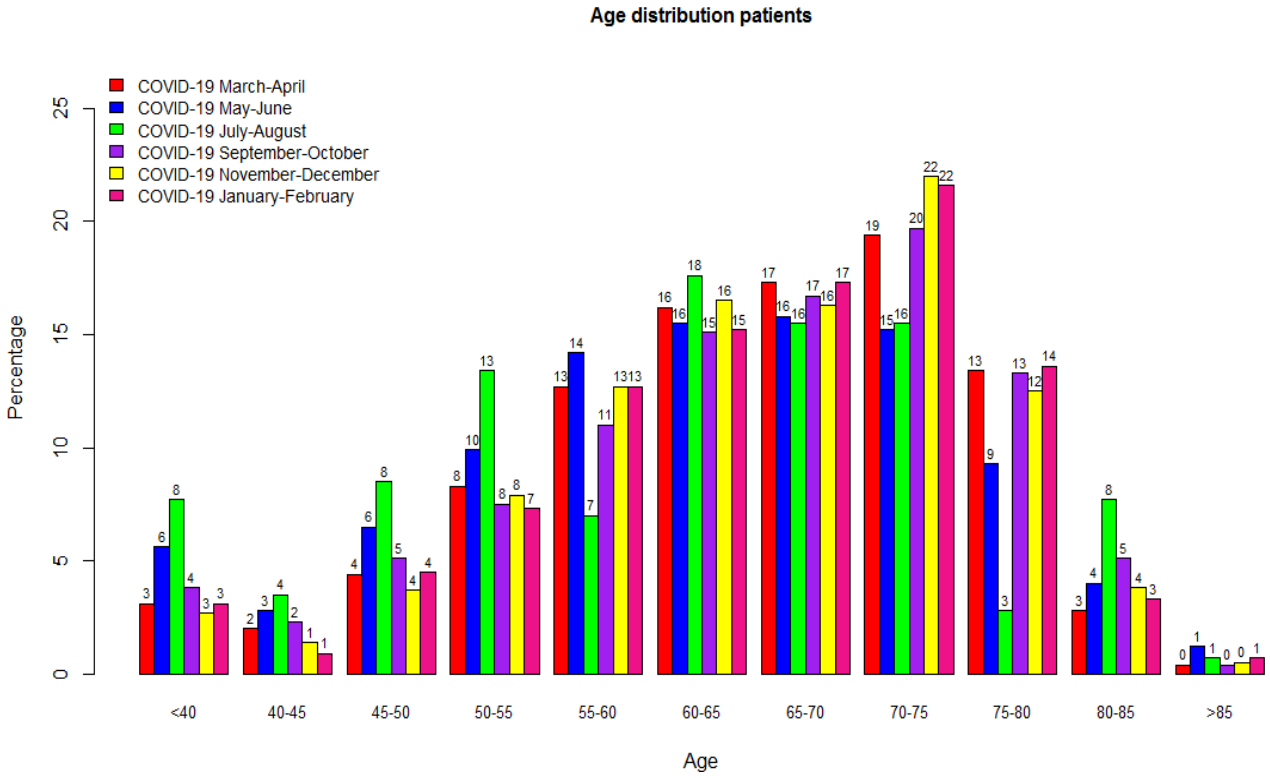
COVID-19 is a new clinical condition for which new knowledge is continuously being obtained, new treatment methods are used and as a result the prognoses / outcomes of the patients may change. To provide insight into these changes, the section below of the report will break down some important patient characteristics and outcomes into two-month periods of the COVID-19 epidemic.

The table below shows the number of COVID-19 patients per two months.

	Number of patients	**Number of deceased patients (%) ***	**Number of patients linked to clinical data**
Maart-april	2675	813 (30.4)	2543
Mei-juni	206	37 (18)	190
Juli-augustus	131	33 (25.2)	114
September-oktober	1427	459 (32.2)	1132
November-december	2226	626 (28.1)	1256
1 till 19 January 2021	*701*	*67 (9.6)*	*81*

