Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

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CRITICAL CARE

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

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Abstract

Background: Patients with COVID-19 can require critical care for prolonged periods. Patients with persistent critical Illness can have complex recovery trajectories, but this has not been studied for patients with COVID-19. We examined the prevalence, risk factors, and long-term outcomes of critically ill patients with COVID-19 and persistent critical illness.
Methods: This was a national cohort study of all adults admitted to Scottish critical care units with COVID-19 from March 1, 2020 to September 4, 20. Persistent critical illness was defined as a critical care length of stay (LOS) of ≥10 days. Outcomes included 1-yr mortality and hospital readmission after 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: A total of 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. Patients with persistent critical illness 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 included age, illness severity, organ support on admission, and fewer comorbidities.
Conclusions: Almost half of all patients with COVID-19 admitted to critical care developed persistent critical illness, with high resource use in critical care and beyond. However, persistent critical illness was not associated with significantly worse long-term outcomes compared with patients who were critically ill for shorter periods.

Keywords: COVID-19; intensive care; long-term ventilation; mortality; outcome; readmission

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Editor's key points

- Prolonged critical illness is associated with important impacts on long-term functional outcomes for patients.
- Large numbers of patients developed prolonged critical illness as a result of COVID-19, but the epidemiology of this problem is not well described.
- In this study, prolonged critical illness attributable to COVID-19 was associated with worse patient outcomes in the short term, but long-term survival was similar to that of patients with shorter periods of critical illness.
- Good long-term survival rates after COVID-19 critical illness may mask a high incidence of poor functional outcomes impacting patient quality of life.

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 WHO.[1] The related severe acute hypoxaemic respiratory failure, which severe COVID-19 infection may cause, often necessitates admission to an ICU for mechanical ventilation and multi-organ support.[2] Evidence is emerging internationally on the clinical characteristics of those patients admitted to ICU as a result of 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-yr national cohort study in Australia and New Zealand, it was found that 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 patients with COVID-19 may be helpful to guide decisions around resource allocation and rehabilitation needs.

Therefore, this complete prospective national cohort study had 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 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, 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 data sets are national data sets, capturing all patients in Scotland.

Participants

A cohort study design was used. Scottish residents comprised the cohort, who were aged ≥16 yr admitted to general ICUs and combined ICU/high-dependency units (HDUs) in Scotland from March 1, 2020 to September 4, 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 September 25, 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 (LOS) 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 have demonstrated that the clinical course and case-mix of critically ill patients with COVID-19 are changing across different 'waves' of the pandemic.[12,13] Furthermore, previous work has demonstrated that the focus of clinical care for patients in the ICU 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 who had been discharged or died on or before September 25, 2021.

Other variables

Patient characteristic variables were sex, age, and ethnicity. Ethnicity was derived from categories of Scotland's Census 2011 with low frequencies aggregated.[14] Socio-economic deprivation was defined using quintiles of the Scottish Index of Multiple Deprivation (SIMD version 2020).[15] The 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 Scale, and comorbidities. The SICSAG-defined severe comorbidities were combined with Charlson-defined comorbidities as described previously[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, Pao_2:FiO_2 ratio, the Acute Physiology Score (APS) of the Acute Physiology and Chronic Health Evaluation (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 χ^2, Kruskal–Wallis, and log-rank tests. Daily frequency of bed occupancy and organ support activity was derived from augmented care period 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[18] competing risk analysis, using death before 10 days as a competing risk to help control for survivor bias. Because of 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 *vs* 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 *vs* those who were discharged before 10 days. Maximum follow-up was truncated to 1 yr, 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 after critical care discharge were investigated using Cox regression in univariable and multivariable models. Risk factors associated with emergency hospital readmission after hospital discharge were investigated using Fine and Gray[18] competing risk analysis, with death after hospital discharge as a competing risk.

Additional analyses

We repeated Fine and Gray[18] 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 previously.

Data were analysed using R version 3.6.1. (R Foundation for Statistical Computing, Vienna, Austria).[19] We used a significance level of 5%, 95% confidence intervals (CIs), 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 case 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

The Scottish Intensive Care Society Audit Group 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.

