Prevalence, characteristics and longer-term outcomes of patients with persistent critical illness due to COVID-19 in Scotland: a national cohort study

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Abstract

Background

Patients with coronavirus disease (COVID-19) can require critical care for prolonged periods. Patients with Persistent Critical Illness can have complex recovery trajectories but this has not been researched for patients with COVID-19. This study aims to examine prevalence, risk factors and long-term outcomes of critically ill COVID-19 patients with Persistent Critical Illness.

Methods

A national cohort study of all adults admitted to Scottish critical care units with COVID-19 from 01/03/20-04/09/21. Persistent Critical Illness was defined as a critical care length of stay (LOS) of ≥10 days. Outcomes included one-year mortality and hospital readmission following critical care discharge. Fine and Gray competing risk analysis was used to identify factors associated with Persistent Critical Illness with death as a competing risk.

Results

2236 patients with COVID-19 were admitted to critical care. 1045 patients were identified as developing Persistent Critical Illness, comprising 46.7% of the cohort but using 80.6% of bed-days. Persistent Critical Illness patients used more organ support, had longer post-critical care LOS and longer total hospital LOS. Persistent Critical Illness was not significantly associated with long-term mortality or hospital readmission. Risk factors associated with increased hazard of Persistent Critical Illness include age, illness severity, organ support on admission and fewer comorbidities.

Conclusion

Almost half of all critical care patients with COVID-19 develop Persistent Critical Illness, with high resource use in critical care and beyond. Through improved identification of Persistent Critical Illness, services and care packages can be developed and targeted at the longer-term effects of COVID-19 on patients and their families.

Introduction

Coronavirus disease 2019 (COVID-19), caused by the Severe Acute Respiratory Syndrome Coronavirus-2 (SARS-CoV-2) was declared a global pandemic in March 2020 by the World Health Organisation[1]. The related severe acute hypoxemic respiratory failure which severe COVID-19 infection may cause, often necessitates admission to an intensive care unit (ICU) for mechanical ventilation and multi-organ support[2]. Evidence is emerging internationally on the clinical characteristics of those patients admitted to ICU due to COVID-19[3-4]. These data have shown that these patients often have a high severity of illness, requiring extended ICU stays and high resource use[5].

Previous research has characterised the 'Persistent Critical Illness' cohort, a patient group with extended ICU stays and high hospital resource use, often followed with complicated recovery trajectories[6-10]. For example, in a 14-year national cohort study in Australia and New Zealand found the Persistent Critical Illness cohort accounted for 5.0% of the patients admitted to ICU, but almost a third of ICU bed-days[9]. Limited data exist regarding the Persistent Critical Illness cohort in the context of the COVID-19 pandemic, especially in relation to longer-term outcomes and ongoing resource use. A greater understanding of Persistent Critical Illness prevalence in COVID-19 patients may be helpful to guide decisions around resource allocation and rehabilitation needs.

Therefore, this complete prospective national cohort study has two aims. Firstly, examine the profile, prevalence and outcomes of patients admitted to critical care who develop Persistent Critical Illness. Secondly, we describe the risk factors for developing Persistent Critical Illness in patients admitted to critical care with COVID-19.

Methods

Study setting and databases

The Community Health Index (CHI) number, a unique identifier used in Scottish health systems, was used to line the following Public Health Scotland databases: Electronic Communication of Surveillance in Scotland (ECOSS) database, which captures all virology testing in Scotland; Scottish Morbidity Record 01 (SMR01), which captures all acute hospital activity; National Records of Scotland death records; and the Scottish Intensive Care Society Audit Group (SICSAG) database. The SICSAG database captures all adult general intensive care (ICU) activity within Scotland. Data are entered prospectively and are subject to regular validation assessments[11]. These datasets are national datasets, capturing all patients in Scotland.

Participants

A cohort study design was used. Scottish residents comprised the cohort, who were aged ≥16 years admitted to general ICUs and combined ICU/high dependency units (HDUs) in Scotland from 01/03/2020 to 04/09/2021 with a positive polymerase chain reaction test for nucleic acid for SARS-CoV-2 before or during critical care admission. Records generated through moving between HDUs and ICUs were merged to create a continuous critical care stay. We included only the first admission for patients with multiple, non-continuous critical care admissions. Patients admitted to standalone HDUs with no subsequent ICU/combined ICU/HDU admission were not included. Follow-up was available up to 25/09/2021, providing at least 21 days follow up for all patients from critical care admission.