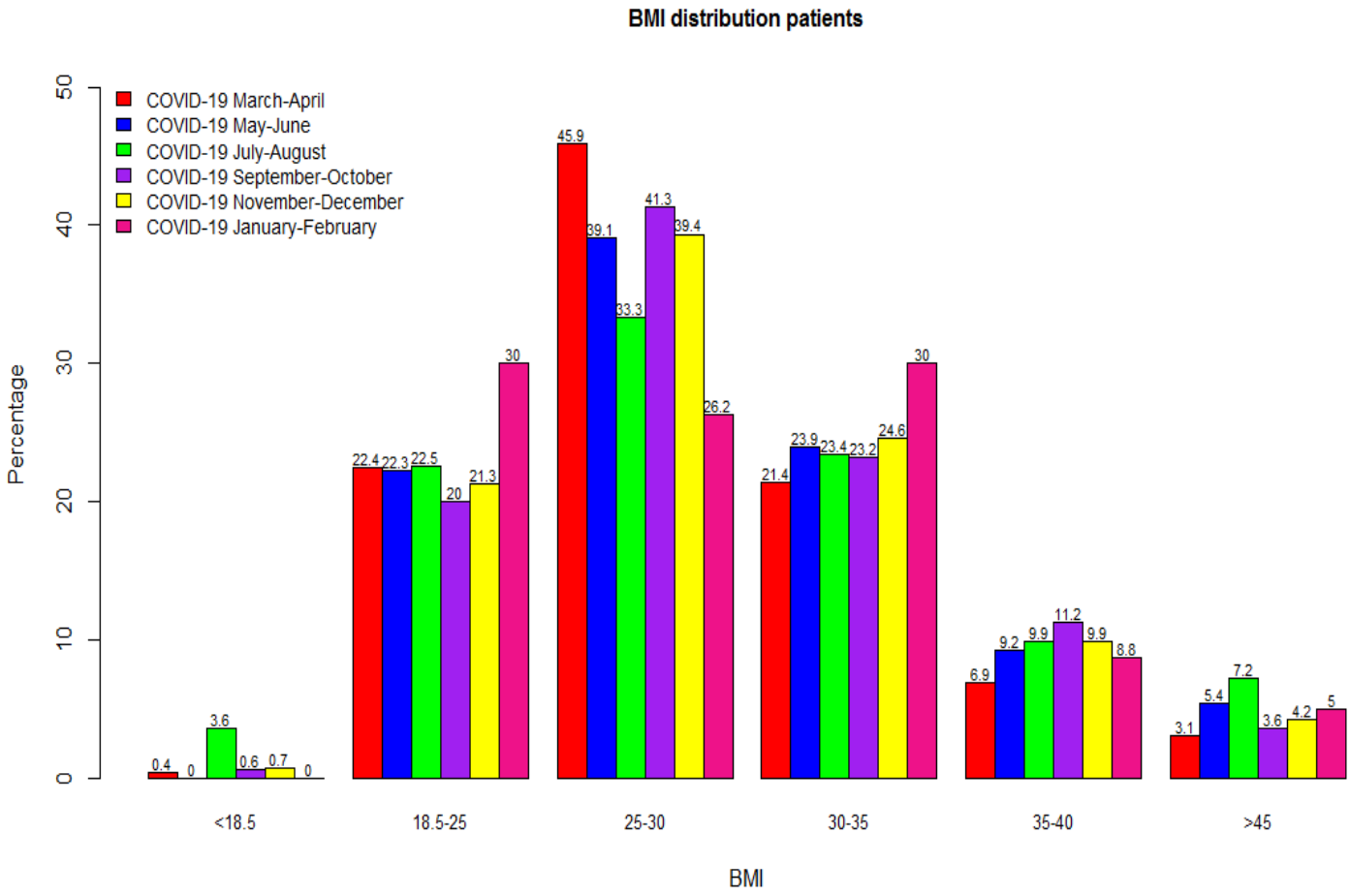
* Note a large proportion of patients from the more recent periods are still hospitalized of which a considerable part may still die, so the numbers can still rise (considerably).

The figure and table below shows the age distribution of the admitted COVID-19 patients over different time periods.



