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.

From February 25, 2021, all individual episodes of patients who have had multiple proven COVID-19 episodes will be included. An episode is defined as a consecutive hospital admission period (in one or more hospitals) in which a patient has tested positive at any time. Once a patient is discharged from hospital and after more than three days is re-admitted to hospital with proven COVID-19, this new hospitalization will be considered as a new COVID-19 episode. This allows one patient to have multiple COVID-19 episodes. This report uses data from all recorded episodes.

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 episodes can be linked this could lead to bias: a distortion of the results can occur if the linked episodes differ from the non-linked episodes, for instance because the patients of linked episodes have been discharged relatively quickly, or because they died. If more data are available, there will be more certainty about the shown differences between time periods and the associations between patient characteristics and their outcomes.

The data included in this report has been processed by the compilers with the utmost care. The compiler cannot be held liable in any way for information that is nevertheless incomplete or incorrect.In the table below the total number of admitted COVID-19 episodes, the COVID-19 episodes linked to the clinical data, and SARI patients are shown.

	Number of patients	Number of hospitals
All COVID-19 episodes	8538	72
Linked COVID-19 episodes	6958	69
SARI patients in 2017-2019	19835	80

Comparison COVID-19 with SARI

In this report, the data of the COVID-19 episodes 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.

ICU length of stay

The table below shows the mean ICU length of stay of all COVID-19 episodes and admitted SARI patients, of the COVID-19 episodes of which the patients are still in the ICU, and of COVID-19 episodes and SARI patients who have been discharged recently split up into different discharge destinations. If a COVID-19 patient has been transferred to another ICU during the episode, all ICU length of stays will be added up together. The length of stay is calculated in days ((discharge date - admission date)+1).

	Number of COVID-19 episodes	Mean length of stay (SD)	Number of SARI patients	Mean length of stay (SD)
Patients who are currently being treated in the ICU *	526	8.9 (12.8)	0	-
Discharged to nursing ward in same or different hospital	5533	17 (18.9)	14106	5.9 (9.6)
Other discharge destination	318	17.7 (24.1)	2290	7.2 (11.2)
Died in the ICU	2161	16.8 (16.2)	3439	7.1 (10.5)
TOTAL	8538	16.9 (18.4)	19835	6.3 (10)

N.B. For the COVID-19 episodes of which the patient is currently admitted, it concerns the ICU length of stay up till the moment that this report was generated and not the final total length of stay.

The figure and table below show the age distribution of all COVID-19 episodes, the linked COVID-19 episodes and the SARI patients.
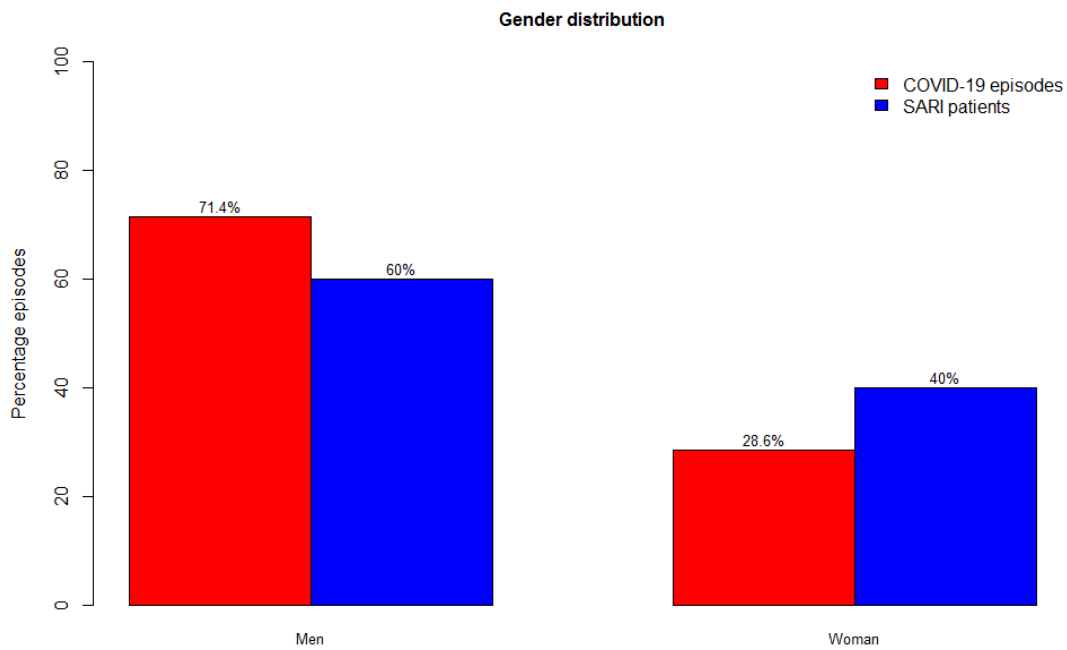
Age distribution patients
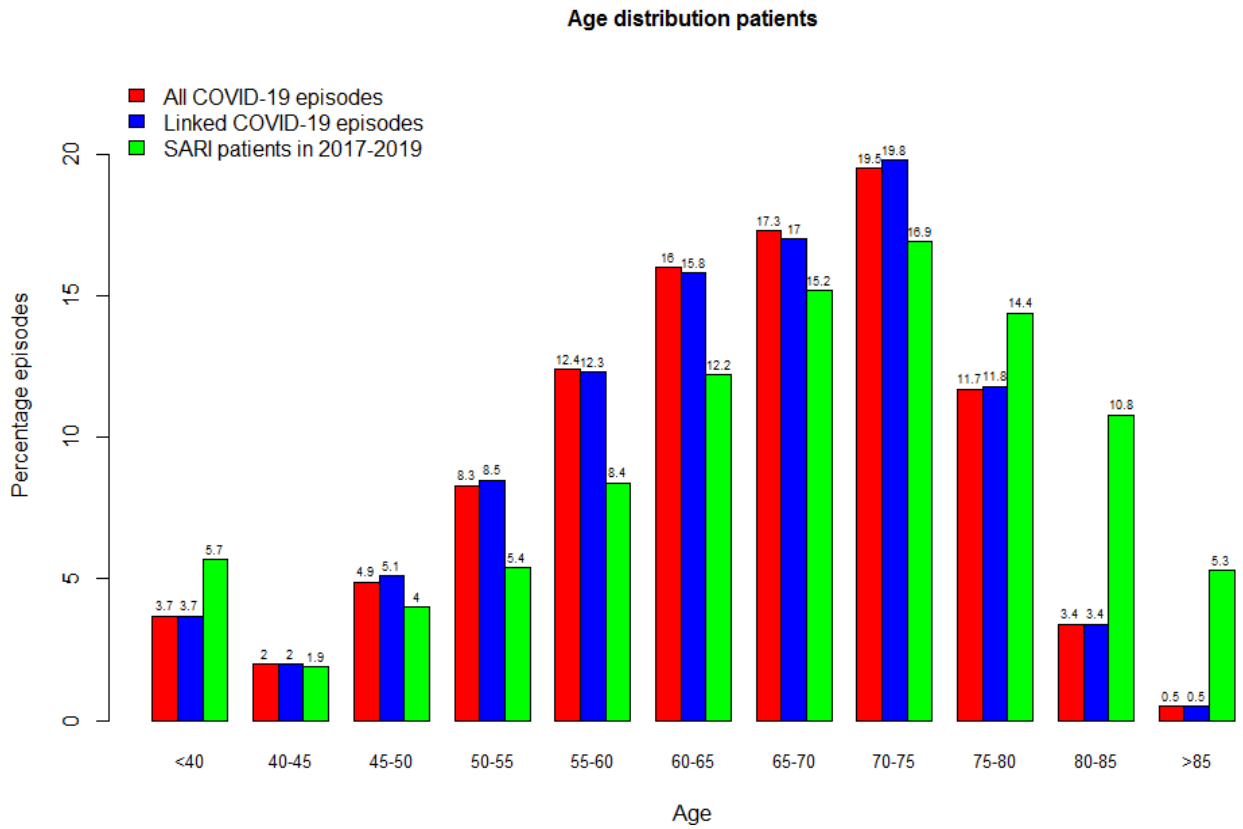
|	Mean age (SD)
All COVID-19 episodes	63.7 (11.4)
Linked COVID-19 episodes	63.7 (11.4)
SARI patients in 2017-2019	66.3 (14.2)

