CHEST

Days Spent at Home and Mortality After Critical Illness

A Cluster Analysis Using Nationwide Data

Guillaume L. Martin, MD; Alice Atramont, MD; Marjorie Mazars, MSc; Ayden Tajahmady, MD; Emin Agamaliyev, PhD; Mervyn Singer, FRCP; Marc Leone, MD; and Matthieu Legrand, MD

BACKGROUND: Beyond the question of short-term survival, days spent at home could be considered a patient-centered outcome in critical care trials.

RESEARCH QUESTION: What are the days spent at home and health care trajectories during the year after surviving critical illness?

STUDY DESIGN AND METHODS: Data were extracted on adult survivors spending at least 2 nights in a French ICU during 2018 who were treated with invasive mechanical ventilation or vasopressors or inotropes. Trauma, burn, organ transplant, stroke, and neurosurgical patients were excluded. Stays at home, death, and hospitalizations were reported before and after ICU stay, using state sequence analysis. An unsupervised clustering method was performed to identify cohorts based on post-ICU trajectories.

RESULTS: Of 77,132 ICU survivors, 89% returned home. In the year after discharge, these patients spent a median of 330 (interquartile range [IQR], 283-349) days at home. At 1 year, 77% of patients were still at home and 17% had died. Fifty-one percent had been re-hospitalized, and 10% required a further ICU admission. Forty-eight percent used rehabilitation facilities, and 5.7%, hospital at home. Three clusters of patients with distinct post-ICU trajectories were identified. Patients in cluster 1 (68% of total) survived and spent most of the year at home (338 [323-354] days). Patients in cluster 2 (18%) had more complex trajectories, but most could return home (91%), spending 242 (174-277) days at home. Patients in cluster 3 (14%) died, with only 37% returning home for 45 (15-90) days.

INTERPRETATION: Many patients had complex health care trajectories after surviving critical illness. Wide variations in the ability to return home after ICU discharge were observed between clusters, which represents an important patient-centered outcome.

CHEST 2022; ■(■):■-■

KEY WORDS: intensive care; outcome; PICS; trajectory

ABBREVIATIONS: ACH = acute care hospitals; CNAM = Caisse Nationale de l'Assurance Maladie; FROG-ICU = French and European Outcome reGistry in Intensive Care Units; HAH = hospital at home; IQR = interquartile range; PICS = post-ICU syndrome; PW = psychiatric wards; RF = rehabilitation facilities; SAPS II = Simplified Acute Physiology Score II; SNDS = Système National des Données de Santé; SNH = skilled nursing homes

AFFILIATIONS: From the Caisse Nationale de l'Assurance Maladie (G. L. M., A. A., M. M., A. T., and E. A.), Paris, France; the Bloomsbury Institute for Intensive Care Medicine, Division of Medicine (M. S.), University College London, London, United Kingdom; Aix-Marseille University, Assistance Publique Hôpitaux de Marseille, Department of Anesthesia and Intensive Care Unit (M. Leone), Hospital Nord, Marseille, France; Société Française d'Anesthésie et de Réanimation (SFAR) (M. Leone And M. Legrand), Paris, France; the Department of Anesthesia and Perioperative Care (M. Legrand), Division of Critical Care Medicine, UCSF, San Francisco, CA; and the INI-CRCT network (M. Legrand), Nancy, France.

CORRESPONDENCE TO: Matthieu Legrand, MD; email: matthieu.legrand@ucsf.edu

DOI: https://doi.org/10.1016/j.chest.2022.10.008

Take-home Points

Study question: How many days did patients spend at home during the year after surviving critical illness?

Results: Among patients surviving an ICU stay, 89% returned home (for a median 330 [interquartile range (IQR), 283-349] days) but with wide variability between clusters, and only 37% of patients who ultimately died after ICU discharge could return home for 45 (15-90) days.

Interpretation: Many patients had complex health care trajectories after surviving critical illness, with large variability in their ability to return home.

Stay in an ICU represents a major life event, impacting the physical, cognitive, and mental health of many survivors.[1-5] Beyond the legitimate question of short-term survival, outcomes research in critical care is increasingly focusing on longer-term survival and quality of life. In this regard, the post-ICU syndrome (PICS) has been increasingly recognized as a major clinical entity.[1,6,7] Defined as impairments in cognition, mental health, and physical function after critical care, it affects 33% to 99% of survivors.[8] Although small cohorts have reported quality of life or functional status after critical illness, the ability of the patient to return home and their subsequent health care trajectories in large populations remains underexplored.[7,9-11] Data from large-scale population-based cohorts are needed to better delineate patient needs and to inform patients, relatives, and policy-makers.[12-14]

The main objective of this study was to report outcomes and health care trajectories during the year after ICU discharge in adult patients admitted to French ICUs in 2018, using state sequence analysis. We focused on their ability to return home, days spent at home, and health care trajectories.

Study Design and Methods

Data Source

France has a mandatory public health insurance system that covers the entire population, ie, 67 million inhabitants. The National Health Data System (Système National des Données de Santé, SNDS) comprehensively collects anonymized individual health care consumption data, reimbursed to beneficiaries of the various French public health insurance schemes.[15] The SNDS includes outpatient data (pharmacy reimbursement claims, health care professional visits, and laboratory or imaging claims) and is linked to data collected on public and private hospital admissions via the Programme de Médicalisation des Systèmes d'Information, the national hospital discharge database. The Programme de Médicalisation des Systèmes d'Information comprises information regarding admissions to acute care hospitals (ACH), psychiatric wards (PW) use of rehabilitation facilities (RF) and hospital at home (HAH). The SNDS is also linked to a specific database for skilled nursing homes (SNH). The SNDS collects demographic data, date of death, and long-term chronic diseases eligible for 100% reimbursement of health care expenditure. Hospital stays in ACH are classified by the *Groupes Homogènes de Malades* system, a French adaptation of diagnosis-related groups. Long-term chronic diseases and hospital diagnoses are coded according to the International Statistical Classification of Diseases, 10th Revision. Procedures are coded according to the *Classification Commune des Actes Médicaux*, a French classification of medical procedures.

The use of SNDS data by the *Caisse Nationale de l'Assurance Maladie* (CNAM), the French National Health Insurance Fund, has been approved by decree and by the French data protection authority (*Commission Nationale de l'Informatique et des Libertés*). CNAM has permanent access to SNDS data in application of the provisions of article R. 1461-12 of the French public health code.

Study Population Selection

Inclusion criteria were patients aged 18 years and older, admitted to a French adult ICU between January 1, 2018 and December 31, 2018, for at least 2 consecutive nights, requiring invasive mechanical ventilation or vasopressors or inotropes. Patients admitted to the ICU for trauma, burn injuries, organ transplant, stroke, or intracranial surgery were excluded from analysis because these causes of admission intrinsically affect the patient's ability to return home and reflect highly specific populations with distinct trajectories. Patients with no health care reimbursement in 2017 or with data linkage problems were also excluded. For each patient, if several ACH admissions met the selection criteria, the first was considered the index stay. Because the study focused on post-ICU trajectories, only patients discharged alive after the index ICU admission were included.

Data Collection and Statistical Analysis

Data were extracted on age, sex, and selected preexisting comorbidities identified by algorithms applied to the patients' 2017 data. These algorithms, developed by CNAM, combine inpatient diagnoses, long-term disease information, and pharmacy reimbursement claims, and are applied annually to each beneficiary, providing information on 58 health conditions.[16]

For the index stay, the cause of hospitalization (based on the *Groupes Homogènes de Malades* classification, summarized into 10 categories), ICU procedures, length of ICU stay, and the Simplified Acute Physiology Score II (SAPS II) on ICU admission were identified.

For each patient, a daily state sequence was created to analyze care pathways in the 365 days preceding and the 365 days after ICU discharge (baseline date, e-Fig 1). A sequence refers to the daily succession of the different events (states) defining the patient's trajectory. Subsequent states were collected: death, hospital stays in ACH (at least 1 night), RF, PW (only full-time hospitalization), HAH, and SNH stays. Among ACH stays, ICU admissions were specifically identified. When neither hospitalized nor deceased, patients were considered to be at home. Patients with SNH stays after the index stay were considered at home if they were already in a SNH before the index stay. When multiple states overlapped on the same day, we used the following priority rule to define the chosen state: Death > ICU > ACH > RF > PW > HAH > SNH > Home. To facilitate visualization and clustering operations (see later

FLA 5.6.0 DTD ■ CHEST5324_proof ■ 23 November 2022 ■ 3:03 pm ■ EO: CHEST-22-1073

Q6 discussion), the daily state sequence was aggregated in a weekly state sequence, selecting the most frequent state presented by each patient during each week of the year before and after ICU discharge (52 weeks per year). If an equal number of events occurred during the same week for concurrent states, the previously described priority rule was used to define the weekly state.

Descriptive statistics were reported based on the individual daily state sequences (for each state: number of patients with at least one admission, number of admissions, cumulative length of admissions). Health care trajectories before and after ICU discharge were represented using distribution plots (transversal distribution of the different states each week) and sequence index plots (superposition of all the individual weekly state sequences).