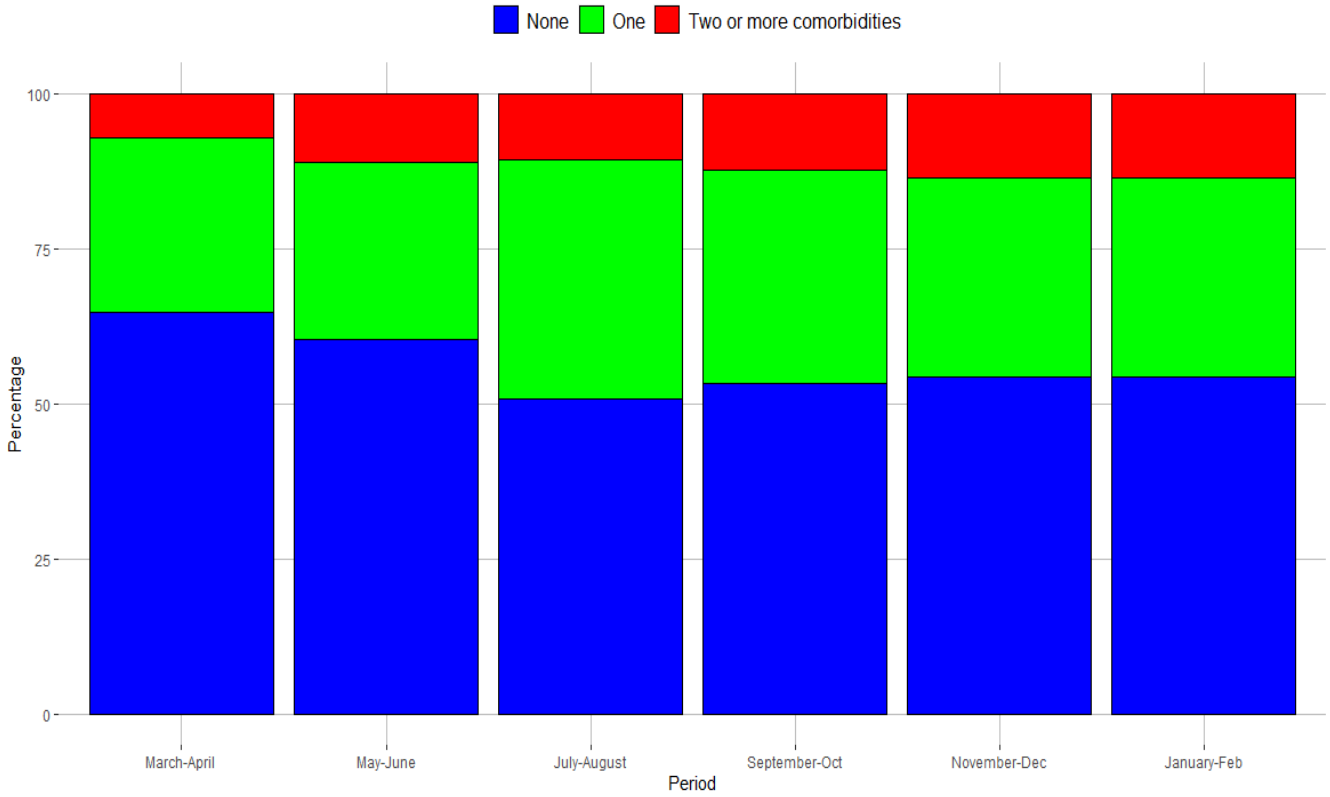
	Mean age (SD)	Median Age (IQR)
March-April	64 (11)	66 (58-73)
Mei-June	61.8 (12.7)	63 (55-71)
July-August	60.4 (13.4)	64 (51-70)
September-October	64.3 (11.8)	66 (57-73)
November-December	64.8 (10.7)	66 (58-73)
1 till 19 January 2021	*64.7 (10.9)*	*66 (59-73)*

The figure and table below shows the BMI distribution of the admitted COVID-19 patients over different time periods.



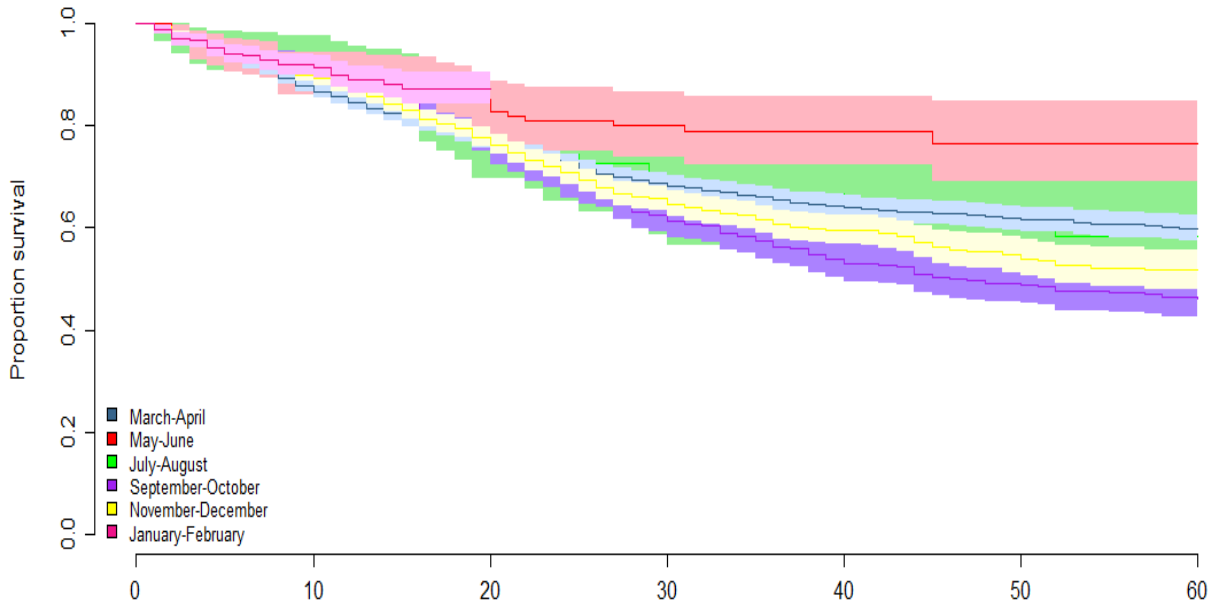
	Mean BMI (SD)	Median BMI (IQR)
March-April	28.7 (4.9)	27.8 (25.2-31.1)
May-June	29.4 (5.7)	28.4 (25.3-32.4)
July-August	29.5 (6.7)	28.1 (24.9-33.3)
September-October	29.3 (5.3)	28.7 (25.7-32)
November-December	29.3 (5.4)	28.3 (25.4-32.3)
1 till 19 January 2021	*29.3 (6.4)*	*29.1 (24.7-32.1)*