Variables

Exposure: The primary exposure of interest was Persistent Critical Illness, defined as a length of stay in critical care of at least 10 days duration, consistent with literature relating to a pan-ICU population[9-10].

However, the clinical course of patients admitted to critical care with COVID-19 is still evolving. Indeed, data has demonstrated that the clinical course and case-mix of critically ill COVID-19 patients is changing across different 'waves' of the pandemic[12,13]. Furthermore, previous work has demonstrated that the focus of clinical care for ICU patients may differ from those remaining in ICUs beyond 21 days, regardless of their diagnosis[8]. Thus, to ensure an inclusive definition, we utilised a 21-day cut-off point to define Persistent Critical Illness in a sensitivity analysis.

Outcomes: Outcomes included mortality (at critical care discharge and hospital discharge), critical care interventions (type/duration of organ support during critical care stay), resource use (duration of critical care and post-critical care hospital stay (for critical care survivors)) and post-critical care

outcomes (post-critical care mortality and post-hospital discharge hospital readmission risk). Critical care outcomes were available for those had been discharged or died on or before 25/09/2021.

Other variables: Demographic variables were sex, age and ethnicity. Ethnicity was derived from categories of the Scottish Census 2011 with low frequencies aggregated[14]. Socioeconomic deprivation was defined using quintiles of the Scottish Index of Multiple Deprivation (SIMD Version 2020)[15]. SIMD is an area-based ranking index based on postcode of residence. Previous health status comprised the number of emergency acute hospital admissions in the year before admission, Clinical Frailty Score, and comorbidities. SICSAG-defined severe comorbidities were combined with Charlson-defined comorbidities as previously described[16-17] and represented as individual comorbidities for the most prevalent comorbidities, and a count. Acute illness variables comprised duration from hospital admission to critical care admission, PaO2:FiO2 (PF) ratio, the Acute Physiology Score (APS) of the APACHE II model (grouped as tertiles) and number of organ systems supported at critical care admission (cardiovascular, respiratory and renal support).

Statistical analysis

Baseline characteristics and outcomes were stratified in tables by exposure status (Persistent Critical Illness vs Discharged alive before day 10 vs Died before day 10), and outcomes were compared using chi-square, Kruskal Wallis and log-rank tests. Daily frequency of bed occupancy and organ support activity was derived from Augmented Care Period (ACP) data and presented stratified by exposure status[11,12,16].

Univariable and multivariable associations of patient characteristics with development of Persistent Critical Illness as an outcome were assessed using Fine and Gray competing risk analysis[18], using death before 10 days as a competing risk to help control for survivor bias. Due to its non-linear association with outcomes, age was categorised into easily interpretable and similarly sized groups. Comorbidity counts were used in preference to individual comorbidities to reduce degrees of freedom of the models.

A Kaplan-Meier plot was presented for the cohort who survived to critical care discharge to explore post-critical care survival stratified by those who spent at least 10 days in critical care versus those who were discharged before 10 days. A Cumulative incidence plot was presented for those who survived to hospital discharge to explore emergency hospital readmission, stratified by those who spent at least 10 days in critical care versus those who were discharged before 10 days. Maximum follow-up was truncated to 1 year, as data were sparse beyond this. One-year outcomes for both post-critical care survival and emergency hospital readmission were presented using these methods. Risk factors associated with survival following critical care discharge were investigated using Cox regression

in univariable and multivariable models. Risk factors associated with emergency hospital readmission following hospital discharge were investigated using Fine and Gray competing risk analysis, with death following hospital discharge as a competing risk.

Additional analyses

We repeated Fine and Gray competing risk models identifying risk factors associated with developing Persistent Critical Illness, where Persistent Critical Illness was redefined as a critical care stay of at least 21 days as explained above.

Data were analysed using R Version 3.6.1[19]. We used a significance level of 5%, 95% confidence intervals (CI) and two-sided p values. Appropriate measures of central tendency and dispersion were presented for continuous variables. An indicator variable was created for missing data for APS and ethnicity. A complete cases analysis was performed for all other variables in analyses. No sample size calculation was performed as this was defined by the number of admissions to Scottish critical care units.