Results

Patient characteristics

Between March 1, 2020 and September 4, 2021, 2236 patients with laboratory-confirmed COVID-19 were admitted to 24 ICUs across Scotland. Baseline patient and clinical characteristics, stratified by persistent critical illness status, are presented in Table 1. Twenty-three patients remained in critical care units on the censor date (Supplementary 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 yr (inter-quartile range [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 with the cohort who was 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 with 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%). Multi-organ support was more frequent in the persistent critical illness (41.2%) and died before 10 days (46.9%) cohorts compared with those discharged before 10 days (14.9%). Advanced respiratory support was required on admission in less than half of the patients overall (42.3%), but it was more common in the persistent critical illness (56.7%) and died before 10 days (54.9%) cohorts, compared with 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 September 25, 2021 and are described in Supplementary 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 renal replacement therapy (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 noninvasive ventilation showed more variation (54.8% [persistent critical illness], 40.9% [died before 10 days], and 65.2% [discharged before 10 days]; $P<0.001$) (Supplementary Fig

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, patients with persistent critical illness had a longer total hospital LOS (28 days *vs* 8 days [died before 10 days] and 12 days

Table 1 Baseline characteristics. 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 past 10 days from admission. Twenty-six records have an unknown SIMD quintile; 103 records have unknown ethnicity. Percentages for organ support, advanced respiratory support, noninvasive ventilation, cardiovascular support, and renal replacement therapy are based on complete recording of these data corresponding to admission date; 0 record(s) are currently missing. Eighty-one patients lack APACHE data; 81 patients lack APS data. *Output suppressed because of disclosure risk. APACHE, Acute Physiology and Chronic Health Evaluation; APS, Acute Physiology Score; IQR, inter-quartile range; PF, Pao_2:FiO_2; SIMD, Scottish Index of Multiple Deprivation.

	All	Discharged before 10 days	Died before 10 days	Persistent critical illness
Number of patients *n*	2236	854	337	1045
Age on admission (yr), median (IQR)	59 (51–67)	56 (45–64)	64 (57–72)	60 (52–67)
Sex, *n* (%)				
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)
Socio-economic status quintile (SIMD), *n* (%)				
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, *n* (%)				
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, *n* (%)				
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)
Comorbidities, *n* (%)				
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, *n* (%)				
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, *n* (%)				
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, *n* (%)				
0	248 (11.1)	185 (21.7)	15 (4.5)	48 (4.6)
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)
Noninvasive 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)

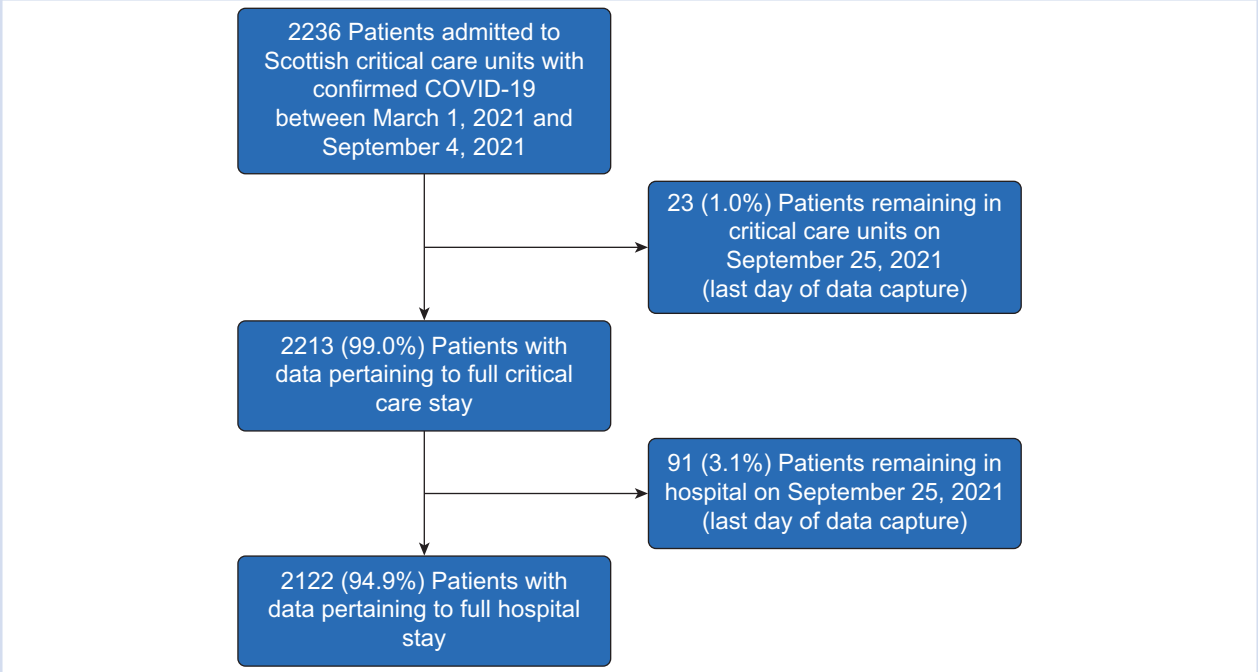

Fig 1. Cohort derivation flow diagram.