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 episodes 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 episodes and the SARI patients is shown.

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

BMI distribution
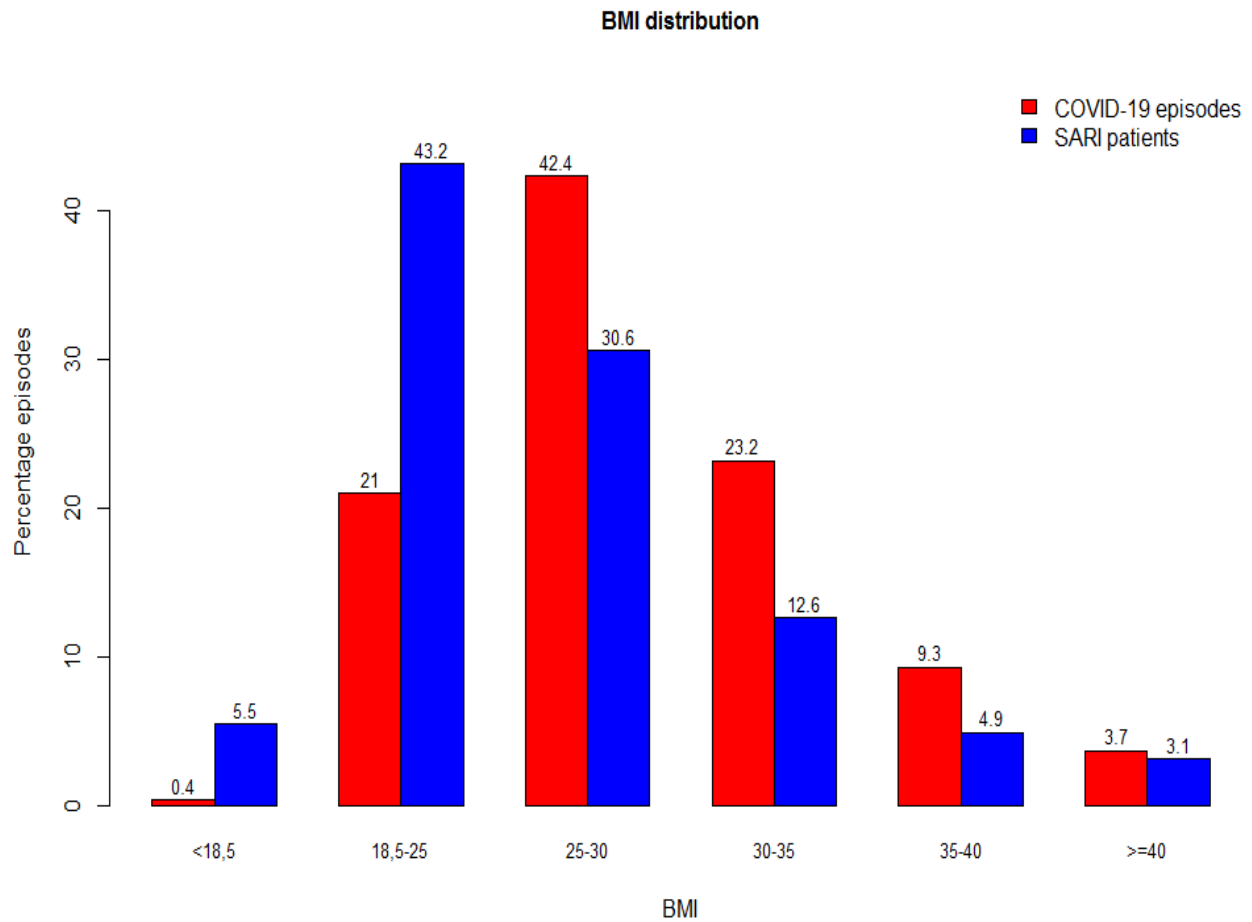
	Mean BMI (SD)
Linked COVID-19 episodes	29.1 (5.3)
SARI patients in 2017-2019	26.2 (6)