In the graph below, the percentage of COVID-19 patients without, with one or with two or more comorbidities are given for different periods.



**Note since the report of 2020-12-10 diabetes is also counted as a comorbidity, as a result of this the percentage of patients with one or more comorbidities may have increased compared to previous reports.*

The figure below shows an initial estimate per period of the percentage of COVID-19 patients (the vertical axis) who will survive hospitalization, including admission to the ICU, until a certain moment (the horizontal axis) after the start of the ICU admission.
These estimates must be interpreted with caution, because the patients who are currently being treated have also been included and the outcome of them is therefore not yet known.



Number of patients

March-April	2675	2197	1512	976	641	401	244
May-June	206	155	109	72	44	28	18
July-August	131	100	47	36	26	20	16
September-Oct.	1427	1161	650	370	250	179	114
November-Dec.	2226	1753	1074	523	280	148	78
January-Feb.	701	382	26				

The table below shows the (univariate) Odds Ratio (OR) of the two monthly periods. An OR shows approximately how much the risk of dying is increased in relation to the reference group, i.e. the months March and April. The 95% confidence interval of the OR indicates whether the relationship found between the period and mortality is significant (confidence interval includes 1 NOT) or not significant (confidence interval includes 1 DO). Note this is a univariate analysis meaning that no adjustment has been made for differences in patient characteristics over time. It is also important to realize that a large proportion of patients from the more recent periods are still hospitalized. These are included in the calculations as survivors, while a considerable part may still die, so that the odds ratio can still rise (considerably).

	Odds ratio (CI)
Period March-April	Reference
Period May-June	0.5 (0.35-0.72)
Period July-August	0.77 (0.52-1.15)
Period September-October	1.09 (0.95-1.25)
Period November-December	0.9 (0.79-1.01)
Period 1 till 19 January 2021	*0.24 (0.19-0.32)*

COVID-19 and SOFA

For this report, the data of the COVID-19 patients are also linked to the information about organ failure that is supplied to NICE in the Sequential Organ Failure Assessment (SOFA) registration module. In the table below, in addition to the number of COVID-19 patients that could be linked to the clinical information, the number of COVID-19 patients that could be linked to the SOFA data is shown.

	Number of COVID-19 patients
Linked to clinical (MDS) data	5326
Linked to organ failure (SOFA) data	2914

The table below shows how many COVID-19 and SARI patients received treatment with different types of organ support. For the patients receiving the particular organ support it is also shown how many calendar days they received this support on average during the ICU admission. Finally, the average number of calendar days on which the measured platelet was <50 is shown.

	COVID-19 patients N (%)	**Mean number of days (SE)**	**SARI patients N (%)**	**Mean number of days (SE)**
Basic respiratory support	2156 (74)	10.8 (11.1)	5122 (59.1)	6.5 (8.5)
Advanced respiratory support	23 (0.8)	2.8 (3.2)	170 (2)	3.7 (6.7)
Artificial liver support	2 (0.1)	1.5 (0.7)	0 (0)	-
Cardiac support using cardiac assist device	13 (0.4)	12.6 (19.1)	57 (0.7)	10.4 (14.3)
Renal support using renal replacement therapy	301 (10.3)	10 (9.5)	564 (6.5)	8.1 (9.4)
Measured platelets value <50	114 (3.9)	2.7 (3.3)	511 (5.9)	4.8 (5.6)