

# Readmissions, post-discharge mortality and sustained recovery among patients admitted to hospital with COVID-19

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1 **Abstract**

2 **Background**

3 Many interventional in-patient COVID-19 trials assess primary outcomes through day 28 post-  
4 randomization. Since a proportion of patients experience protracted disease or relapse, such follow-  
5 up period may not fully capture the course of the disease, even when randomization occurs a few  
6 days after hospitalization.

7 **Methods**

8 Among adults hospitalized with COVID-19 in Eastern Denmark from March 18, 2020 - January 12,  
9 2021 we assessed: all-cause mortality, recovery and sustained recovery 90 days after admission, and  
10 readmission and all-cause mortality 90 days after discharge. Recovery was defined as hospital  
11 discharge and sustained recovery as recovery and alive without readmissions for 14 consecutive  
12 days.

13 **Results**

14 Among 3,386 patients included in the study 2,796 (82.6%) reached recovery and 2,600 (77.0%)  
15 achieved sustained recovery. Of those discharged from hospital, 556 (19.9%) were readmitted, and  
16 289 (10.3%) died. Overall, the median time to recovery was 6 days (Interquartile range (IQR), 3-  
17 10), and 19 days (IQR, 11-33) among patients in intensive care in the first two days of admission.

18 **Conclusions**

19 Post-discharge readmission and mortality rates were substantial. Therefore, sustained recovery  
20 should be favored to recovery outcomes in clinical COVID-19 trials. A 28-day follow-up period  
21 may be too short the critically ill.

22 **Keywords: COVID-19; sustained recovery; readmission; post-discharge mortality; SARS-CoV-2.**

23

# 1 **Introduction**

2 Previous studies have indicated that some patients with COVID-19 have protracted disease and that  
3 rates of post-discharge mortality and readmissions can be substantial.[1, 2] This could potentially  
4 have affected the validity of results of clinical trials, since many interventional clinical trials of  
5 COVID-19 treatments evaluated outcomes at day 28 after randomization. [3-9] Reported estimates  
6 on length of hospital stay for COVID-19 patients with critical illness vary, but exceeds 28 days  
7 since admission for a notable proportion of the critical ill patients in some studies.[10, 11] For such  
8 patients, a primary outcome assessed during a 28-day follow-up period may not capture the full  
9 course of the disease, and also may cover little or none of the post-discharge time period after initial  
10 recovery. Further, if rates of readmissions and post-discharge deaths are substantial, a significant  
11 number of patients classified as recovered, may not truly have recovered from COVID-19. The  
12 *Accelerating COVID-19 therapeutic interventions and vaccines 3 (ACTIV-3): Therapeutics for*  
13 *Inpatients With COVID-19 (TICO)* trial, a large multisite trial of multiple treatments for  
14 hospitalized COVID-19 patients, introduced the outcome *sustained recovery*. Sustained recovery  
15 was defined as discharge from hospital and remaining alive and discharged for 14 days, thereby  
16 accounting for post-discharge readmissions and deaths in treatment effect estimates.[12, 13] This  
17 definition was developed in July 2020, and was based on preliminary findings from cohort studies  
18 including the one described here.

19 To evaluate sustained recovery as an outcome and to assess the optimal time point to estimate rates  
20 of sustained recovery, we examined longer-term all-cause mortality, post-discharge mortality,  
21 readmissions, recovery and sustained recovery among patients hospitalized with COVID-19. In  
22 secondary analyses, we compared these outcomes 1) before and after dexamethasone and  
23 remdesivir were introduced as standard of care and 2) between subgroups defined by disease

1 severity during index admission.

2

## 3 **Methods**

### 4 **Study setting**

5 This study was a multicenter cohort study in Eastern Denmark, a region with 2.7 million  
6 inhabitants. All patients with COVID-19 in need of in-patient care treated at public hospitals were  
7 eligible for this study. A total of 10 hospitals contributed with data to this study. All hospitals used  
8 an identical software, *Sundhedsplatformen*, for electronic health records (EHR), by EPIC,  
9 Wisconsin[14]. During surges of COVID-19 related hospital admissions it was necessary to  
10 postpone elective surgery and reallocate hospital resources, but the capacity for hospital admissions  
11 and intensive care was not saturated at any point in time. In June 2020, remdesivir and  
12 dexamethasone were introduced as standard of care in treatment of COVID-19 patients in Denmark.  
13 Community transmission of SARS-CoV-2 was low in June 2020 and this timepoint separated the  
14 first and second wave of COVID-19 related hospital admissions.

15

### 16 **Data sources**

17 Data were obtained from EHR and merged with data on vital status from the Danish civil  
18 registration system, using the unique civil registration number that is assigned to all Danish citizens,  
19 ensuring near-complete ascertainment of mortality. Data freeze was May 26<sup>th</sup>, 2021.