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

	COVID-19 episodes N(%)	SARI patients N(%)
COPD/Respiratory insufficiency	898 (12.9)	7549 (38.1)
Renal failure	308 (4.4)	1717 (8.7)
Cirrhosis	26 (0.4)	239 (1.2)
Cardiovascular insufficiency	111 (1.6)	760 (3.8)
Malignancy/Haematological insufficiency	202 (2.9)	1960 (9.9)
Immunological insufficiency	637 (9.2)	3807 (19.2)
Diabetes	1619 (23.3)	4006 (20.2)
Mechanically ventilated at ICU admission	2470 (35.5)	7941 (40)
Mechanically ventilated within the 1st 24 hours	4611 (66.3)	11153 (56.2)

In the graph below, the percentage of COVID-19 episodes of which the patient had no, one or more than one comorbidities are given for different age groups.
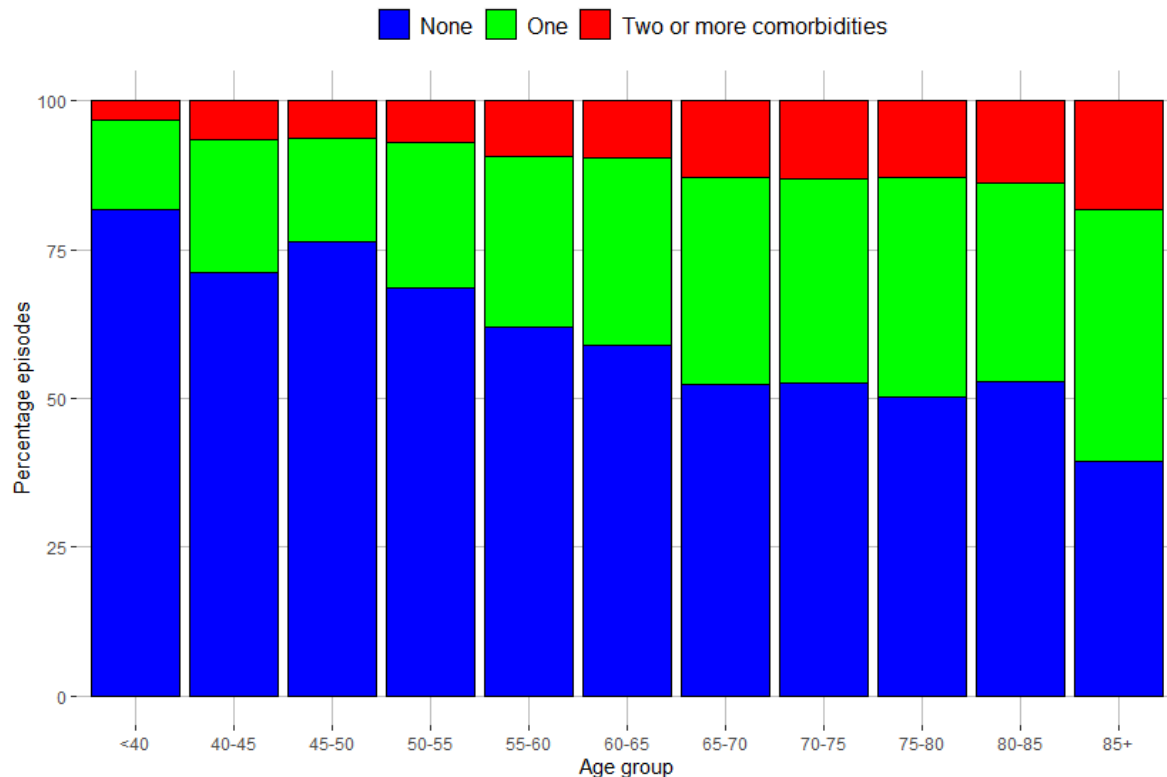
Note since the report of 2020-12-10 diabetes is also counted as a comorbidity, as a result of this the percentage of episodes of which patient had one or more comorbidities may have increased compared to previous reports.

Patient outcomes and determinants

In the table below important characteristics belonging to COVID-19 episodes of which the patient died are compared with COVID-19 episodes of which the patient survived.
N.B. This analysis excludes the episodes of which the patient is still admitted at the Intensive Care. However, the number of these episodes 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 episodes of which the patient deceased and survived has been displayed. The column containing the P-value shows whether the differences between the episodes of deceased and survived 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 probably 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 episodes	4576 (69.1)	2048 (30.9)			334
Age groups			<0.001		
<40	229 (92.7)	18 (7.3)		reference	10
40-45	119 (90.2)	13 (9.8)		reference	7
45-50	305 (90.2)	33 (9.8)		reference	16
50-55	489 (86.4)	77 (13.6)		1.63 (1.14-2.31)	22
55-60	681 (84.1)	129 (15.9)		1.96 (1.42-2.69)	48
60-65	797 (76.7)	242 (23.3)		3.14 (2.34-4.21)	60
65-70	738 (66.1)	379 (33.9)		5.3 (3.99-7.05)	64
70-75	734 (55.8)	582 (44.2)		8.19 (6.2-10.82)	63
75-80	382 (48.2)	411 (51.8)		11.11 (8.3-14.88)	30
80-85	83 (36.7)	143 (63.3)		17.79 (12.26-25.83)	12
>85	11 (34.4)	21 (65.6)		19.72 (9.1-42.72)	1
Gender			<0.001		
Men	3185 (67.5)	1533 (32.5)		reference	253
Woman	1391 (73)	515 (27)		0.77 (0.68-0.87)	81
BMI groups			<0.001		
<18.5	15 (55.6)	12 (44.4)		1.45 (0.67-3.12)	2
18.5-25	876 (64.8)	476 (35.2)		reference	68
25-30	1901 (69.3)	841 (30.7)		0.8 (0.7-0.92)	133