Based on the post-ICU weekly state sequences, an unsupervised clustering method was used to identify groups of patients with similar trajectories after ICU discharge. The (dis)similarity between sequences was first measured: pairwise distances were computed between individual sequences by optimal matching, using the Longest Common Subsequence method.[17] The partition around medoids clustering algorithm was then applied, using previously computed distances.[18] This algorithm is intended to find a prespecified number of k representative sequences, called medoids, and attributes other sequences to the closest medoid. It aims to reduce the sum of dissimilarities between the medoid (center of the cluster) and the attributed sequences. The number of clusters was determined according to both statistical criteria and clinical appraisal of the clustering results. Sensitivity analyses using other sequence dissimilarity methods (optimal matching with different costs, Hamming distance)[17] and clustering algorithms (hierarchical ascendant classification, using Ward's method) were conducted. Overall, results were similar across analyses, and the approach combining longest common subsequence and partition around medoids was chosen for its robustness.

A multinomial logistic regression model was then used to assess baseline factors associated with the subsequently created clusters. Multivariable analysis was adjusted for baseline factors considered clinically relevant.

Data from the year before ICU discharge that was used as an exploratory analysis aimed to describe whether it differed from post-ICU clusters.

Results are presented as percentage or median and interquartile range (IQR) or ORs and 95% CI. Analyses were performed using SAS software (version 9.4, SAS Institute Inc) and R version 3.5.2 (packages TraMineR version 2.0-11 and WeightedCluster version 1.4 for sequence analysis and clustering).[17,18]

Results

Baseline Characteristics

Of 222,896 patients admitted to a French adult ICU during the study period, 96,177 met the selection criteria. Of these, 20% died before ICU discharge, leaving 77,132 patients in the final cohort (Table 1 and e-Fig 2). Baseline patient characteristics are shown in Table 1. Median age was 67 years (IQR, 57-75), with 58% patients older than 65 years and 27% older than 75 years (Table 1). The most frequent comorbidities were diabetes (24%), chronic respiratory disease (19%), psychiatric disorders (14%), chronic heart failure (10%), and active cancer (10%). The median SAPS II score was 41 (30-55). Postoperative care was the main reason for admission (30% cardiac, 23% noncardiac), followed by respiratory diseases (14%). Invasive mechanical ventilation, vasopressors or inotropes, and renal replacement therapy were used in 83%, 65%, and 9.1% of patients, respectively. The median length of index ACH stay (including contiguous ACH stays) was 18 days (11-33). The median ICU length of stay was 5 days (3-10); 24% of ICU stays exceeded 10 days. Patients were admitted directly to intensive or transitional care units, or via the ED for 62% of index stays.

Health Care Trajectories After ICU Discharge

Three clusters were identified based on the patients' post-ICU trajectories (Tables 2 and 3). Figure 1 shows the state distribution plots and sequence index plots of care pathways before and after ICU discharge for all patients and for each of the three clusters.

Among the 77,132 patients discharged alive from the index ICU stay, 4,360 (5.7%), 6,124 (7.9%), and 7,424 (9.6%) died within the 30, 60, and 90 days after ICU discharge, respectively. The median duration before death was 71 (19-180) days. Six percent of patients (n = 4,615) died during the index ACH stay (and contiguous ACH stays).

Eighty-nine percent of patients returned home at some point during the year after ICU discharge, for a median cumulative duration of 330 (283-349) days (Table 2). They returned home 18 (7-37) days after ICU discharge. During the 1-year follow-up, 51% of patients required re-hospitalization in an ACH for a median 11 (4-25) days, and 10% an ICU readmission for 5 (2-11) days. Approximately 44% of acute care readmissions were through the ED or transitional/ICUs. The main reasons for readmissions in ACH were cardiovascular diseases (16%), noncardiac surgery (16%), GI diseases (13%), and respiratory diseases (12%). Cardiac surgery, which represented 30% of the index stays, only accounted for 2% of the ACH readmissions. The main reasons for ICU readmissions were respiratory diseases (25%), noncardiac surgery (22%), and cardiovascular diseases (12%).

Regarding other stays, 48% of patients were admitted at least once to RF for 29 (21-54) days, 5.7% had HAH stays, 5.2% were admitted to a PW, and 2% to a SNH

FLA 5.6.0 DTD ■ CHEST5324_proof ■ 23 November 2022 ■ 3:03 pm ■ EO: CHEST-22-1073

TABLE 1] Characteristics of Patients and Index Stays

	No.	%
No. of patients	77,132	100
Age, y		
18-34	3,335	4.3
35-44	3,881	5.0
45-54	8,736	11.3
55-64	16,279	21.1
65-69	11,872	15.4
70-74	12,141	15.7
75-79	9,564	12.4
80-84	7,005	9.1
85-89	3,465	4.5
≥90	854	1.1
Age in y, median (IQR)	67 (57-75)	…
Sex		
Male	49,914	64.7
Female	27,218	35.3
Comorbidities		
Heart failure	7,850	10.2
Cerebrovascular disease	4,541	5.9
Diabetes	18,626	24.1
Active cancer	7,960	10.3
Dementia	1,236	1.6
Chronic respiratory disease	14,784	19.2
End-stage renal disease	1,610	2.1
Liver disease	3,834	5.0
Psychiatric disease	11,121	14.4
Reason for hospitalization		
Cardiac surgery	23,157	30.0
Noncardiac surgery	18,036	23.4
Respiratory diseases	11,076	14.4
Cardiovascular diseases	8,031	10.4
Poisoning	4,264	5.5
Neurological diseases (except stroke)	3,486	4.5
GI diseases	3,153	4.1
Renal or metabolic diseases	2,396	3.1
Infectious diseases	1,546	2.0
Miscellaneous	1,987	2.6
Length of index ACH stay in days, median (IQR)[a]	18 (11-33)	…
Length of ICU stay in days, median (IQR)	5 (3-10)	…
2-3 days (Quartile 1)	27,387	35.5
4-5 days (Quartile 2)	15,065	19.5
6-10 days (Quartile 3)	16,401	21.3
> 10 days (Quartile 4)	18,279	23.7
ICU procedures[a]		
Invasive mechanical ventilation	64,263	83.3
Vasopressors or inotropes	50.271	65.2
Noninvasive mechanical ventilation	25.388	32.9
Fluid resuscitation	16,000	20.7
Renal replacement therapy	7,012	9.1
Transcutaneous temporary cardiac stimulation	4,704	6.1
Administration of blood products	4,438	5.8
Transcutaneous drainage of a pericardial collection	2,114	2.7
CPR with intubation	1,338	1.7
Emergency external electrical cardioversion	1,071	1.4
Mechanical circulatory support	938	1.2
Tracheostomy	3,686	4.8
Gastrostomy	1,614	2.1
SAPS II, median (IQR)	41 (30-55)	…
SAPS II, missing data	71	…

ACH = acute care hospital; IQR = interquartile range; SAPS II = Simplified Acute Physiology Score II.
[a]Including contiguous ACH stays.

facility. At 1 year post-ICU discharge, 77% of patients were at home and 17% had died.

Over the year preceding the index ICU stay, 99% were at home for a median cumulative duration of 351 (333-358) days, 56% were hospitalized in an ACH for a median 7 (3-18) days, and 4.9% had been admitted to an ICU for a median 4 (2-9) days (e-Table 1 and Figure 2).

Health Care Trajectories Among Clusters

We identified three clusters with very distinct characteristics and outcomes (Figs 1 and 2). Cluster 1 (n = 52,254, 68%) was characterized by an early return to home and, mostly, a hospital-free trajectory for the year after ICU discharge. Patients could be discharged home in 99.8% of cases, for a median 338 (323-354) days. The median time before home discharge was 13 (6-28) days. At 1 year, 98% were still alive and 95% were at home. Nonetheless, 47% required rehospitalization in an ACH a median 2 (1-3) times for a median of 8 (3-17) days; 6.5% were readmitted to an ICU for a median 4 (2-8) days, and 42% were admitted to RFs for 22 (19-29) days. Cluster 1 included the highest rate of patients admitted to a PW (6.3%, for 33 (14-79) days). HAH or SNH

FLA 5.6.0 DTD ■ CHEST5324_proof ■ 23 November 2022 ■ 3:03 pm ■ EO: CHEST-22-1073

admissions were infrequent. The progression of "ACH-to-Home" (23%) or "ACH-to-RF-to-Home" (17%) were the two main distinct state sequences in this cluster. Over the year preceding ICU discharge, 99% of patients in this cluster were at home for a median of 354 (343-359) days. Fifty-four percent had been hospitalized in an ACH for 6 (2-14) days, and 5.8% stayed in RFs (e-Table 1).