Approvals

SICSAG received approval by the Public Benefit and Privacy Panel for Health and Social Care (1920-0093) to undertake work relating to the COVID-19 pandemic.

Role of the funding source

The funder had no role in the study design; in the collection, analysis and interpretation of the data; in the writing of the report; and in the decision to submit the paper for publication.

Results

Patient Demographics

Between 01/03/2020 and 04/09/2021, 2236 patients with laboratory confirmed COVID-19 were admitted to 24 ICUs across Scotland. Baseline demographic and clinical characteristics, stratified by Persistent Critical Illness status, are presented in Table 1. 23 patients remained in critical care units on the censor date (e-Table 1). Figure 1 shows cohort derivation and flow.

There were 1045 patients with Persistent Critical Illness, representing 46.7% of all admissions. Median age was 59 years (IQR 51, 67) and differed by exposure status: Discharged before 10 days 56 (45,64), Died before 10 days 64 (57,72), and Persistent Critical Illness 60 (52,67). There was a greater proportion of patients living in more deprived neighbourhoods in the Persistent Critical Illness cohort (31.1% most deprived, 12.8% least deprived) compared to the cohort who were discharged before 10 days (25.5% most deprived, 12.3% least deprived).

Almost two thirds of patients overall had no comorbidities (63.4%). The most common comorbidities were respiratory disease (12.3%) and diabetes (11.6%). Comorbidities were more frequent in the group who died before 10 days (55.8%) compared to those discharged before 10 days (44.0%) and Persistent Critical Illness (42.5%) cohorts. Additionally, a smaller proportion of the Persistent Critical Illness cohort had multiple comorbidities (12.8% vs 15.5% in those who were discharged before 10 days and 30.3% in those who died before 10 days). More than three quarters (76.9%) of patients had no emergency admissions in the preceding year. Most patients overall were non-frail (61.1%), although 24.8% were missing frailty data. The proportion of non-frail patients was similar in the Persistent Critical Illness (62.3%) and discharged before 10 days cohorts (66.7%). Those who died before 10 days were less likely to be non-frail (43.3%).

Most patients had one organ system supported on critical care admission (56.9%). Multiorgan support was more frequent in the Persistent Critical Illness (41.2%) and died before 10 days (46.9%) cohorts compared to those discharged before 10 days (14.9%). Advanced respiratory support was required on admission in less than half of patients overall (42.3%), but was more common in the Persistent Critical Illness (56.7%) and died before 10 days (54.9%) cohorts, compared to those discharged before 10 days (19.6%).

Interventions, Resource Use and Outcomes

Complete organ support data were available for 2313 (99.0%) patients. The remaining 23 patients were still present in critical care on 25/09/21 and are described in e-Table 1. 1393 patients (62.3%) received advanced respiratory support during their critical care stay, 1405 (62.8%) received cardiovascular support and 411 (18.4%) received RRT. The Persistent Critical Illness cohort received more advanced respiratory support (91.5% vs 69.7% (Died before 10 days) and 23.7% (Discharged before 10 days),p<0.001), cardiovascular support (91.0% vs 74.2% (Died before 10 days) and 23.9% (Discharged before 10 days),p<0.001) and RRT (30.8% vs 20.2% (Died before 10 days) and 2.5% (Discharged before 10 days),p<0.001) but NIV showed more variation (54.8% (Persistent Critical Illness), 40.9% (Died before 10 days), 65.2% (Discharged before 10 days),p<0.001) (e-Figure 1). The Persistent Critical Illness cohort received longer durations of organ support in all categories.

Median critical care LOS overall was 9 days (IQR 4,18). In the Persistent Critical Illness cohort the median LOS was 19 days vs 5 days in the Died before 10 days cohort and 4 days in the Discharged before 10 days cohort. Compared with the other cohorts, Persistent Critical Illness patients had a longer total hospital LOS (28 days vs 8 days (Died before 10 days) and 12 days (Discharged before 10 days)) and spent longer in hospital after critical care discharge (Persistent Critical Illness (14 days) vs discharged before 10 days (6 days),p<0.001).