[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 they used 80.6% of critical care bed-days. Figure 2 illustrates how proportions of patients

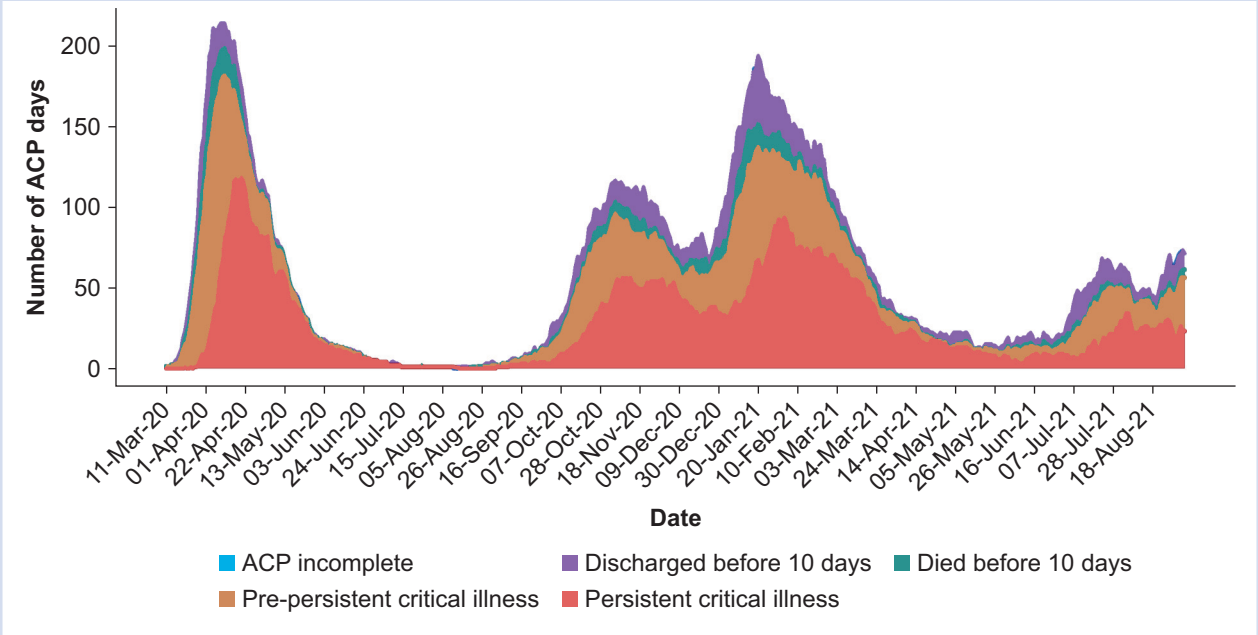

Fig 2. Daily frequency of critical care bed occupancy stratified by critical care stay length and outcome. Bed occupancy is derived from augmented care period (ACP) days. Pre-persistent critical illness indicates bed days for patients who would go on to stay ≥10 days in critical care, but at that point 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.

present in critical care differed over time. At the peak of Wave 1 (April 10, 2020), a similar proportion of persistent critical illness and shorter-stay patients was 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 (January 20, 2021) 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 after critical care discharge but before hospital discharge was lower in patients with persistent critical illness compared with patients discharged from critical care before 10 days (2.4% *vs* 4.9%). Measured after critical care discharge, 1 yr 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%]) (Fig. 3a). For the cohort who survived to critical care discharge, factors associated with mortality after critical care discharge are presented in Supplementary Table 2. After adjustment for confounders, persistent critical illness was not associated with mortality after critical care discharge (hazard ratio [HR] 0.60 [0.25–1.44]; P=0.254). Acute hospital 1 yr 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%]) (Fig. 3b). Factors associated with readmission are presented in Supplementary 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 two or more comorbidities and two or more prior emergency admissions in the year before 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; two 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 the 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 (two 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 (two 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 (Supplementary Tables 4 and 5). Similar factors remained associated with the development of persistent critical illness in both univariable and multivariable analysis: age group, presence of comorbidities,

Table 2 Outcomes. 'Persistent critical illness' indicates patients who stayed ≥10 days in the ICU. 'Short stay' indicates patients who stayed fewer than 10 days in the ICU. This table includes data from 23 patients who were still in the ICU at the time of data extraction, and therefore have not had an entire ICU stay. '–' indicates significance testing was not performed because of confounding by indication. IQR, inter-quartile range.