20

### 21 **Study population**

22 We included adult patients, aged  $\geq 18$  years, admitted to hospital with an international classification  
23 of diseases, 10th revision (ICD-10) diagnosis code of COVID-19 between March 18<sup>th</sup>, 2020 and Jan

1 12<sup>th</sup>, 2021, and fulfilling the following criteria: a positive SARS-CoV-2 PCR between 30 days  
2 before and 7 days after the date of admission, duration of hospital admission more than 48 hours  
3 and at least one measurement of vital signs during this admission. The first admission fulfilling  
4 these criteria was defined as the *index admission*. The inclusion criteria of both a measurement of  
5 vital signs and at least a 48-hour in-patient stay was introduced, since out-patients that visited  
6 hospitals for COVID-19 tests, were included on in-patient EHR lists in some hospitals during  
7 March 2020. Further, the 48-hour criterium was introduced to include only patients who had  
8 moderate/severe COVID-19 and to be comparable to patients included in clinical trials of patients  
9 hospitalized with COVID-19, and who are often randomized a few days after admission.

## 11 **Definitions**

12 Baseline was defined as time of index admission. A subsequent admission with a duration of more  
13 than 48 hours and within 90 days after discharge the index admission was categorized as a  
14 readmission. If a hospital admission occurred less than 48 hours after discharge from a previous  
15 admission, the two admissions were regarded as one admission. Patients with index admissions of  
16 more than 90 days were excluded from analysis of post-discharge outcomes. Discharge was defined  
17 as the date of discharge from hospital as we did not have information on whether patients were  
18 discharged to home, elderly homes, rehabilitation etc.

19 Disease severity was assessed by the maximum levels of respiratory support given until different  
20 timepoints of the index admission and categorized for each patient on an ordinal scale grouped as 0-  
21 5 L O<sub>2</sub>/min, >5-15 L O<sub>2</sub>/min, 'more than 15L O<sub>2</sub>/min without ICU admission' or ICU admission.

22 Comorbidities at baseline were determined using ICD-10 codes from hospital records prior to the  
23 index admission and categorized in meta categories from the Charlson comorbidity index and the

1 Elixhauser index.[15, 16] The complete ICD-10 categorization used is available in supplemental  
2 material (see Supplemental Material Table S1).

3

#### 4 **Outcomes**

5 The outcomes were ‘death within 90 days from index admission’, ‘death within 90 days from  
6 discharge from index admission’, ‘readmission within 90 days from discharge from index  
7 admission’, and a combined endpoint of ‘readmission or death (whichever came first) within 90  
8 days from discharge from index admission’, ‘recovery within 90 days from index admission’ and  
9 ‘sustained recovery within 90 days from index admission’. Recovery was defined as discharge from  
10 index admission. Sustained recovery was defined as discharge from the index admission, and being  
11 alive without readmissions for 14 consecutive days. If a patient was readmitted before reaching  
12 sustained recovery, the 14 consecutive days event free period could be achieved after discharge  
13 from a readmission.

14

#### 15 **Statistical analyses**

16 All patients were included from 48 hours after the index admission to outcome of interest or ‘90  
17 days after index admission’ or ‘90 days after discharge from index admission’, as specified in the  
18 outcomes or freeze date the 26<sup>th</sup> of May 2021. Patient characteristics were presented overall,  
19 stratified by wave, and stratified by the maximum disease severity in the first 14 days of index  
20 admission. Kaplan Meier method was used to estimate the risk of ‘death within 90 days after index  
21 admission’, ‘death within 90 days after discharge from index admission’ and ‘readmission or death  
22 within 90 days after discharge from index admission’. ‘Recovery with 90 days after index  
23 admission’, ‘sustained recovery with 90 days after index admission’ and ‘readmission within 90  
24 days after discharge from index admission’ were illustrated by cumulative incidence curves. In

1 analysis stratified for disease severity, we stratified by the maximum level of respiratory support in  
2 the first 2 and 14 days of index admission. Recovery could first occur 2 days after index admission  
3 due to the inclusion criteria. Sustained recovery could first occur from day 16 since index  
4 admission, due to the outcome definition and inclusion criteria. Multivariable Cox regression  
5 analysis assessed the factors associated with ‘death’, and ‘readmission or death’ by comparing  
6 cause-specific hazards. Multivariable Fine-Gray models compared the sub distribution hazard for  
7 ‘recovery’, ‘sustained recovery’ and ‘readmission’. Variables of interest included wave, age, sex,  
8 and individual comorbidities of cardiovascular disease, hypertension, diabetes mellitus, chronic  
9 pulmonary disease, renal disease, malignancy, neurological disease and moderate to severe liver  
10 disease defined from the comorbidities meta categories. The statistical software R and the packages  
11 *survival*, *mstate*, *cmprisk* and *tidyverse* were used for data analyses.

## 13 **Results**

### 14 **Study population**

15 We included 3,386 adult patients admitted to hospital with COVID-19 in the study period: 1,137  
16 and 2,249 in the first and second waves, respectively (see Supplemental Material Figure 1). The  
17 median age was 74 years [IQR 61 - 82] and 54.7% were male. The duration of the index admission  
18 was median 6.8 days [IQR 4.1 - 11.7] and 590 died during index admission (Table 1). The baseline  
19 characteristics were similar between patients admitted during the first and the second wave.  
20 Baseline characteristics of the total cohort and survivors of the index admission are summarized in  
21 Table 1. Characteristics stratified by disease severity during the index admission are summarized in  
22 see Supplemental Material Table S2 and for survivors of the index admission in see Supplemental  
23 Material Table S3. Data on treatment with remdesivir and dexamethasone in the first and second

1 wave are displayed in see Supplemental Material Table S4.