Patients who developed Persistent Critical Illness comprised 46.7% of the cohort but used 80.6% of critical care bed-days. Figure 2 illustrates how proportions of patients present in critical cares differed over time. At the peak of Wave 1 (10/04/20) a similar proportion of Persistent Critical Illness and shorter stay patients were present in units (46.9% shorter stay vs 53.1% Persistent Critical Illness). Two weeks after this peak the majority of patients present in units had Persistent Critical Illness (66.4% vs 33.6% shorter stay). The peak of Wave 2 (20/01/21) revealed a lower proportion of patients with Persistent Critical Illness (34.7% vs 65.3% shorter stay patients). Two weeks later the majority of patients had Persistent Critical Illness but the difference was less pronounced compared with Wave 1 (57.8% Persistent Critical Illness vs 42.2% shorter stay).

Overall, 761 patients (34.0%) died before critical care discharge and 848 (37.9%) patients died before ultimate hospital discharge (Table 2). Mortality following critical care discharge but prior to hospital discharge was lower in Persistent Critical Illness patients compared with patients discharged from critical care before 10 days (2.4% vs 4.9%). Measured after critical care discharge, 1-year mortality was low in both groups (Persistent Critical Illness 6.6%(CI 4.3%,8.9%) vs Discharged before 10 days

9.5%(7.5%,11.5%)) (Figure 3A). For the cohort who survived to critical care discharge, factors associated with mortality following critical care discharge are presented in e-Table 2. After adjustment for confounders, Persistent Critical Illness was not associated with mortality following critical care discharge (HR 0.60 (0.25,1.44),p=0.254). Acute hospital 1-year readmission risk was similar between groups (Persistent Critical Illness 23.4%(19.2%,27.3%) vs discharged before 10 days 24.1% (19.8%,28.1%))(Figure 3B). Factors associated with readmission are presented in e-Table 3. After confounder adjustment, there was no significant association between Persistent Critical Illness and hospital readmission (HR 1.31 (0.99,1.73),p=0.055).

Risk factors associated with persistent critical illness

In univariable models, several patient characteristics were associated with Persistent Critical Illness status (Table 3). Age had a non-linear relationship with Persistent Critical Illness, with the highest hazard ratio in age group 60-69 (HR 1.33(1.12,1.59),p=0.002) relative to over 70. Having 2 or more comorbidities, and 2 or more prior emergency admissions in the year prior to critical care admission, were both associated with reduced hazard of Persistent Critical Illness (HR 0.66(0.55,0.80),p<0.001 and HR 0.48(0.34,0.66),p<0.001). In contrast, APS and organ support on admission, both markers of illness severity, were associated with increased hazard of Persistent Critical Illness: (APS tertile 3 vs 1: HR 1.83(1.52,2.19),p<0.001; 2 or more organs supported on admission vs none: HR 4.12(3.06,5.56),p<0.001).

In multivariable models, these associations were maintained. The age group with highest hazard of Persistent Critical Illness was 60-69 (HR 1.26(1.05,1.50),p=0.011). Presence of comorbidities was associated with reduced odds of Persistent Critical Illness (2 or more vs 0 comorbidities HR 0.70(0.57,0.86),p=0.001). Increasing APS was associated with increased hazard of Persistent Critical Illness (Tertile 3 vs 1: HR 1.56(1.28,1.89),p<0.001) as was organ support on admission (2 or more vs no organs supported: HR 3.05(2.24,4.16),p<0.001).

Additional analyses

A sensitivity analysis modelled risk factors relating to Persistent Critical Illness by defining it as spending more than or equal to 21 days in critical care(e-Tables 4-5). Similar factors remained associated with the development of Persistent Critical Illness in both univariable and multivariable analysis: Age group, presence of comorbidities, previous emergencies (both associated with reduced hazard of persistent critical illness), APS and number of organs supported (both associated with an increased hazard of persistent critical illness).

Discussion

This complete national cohort study has demonstrated that almost half of all patients admitted to critical care with COVID-19 developed Persistent Critical Illness, with a critical care stay greater than 10 days. This had a significant impact on bed capacity as Persistent Critical Illness patients accrued over four fifths of all critical care beds occupied by patients with COVID-19 during the study period. For those who survived to critical care discharge, post-critical care discharge mortality was lower in Persistent Critical Illness patients compared with those who had a shorter critical care stay. This lower mortality was noted in spite of a longer post-critical care hospital stay and a similar rate of acute hospital readmissions in the Persistent Critical Illness group. Factors associated with increased hazard of developing Persistent Critical Illness included severity of illness, and absence of comorbidities.