	COVID-19 survivors N (%)	COVID-19 deceased N (%)	P-value	Odds ratio (95% CI)	COVID-19 still in hospital N
30-35	1082 (72.2)	417 (27.8)		0.7 (0.6-0.82)	70
35-40	421 (71.2)	170 (28.8)		0.73 (0.6-0.9)	36
>40	174 (72.5)	66 (27.5)		0.69 (0.51-0.93)	13
Comorbidities					
COPD & respiratory insufficiency No	4076 (70.6)	1694 (29.4)	<0.001	reference	290
COPD & respiratory insufficiency Yes	500 (58.5)	354 (41.5)		1.7 (1.47-1.97)	44
Renal failure No	4461 (70.4)	1877 (29.6)	<0.001	reference	312
Renal failure Yes	115 (40.2)	171 (59.8)		3.53 (2.77-4.5)	22
Cardiovascular insufficiency No	4527 (69.5)	1991 (30.5)	<0.001	reference	329
Cardiovascular insufficiency Yes	49 (46.2)	57 (53.8)		2.64 (1.8-3.89)	5
Malignancy No	4486 (69.8)	1942 (30.2)	<0.001	reference	328
Malignancy Yes	90 (45.9)	106 (54.1)		2.72 (2.04-3.62)	6
Immunological insufficiency No	4237 (70.4)	1784 (29.6)	<0.001	reference	300
Immunological insufficiency Yes	339 (56.2)	264 (43.8)		1.85 (1.56-2.19)	34
Number of comorbidities			<0.001		
None	2910 (75.2)	959 (24.8)		reference	194
1	1334 (65)	717 (35)		1.62 (1.44-1.82)	103
>1	332 (47.2)	372 (52.8)		3.36 (2.85-3.97)	37
Diagnoses at ICU-admission					
Cardiopulmonary resuscitation No	4557 (69.6)	1988 (30.4)	<0.001	reference	331
Cardiopulmonary resuscitation Yes	19 (24.1)	60 (75.9)		7.24 (4.31-12.16)	3
Mechanical ventilation at admission No	3066 (72)	1195 (28)	<0.001	reference	227
Mechanical ventilation at admission Yes	1510 (63.9)	853 (36.1)		1.45 (1.3-1.61)	107
Gastrointestinal bleeding No	4563 (69.1)	2041 (30.9)	0.822	reference	334
Gastrointestinal bleeding Yes	13 (65)	7 (35)		1.2 (0.48-3.02)	0
Diabetes No	3620 (71.3)	1457 (28.7)	<0.001	reference	262
Diabetes Yes	956 (61.8)	591 (38.2)		1.54 (1.36-1.73)	72
Diagnoses in 1st 24 hours of ICU-admission					
Acute renal failure No	4351 (71.3)	1755 (28.7)	<0.001	reference	309
Acute renal failure Yes	225 (43.4)	293 (56.6)		3.23 (2.69-3.87)	25
Mechanical ventilation within the 1st 24 hours No	1692 (76)	534 (24)	<0.001	reference	121
Mechanical ventilation within the 1st 24 hours Yes	2884 (65.6)	1514 (34.4)		1.66 (1.48-1.87)	213
Confirmed infection No	971 (70.8)	400 (29.2)	0.125	reference	69
Confirmed infection Yes	3605 (68.6)	1648 (31.4)		1.11 (0.97-1.26)	265
Vasoactive medication No	2233 (75.5)	725 (24.5)	<0.001	reference	154
Vasoactive medication Yes	2343 (63.9)	1323 (36.1)		1.74 (1.56-1.94)	180

Kaplan Meier survival curve

In the figure below, one can see a first estimate of the percentage of COVID-19 episodes (the vertical axis) of which patients 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 episodes (black line), the linked COVID-19 episodes (the red line) and the SARI patients from the years 2017-2019 (blue line). The second figure shows the linked COVID-19 episodes of which the patient has (dotted) or has not (solid) been mechanically ventilated at the first day of admission.