Cluster 2 (n = 13,775, 18%) gathered patients with more complex and heterogeneous pathways. Despite the heterogeneity of the individual sequences, the transversal state distribution showed that in the first 3 weeks after ICU discharge, patients were mostly in an ACH. Over the following 10 weeks, 40% to 57% were in RFs and, subsequently, home discharge was achieved in 43% to 70% (Fig 1A). In this cluster, despite more frequent rehospitalizations, 91% of patients returned home for 242 (174-277) days. The median time before discharge home was 70 (37-112) days. At 1 year post-ICU discharge, 92% had survived, and 70% were at home. Of note, 71% required rehospitalization at least once in an ACH during the year after ICU discharge, with 2 (1-4) stays for 21 (8-45) days. In addition, 89%, 12%, 8%, and 4% were admitted to RFs (for 66 [45-111] days), HAH, SNH, or PWs, respectively. Regarding the year preceding ICU discharge, 99% of these patients were at home, and 56% were hospitalized in an ACH for a median 10 (4-25) days, and 5.6% required ICU admission for 5 (2-12) days (e-Table 1). Sixteen percent spent 37 (20-72) days in RFs.

Cluster 3 (n = 11,103; 14%) gathered patients who died during the year after ICU discharge. Over the year after ICU discharge, only 37% returned home for a median of 45 (15-90) days, with none at home at 1 year post-ICU discharge (Table 2). The median time before discharge home was 16 (8-38) days. The progression from "ACH-to-Death" was the most frequent distinct state sequence in this cluster, accounting for 39% of the individual daily sequences. Forty-four percent were rehospitalized in an ACH for a median of 19 (8-37) days with a median of 2 (1-3) stays, 28% were admitted to RFs for 29 (14-55) days, and 11% had HAH stays for 28 (11-67) days. During the year preceding ICU discharge, 98% were at home, 66% required at least one ACH stay for 16 (7-32) days, 7.9% an ICU admission for 5 (2-10) days, and 16% an admission to RFs for 31 (16-59) days (e-Table 1).

Risk Factors to Belong to a Cluster

Patients in clusters 2 and 3 were older and had more comorbidities than patients in cluster 1 (Table 3). They were less frequently hospitalized for cardiac surgery, had longer index ICU stays, had higher SAPS II scores, and more frequently required renal replacement therapy, blood transfusion, mechanical circulatory support, gastrostomy, and tracheotomy than patients in cluster 1. Compared with cluster 1, patients in cluster 2 were more often women, whereas patients in cluster 3 were more often men. These results were confirmed for variables included in the multivariable analysis (Table 3 and Fig 3). Compared with cluster 1, the risk associated with being in cluster 3 increased from 1.65 (1.30-2.08) for patients aged 35 to 44 years to 21.58 [16.83-27.65] for patients over 90 years compared with patients aged 18 to 34 years. The comorbidities most strongly associated with cluster 3 were active cancer (OR = 2.27 [2.14-2.42]), liver disease, dementia, and heart failure, with an OR of approximately 1.8 (Fig 3). Using cardiac surgery as the reference, all other reasons for hospitalization were positively associated with cluster 3 and also with cluster 2 except respiratory diseases and poisoning. Gastrostomy was a strong risk factor for belonging to clusters 2 and 3.

Discussion

In this large retrospective population study of critically ill adults surviving an admission to a French ICU in 2018, 89% returned home for a median duration of 330 (283-349) days, and 17% died over the year after ICU discharge. Rehospitalizations in acute care units and ICUs were needed for 51% and 10% of patients, respectively. There was wide heterogeneity in their ability to return home. We identified three clusters reflecting three distinct post-ICU trajectories. Many patients had complex trajectories with alternating periods at home and hospital. Most patients who died during the year after discharge could not return home, and those who did managed to stay home for only a short period.

We previously reported that ICU survivors had a high risk of dying over subsequent years.[19] In this study, we confirmed an ICU mortality of approximately 20% and an additional mortality rate of 17% in the year after ICU discharge. Albeit important, mortality may not be the worst outcome considered by patients or their relatives.[14,20,21] Several observational studies reported poor quality of life of altered functional status after surviving a critical illness.[4,5,22,23] Only a few randomized controlled trials have explored functional outcomes as a crucial end point. The conventional ventilation or extracorporeal membrane oxygenation for severe adult

FLA 5.6.0 DTD ■ CHEST5324_proof ■ 23 November 2022 ■ 3:03 pm ■ EO: CHEST-22-1073

TABLE 2] Description of Hospital and SNH Stays, Home Stays, and Death in the Year (365 Days) After ICU Discharge, for All Patients and by Cluster

	All Patients	Cluster 1	Cluster 2	Cluster 3
No. of patients	77,132	52,254	13,775	11,103
ACH				
Index stay (and contiguous stays)				
Patients with at least one stay, No. (%)	73,264 (95.0)	49,043 (93.9)	13,441 (97.6)	10,780 (97.1)
Cumulative LOS, days, median (IQR)[a]	10 (6-18)	8 (5-13)	20 (11-35)	14 (7-26)
Rehospitalization(s) in ACH				
No. of patients with at least one stay, No. (%)	39,130 (50.7)	24,489 (46.9)	9,765 (70.9)	4,876 (43.9)
No. of stays, median (IQR)[a]	2 (1-3)	2 (1-3)	2 (1-4)	2 (1-3)
Cumulative LOS, days, median (IQR)[a]	11 (4-25)	8 (3-17)	21 (8-45)	19 (8-37)
ICU				
No. of patients with at least one stay, No. (%)	7,638 (9.9)	3,408 (6.5)	2,381 (17.3)	1,849 (16.7)
No. of stays, median (IQR)[a]	1 (1-1)	1 (1-1)	1 (1-1)	1 (1-1)
Cumulative LOS, days, median (IQR)[a]	5 (2-11)	4 (2-8)	6 (3-13)	6 (3-15)
RF				
No. of patients with at least one stay, No. (%)	37,256 (48.3)	21,898 (41.9)	12,292 (89.2)	3,066 (27.6)
No. of stays, median (IQR)[a]	1 (1-2)	1 (1-1)	2 (1-2)	1 (1-2)
Cumulative LOS, days, median (IQR)[a]	29 (21-54)	22 (19-29)	66 (45-111)	29 (14-55)
HAH				
No. of patients with at least one stay, No. (%)	4,359 (5.7)	1,456 (2.8)	1,718 (12.5)	1,185 (10.7)
No. of stays, median (IQR)[a]	1 (1-2)	1 (1-1)	1 (1-3)	1 (1-2)
Cumulative LOS, days, median (IQR)[a]	35 (15-86)	24 (12-45)	68 (29-138)	28 (11-67)
PW				
No. of patients with at least one stay, No. (%)	4,045 (5.2)	3,285 (6.3)	574 (4.2)	186 (1.7)
No. of stays, median (IQR)[a]	1 (1-2)	1 (1-2)	2 (1-3)	1 (1-2)
Cumulative LOS, days, median (IQR)[a]	36 (15-87)	33 (14-79)	61 (27-129)	28 (12-85)
SNH[b]				
No. of patients with at least one stay, No. (%)[a]	1,635 (2.1)	161 (0.3)	1,102 (8.0)	372 (3.4)
Cumulative LOS, days, median (IQR)[a]	157 (49-270)	67 (21-218)	215 (104-282)	53 (21-128)
Home				
No. of patients with at least one stay, No. (%)	68,873 (89.3)	52,158 (99.8)	12,557 (91.2)	4,158 (37.4)
Cumulative LOS, days, median (IQR)[a]	330 (283-349)	338 (323-354)	242 (174-277)	45 (15-90)
No. of patients at home at 1 year, No. (%)	59,123 (76.7)	49,414 (94.6)	9,709 (70.5)	0 (0.0)
Home (including HAH)				
No. of patients with at least one stay, No. (%)	69,774 (90.5)	52,173 (99.8)	12,826 (93.1)	4,775 (43.0)
Cumulative LOS, days, median (IQR)[a]	330 (285-349)	338 (324-354)	249 (187-282)	49 (18-96)
No. of patients at home at 1 year, No. (%)	59,595 (77.3)	49,526 (94.8)	10,049 (73.0)	20 (0.2)
Death				
No. of deaths, No. (%)	13,292 (17.2)	1,150 (2.2)	1,104 (8.0)	1,1038 (99.4)
Cumulative length, days, median (IQR)[c]	294 (185-346)	71 (34-116)	74 (41-110)	316 (249-351)

ACH = acute care hospital; HAH = hospital at home; IQR = interquartile range; LOS = length of stay; PW = psychiatric ward; RF = rehabilitation facilities; SNH = skilled nursing home.
[a]Among patients with at least one stay.
[b]Patients with SNH stays after the index stay were considered at home if they were already in SNH before the index stay.
[c]Among deceased patients.