Similar to previous evidence, COVID-19 patients who developed Persistent Critical Illness contributed a smaller proportion of total patient numbers, but higher resource use in terms of care delivery in the hospital environment[20-21] However, the number of patients who developed Persistent Critical Illness in the COVID-19 critical care population is greater than described in previous studies relating to general critical care patients. For example, in two previous Scottish studies, less than 10% of patients developed Persistent Critical Illness[8,22]. This data demonstrates that describing the absolute number of COVID-19 cases admitted to critical care, does not capture the full clinical impact associated with the pandemic. A greater number of patient bed days were required for this cohort alongside more complex care delivery, reflected in a higher degree of organ support. This contextual and demographic data is key to understanding how best to plan services moving forward for both COVID-19 patients, as well as non-COVID-19 patients requiring critical care services.

In this national cohort, age, illness severity and organ support on admission to critical care, were risk factors associated with the development of Persistent Critical Illness. These risk factors are consistent with previous research examining the development of Persistent Critical Illness in the non-COVID-19 critical care cohort[23]. However, in contrast to previous literature on a pan-ICU population, long-term survival was higher in this Persistent Critical Illness cohort. Moreover, one year readmission risk was lower in this COVID-19 cohort in comparison to previous research describing non-COVID-19 cohorts[17,24]. We hypothesise that these differences may be partly driven by the higher mortality in patients with multimorbidity and pre-existing poor health in the short stay COVID-19 cohorts. Complex multimorbidity is known to negatively impact both short and long-term outcomes from critical care[25-26]. Research examining the interplay between COVID-19 and pre-existing comorbidities is urgently required in order to understand optimal management for these patients.

Persistent Critical Illness patients have complex needs which often required specialist interventions, especially in relation to communication and rehabilitation, both during the critical care stay and after discharge[27]. These adaptations to care are crucial to ensure optimal outcomes and experience. Due to the demanding workload and the challenges which critical care staffing experienced during the pandemic, many of these adaptations may not have been routinely adopted[28]. Additionally, family caregivers had limited access during the pandemic to patient visiting and bedside clinician updates. As such, both patients, and family caregivers, may have complex challenges following hospital discharge. These challenges, and the burdens associated with Persistent Critical Illness, are not captured when assessing survival following critical care discharge[29]. Future research should focus on the ongoing symptomatology suffered by these patients and their caregivers, the impact of post-critical care interventions to address these rehabilitation needs, and how this may differ from other critical care patients. Clinicians should also strive to understand the impact of the pandemic on families and how this can be mitigated in future waves.

This study has several strengths. Firstly, by linking multiple datasets of routinely collected data, we are confident that we have complete outcome data and high percentage of organ support data so can make a good assessment of the link between critical care and outcome. By linking with the ECOSS database, which records all patients with a positive COVID-19 polymerase chain reaction swab, we are confident that all patients in the cohort were suffering from confirmed COVID-19 disease. Additionally, by including variables such as socioeconomic status in the logistic regression we were able to identify more holistic variables associated with long critical care stay than other datasets may be able to provide. Our analyses allowed for the competing risk of death to be evaluated in associations such as the non-linear relationship between age and Persistent Critical Illness.

There are a number of potential limitations with this study. Firstly, due to the changes in service provision during the pandemic, some patients which usually would have been cared for in an HDU environment, may have received additional respiratory support outside traditional critical care areas and therefore do not contribute to our dataset. This may result in some under reporting regarding the duration of organ support or critical care stay in our patients. Additionally, the routine data collected did not take into account any of the potential disease modifying agents which were identified as the pandemic developed, such as Dexamethasone and Tocilizumab. Although there is evidence to suggest they decrease mortality in patients with COVID-19, our study is unable to identify if they have any impact on the development or duration of Persistent Critical Illness. Finally, our reporting of ethnicity

data is relatively restricted due to the small numbers of non-white patients and aggregate reporting requirements for small groups. Additionally, within this relatively small population, there were a number of patients with unknown ethnicity, therefore further weakening the confidence in any assessment of the impact of ethnicity.

Conclusion

Almost half of patients admitted to critical care in Scotland with COVID-19 developed persisting critical illness. This group of patients used more than four fifths of all bed-days occupied by patients with COVID-19 and used more post-critical care and post-hospital discharge resource, but had better long-term mortality. Clinical services need to continue to develop to meet the substantial care needs for this group of patients and their families.