Patients admitted before September 4, 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
Noninvasive respiratory support, *n* (%)	1268 (56.7)	557 (65.2)	138 (40.9)	573 (54.8)	<0.001
Combined advanced or noninvasive 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
Renal support, *n* (%)	411 (18.4)	21 (2.5)	68 (20.2)	322 (30.8)	<0.001
Duration of organ support (days), median (IQR)					
Advanced respiratory support	13 (7–22)	4 (2–6)	6 (3–8)	17 (12–28)	–
Noninvasive respiratory support	3 (2–6)	4 (2–6)	4 (2–6.8)	3 (2–7)	–
Combined advanced or noninvasive respiratory support	10 (5–19)	4 (3–6)	6 (3–8)	19 (13–28)	–
Cardiovascular support	6 (3–11)	2 (1–3)	4 (2–5)	9 (5–14)	–
Renal support	8 (3–15)	4 (2–5)	3 (2–5)	10 (4–17)	–

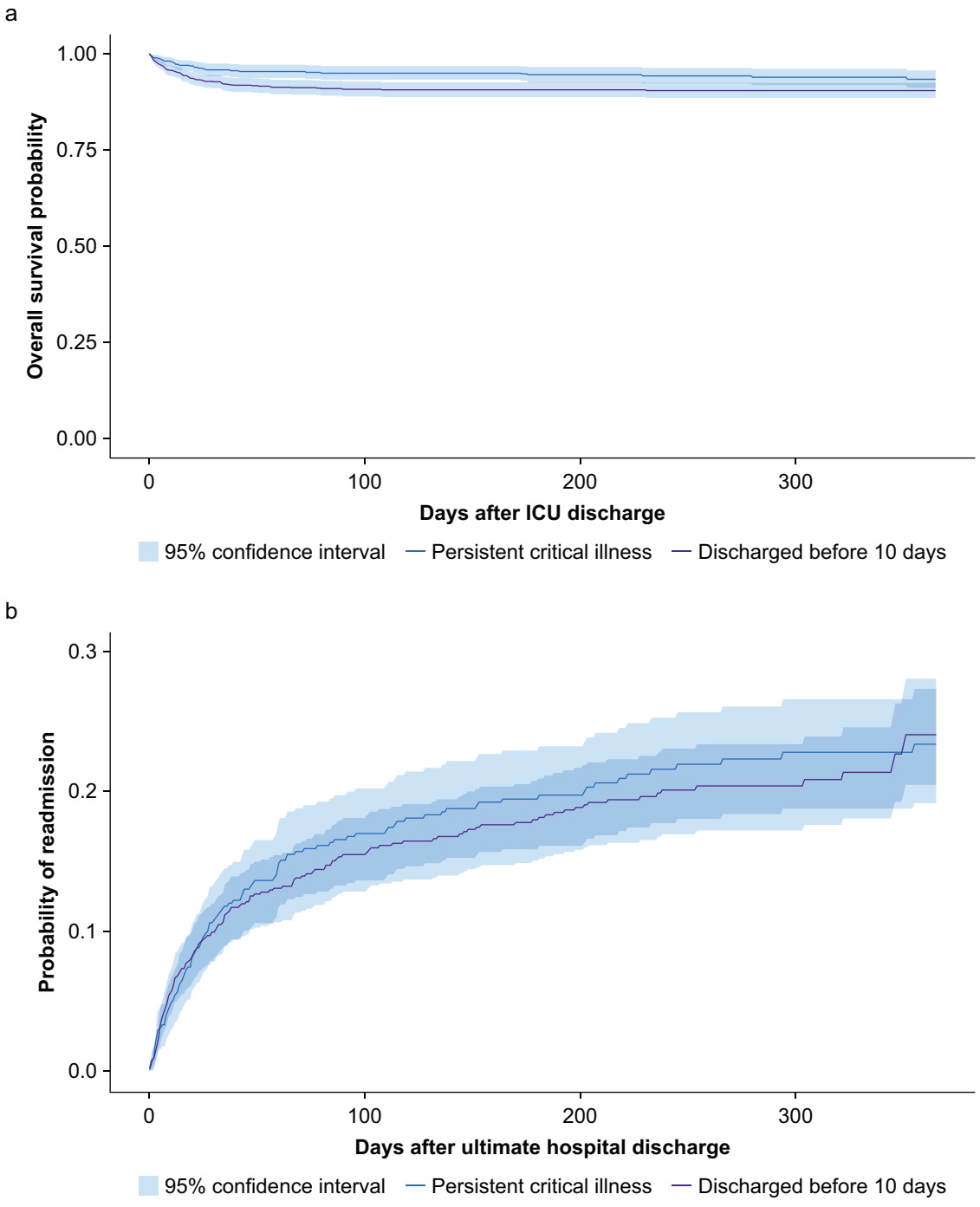

Fig 3. Outcomes after critical care discharge. (a) Survival probability after critical care discharge, stratified by stay length. Graph is calculated using Kaplan–Meier estimates with 95% confidence intervals. (b) Emergency hospital readmission probability after ultimate hospital discharge, stratified by stay length. Graph is calculated using Kaplan–Meier estimates with 95% confidence intervals.

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

In this cohort study, we demonstrated that almost half of all patients admitted to critical care with COVID-19 developed

Table 3 Factors associated with persistent critical illness with death before 10 days as competing risk (Fine and Gray[18] models). 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. APS, Acute Physiology Score; CI, confidence interval; SIMD, Scottish Index of Multiple Deprivation. Number of observations=2210. Number of events=1030.

	Univariable models		Multivariable models	
	Hazard ratio (95% CI)	P-value	Hazard ratio (95% CI)	P-value
Age (reference=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 (reference=white)				
Other ethnicities	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 (reference=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 (reference=none)				
One comorbidity	0.90 (0.77–1.05)	0.19	0.84 (0.72–0.99)	0.04
Two or more comorbidities	0.66 (0.55–0.80)	<0.001	0.70 (0.57–0.86)	0.001
Prior emergencies (reference=none)				
One emergency	0.80 (0.68–0.95)	0.01	0.89 (0.75–1.07)	0.21
Two or more emergencies	0.48 (0.34–0.66)	<0.001	0.59 (0.42–0.84)	0.003
APS tertile (reference=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 (reference=none)				
One organ	2.70 (2.01–3.62)	<0.001	2.26 (1.68–3.04)	<0.001
Two or more organs	4.12 (3.06–5.56)	<0.001	3.05 (2.24–4.16)	<0.001

persistent critical illness, with a critical care stay greater than 10 days. This had a significant impact on bed capacity as patients with persistent critical illness accrued over four-fifths of all critical care beds occupied by patients with COVID-19 during the study period. However, 1 yr mortality was not significantly lower amongst patients with persistent critical illness compared with those who had a shorter critical care stay. This may reflect the nature of COVID-19 and critical care admission and discharge patterns at times of exceptionally high demand. Factors associated with increased hazard of developing persistent critical illness included severity of illness and absence of comorbidities.