2

### 3 **Overall outcomes**

4 In the total cohort, 2796 (82.6%) were discharged within 90 days after admission (Table 2), and  
5 thereby reached the outcome “recovery”; 861 patients 25.4% [95% CI 24.0% - 26.9%] died within  
6 90 days from index admission (Figure 1A)..

### 7 **Readmissions and post-discharge mortality**

8 Of the 2796 who recovered, 19.9% had been readmitted 90 days after initial recovery (Figure 1C)  
9 with 10.9% [95% CI 9.8% -12.1%] readmitted after 14 days. In total, 10.3% [95% 9.2, 11.5] died  
10 after recovery, 5.4% [95% CI 4.6% - 6.2%] died within the first 14 days post-discharge (Figure  
11 1B). In the combined outcome, 25.8% [95% CI 24.1, 27.4] were readmitted or died with in the 90  
12 days following discharge from index admission (Figure 1D). The rates of readmission and post-  
13 discharge death were highest in the first 14 days after discharge and then leveled off to a more  
14 constant rate (Figure 1B-1D, Table 2).

### 15 **Recovery and Sustained recovery**

16 At 90 days after index admission, significantly more patients had reached the outcome recovery  
17 than sustained recovery (Table 2, Figure 2A). The cumulative incidence of recovery was 78.6%  
18 [95% CI 77.2-80.0] at day 28 and 82.6% [95% CI 81.3-83.9] at day 90. The cumulative incidence  
19 of sustained recovery was 71.1% [95% CI: 69.6 - 72.7] at day 42 and 76.8% [95% CI 75.4 - 78.2]  
20 at day 90 (Fig. 2A). The median time to recovery was 6 days (IQR: 3-10) and median time to  
21 sustained recovery was 20 days (IQR: 18 - 26). Risk factors for failure to reach sustained recovery  
22 was older age, male sex, and cardiovascular disease, diabetes mellitus, chronic pulmonary disease,  
23 renal disease, malignancies, and neurological disease. (Table 3)



## 1 **Outcomes by wave**

2 The all-cause mortality rate was lower in the second wave than the first wave (Supplemental  
3 Material Fig. S6, Table 2). From the first to the second wave readmission rates increased but post-  
4 discharge mortality rates did not change significantly (Table 2, Supplemental S6 1B-1D). Rates of  
5 both recovery and sustained recovery were higher in the second wave compared to the first, hazard  
6 ratio 1.39 [1.29, 1.50] and 1.28 [95% CI 1.19 - 1.39], respectively (Table 2, Supplemental Material  
7 Figure S4 and S7).

## 9 **Outcomes by COVID-19 disease severity**

10 The post-discharge mortality was substantial across subgroups defined by disease severity during  
11 the admission, except in the ICU subgroup (Table 2, Supplemental Material Figure S3). In a  
12 sensitivity analysis, patients were binned by index admission duration of 14, 28, 60 and 90 days and  
13 the results were similar (Data not shown).

14  
15 Rates of sustained recovery decreased with increasing levels of respiratory support (Table 2, Figure  
16 2B). The subgroup which received >15L of oxygen had a lower cumulative incidence of sustained  
17 recovery than the ICU subgroup. We did not have access to information on clinical decisions to  
18 abstain from ICU treatment. In a sensitivity analysis we included only patients below 70 years of  
19 age. Exclusion of patients aged 70+ years resulted in a significant increase in the estimates of  
20 cumulative incidence of sustained recovery among patients receiving oxygen supplementation 5-15  
21 L/min or >15 L/min (see Supplemental Material Figure S2).

22 Patients treated in the ICU had prolonged time to sustained recovery, median 36 days [IQR 28 - 49].  
23 In this subgroup, the cumulative incidence of sustained recovery increased from 38.0% [95% CI  
24 33.4% - 42.7%] at day 42 to 60.0% [95% CI 55.4% - 64.7%] at day 90 after index admission

1 (Table 2, Figure 2B). The relative rate of sustained recovery for the ICU group compared to the 0-5  
2 L O<sub>2</sub>/min subgroup increased significantly from 0·15 [95% CI 0·13 - 0·17] in analyses with 42 days  
3 of follow-up to 0·21 [95% CI 0·19 - 0·23] with 90 days of follow-up (see Table2 and Supplemental  
4 Material Figure S5).

5 Among patients in intensive care units during the first 2 days of admission, median time to recovery  
6 and sustained recovery was 19 (IRQ, 11-33) and 36 (IQR 26-48) days, respectively.

## 8 **Discussion**

9 We examined all-cause mortality, post-discharge mortality, readmissions, recovery, and sustained  
10 recovery in a large, population-based cohort of patients admitted to hospital with COVID-19 in  
11 Eastern Denmark. Readmissions and post-discharge mortality rates were substantial and a large  
12 proportion of patients with critical illness had protracted time to recovery.

13  
14 In the total cohort, the cumulative incidence curves leveled out around day 28 for the outcome  
15 recovery and day 42 for sustained recovery. But among patients who received oxygen  
16 supplementation >15 l O<sub>2</sub>/min or were admitted to the ICU during the index admission, the  
17 cumulative incidence of sustained recovery was substantially higher at day 90 compared to day 42.