Authors' contributions, transparency statement and data access

NL affirms that the manuscript is an honest, accurate, and transparent account of the study being reported; that no important aspects of the study have been omitted; and that any discrepancies from the study as planned have been explained. NL, JM, NS, MB, CK and KP contributed to conception and design of the work. All authors contributed to data acquisition or analysis. All authors contributed to interpretation of data for the work. NL, JM, NS, MB, CK and KP drafted the work. All authors revised it critically for important intellectual content. All authors gave final approval of the version to be published. All authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. Since analyses involved data on unconsented participants, we are unable to share individual level data.

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Competing Interests and Funding

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Tables

Table 1: Baseline characteristics

Number of patients		**All**	**Discharged before 10 days**	**Died before 10 days**	**Persistent Critical Illness**
	n	2236	854	337	1045
Age on admission (years)	Median (IQR)	59 (51,67)	56 (45,64)	64 (57,72)	60 (52,67)
Sex	Female	751 (33.6%)	315 (36.9%)	109 (32.3%)	327 (31.3%)
	Male	1485 (66.4%)	539 (63.1%)	228 (67.7%)	718 (68.7%)
Socioeconomic status quintile (SIMD)	1 - Most deprived	636 (28.8%)	216 (25.5%)	99 (29.8%)	321 (31.1%)
	2	542 (24.5%)	227 (26.8%)	73 (22.0%)	242 (23.5%)
	3	407 (18.4%)	171 (20.2%)	58 (17.5%)	178 (17.3%)
	4	348 (15.7%)	129 (15.2%)	61 (18.4%)	158 (15.3%)
	5 - Least deprived	277 (12.5%)	104 (12.3%)	41 (12.3%)	132 (12.8%)
Ethnicity	White	1945 (91.2%)	749 (92.0%)	296 (91.6%)	900 (90.4%)
	Black/Caribbean /African	37 (1.7%)	*	*	*
	Asian	121 (5.7%)	39 (4.8%)	21 (6.5%)	61 (6.1%)
	Other	30 (1.4%)	*	*	*
Previous health status					
Comorbidity count	0	1418 (63.4%)	564 (66.0%)	149 (44.2%)	705 (67.5%)
	1	450 (20.1%)	158 (18.5%)	86 (25.5%)	206 (19.7%)
	2 plus	368 (16.5%)	132 (15.5%)	102 (30.3%)	134 (12.8%)

Number of patients		All	Discharged before 10 days	Died before 10 days	Persistent Critical Illness
Comorbidities	Cardiovascular disease	229 (10.2%)	74 (8.7%)	68 (20.2%)	87 (8.3%)
	Respiratory disease	275 (12.3%)	117 (13.7%)	56 (16.6%)	102 (9.8%)
	Diabetes Mellitus	259 (11.6%)	92 (10.8%)	59 (17.5%)	108 (10.3%)
	Cancer	154 (6.9%)	52 (6.1%)	37 (11.0%)	65 (6.2%)
	Other	303 (13.6%)	109 (12.8%)	74 (22.0%)	120 (11.5%)
Emergency hospital admissions in previous year	0	1719 (76.9%)	633 (74.1%)	238 (70.6%)	848 (81.1%)
	1	382 (17.1%)	146 (17.1%)	76 (22.6%)	160 (15.3%)
	2 plus	135 (6.0%)	75 (8.8%)	23 (6.8%)	37 (3.5%)
Clinical frailty score (CFS)	Non-frail	1367 (61.1%)	570 (66.7%)	146 (43.3%)	651 (62.3%)
	Vulnerable	184 (8.2%)	62 (7.3%)	43 (12.8%)	79 (7.6%)
	Frail	130 (5.8%)	55 (6.4%)	52 (15.4%)	23 (2.2%)
	Not known	555 (24.8%)	167 (19.6%)	96 (28.5%)	292 (27.9%)
Illness severity and organ support					
APACHE II score	Median (IQR)	15 (11,18)	12 (9,15)	18 (15,23)	15 (13,19)
APS	Median (IQR)	7 (4,10)	5 (2,8)	9 (5,14)	7 (4,11)
PF ratio (kPa)	Median (IQR)	12.9 (9.2,18.6)	15.0 (10.6,22.6)	11.7 (8.6,17.0)	11.8 (8.8,16.6)
Time from hospital admission to ICU admission (days)	Median (IQR)	1 (0,4)	1 (0,3)	2 (0,5)	1 (0,4)
Number of organ systems supported on ICU admission	0	248 (11.1%)	185 (21.7%)	15 (4.5%)	48 (4.6%)