FLA 5.6.0 DTD ■ CHEST5324_proof ■ 23 November 2022 ■ 3:03 pm ■ EO: CHEST-22-1073

TABLE 3] Characteristics of Patients and Index Stays by Cluster, and Factors Associated With Clusters in Multinomial Logistic Regression Models

	Cluster 1		Cluster 2		Cluster 3		Cluster 2		Cluster 3	
	No.	%	No.	%	No.	%	(Ref. = Cluster 1)		(Ref. = Cluster 1)	
No. of patients	52,254	100	13,775	100	11,103	100	OR	95% CI	OR	95% CI
Age category, y										
18-34	2,765	5.3	454	3.3	116	1.0	1.00	Ref.	1.00	Ref.
35-44	3,064	5.9	586	4.3	231	2.1	1.09	(0.95-1.26)	1.70	(1.35-2.15)
45-54	6,595	12.6	1,431	10.4	710	6.4	1.28	(1.13-1.44)	2.49	(2.02-3.06)
55-64	11,553	22.1	2,790	20.3	1,936	17.4	1.39	(1.24-1.56)	3.78	(3.10-4.61)
65-69	8,081	15.5	2,172	15.8	1,619	14.6	1.63	(1.44-1.83)	4.81	(3.94-5.87)
70-74	8,218	15.7	2,130	15.5	1,793	16.1	1.63	(1.45-1.84)	5.74	(4.70-7.01)
75-79	6,108	11.7	1815	13.2	1,641	14.8	1.93	(1.71-2.18)	7.36	(6.02-9.00)
80-84	4,014	7.7	1,397	10.1	1,594	14.4	2.26	(1.99-2.56)	10.57	(8.64-12.95)
85-89	1,535	2.9	817	5.9	1,113	10.0	3.30	(2.87-3.79)	16.36	(13.27-20.17)
≥ 90	321	0.6	183	1.3	350	3.2	3.65	(2.94-4.52)	24.37	(18.99-31.26)
Age, years, median (IQR)	66 (55-74)		68 (59-77)		72 (64-80)					
Sex										
Male	33,945	65.0	8,656	62.8	7,313	65.9	1.00	Ref.	1.00	Ref.
Female	18,309	35.0	5,119	37.2	3,790	34.1	1.09	(1.04-1.13)	0.89	(0.84-0.93)
Comorbidities										
Heart failure	4,210	8.1	1,615	11.7	2,025	18.2	1.31	(1.23-1.40)	1.79	(1.68-1.92)
Cerebrovascular disease	2,670	5.1	976	7.1	895	8.1	1.20	(1.11-1.30)	1.16	(1.06-1.26)
Diabetes	11,677	22.3	3,618	26.3	3,331	30.0	1.13	(1.08-1.18)	1.17	(1.11-1.23)
Active cancer	4,293	8.2	1,368	9.9	2,299	20.7	1.06	(0.99-1.14)	2.22	(2.09-2.36)
Dementia	539	1.0	277	2.0	420	3.8	0.98	(0.93-1.03)	1.10	(1.04-1.16)
Chronic respiratory disease	9,063	17.3	2,789	20.2	2,932	26.4	0.95	(0.83-1.09)	1.35	(1.18-1.55)
End-stage renal disease	906	1.7	312	2.3	392	3.5	1.36	(1.25-1.49)	1.89	(1.73-2.07)
Liver disease	2,100	4.0	786	5.7	948	8.5	1.34	(1.27-1.43)	1.26	(1.18-1.35)
Psychiatric disease	7,298	14.0	2,176	15.8	1,647	14.8	1.34	(1.15-1.56)	1.81	(1.57-2.08)
Reason for hospitalization										
Cardiac surgery	19,264	36.9	3,175	23.0	718	6.5	1.00	Ref.	1.00	Ref.

Q12

(Continued)

TABLE 3] *(Continued)*

	Cluster 1		Cluster 2		Cluster 3		Cluster 2		Cluster 3	
	No.	%	No.	%	No.	%	(Ref. = Cluster 1)		(Ref. = Cluster 1)	
Non-cardiac surgery	10,509	20.1	4,369	31.7	3,158	28.4	1.72	(1.61-1.83)	5.27	(4.79-5.80)
Respiratory diseases	6,699	12.8	2,021	14.7	2,356	21.2	1.03	(0.95-1.11)	5.65	(5.09-6.26)
Cardiovascular diseases	4,699	9.0	1,542	11.2	1,790	16.1	1.42	(1.32-1.53)	6.83	(6.17-7.57)
Poisoning	3,738	7.2	308	2.2	218	2.0	0.54	(0.47-0.61)	2.44	(2.06-2.89)
Neurological diseases (except stroke)	2,246	4.3	752	5.5	488	4.4	1.62	(1.46-1.79)	5.48	(4.79-6.28)
GI diseases	1,786	3.4	540	3.9	827	7.4	1.30	(1.17-1.46)	8.44	(7.46-9.56)
Renal or metabolic diseases	1,395	2.7	452	3.3	549	4.9	1.27	(1.12-1.43)	6.44	(5.60-7.39)
Infectious diseases	840	1.6	314	2.3	392	3.5	1.68	(1.46-1.94)	8.99	(7.70-10.49)
Miscellaneous	1.078	2.1	302	2.2	607	5.5	1.42	(1.24-1.64)	14.03	(12.19-16.15)
Length of index ACH stay in days, median (IQR)[a]	15 (10-24)		37 (21-61)		29 (17-49)					
Length of ICU stay, days, median (IQR)	4 (2-8)		8 (4-18)		7 (4-15)					
2-3 days (Quartile 1)	21,979	42.1	3,021	21.9	2,387	21.5	1.00	Ref.	1.00	Ref.
4-5 days (Quartile 2)	11,036	21.1	2,115	15.4	914	17.2	1.25	(1.17-1.33)	1.23	(1.15-1.32)
6-10 days (Quartile 3)	10,646	20.4	2,985	21.7	2,770	24.9	1.68	(1.58-1.78)	1.54	(1.44-1.64)
> 10 days (Quartile 4)	8,593	16.4	5,654	41.0	4,032	36.3	3.49	(3.29-3.71)	2.54	(2.37-2.72)
ICU procedures										
Invasive mechanical ventilation	44,382	84.9	11,610	84.3	8,271	74.5				
Vasopressors or inotropes	31,553	60.4	10,162	73.8	8,556	77.1				
Noninvasive mechanical ventilation	15,688	30.0	5,353	38.9	4,347	39.2	0.99	(0.94-1.03)	0.97	(0.92-1.02)
Fluid resuscitation	9,485	18.2	3,618	26.3	2,897	26.1	1.14	(1.09-1.20)	1.08	(1.03-1.14)
Renal replacement therapy	3,354	6.4	2,031	14.7	1,627	14.7	1.34	(1.25-1.43)	1.31	(1.22-1.41)
Transcutaneous temporary cardiac stimulation	3,809	7.3	716	5.2	179	1.6	1.00	(0.91-1.10)	0.84	(0.71-1.00)
Administration of blood products	485	4.8	1,154	8.4	799	7.2	1.29	(1.19-1.40)	1.36	(1.24-1.49)
Transcutaneous drainage of a pericardial collection	1,684	3.2	345	2.5	85	0.8	1.19	(1.05-1.35)	0.95	(0.75-1.20)
CPR with intubation	695	1.3	347	2.5	296	2.7	1.12	(0.97-1.29)	1.36	(1.16-1.58)

(Continued)

FLA 5.6.0 DTD ■ CHEST5324_proof ■ 23 November 2022 ■ 3:03 pm ■ EO: CHEST-22-1073

TABLE 3] (Continued)

	Cluster 1		Cluster 2		Cluster 3		Cluster 2 (Ref. = Cluster 1)		Cluster 3 (Ref. = Cluster 1)	
	No.	%	No.	%	No.	%				
Emergency external electrical cardioversion	589	1.1	291	2.1	191	1.7	1.19	(1.02-1.40)	1.15	(0.96-1.39)
Mechanical circulatory support	516	1.0	335	2.4	87	0.8	1.82	(1.56-2.12)	1.76	(1.37-2.25)
Tracheostomy	1,533	2.9	1,258	9.1	895	8.1	1.65	(1.51-1.80)	1.52	(1.37-1.67)
Gastrostomy	398	0.8	668	4.8	548	4.9	3.67	(3.21-4.21)	4.31	(3.73-4.98)
SAPS II, median (IQR)	38 (28-51)	...	46 (34-59)	...	51 (40-64)	...	...	...	...	...
SAPS II, missing data	48	0.1	12	0.1	11	0.1	...	...	...	...

ACH = acute care hospital; IQR = interquartile range; SAPS II = Simplified Acute Physiology Score II.
[a]Including contiguous ACH stays.

respiratory failure trial, for instance, explored the impact of extracorporeal membrane oxygenation in patients with severe acute respiratory distress syndrome on death or severe disability at 6 months.[24] Recently, ability to return home and hospital-free days have been proposed as significant patient-centered outcomes in ICU survivors.[25,26] Implementing strategies to accelerate and improve recovery and the ability to return home are advocated by both critical illness survivors and clinicians.[27]

Quality of life in ICU survivors should be viewed as a main goal of ICU management. In the year preceding the ICU discharge, 99% of our cohort were at home for a median of 351 (333-358) days, although 56% were hospitalized in an acute care unit for 7 (3-18) days during 1 (1-3) stays, and 5% had an ICU stay. During the year after ICU discharge, 89% of the patients returned home, 51% were re-hospitalized in an ACH for 11 (4-25) days, and 10% spent 5 (2-11) days in an ICU. Of note, half of the patients were admitted at least once to an RF for a median of 29 (21-54) days, which represents a significant increase in health care resource utilization. The days spent at home during the year preceding admission was not a major discriminant of post-ICU trajectories.