18 In adjusted analysis, comparing rates of sustained recovery between patients admitted to the ICU  
19 and patients receiving <5 l O<sub>2</sub>/min during index admission, the risk ratio changed significantly from  
20 day 42 to day 90. These results indicate that a prolonged follow-up of 60 - 90 days is needed in  
21 interventional studies to assess treatment effects in critically ill COVID-19 patients.

22 The ACTIV-3:TICO trial, reported similar cumulative incidence rates of sustained recovery as this  
23 study, although the time to sustained recovery was shorter.[12] The median age in the ACTIV-  
24 3:TICO-trial was 12 years lower, which may explain part of the difference. They also reported

1 worse pulmonary status at baseline was associated with lower rates of sustained recovery. Our  
2 results are also in line with a meta-analysis of hospitalized COVID-19 patients, that reported a  
3 median length of stay in hospital of 5 days, but the length of stay increased with disease  
4 severity.[17] Also, in a large cohort study of 4,244 critical ill patients with COVID-19, a notable  
5 proportion of patients had protracted disease course with long hospital admission.[11]  
6  
7 The estimates of incidence of readmissions in the present study were similar to readmissions rates  
8 reported in studies from the UK and US where 23% and 20% of hospitalized COVID-19 patients  
9 had been readmitted at day 60.[1, 2] Other studies have reported lower readmission rates. These  
10 studies have either reported on cohorts with lower median age, with a shorter follow-up period or  
11 less complete rates of follow-up than this study.[18-22] Our estimates of post-discharge mortality ( $\approx$   
12 10%) were similar to studies from US and UK. The incidence of post-discharge mortality in the  
13 ICU subgroup was much lower than other subgroups. Those in the ICU subgroup, were younger  
14 and the prevalence of comorbidities lower compared to other subgroups. (Supplementary Appendix  
15 Table S3). In adjusted analysis comparing the ICU group to those with minimal oxygen supply the  
16 hazard ratio of post-discharge mortality was 0.58 but did not reach statistical significance. (Table  
17 2). Overall, we found a high incidence of post-discharge events in the first 14 days following  
18 discharge from the index admission, indicating that a 14-day post-discharge event-free period for  
19 the sustained recovery definition capture the majority of post-discharge COVID-19 associated  
20 events. A substantial number of events occurs after the initial 14 days from discharge and the event  
21 free period in the sustained recovery definition can be prolonged (see Supplemental Material Table  
22 S5).

23

1 From the first to the second wave, we found that rates of in-hospital mortality declined, rates of  
2 readmissions in the first two weeks after discharge increased, while rates of post-discharge  
3 mortality did not change significantly; resulting in higher rates of recovery and sustained recovery  
4 in the second wave than in the first wave. The introduction of remdesivir and dexamethasone as  
5 standard of care partly explain the better outcomes, but other improvements in management and  
6 treatment are also likely to have contributed. The national vaccine program started in late December  
7 2020. Therefore, very few participants, if any, in our study would have been vaccinated prior to the  
8 index admission, further vaccination was only recommended for patients sick with with COVID-19  
9 after they had fully recovered. This the availability of vaccines is not like to explain the difference.

10  
11 One limitation of the study is that we could not determine if readmissions or deaths were  
12 attributable to COVID-19. A large proportion of the study population had co-morbidities and thus it  
13 is likely that some of the events, especially in the last part of the follow-up period, were unrelated to  
14 COVID-19. Data on comorbidities were obtained using diagnose codes from prior hospital contacts  
15 and thus may be underreported. The inclusion criteria of minimum 48 hours admission duration  
16 excluded patients that died earlier and could neither achieve recovery nor sustained recovery.  
17 Readmissions separated by less than 48 hours were merged, which would not affect sustained  
18 recovery, due to the inherent event free period, but may have decreased rates of post-discharge  
19 outcomes and recovery. Some patients did not have records of oxygen supply and were categorized  
20 in the lowest respiratory support subgroup. We cannot exclude that patients may not have had all  
21 changes in respiratory support recorded in their medical records, but do not believe that this would  
22 change the conclusions of this study. Unfortunately, we could not assess outcomes in nursing  
23 homes et cetera nor long covid and post-covid conditions.

1 Strengths of the study include the large, population-based study population and the near-complete  
2 follow-up due to the high quality of the registry data used for the study. All COVID-19 patients in  
3 the region where the study was conducted were treated at public hospitals, with identical EHR  
4 software and a common treatment protocol. Data on deaths were collected from the Danish civil  
5 registration system, which is up to date and hence fully ascertain survival status.  
6 We conclude that rates of adverse outcomes within 14 days after discharge of a hospital admission  
7 for COVID-19 are substantial, favoring the use of sustained recovery as outcome as opposed to  
8 recovery in clinical COVID studies. A follow-up period of 28 days to assess outcomes in studies of  
9 treatments for COVID-19 may be too short for the critical ill.

## 11 **NOTES**

### 12 **Contributors**

13 JL, MH and KSM designed the study. AZ and KSM verified the raw data. JR oversaw the statistical  
14 analysis done by KSM. KSM and MH drafted the manuscript. All authors were involved in the  
15 interpretation of results and critically reviewed the first draft and approved the final version of the  
16 manuscript. All authors had full access to all the data.

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19 This study was approved by the Danish National Ethics Committee.