Number of patients		All	Discharged before 10 days	Died before 10 days	Persistent Critical Illness
	1	1272 (56.9%)	542 (63.5%)	164 (48.7%)	566 (54.2%)
	2 or more	716 (32.0%)	127 (14.9%)	158 (46.9%)	431 (41.2%)
Advanced respiratory support on admission	n (%)	945 (42.3%)	167 (19.6%)	185 (54.9%)	593 (56.7%)
Non-invasive respiratory support on admission	n (%)	1002 (44.8%)	471 (55.2%)	130 (38.6%)	401 (38.4%)
Other basic respiratory support on admission	n (%)	289 (12.9%)	216 (25.3%)	22 (6.5%)	51 (4.9%)
Cardiovascular support on admission	n (%)	743 (33.2%)	150 (17.6%)	163 (48.4%)	430 (41.1%)
Renal replacement therapy on admission	n (%)	44 (2.0%)	12 (1.4%)	9 (2.7%)	23 (2.2%)

*Note: Died indicates patients who died less than 10 days after ICU admission. Long stay indicates patients who were still in ICU >=10 days after admission. Short stay indicates patients who were discharged alive before 10 days but who remained alive past10 days from admission. 26 records have an unknown SIMD quintile. 103 records have unknown ethnicity. Percentages for organ support, advanced respiratory support, non-invasive ventilation, cardiovascular support and renal replacement therapy are based on complete recording of this data corresponding to admission date - 0 record(s) are currently missing. 81 patients lack APACHE data. 81 patients lack APS data. *Output suppressed due to disclosure risk.

Table 2: Outcomes

Patients admitted before 04 September 2021		All	Discharged before 10 days	Died before 10 days	Persistent Critical Illness	p-value
Number of patients	n	2236	854	337	1045	-
Outcome						
Died before ICU discharge	n (%)	761 (34.0%)	0 (0%)	313 (92.9%)	448 (42.9%)	-
Died before Ultimate hospital discharge	n (%)	848 (37.9%)	42 (4.9%)	333 (98.8%)	473 (45.3%)	-
Length of stay (days)						
ICU Length of Stay	Median (IQR)	9 (4,18)	4 (2,6)	5 (2,7)	19 (13,30)	-
Post-ICU hospital stay (for patients discharged alive from ICU)	Median (IQR)	9 (4,18)	6 (4,12)	3 (2,5)	14 (8,24)	<0.001
Total Hospital stay	Median (IQR)	17 (10,31)	12 (8,20)	8 (5,12)	28 (19,48)	-
Organ support during ICU stay						
Advanced respiratory support	n (%)	1393 (62.3%)	202 (23.7%)	235 (69.7%)	956 (91.5%)	<0.001
Non-invasive respiratory support	n (%)	1268 (56.7%)	557 (65.2%)	138 (40.9%)	573 (54.8%)	<0.001
Combined advanced or non-invasive respiratory support	n (%)	2057 (92.0%)	685 (80.2%)	329 (97.6%)	1043 (99.8%)	<0.001
Cardiovascular support	n (%)	1405 (62.8%)	204 (23.9%)	250 (74.2%)	951 (91.0%)	<0.001

Patients admitted before 04 September 2021		All	Discharged before 10 days	Died before 10 days	Persistent Critical Illness	p-value
Renal support	n (%)	411 (18.4%)	21 (2.5%)	68 (20.2%)	322 (30.8%)	<0.001
Duration of organ support (days)						
Advanced respiratory support	Median (IQR)	13 (7,22)	4 (2,6)	6 (3,8)	17 (12,28)	-
Non-invasive respiratory support	Median (IQR)	3 (2,6)	4 (2,6)	4 (2,6.8)	3 (2,7)	-
Combined advanced or non-invasive respiratory support	Median (IQR)	10 (5,19)	4 (3,6)	6 (3,8)	19 (13,28)	-
Cardiovascular support	Median (IQR)	6 (3,11)	2 (1,3)	4 (2,5)	9 (5,14)	-
Renal support	Median (IQR)	8 (3,15)	4 (2,5)	3 (2,5)	10 (4,17)	-

Persistent Critical Illness indicates patients who stayed >=10 days in ICU. Short stay indicates patients who stayed fewer than 10 days on ICU. This table includes data from 23 patients who were still in ICU at the time of the data extract and therefore have not had an entire ICU stay. “-“ indicates significance testing was not performed due to confounding by indication.