Large variations in postdischarge trajectories were identified in the three different clusters. Cluster 1 gathered survivors who returned home after ICU discharge and survived, although many required several acute hospitalizations, and 42% were admitted to an RF. Cluster 2 included patients who had more complex health care trajectories, with 71% requiring a new acute hospitalization and 17% an ICU readmission. Most were admitted to long-term care facilities. Cluster 3 mainly comprised patients who died during the year after ICU discharge, with only 37% able to return home (43% including receipt of HAH) for a short period. Patients in clusters 2 and 3 were more likely to have prolonged ICU stays (>10 days), receive renal replacement therapy, or have a tracheotomy or gastrostomy performed.[28] Most had complex trajectories with large utilization of health care resources. In the general population in France in 2018, approximately 15/1,000 inhabitants were admitted for hospitalizations in RF, and 107/1,000 inhabitants for overnight hospitalizations in ACH. Admissions to RF vary across hospitals and regions, depending on ease of access or the population profile, and these are decided on a case-by-case basis by physicians, with no specific economic or clinical criteria.

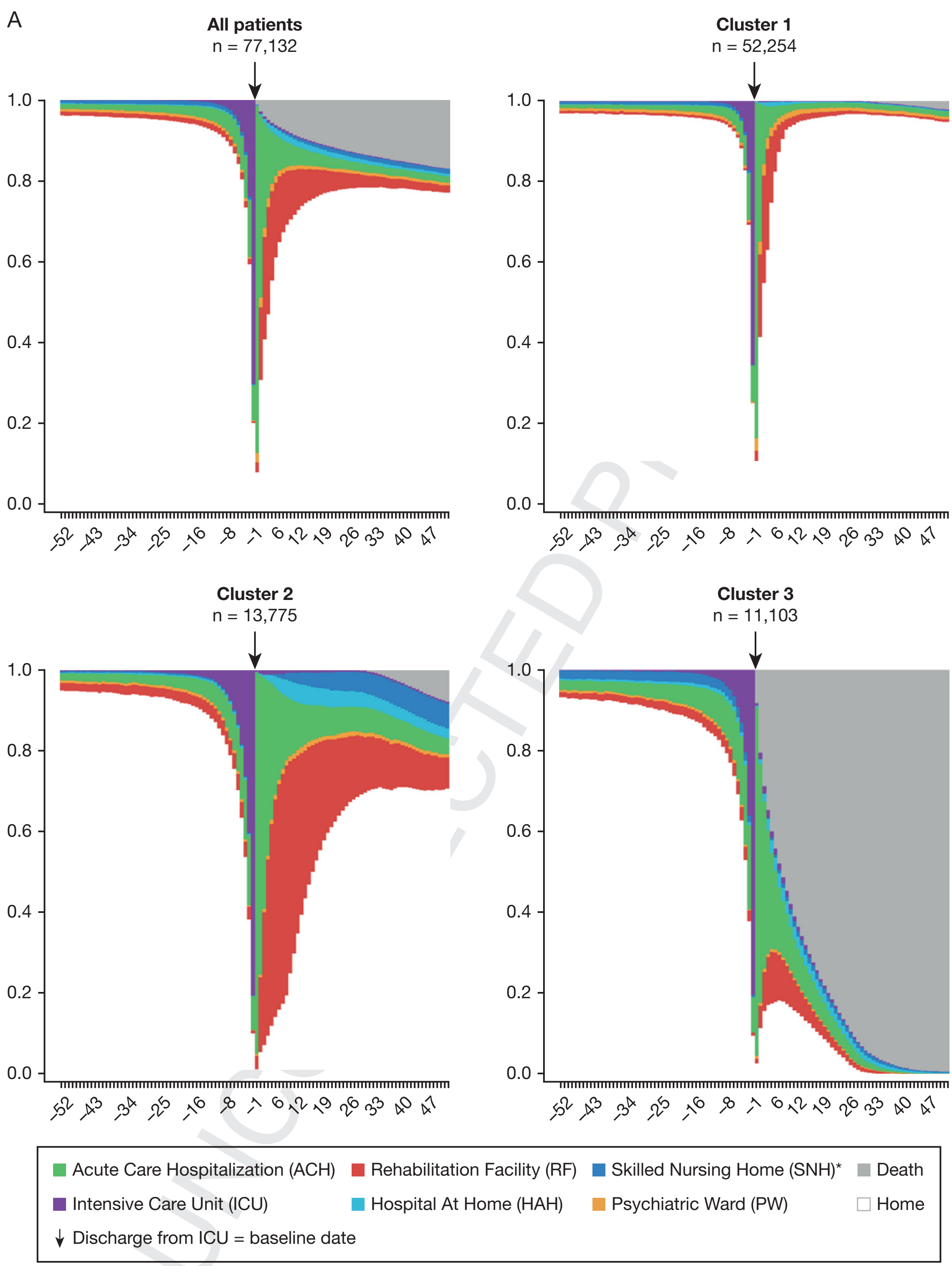
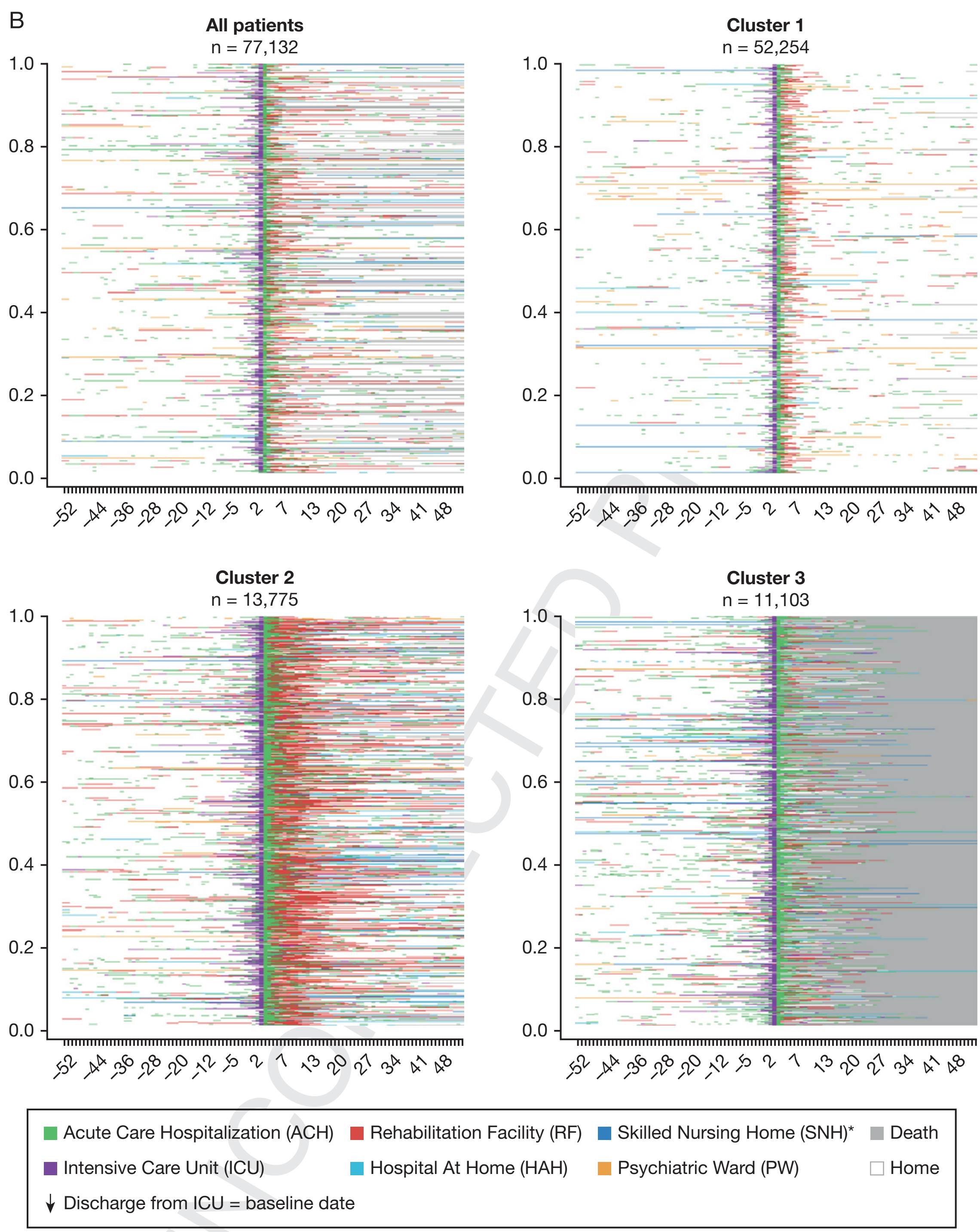


