ORCA – Online Research @ Cardiff

Risk factors for 1-year mortality and hospital utilisation patterns in critical care survivors: a retrospective, observational, population-based data-linkage study

Short title: Risk factors of long-term mortality and hospital utilisation after ICU discharge

Tamas Szakmany MD, PhD, EDIC, DESA, FRCA, FFICM[1,*,$], Angharad M Walters MSc[2,*], Richard Pugh FRCA, FFICM[3], Ceri Battle PhD[4], Damon M Berridge PhD[2], Ronan A Lyons MD[2]

[*]Contributed equally to the manuscript

[1]Department of Anaesthesia, Intensive Care and Pain Medicine, Division of Population Medicine, Cardiff University, Heath Park Campus, Cardiff, CF14 4XN, UK

[2]Health Data Research UK, Swansea University Medical School, Data Science Building, Singleton Park, Swansea, SA2 8PP

[3]Anaesthetic Department, Glan Clywdd Hospital, Betsi Cadwaladar University Health Board, Rhuddlan Road, Bodelwyddan, Rhyl, LL18 5UJ, UK

[4]Critical Care Directorate, Morriston Hospital, Abertawe Bro Morgannwg University Health Board, Heol Maes Eglwys, Swansea, SA6 6NL, UK

[$]Corresponding author:

Dr Tamas Szakmany MD, PhD, EDIC, DESA, FRCA, FFICM

Senior Lecturer in Intensive Care, Department of Anaesthesia, Intensive Care and Pain Medicine, Division of Population Medicine, Cardiff University, Heath Park Campus, Cardiff, CF14 4XN, UK

Tel/Fax: +442920723112

e-mail: szakmanyt1@cardiff.ac.uk

No reprints will be ordered

Authors contributions

TSZ conceived and supervised the study, performed data interpretation, and developed the manuscript. AMW

extracted data, performed data analysis, and developed the manuscript. RP conceived the study, performed data

interpretation, and provided input on manuscript development. CB provided input on data interpretation, helped

write the manuscript, and provided critical input on its revisions. DMB performed data analysis and provided

critical input on manuscript revisions. RAL supervised the study, provided input on data interpretation, helped

write the manuscript, and provided critical input on its revisions.

Word count: 2983

Abstract

Objective: Clear understanding of the long-term consequences of critical care survivorship is essential. We investigated the care process and individual factors associated with long-term mortality among ICU survivors and explored hospital use in this group.

Design: Population based data linkage study using the Secure Anonymised Information Linkage (SAIL) databank.

Setting: All ICUs between 2006-2013 in Wales, UK.

Patients: We identified 40,631 patients discharged alive from Welsh adult ICUs.

Intervention: none.

Measurements and Main results: Primary outcome was 365-day survival. The secondary outcomes were 30 and 90-day survival and hospital utilisation in the 365 days following ICU discharge. Kaplan-Meier curves were plotted to compare survival rates. Cox proportional hazards regression models were used to determine risk factors of mortality. 7,883 (19.4%) patients died during the 1-year follow-up period. In the multivariable Cox regression analysis, advanced age and comorbidities were significant determinants of long-term mortality. Expedited discharge due to ICU bed shortage was associated with higher risk. The rate of hospitalisation in the year prior to the critical care admission was 28 hospitalised days/1000 days, post critical care was 88 hospitalised days/1000 days for those who were still alive; and 57 hospitalised days/1000 days and 412 hospitalised days/1000 days for those who died by the end of the study, respectively.

Conclusions: One in five ICU survivors die within one year, with advanced age and comorbidity being significant predictors of outcome, leading to high resource use. Care process factors indicating high system stress were associated with increased risk. More detailed understanding is needed on the effects of the potentially modifiable factors to optimise service delivery and improve long-term outcomes of the critically ill.