These estimations have to be interpreted with care, because the episodes of which the patient is 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 episodes 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.
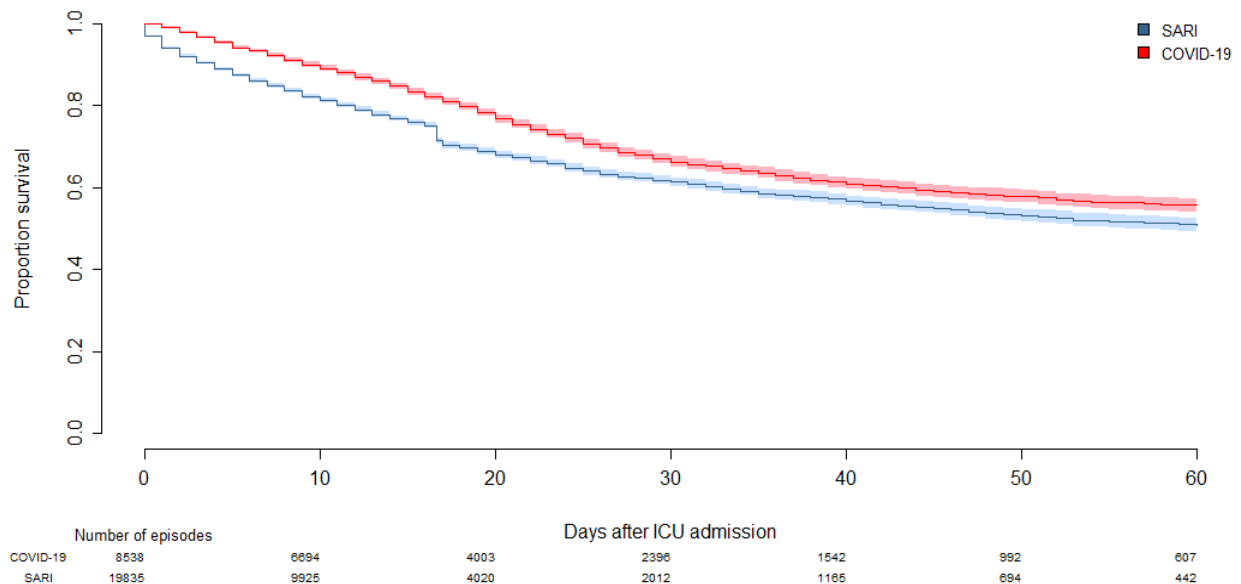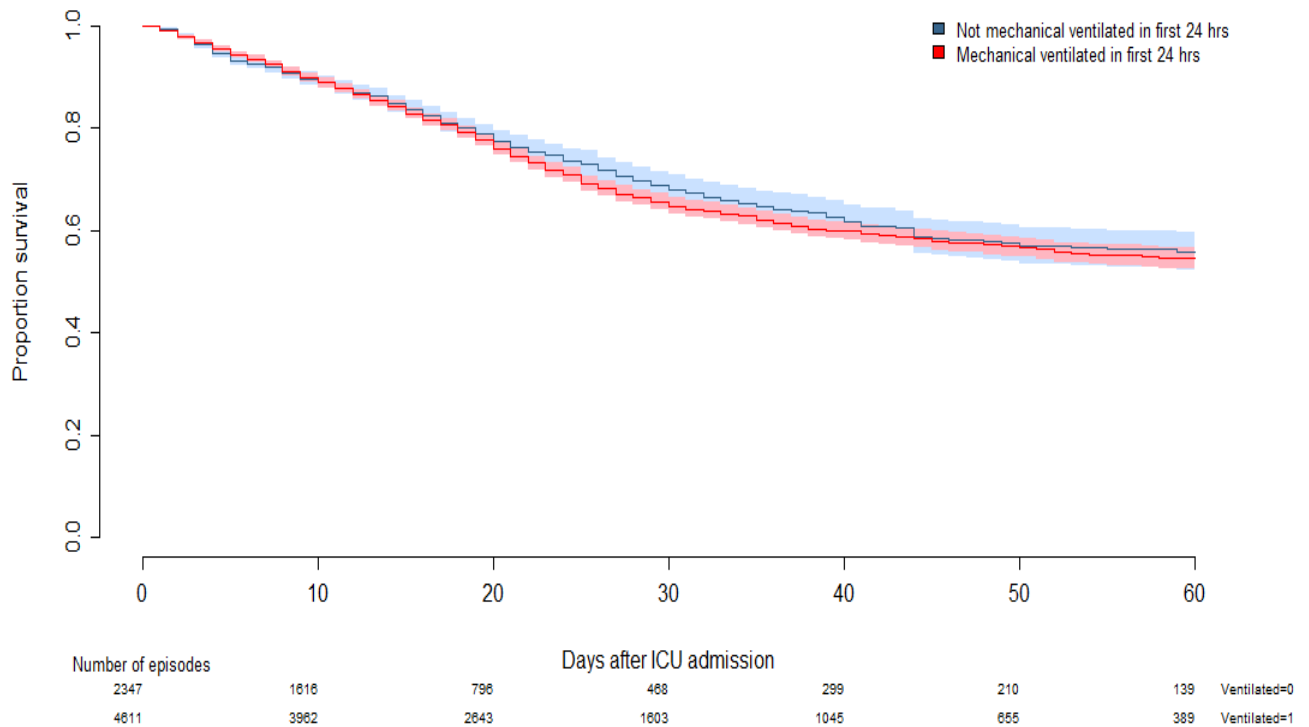
Variations over time

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 episodes per two months.

|	Number of episodes	Number of episodes of which the patient is deceased (%) *	Number of episodes linked to clinical data (%)
March-April 2020	2671	807 (30.2)	2577 (96.5)
Mei-June 2020	202	36 (17.8)	191 (94.6)
July-August 2020	125	31 (24.8)	115 (92)
Sept-Oct 2020	1433	457 (31.9)	1319 (92)
November-Dec 2020	2234	694 (31.1)	1885 (84.4)
Jan-Feb 2021	1860	363 (19.5)	863 (46.4)