Figure 1 – *State distribution plot (A) and sequence index plots (B, C, D) of* ***health care*** *trajectories during the 52 weeks before and after ICU discharge, for all patients and by cluster. A, State distribution plots (transversal distribution of the different states each week); B, C, D, Sequence index plots (superposition of the longitudinal individual sequences of patients): unsorted (B), sorted by states from start of the post-ICU trajectory (C) and sorted by states from end (D). *Patients already admitted to SNH before ICU admission are represented as "Home" after ICU discharge. In all figures, the x axis represents week numbering, before and after ICU discharge. The baseline date (ICU discharge) is set at the beginning of week 1. In A, the y axis represents the proportion of patients. In B, C, and D, one line represents one patient sequence. SNH = skilled nursing home.*

FLA 5.6.0 DTD ■ CHEST5324_proof ■ 23 November 2022 ■ 3:03 pm ■ EO: CHEST-22-1073



print & web 4C/FPO

Figure 1 – *Continued*

Our study reports at a national scale the trajectories of patients after ICU discharge and adds to the literature of post-ICU outcomes. Among 1,083 Medicare survivors of sepsis, of whom only 38% required ICU admission, 63% were readmitted in the first year after discharge, spending a median 16 days (IQR, 2-45) in an inpatient health care facility.[25] Among patients with septic shock, only a third of survivors had not returned to independent living by 6 months after discharge. In our study, the identification of clusters of patients provides important insights into the population more likely to return home after an ICU

FLA 5.6.0 DTD ■ CHEST5324_proof ■ 23 November 2022 ■ 3:03 pm ■ EO: CHEST-22-1073

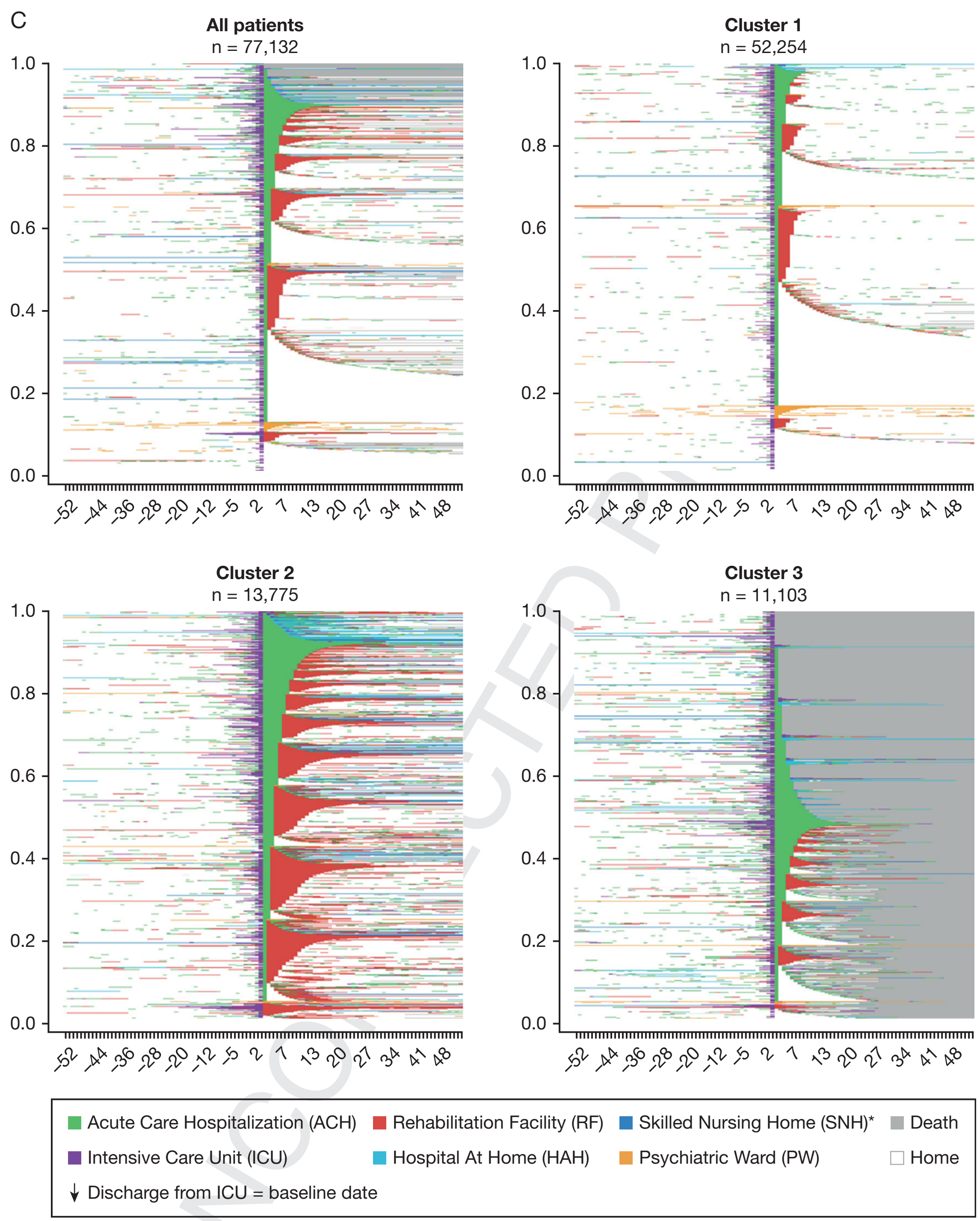
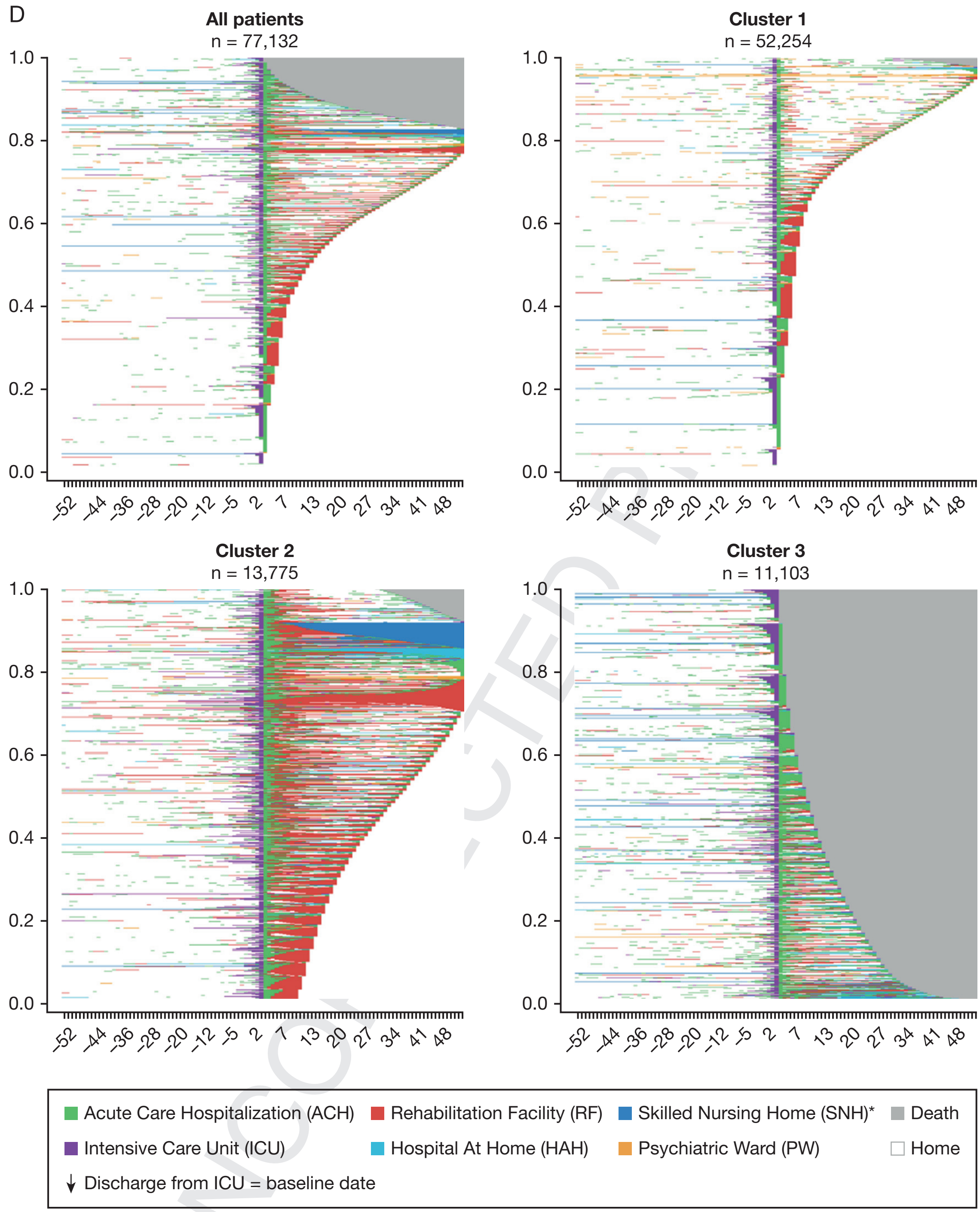