Table 3: Factors associated with Persistent Critical Illness with death before 10 days as competing risk (Fine and Gray models)

	Univariable models		Multivariable model	
	Hazard ratio (95% CI)	**p-value**	**Hazard ratio (95% CI)**	**p-value**
Age (ref=70+)				
60-69	1.33 (1.12,1.59)	0.002	1.26 (1.05,1.50)	0.01
50-59	1.15 (0.95,1.38)	0.14	1.12 (0.93,1.35)	0.23
16-49	0.79 (0.64,0.97)	0.02	0.84 (0.68,1.04)	0.10
Sex - male vs female	1.15 (1.00,1.31)	0.04	1.10 (0.96,1.26)	0.16
Ethnicity (ref=White)				
Other ethnicity	1.16 (0.94,1.43)	0.18	1.02 (0.82,1.27)	0.83
Unknown ethnicity	1.03 (0.77,1.37)	0.86	0.90 (0.67,1.21)	0.50
SIMD (ref=5 - Least deprived)				
4	0.94 (0.74,1.18)	0.58	0.92 (0.73,1.16)	0.48
3	0.89 (0.71,1.12)	0.32	0.94 (0.75,1.17)	0.57
2	0.92 (0.74,1.13)	0.42	0.95 (0.77,1.18)	0.64
1 - Most deprived	1.08 (0.88,1.33)	0.45	1.07 (0.87,1.31)	0.52
Comorbidities (ref=none)				
1 comorbidity	0.90 (0.77,1.05)	0.19	0.84 (0.72,0.99)	0.04
2 or more comorbidities	0.66 (0.55,0.80)	<0.001	0.70 (0.57,0.86)	0.001
Prior emergencies (ref=none)				
1 emergency	0.80 (0.68,0.95)	0.01	0.89 (0.75,1.07)	0.21
2 or more emergencies	0.48 (0.34,0.66)	<0.001	0.59 (0.42,0.84)	0.003

	Univariable models		Multivariable model	
	Hazard ratio (95% CI)	**p-value**	**Hazard ratio (95% CI)**	**p-value**
APS Tertile (ref=1 (1-3))				
Tertile 2 (4-8)	1.80 (1.51,2.15)	<0.001	1.59 (1.33,1.90)	<0.001
Tertile 3 (9-31)	1.83 (1.52,2.19)	<0.001	1.56 (1.28,1.89)	<0.001
APS missing	0.54 (0.32,0.91)	0.02	0.57 (0.34,0.97)	0.04
Organs supported on admission (ref=none)				
1 organ	2.70 (2.01,3.62)	<0.001	2.26 (1.68,3.04)	<0.001
2 or more organs	4.12 (3.06,5.56)	<0.001	3.05 (2.24,4.16)	<0.001

Fine and Gray competing risks analysis showing univariable Hazard ratios of Persistent Critical Illness with death before 10 days in critical care as a competing risk. CI=Confidence Intervals; SIMD= Scottish Index of Multiple Deprivation; APS = Acute Physiology score. Number of Observations = 2210. Number of Events = 1030

Figure Legends

Figure 1: Cohort derivation flow diagram

Figure 2: Daily frequency of critical care bed occupancy stratified by critical care stay length and outcome

Bed occupancy is derived from Augmented Care Period (ACP) days. Pre-Persistent Critical Illness indicates bed-days for patients who would go on to stay >=10 days in critical care, but at that point in time had stayed <10 days in critical care. Persistent Critical Illness indicates bed days for patients who had stayed >=10 days in critical care.

Figure 3: Outcomes following Critical Care discharge

A shows survival probability following critical care discharge, stratified by stay length. Graph is calculated using Kaplan-Meier estimates with 95% Confidence intervals. B shows emergency hospital readmission probability following ultimate hospital discharge, stratified by stay length. Graph is calculated using Kaplan-Meier estimates with 95% Confidence intervals.