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## 1 **Declaration of Interests**

2 CUN: Research support and consultancy fees outside this study from Abbvie AstraZeneca  
3 (consulting fees paid to author), Janssen (consulting fees paid to author), Takeda consulting fees  
4 paid to author), CSL Behring (consulting fees paid to author), Beigene (consulting fees paid to  
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6 Society; from Ministry of Higher Education and Science (0238-00006B) for this study. CUN also  
7 reports grants or contracts from Novo Nordisk Foundation, Danish Cancer Society, AstraZeneca,  
8 Abbvie, Janssen, EU (ERAPERMED) (through institution).

9 KSM: Lecturing fee outside this study from GSK

10 MH: Consultancy, congress, and lecturing fees outside this study from Gilead (paid to author),  
11 GSK (paid to author), MDS (unpaid), AstraZeneca and Sobi; including fee for online participation  
12 in congress from Gilead and GSK, participation on a Data Safety Monitoring Board or Advisory  
13 Board for Gilead, GSK, MSD, AstraZeneca, and Sobi (paid to author).

14 CM reports Participation on a Data Safety Monitoring Board or Advisory Board for INSIGHT SSC  
15 (International Network for Strategic Initiatives in Global HIV Trials) (Unpaid participation).

16 KSM, JR, AGZ, SRO, CUN, TJ, LW, JUJ, CM, JL, and MH declare no competing interests.

17

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19

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ACCEPTED MANUSCRIPT



1 **Tables**

2 **Table 1: Patient characteristics**

Variable	All patients			Recovery within 90 days from index admission		
	Total cohort n = 3,386	First wave (1) n = 1,137	Second wave (2) n = 2,249	Total cohort n = 2,796	First wave (1) n = 872	Second wave (2) n = 1,924
<b>Patient Age</b>						
18 to 49 years (%)	371 (11.0)	126 (11.1)	245 (10.9)	367 (13.1)	124 (14.2)	243 (12.6)
50 to 69 years (%)	978 (28.9)	340 (29.9)	638 (28.4)	874 (31.3)	290 (33.3)	584 (30.4)
70 to 79 years (%)	928 (27.4)	325 (28.6)	603 (26.8)	757 (27.1)	241 (27.6)	516 (26.8)
80 to 100 years (%)	1,109 (32.8)	346 (30.4)	763 (33.9)	798 (28.5)	217 (24.9)	581 (30.2)
Male (%)	1,852 (54.7)	622 (54.7)	1,230 (54.7)	1,498 (53.6)	455 (52.2)	1,043 (54.2)
<b>Comorbidities at baseline</b>						
Cardiovascular disease (%)	1,237 (36.5)	378 (33.2)	859 (38.2)	945 (33.8)	269 (30.8)	676 (35.1)
Hypertension (%)	815 (24.1)	256 (22.5)	559 (24.9)	639 (22.9)	188 (21.6)	451 (23.4)
Diabetes Mellitus (%)	567 (16.7)	186 (16.4)	381 (16.9)	438 (15.7)	133 (15.3)	305 (15.9)
Chronic Pulmonary Disease (%)	481 (14.2)	153 (13.5)	328 (14.6)	382 (13.7)	114 (13.1)	268 (13.9)
Renal Disease (%)	231 (6.8)	72 (6.3)	159 (7.1)	157 (5.6)	47 (5.4)	110 (5.7)
Malignancy (%)	443 (13.1)	136 (12.0)	307 (13.7)	343 (12.3)	95 (10.9)	248 (12.9)
Neurological Disease (%)	412 (12.2)	143 (12.6)	269 (12.0)	301 (10.8)	90 (10.3)	211 (11.0)
Moderate/Severe Liver Disease (%)	18 (0.5)	6 (0.5)	12 (0.5)	15 (0.5)	4 (0.5)	11 (0.6)
Time from index admission to PCR test, days, median (IQR)	0.3 (-2.9 - 0.7)	0.4 (-1.5 - 0.6)	0.3 (-3.4 - 0.8)	0.3 (-3.2 - 0.7)	0.4 (-2.5 - 0.6)	0.3 (-3.5 - 0.8)
Duration of index admission, days, median (IQR)	6.8 (4.1 - 11.7)	7.3 (4.2 - 13.2)	6.4 (4.0 - 10.7)	6.1 (4.0 - 10.6)	7.0 (4.1 - 13.0)	6.0 (4.0 - 9.8)
Died during index admission (%)	590 (17.4)	265 (23.3)	325 (14.4)	0 (0.0)	0 (0.0)	0 (0.0)
<b>Maximum level of respiratory support in first 14 days of index admission</b>						
< 5 L O <sub>2</sub> /min (%)	2,111 (62.3)	642 (56.5)	1,469 (65.3)	2,018 (72.2)	610 (70.0)	1,408 (73.2)
5-15 L O <sub>2</sub> /min (%)	509 (15.0)	181 (15.9)	328 (14.6)	368 (13.2)	120 (13.8)	248 (12.9)

> 15 L O <sub>2</sub> /min (%)	348 (10.3)	140 (12.3)	208 (9.2)	150 (5.4)	49 (5.6)	101 (5.2)
ICU (%)	418 (12.3)	174 (15.3)	244 (10.8)	260 (9.3)	93 (10.7)	167 (8.7)