Figure 1 – *Continued*

stay and those more likely to have complex trajectories with a requirement for complex care. Although these data are not intended for decision-making at the individual level, they nonetheless provide valuable information on the health care intensity of different populations after an ICU admission. Most of the patients who died during the year after ICU discharge never went home, except for short periods, and they spent most of their time in acute care units and RFs. Of note, 98% of them were at home in the year before ICU admission, excluding such criteria as a predictor of post-ICU outcomes. These results reinforce the need for accurate predictive and prognostic tools in patients discharged from the ICU.[29]

FLA 5.6.0 DTD ■ CHEST5324_proof ■ 23 November 2022 ■ 3:03 pm ■ EO: CHEST-22-1073



print & web 4C/FPO

Figure 1 – *Continued*

Cluster 2 gathers populations most likely to benefit from strategies aimed at improving post-ICU outcomes. Although large-scale, multicenter studies are still lacking, interdisciplinary and collaborative rehabilitation interventions are feasible and may improve post-ICU outcomes. In a randomized controlled trial, early mobilization in patients with sepsis was associated with an increased likelihood of being discharged directly home (51% vs 27%, $P < .001$).[30] Long-term consequences of critical illness, including respiratory and cardiovascular complications, neuromuscular weakness, neurological disorders, cognitive decline, depression, posttraumatic stress disorders, and decompensation or progression of underlying

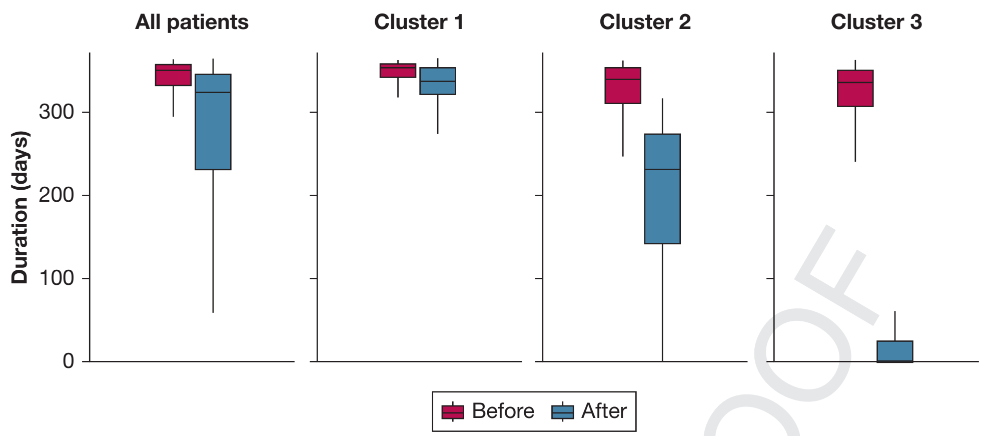


Figure 2 – *Distribution of the number of days spent at home during the year before and the year after ICU discharge, for all patients and by cluster, during the year before ICU discharge. "Home" included skilled nursing home (SNH); during the year after ICU discharge, "Home" included SNH only for patients who were already in SNH before ICU discharge. All patients, including those without any return to home (ie, number of days at home = 0) are plotted.*

comorbidities of critical illness, have been increasingly recognized.[22,23,31-37] This has been reported as an umbrella syndrome—PICS—corresponding to a global health impairment that includes physical, psychological, and cognitive symptoms after critical illness.[8] PICS may explain the high utilization of health care resources after ICU discharge, especially RF and psychiatric hospitalization. This last form of hospitalization was needed by 6% of cluster 1 patients. In the French and European Outcome reGistry in Intensive Care Units (FROG-ICU) cohort, 22% and 19%, respectively, showed symptoms of anxiety or depression.[38,39] In a

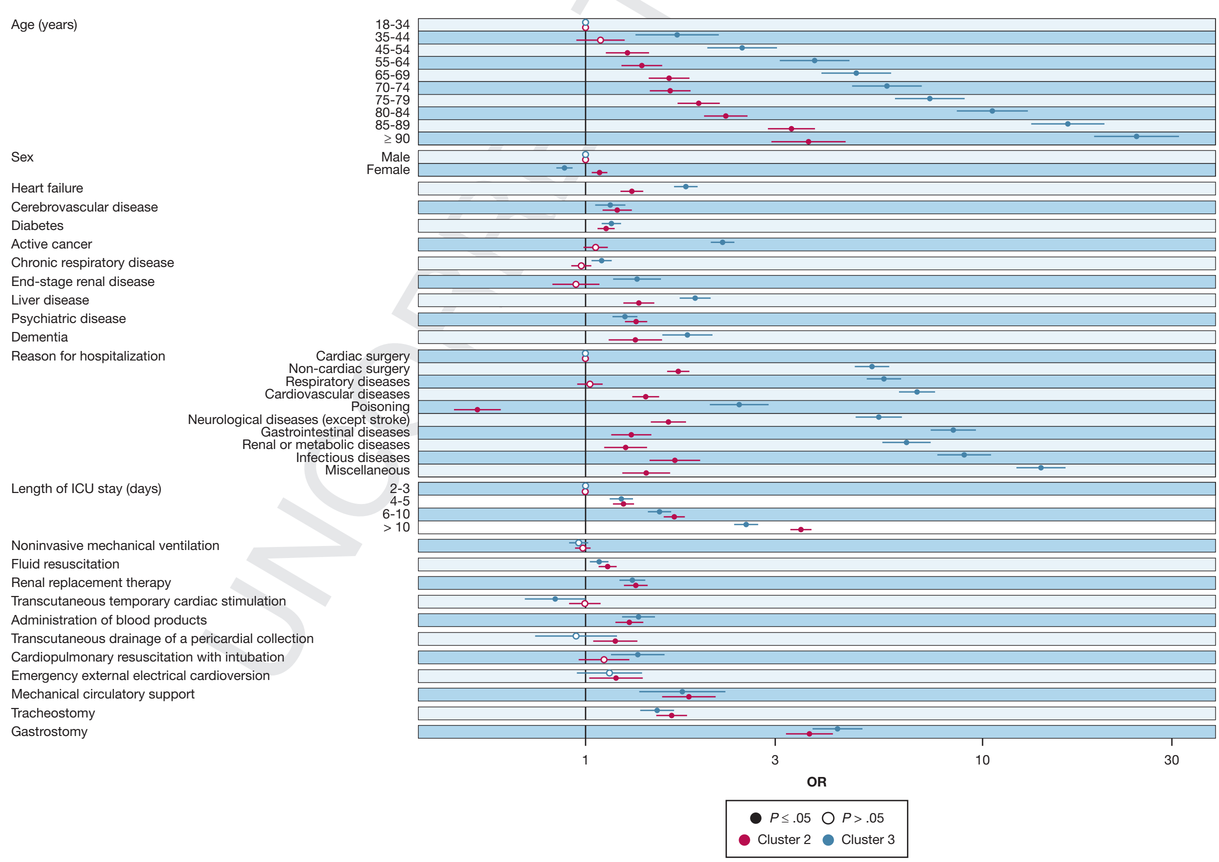


Figure 3 – *Factors associated with being in clusters 2 or 3 in multinomial logistic regression models, with cluster 1 taken as a reference.* Q16

prospective, multicenter cohort, a history of anxiety or depression, prolonged duration of mechanical ventilation, and inability of a home discharge were associated with long-term disability.[12]

The methodology used in our study has several strengths. First, we used a nationwide administrative database with an excellent capture of health care utilization. Approximately 7% of patients were excluded because of absence of reimbursed health care or linkage issues making it impossible to follow health care trajectories. We excluded patients with specific causes of index hospital stay admission that could have had a major impact on post-ICU trajectories. Sequence analysis allowed us to analyze health care trajectories, considering the different states and their chronological progression, and could thus complement the focus on specific outcomes. Different sequence dissimilarity measures were tested, as well as a hierarchical ascendant clustering method. Although the three-cluster typology remained broadly similar, clusters 1 and 2 could vary in size.

Limitations of our study include the observational design, which prevents any causal association. This study focused on hospitalization data to define health care trajectories; ambulatory care requirements were not analyzed. Moreover, clinical information, functional status, or markers of quality of life are not directly available in the SNDS to assess whether patients who returned home were independent for daily life activities. Hospital bed availability, regional resource differences, and health care provider preferences could have impacted health care trajectories.

Overall, our study highlights the use of a massive claim database to explore long-term outcomes in critically ill patients, including the probability of returning home, which is a major patient-centered outcome. Future articles may further detail predictors of such long-term outcomes.

Interpretation

Most patients surviving a critical illness could return home. Many patients had complex health care trajectories compared with the year before their index ICU admission, but most patients who died after ICU discharge never return home or remain there for short periods, highlighting the need to better identify this subgroup of patients. Days at home should be considered an important patient-centered outcome in future critical care trials.

Acknowledgments

Authors' contributions: M. Leg. takes responsibility for the content of the manuscript, including the data and analysis. G. L. M. and A. A. had full access to all of the data in the study and performed the statistical analysis. G. L. M., A. A., M. M., A. T., E. A., M. S., M. Leone, and M. Legrand contributed substantially to the study design, data analysis, and interpretation, and the writing of the manuscript.