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

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

Age distribution patients
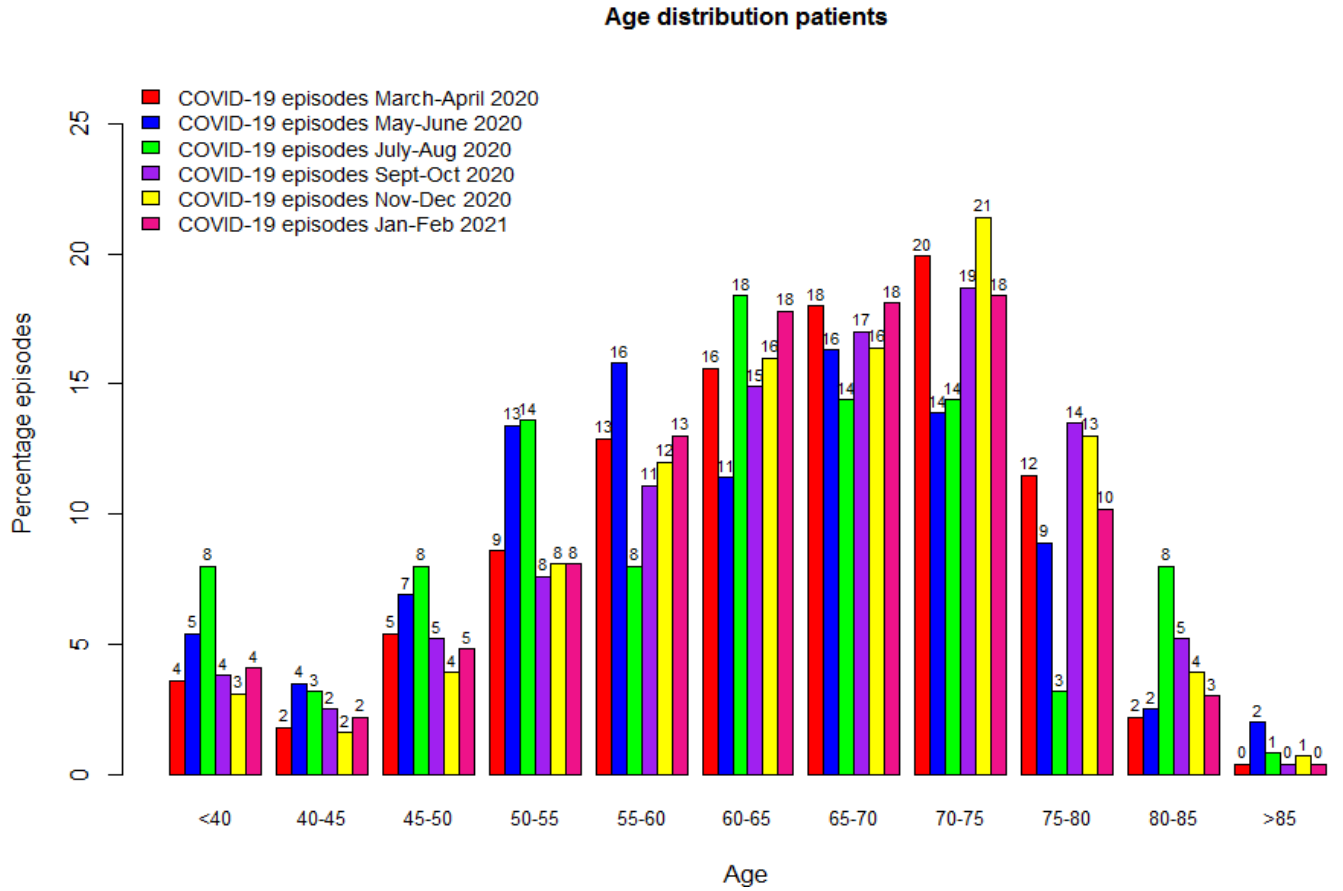
	Mean age (SD)	Median Age (IQR)
March-April 2020	63.4 (11.2)	65 (57-72)
Mei-June 2020	61 (13.1)	61 (53-70)
July-August 2020	60.4 (13.3)	64 (51-70)
Sept-Oct 2020	64.2 (11.9)	66 (57-73)
Nov-Dec 2020	64.7 (11)	66 (58-73)
Jan-Feb 2021	63.1 (11.5)	64.5 (57-71)