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3 **Table 2: Outcomes in analyses in the total cohort, stratified by study period and level of respiratory support in**  
4 **first 14 days of index admission**

	Total cohort	First wave (1)	Second wave (2)	0-5 l/min	5-15 l/min	>15 l/min	ICU
<b>Mortality (3)</b>							
n	n = 3,386	n = 1,137	n = 2,249	n = 2,111	n = 509	n = 348	n = 418
Median time from admission to, days (IQR)	11 (6 - 22)	10 (6 - 18)	13 (7 - 25)	-	-	-	-
Cumulative incidence day 28	20.7 (22.1, 19.4)	24.8 (22.3, 27.3)	18.7 (17.1, 20.3)	-	-	-	-
Cumulative incidence day 90	25.4 (23.9, 26.9)	29.6 (26.8, 32.2)	23.3 (21.6, 25.1)	-	-	-	-
Hazard ratio day 28	-		0.65 (0.56, 0.75)	-	-	-	-
Hazard ratio day 90	-	Ref	0.67 (0.59, 0.77)	-	-	-	-
<b>Post-discharge mortality</b>							
n	n = 2796	n = 872	n = 1,924	n = 2018	n = 368	n = 150	n = 260
Median time from discharge to, days (IQR)	13 (5 - 33)	14 (6 - 38)	13 (5 - 32)	14 (5 - 35)	10 (4 - 21)	18 (5 - 47)	16 (12 - 18)
Cumulative incidence day 14	5.4 (4.6, 6.2)	4.8 (3.4, 6.2)	5.7 (4.6, 6.7)	5.4 (4.4, 6.3)	9.0 (6.0, 11.8)	4.7 (1.2, 8.0)	1.2 (0.0, 2.4)
Cumulative incidence day 90	10.3 (9.2, 11.5)	9.1 (7.1, 10.9)	10.9 (9.5, 12.3)	10.6 (9.3, 11.9)	13.9 (10.3, 17.3)	10.7 (5.6, 15.5)	3.0 (1.0, 5.2)
Hazard ratio day 14	-	Ref	1.01 (0.70, 1.46)	Ref	0.58 (0.37, 0.92)	0.29 (0.13, 0.66)	0.25 (0.06, 1.04)
Hazard ratio day 90	-	Ref	1.08 (0.84, 1.40)	Ref	1.53 (1.12, 2.08)	1.13 (0.68, 1.88)	0.58 (0.28, 1.19)
<b>Readmission (5)</b>	<b>Total</b>	<b>First wave</b>	<b>Second wave</b>	<b>&lt;5 L O<sub>2</sub>/min</b>	<b>5-15 L O<sub>2</sub>/min</b>	<b>&gt;15 L O<sub>2</sub>/min</b>	<b>ICU</b>
n	n = 2796	n = 872	n = 1,924	n = 2018	n = 368	n = 150	n = 260
Median time from discharge to, days (IQR)	12 (4-39)	21 (5-48.75)	10 (4-36.75)	12 (5-38.25)	11 (4-42)	11 (4.5-32.5)	9 (3.75-32.75)
Cumulative incidence day 14 (5)	10.9 (9.8-12.1)	7.6 (5.8-9.3)	12.5 (11.0-14.0)	11.2 (9.9-12.6)	10.3 (7.2-13.4)	12.0 (6.8-17.2)	8.8 (5.4-12.3)
Cumulative incidence day 90 (5)	19.9 (18.4-21.4)	17.2 (14.7-19.7)	21.1 (19.3-22.9)	20.8 (19.0-22.6)	18.8 (14.8-22.7)	20.7 (14.2-27.1)	13.8 (9.7-18.0)