Similar to previous evidence, patients with COVID-19 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 patients admitted to general critical care. For example, in two previous Scottish studies, less than 10% of patients developed persistent critical illness.[8,22] These data demonstrate 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. These contextual and patient characteristics data are key to understanding how best to plan services moving forward for both patients with COVID-19 and those without COVID-19 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, 1-yr readmission risk was lower in this COVID-19 cohort in comparison with 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 to understand optimal management for these patients.

Patients with persistent critical illness 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. Because of the demanding workload and the challenges that

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 after hospital discharge. These challenges, and the burdens associated with persistent critical illness, are not captured when assessing survival after 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 patients admitted to critical care. 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 data sets of routinely collected data, we are confident that we have complete outcome data and high percentage of organ support data so we 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. Additionally, by including variables, such as socio-economic status in the logistic regression, we were able to identify more holistic variables associated with long critical care stay than other data sets 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, because of the changes in service provision during the pandemic, some patients who 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 data set. 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 that 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 because of 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.

Conclusions

Almost half of patients with COVID-19 admitted to critical care in Scotland developed persistent 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. However, 1-yr mortality was not significantly lower amongst patients with persistent critical illness compared with those who had a shorter critical care stay. Clinical services need to continue to develop to meet the substantial care needs for this group of patients and their families.

Authors' contributions

Study conception/design: NIL, JM, NIS, MCB, CTK, KP
Data acquisition/analysis: all authors
Data interpretation: all authors
Drafting of paper: NIL, JM, NIS, MCB, CTK, KP
Critical revision for important intellectual content: all authors
Final approval of paper to be published: all authors
NIL affirms that the paper 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. 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. Because analyses involved data on unconsented participants, the authors are unable to share individual-level data.

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Declarations of interest

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Appendix A. Supplementary data

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