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

BMI distribution patients
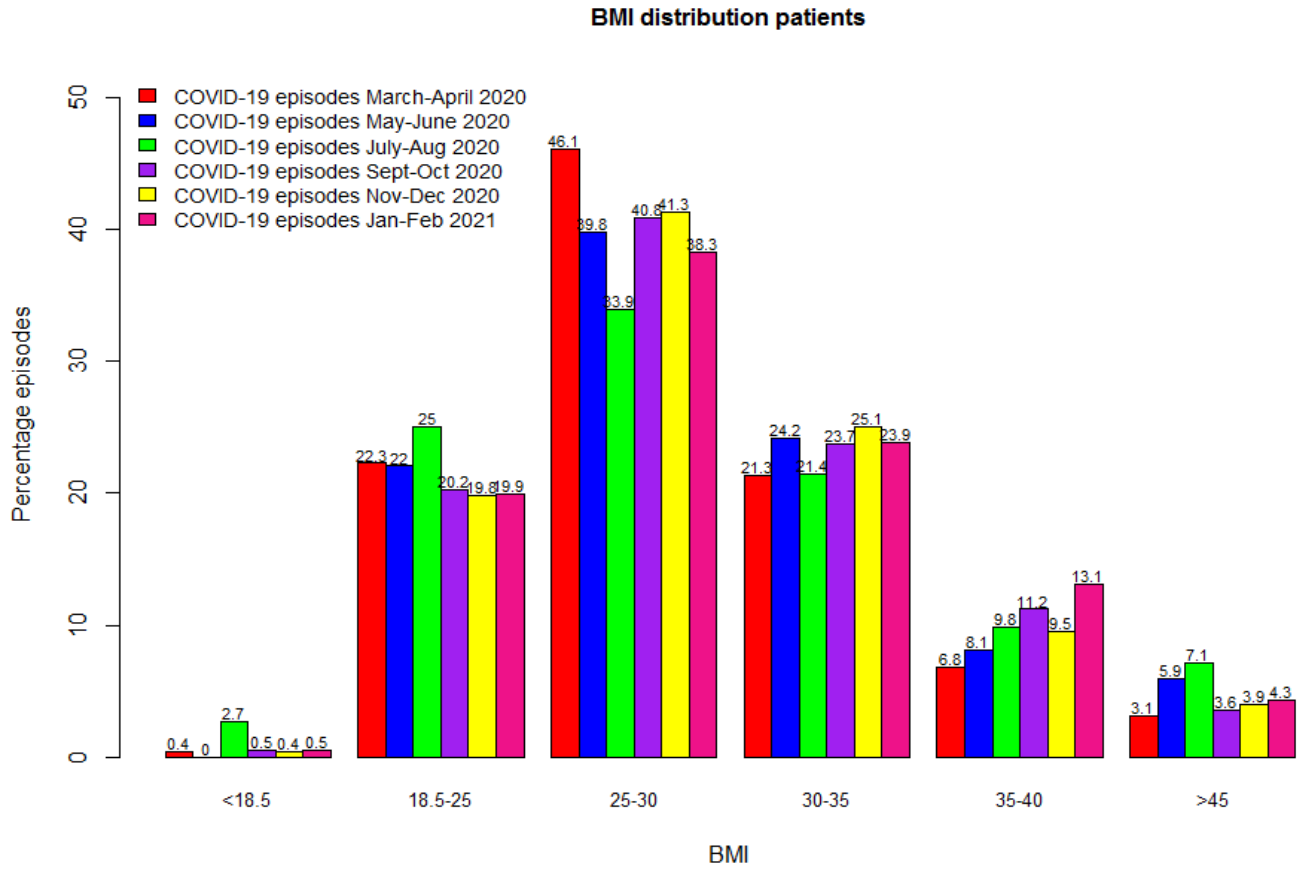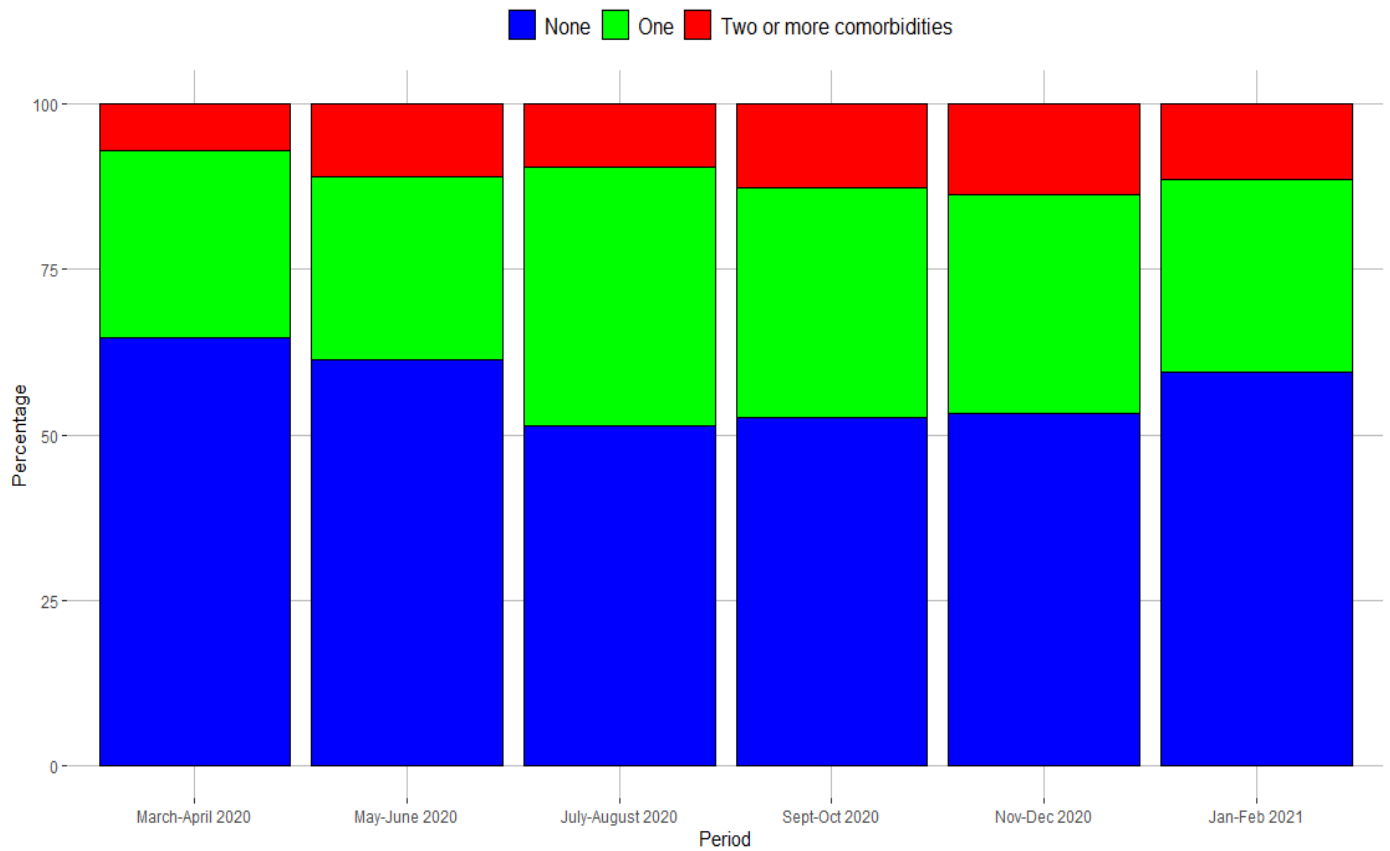

	Mean BMI (SD)	Median BMI (IQR)
March-April 2020	28.7 (4.9)	27.8 (25.3-31.1)
Mei-June 2020	29.4 (5.7)	28.4 (25.3-32.1)
July-August 2020	29.4 (6.7)	27.9 (24.7-33.2)
Sept-Oct 2020	29.3 (5.3)	28.7 (25.6-31.9)
Nov-Dec 2020	29.3 (5.3)	28.4 (25.6-32.3)
Jan-Feb 2021	29.7 (5.7)	28.9 (25.9-32.9)

In the graph below, the percentage episodes of which the patients had no, one or more than one 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 episodes of which patients had no, one or more than one comorbidities may have increased compared to previous reports.

The table below shows per two months period the mean ICU length of stay of all COVID-19 episodes, of the COVID-19 episodes of which the patient is still in the ICU, and of COVID-19 episodes of which the patient has been discharged recently split up into different discharge destinations. If a patient has been transferred to another ICU during an episode, all ICU length of stays will be added up together. The length of stay is calculated in days ((discharge date - admission date)+1).

Note that the most recent period still yields many uncertain results because a large part of this population is still included, so the averages shown will most likely increase.