Risk ratio day 14 (4)	-	Ref	1.58 (1.2, 2.07)	Ref	0.94 (0.67, 1.32)	1.05 (0.65, 1.71)	1.03 (0.66, 1.6)
Risk ratio day 90 (4)	-	Ref	1.18 (0.98, 1.43)	Ref	0.90 (0.69, 1.17)	0.97 (0.68, 1.38)	0.87 (0.62, 1.24)
<b>Readmission or post-discharge mortality</b>							
n	n = 2796	n = 872	n = 1.924	n = 2018	n = 368	n = 150	n = 260
Median time from discharge to, days (IQR)	10 (4-33)	14 (4 - 41)	9 (4 - 30)	10 (4 - 33)	7 (3 -32)	11 (4 - 30)	10 (4 - 28)
Cumulative incidence day 14	15.2 (13.9, 16.5)	11.6 (9.4, 13.7)	16.8 (15.2, 18.5)	15.6 (14.0, 17.2)	16.8 (12.9, 20.6)	16.0 (9.9, 21.7)	9.2 (5.6, 12.7)
Cumulative incidence day 90	25.8 (24.1, 27.4)	22.9 (20.1, 25.7)	27.1 (25.1, 29.0)	26.8 (24.9, 28.7)	27.2 (22.5, 31.6)	27.3 (19.8, 34.1)	15.0 (10.5, 19.2)
Hazard ratio day 14	-	Ref	0.95 (0.76, 1.20)	Ref	1.22 (0.93, 1.61)	0.91 (0.59, 1.39)	0.89 (0.58, 1.37)
Hazard ratio day 90	-	Ref	1.12 (0.95, 1.32)	Ref	1.09 (0.88, 1.35)	1.06 (0.77, 1.46)	0.80 (0.58, 1.12)
<b>Recovery (5)</b>							
n	n = 3386	n = 1,137	n = 2,249	n = 2,111	n = 509	n = 348	n = 418
Median time from admission to, days (IQR)	6 (3-10)	7 (4-12)	6 (3-9)	-	-	-	-
Cumulative incidence day 28 (5)	78.6 (77.2-80.0)	71.9 (69.2-74.5)	82.0 (80.4-83.6)	-	-	-	-
Cumulative incidence day 90 (5)	82.6 (81.3-83.9)	76.7 (74.2-79.2)	85.5 (84.1-87.0)	-	-	-	-
Risk ratio day 28 (4)	-	Ref	1.40 (1.29, 1.51)	-	-	-	-
Risk ratio day 90 (4)	-	Ref	1.39 (1.29, 1.50)	-	-	-	-
<b>Sustained recovery (3,5)</b>							
n	n = 3386	n = 1,137	n = 2,249	n = 2,111	n = 509	n = 348	n = 418
Median time from admission to, days (IQR)	20 (18-26)	21 (18-28)	20 (18-25)	19 (17-22)	22 (19-27)	27 (22-35)	36 (28-49)
Cumulative incidence day 42 (3,5)	71.1 (69.6-72.7)	66.6 (63.8-69.3)	73.5 (71.6-75.3)	85.8 (84.3-87.3)	61.5 (57.3-65.7)	35.9 (30.9-41.0)	38.0 (33.4-42.7)
Cumulative incidence day 90 (5)	76.8 (75.4-78.2)	72.5 (69.9-75.1)	79.0 (77.3-80.7)	89.0 (87.7-90.3)	64.8 (60.7-69.0)	40.2 (35.1-45.4)	60.0 (55.4-64.7)
Risk ratio day 42 (4)	-	Ref	1.28 (1.18, 1.39)	Ref	0.47 (0.42, 0.52)	0.22 (0.19, 0.26)	0.15 (0.13, 0.17)
Risk ratio day 90 (4)	-	Ref	1.28 (1.19, 1.39)	Ref	0.46 (0.41, 0.51)	0.22 (0.19, 0.26)	0.21 (0.19, 0.23)

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2 **Table 3: Risk factors for sustained recovery**

Variables	Hazard Ratio	p-value
<b>Wave</b>		
First wave	—	—
Second wave	1.28 (1.19-1.39)	<0.001
<b>Patient Age (years)</b>		
18 to 49	—	—
50 to 69	0.64 (0.57-0.71)	<0.001
70 to 79	0.49 (0.43-0.55)	<0.001
80 to 100	0.34 (0.30-0.39)	<0.001
<b>Sex</b>		
Female	—	—
Male	0.82 (0.76-0.88)	<0.001
<b>Comorbidities at baseline</b>		
Cardiovascular Disease	0.87 (0.79-0.95)	0.001
Hypertension	1.02 (0.93-1.12)	0.670
Diabetes Mellitus	0.90 (0.81-0.99)	0.038
Chronic pulmonary disease	0.84 (0.76-0.94)	0.003
Renal disease	0.67 (0.56-0.79)	<0.001
Malignancy	0.83 (0.74-0.94)	0.003
Neurological disease	0.68 (0.59-0.77)	<0.001
Moderate/severe liver disease	0.61 (0.33-1.15)	0.130

1 **Footnotes Table 1:**

2 1) Patients admitted to index admission before June 15<sup>th</sup>, 2020.

3 2) Patients admitted to index admission after June 15<sup>th</sup>, 2020.

4 **Footnotes Table 2:**

5 1) Patients admitted to index admission before June 15<sup>th</sup>, 2020.

6 2) Patients admitted to index admission after June 15<sup>th</sup>, 2020.

7 3) The 42 days since index admission timepoint for sustained recovery and 28 days since index  
8 admission for mortality were chosen, since patients reaching sustained recovery commenced  
9 their 14-day event free period 14 days before reaching their outcome. Therefore, day 42 in a  
10 sustained recovery outcome is timewise comparable to a day 28 mortality outcome.

11 4) Multivariate Fine & Grey regression model.