Funding/support: The authors have reported to *CHEST* that no funding was received for this study.

Financial/nonfinancial disclosures: The authors have reported to *CHEST* the following: M. S. reports other from NewB, other from Amormed, other from Biotest, other from Fresenius, grants from Apollo Therapeutics, other from Roche, personal fees from Safeguard Biosystems, personal fees from Aptarion Biotech, personal fees from Pfizer, grants from UCL Technology Fund, outside the submitted work. M. Leone received fees for lectures (AOP) and consulting (Ambu, Gilead, LFB); M. Legrand reports no conflict of interest. G. L. M. reports grants and personal fees from Synapse Medicine, outside the submitted work. None declared (A. A., M. M., A. T., E. A.)

Additional information: The e-Figures and e-Table are available online under "Supplementary Data."

References

1. Gajic O, Ahmad SR, Wilson ME, Kaufman DA. Outcomes of critical illness: what is meaningful? *Curr Opin Crit Care.* 2018;24(5):394-400.
2. Hatch R, Young D, Barber V, Griffiths J, Harrison DA, Watkinson P. Anxiety, depression and post traumatic stress disorder after critical illness: a UK-wide prospective cohort study. *Crit Care.* 2018;22(1):310.
3. Legrand M. Negative trials in critical care medicine and the hurdles. *Lancet Respir Med.* 2018;6(10):e53.
4. Herridge MS, Cheung AM, Tansey CM, et al. One-year outcomes in survivors of the acute respiratory distress syndrome. *N Engl J Med.* 2003;348(8):683-693.
5. Cheung AM, Tansey CM, Tomlinson G, et al. Two-year outcomes, health care use, and costs of survivors of acute respiratory distress syndrome. *Am J Respir Crit Care Med.* 2006;174(5):538-544.
6. Hashem MD, Nallagangula A, Nalamalapu S, et al. Patient outcomes after critical illness: a systematic review of qualitative studies following hospital discharge. *Crit Care.* 2016;20(1):345.
7. Iwashyna TJ, Ely EW, Smith DM, Langa KM. Long-term cognitive impairment and functional disability among survivors of severe sepsis. *JAMA.* 2010;304(16):1787-1794.
8. Kosilek RP, Schmidt K, Baumeister SE, Gensichen J; SMOOTH Study Group. Frequency and risk factors of post-intensive care syndrome components in a multicenter randomized controlled trial of German sepsis survivors. *J Crit Care.* 2021;65:268-273.
9. Elliott D, McKinley S, Alison J, et al. Health-related quality of life and physical recovery after a critical illness: a multi-centre randomised controlled trial of a home-based physical rehabilitation program. *Crit Care.* 2011;15(3):R142.
10. Gandotra S, Files DC, Shields KL, Berry M, Bakhru RN. Activity levels in survivors of the ICU. *Phys Ther.* 2021: pzab135.
11. Geense WW, Boogaard M van den, Peters MAA, et al. Physical, mental, and cognitive health status of ICU survivors before ICU admission: a cohort study. *Crit Care Med.* 2020;48(9):1271-1279.
12. Jouan Y, Grammatico-Guillon L, Teixera N, et al. Healthcare trajectories before and after critical illness: population-based insight on diverse patients clusters. *Ann Intensive Care.* 2019;9(1):126.

13. Jones TK, Fuchs BD, Small DS, et al. Post-acute care use and hospital readmission after sepsis. *Ann Am Thorac Soc.* 2015;12(6):904-913.
14. Auriemma CL, Harhay MO, Haines KJ, Barg FK, Halpern SD, Lyon SM. What matters to patients and their families during and after critical illness: a qualitative study. *Am J Crit Care.* 2021;30(1):11-20.
15. Tuppin P, Rudant J, Constantinou P, et al. Value of a national administrative database to guide public decisions: from the système national d'information interrégimes de l'Assurance Maladie (SNIIRAM) to the système national des données de santé (SNDS) in France. *Rev Epidemiol Sante Publique.* 2017;65(Suppl 4):S149-S167.
16. Rachas A, Gastaldi-Ménager C, Denis P, et al. The economic burden of disease in France from the national health insurance perspective: the healthcare expenditures and conditions mapping used to prepare the French Social Security Funding Act and the Public Health Act. *Med Care.* 2022;60(9):655-664.
17. Studer M. WeightedCluster Library Manual: a practical guide to creating typologies of trajectories in the social sciences with R. 2013. https://www.centre-lives.ch/fr/bibcite/reference/84
18. Gabadinho A, Ritschard G, Müller NS, Studer M. Analyzing and visualizing state sequences in R with TraMineR. *J Statistical Software.* 2011;40:1-37.
19. Atramont A, Lindecker-Cournil V, Rudant J, et al. Association of age with short-term and long-term mortality among patients discharged from intensive care units in France. *JAMA Netw Open.* 2019;2(5):e193215.
20. Auriemma CL, O'Donnell H, Jones J, et al. Patient perspectives on states worse than death: a qualitative study with implications for patient-centered outcomes and values elicitation. *Palliat Med.* 2022;36(2):348-357.
21. Rubin EB, Buehler AE, Halpern SD. States worse than death among hospitalized patients with serious illnesses. *JAMA Intern Med.* 2016;176(10):1557-1559.
22. Wunsch H, Guerra C, Barnato AE, Angus DC, Li G, Linde-Zwirble WT. Three-year outcomes for Medicare beneficiaries who survive intensive care. *JAMA.* 2010;303(9):849-856.
23. Hill AD, Fowler RA, Pinto R, Herridge MS, Cuthbertson BH, Scales DC. Long-term outcomes and healthcare utilization following critical illness: a population-based study. *Crit Care.* 2016;20:76.
24. Peek GJ, Mugford M, Tiruvoipati R, et al. Efficacy and economic assessment of conventional ventilatory support versus extracorporeal membrane oxygenation for severe adult respiratory failure (CESAR): a multicentre randomised controlled trial. *Lancet.* 2009;374(9698):1351-1363.
25. Prescott HC, Langa KM, Liu V, Escobar GJ, Iwashyna TJ. Increased 1-year healthcare use in survivors of severe sepsis. *Am J Respir Crit Care Med.* 2014;190(1):62-69.
26. Groff AC, Colla CH, Lee TH. Days spent at home: a patient-centered goal and outcome. *N Engl J Med.* 2016;375(17):1610-1612.
27. Auriemma CL, Taylor SP, Harhay MO, Courtright KR, Halpern SD. Hospital-free days: a pragmatic and patient-centered outcome for trials among critically and seriously ill patients. *Am J Respir Crit Care Med.* 2021;204(8):902-909.
28. Law AC, Stevens JP, Choi E, et al. Days out of institution after tracheostomy and gastrostomy placement in critically ill older adults. *Ann Am Thorac Soc.* 2022;19(3):424-432.
29. Schofield-Robinson OJ, Lewis SR, Smith AF, McPeake J, Alderson P. Follow-up services for improving long-term outcomes in intensive care unit (ICU) survivors. *Cochrane Database Syst Rev.* 2018;11:CD012701.
30. Major ME, Dettling-Ihnenfeldt D, Ramaekers SPJ, Engelbert RHH, Schaaf M van der. Feasibility of a home-based interdisciplinary rehabilitation program for patients with post-intensive care syndrome: the REACH study. *Crit Care.* 2021;25(1):279.
31. Legrand M, Rossignol P. Cardiovascular consequences of acute kidney injury. *N Engl J Med.* 2020;382(23):2238-2247.
32. Gayat E, Hollinger A, Cariou A, et al. Impact of angiotensin-converting enzyme inhibitors or receptor blockers on post-ICU discharge outcome in patients with acute kidney injury. *Intensive Care Med.* 2018;44(5):598-605.
33. Dick A, Liu H, Zwanziger J, et al. Long-term survival and healthcare utilization outcomes attributable to sepsis and pneumonia. *BMC Health Serv Res.* 2012;12:432.
34. Jackson JC, Ely EW, Morey MC, et al. Cognitive and physical rehabilitation of intensive care unit survivors: results of the RETURN randomized controlled pilot investigation. *Crit Care Med.* 2012;40(4):1088-1097.
35. Wilson ME, Barwise A, Heise KJ, et al. Long-term return to functional baseline after mechanical ventilation in the ICU. *Crit Care Med.* 2018;46(4):562-569.
36. Huang M, Parker AM, Bienvenu OJ, et al. Psychiatric symptoms in acute respiratory distress syndrome survivors: a 1-year national multicenter study. *Crit Care Med.* 2016;44(5):954-965.
37. Neufeld KJ, Leoutsakos J-MS, Yan H, et al. Fatigue symptoms during the first year following ARDS. *Chest.* 2020;158(3):999-1007.
38. Gayat E, Cariou A, Deye N, et al. Determinants of long-term outcome in ICU survivors: results from the FROG-ICU study. *Crit Care.* 2018;22(1):8.
39. Bastian K, Hollinger A, Mebazaa A, et al. Association of social deprivation with 1-year outcome of ICU survivors: results from the FROG-ICU study. *Intensive Care Med.* 2018;44(12):2025-2037.