	Number of episodes	Mean length of ICU stay (SD)
Period March-April 2020		
Patients who are currently being treated in the ICU *	3	13.5 (13.4)
Discharged to nursing ward in same or different hospital	1813	21.9 (17.2)
Other discharge destination	111	25.5 (32.4)
Died in the ICU	744	15.4 (12.9)
TOTAL	**2671**	**20.2 (17.4)**
Period May-June 2020		
Patients who are currently being treated in the ICU *	0	-
Discharged to nursing ward in same or different hospital	161	16.1 (15.9)
Other discharge destination	11	19.1 (30.8)
Died in the ICU	30	13.4 (10.4)
TOTAL	**202**	**15.8 (16.3)**
Period July-August 2020		
Patients who are currently being treated in the ICU *	0	-
Discharged to nursing ward in same or different hospital	94	12.8 (14.2)
Other discharge destination	8	27.6 (24.6)
Died in the ICU	23	20.6 (25)
TOTAL	**125**	**15.2 (17.8)**
Period Sept-Oct 2020		
Patients who are currently being treated in the ICU *	1	103 (-)
Discharged to nursing ward in same or different hospital	981	15.5 (17)
Other discharge destination	48	14 (17.1)
Died in the ICU	403	19.5 (14.1)
TOTAL	**1433**	**16.6 (16.5)**
Period Nov-Dec 2020		
Patients who are currently being treated in the ICU *	29	18 (19)
Discharged to nursing ward in same or different hospital	1490	15.7 (16.3)
Other discharge destination	93	13.2 (16.1)
Died in the ICU	622	17.4 (12.8)
TOTAL	**2234**	**16.1 (15.4)**
Period Jan-Feb 2021		
Patients who are currently being treated in the ICU *	493	7.5 (8.9)
Discharged to nursing ward in same or different hospital	985	10.4 (8.9)
Other discharge destination	46	9.2 (8.6)
Died in the ICU	336	13.8 (9.2)
TOTAL	**1860**	**10.9 (9.1)**

N.B. For the COVID-19 episodes of which the patient is currently admitted, it concerns the ICU length of stay up till the moment
that this report was generated and not the final total length of stay.

The figure below shows an initial estimate per period of the percentage of COVID-19 episodes (the vertical axis) of which the patient sirvived 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.
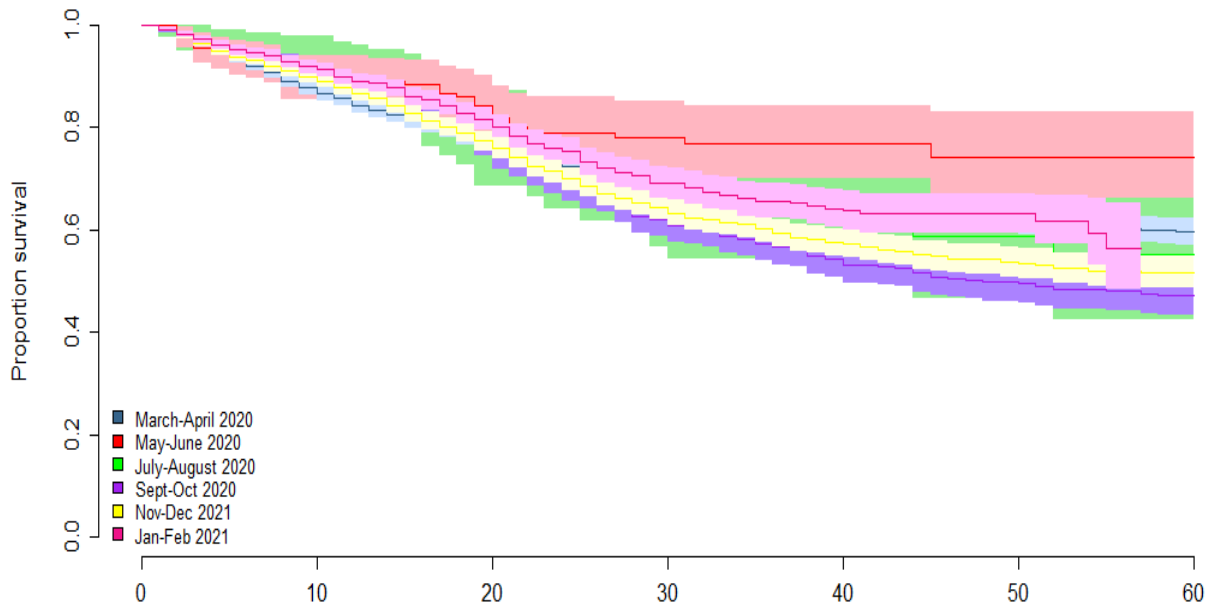
Number of patients						
March-April 2020 2671	2183	1495	959	623	387	228
May-June 2020 202	149	100	66	40	25	15
July-August 2020 125	95	44	32	22	16	11
Sept-Oct 2020 1433	1159	645	362	248	179	120
Nov-Dec 2020 2234	1743	1046	641	453	323	222
Jan-Feb 2021 1860	1352	660	323	145	51	

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 episodes of the more recent periods are still hospitalized. These are included in the calculations as survivors, while a part may still die, so that the odds ratio can still rise (considerably).

	Odds ratio (CI)
Period March-April 2020	Reference
Period May-June 2020	0.5 (0.35-0.72)
Period July-August 2020	0.76 (0.5-1.15)
Period Sept-Oct 2020	1.08 (0.94-1.24)
Period Nov-Dec 2020	1.04 (0.92-1.18)
Period Jan-Feb 2021	0.56 (0.49-0.65)

COVID-19 and SOFA

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

	Number of COVID-19 episodes
Linked to clinical (MDS) data	6958
Linked to organ failure (SOFA) data	3659

The table below shows in how many COVID-19 episodes and how many 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 episodes N (%)	Mean number of days (SE)	SARI patients N (%)	Mean number of days (SE)
Basic respiratory support	2702 (73.8)	10.9 (11.3)	5122 (59.1)	6.5 (8.5)
Advanced respiratory support	27 (0.7)	2.7 (3.1)	169 (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)	9.6 (17.4)	57 (0.7)	10.4 (14.3)
Renal support using renal replacement therapy	354 (9.7)	10 (9.4)	564 (6.5)	8.1 (9.4)
Measured platelets value <50	153 (4.2)	2.8 (3.8)	511 (5.9)	4.8 (5.6)