12 5) Death accounted for as a competing risk

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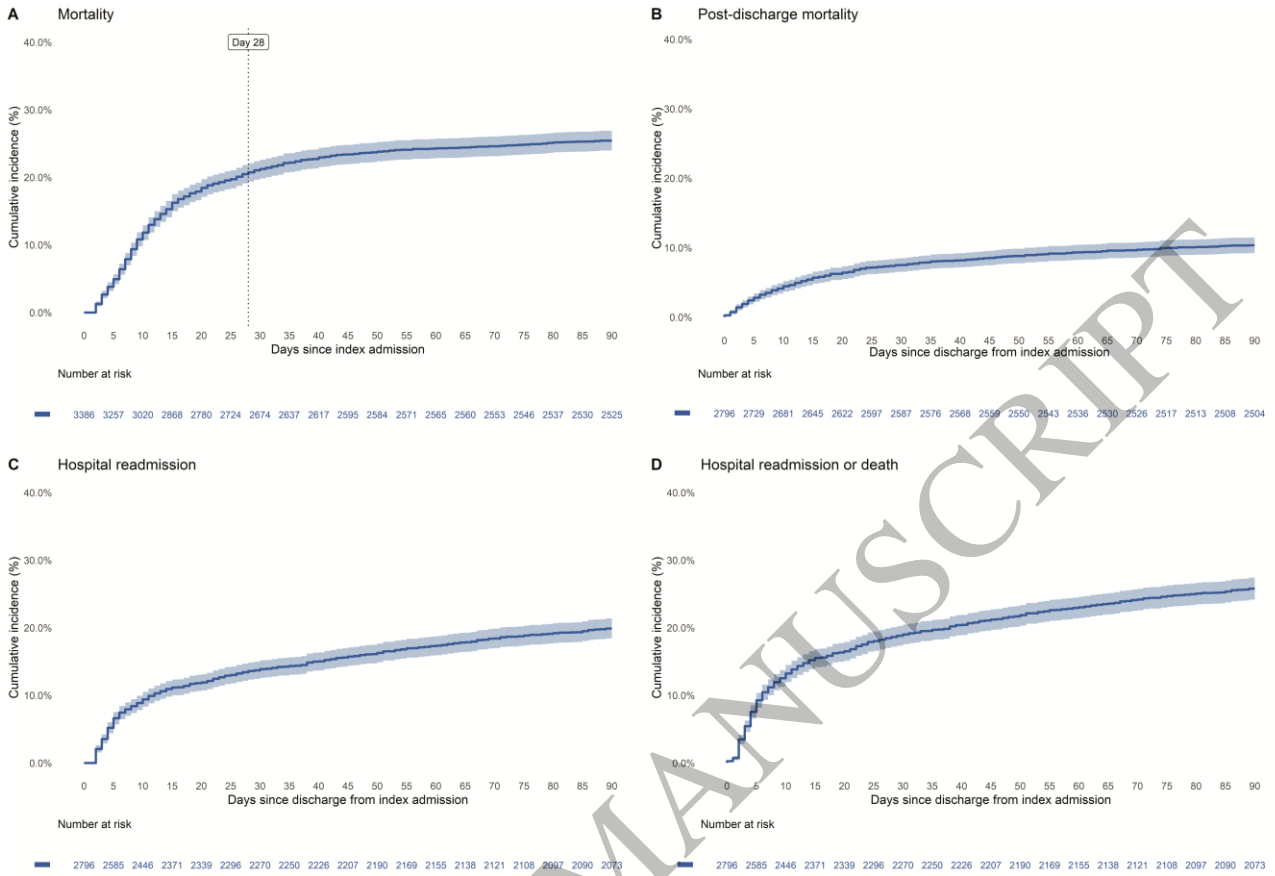
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15 **Figure legends:**

16 **Figure 1:** A) Cumulative incidence of death after index admission B) Cumulative incidence of  
17 death after discharge from index admission. C) Cumulative incidence of hospital readmission after  
18 first hospital discharge from index admission. (2) D) Cumulative incidence of hospital readmission  
19 or death after first hospital discharge from index admission.

20 **Figure 2:** A) Cumulative incidence of recovery and sustained recovery after hospital admission  
21 (2) B) Cumulative incidence of sustained recovery stratified by the maximum level of respiratory  
22 support in the first 14 days of the admission

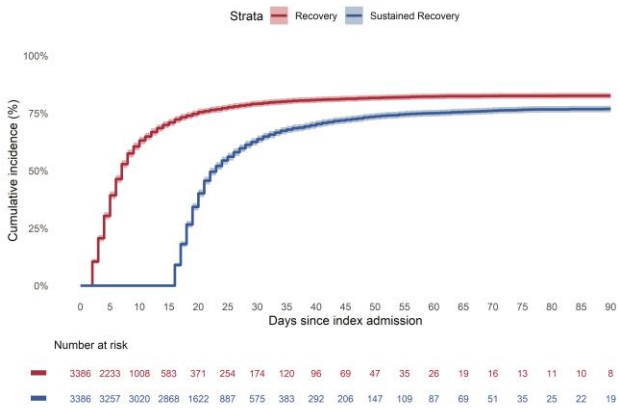
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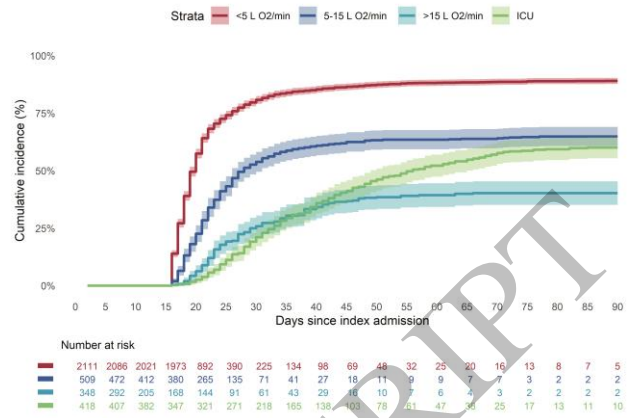
**Figure 1**  
400x280 mm ( x DPI)

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**A Recovery and Sustained Recovery**



**B Sustained recovery**



**Figure 2**  
400x140 mm ( x DPI)

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