Introduction

Demand for critical care services is rising in many countries due to population ageing (1), advances in medical care and changes in patient, public and clinical expectations (2, 3). However, as healthcare becomes more expensive, there is heightened interest in the appropriate use of expensive care modalities, particularly where financial austerity is felt (4). For critical care, a clear understanding of the short- and long-term consequences of intervention is essential if access to critical care resources is to be robust, transparent and equitable (5).

The importance of age, acute physiological derangement and admission diagnosis in predicting intensive care unit (ICU) mortality have been long-established, though historically focus has been predominantly on short-term outcomes (e.g. ICU- or 30-day mortality) (6). More recent studies have suggested that beyond the initial critical illness, the rate and extent of recovery among critical care survivors is more dependent upon chronic morbidity and on sub-acute factors, than on acute illness (7-12) . To date no studies have explored the potential impact of care process factors on the long-term mortality of ICU survivors.

The aim of this study is to investigate care process and patient level factors associated with long-term mortality among ICU survivors. We also set out to explore the hospital use 1 year before critical care admission and 1 year following critical care discharge in this group.

Methods

Datasets

We used the Secure Anonymised Information Linkage (SAIL) databank (www.saildatabank.com) to investigate long-term hospital utilisation and mortality in patients surviving to critical care discharge. The development of the SAIL databank as a secure databank of anonymised person-based records has been described previously (13-15). The analysis of anonymised linked data was approved by the Information Governance Review Panel of the SAIL Collaboration Review System (Longitudinal analysis of Critical Care Outcomes in Wales, Project No: 0634, 20/06/2017)

The datasets linked within the SAIL databank we utilised for this study were: the Welsh Critical Care Dataset (WCCD, collated from the monthly exports of the Critical Care Minimum Dataset from all Welsh ICUs - including organ support, admission and discharge data), the Welsh Demographic Service Dataset (WDSD, demographic data submitted by primary care services), the Patient Episode Database for Wales (PEDW), and

the Annual District Death extract of the Office for National Statistics (ONS, see Supplementary Digital Content (SDC) for further details on Data Sources).

Study cohort

We identified our study population as patients discharged alive from Welsh adult ICUs between April 2006 and December 2013 from the WCCD. This dataset was linked with the WDSD to obtain patient factors such as week of birth, sex, date of death and anonymised address details. We used the week of birth to generate age on discharge date from critical care and anonymised NHS registration address histories to determine time periods over which patients had lived in Wales.

We included the first index critical care admissions for all patients aged 16 years or more discharged alive from critical care. We excluded patients transferred to another ICU, for whom we could not be sure of previous ICU exposure, and we excluded those discharged to palliative care. Furthermore, we limited the cohort to those with high quality matching from the identity linkage and anonymisation process. Patients were followed up until 365 days after ICU discharge, death or outward migration.

Sample classification

We used ICD-10 codes from the PEDW inpatient dataset to determine the reason for the hospital admission and specifically to determine if the admission was due to trauma using a formula we have developed previously and to generate the Comorbidity Index score (16, 17). The modified Charlson Comorbidity Index described by Bottle and Aylin was generated using ICD-10 codes from all hospital admissions in the year preceding the discharge date (17, 18) (see SDC for further details). Scores were categorised into three groups: low (-1-0), medium (1-10) and high (>10) (17). We used anonymised address histories to determine a patient's Welsh Index of Multiple Deprivation (WIMD) 2011 quintile (see SDC for further details).

Description of organisational constrains and care processes

On average, there are 3.2 intensive care beds per 100,000 people in Wales. All Welsh Critical Care units have participated in the Intensive Care National Audit and Research Centre Case Mix Programme (ICNARC CMP) since 2008. The Annual Quality reports generated by ICNARC have indicated that all Welsh critical care units

are within 2SD of the predicted mortality derived from the wider CMP database, with low reported numbers of critical care acquired infections and longer than average delays in discharging patients from critical care. Case mix, acuity, length of stay and number of organs supported among patients admitted to Critical Care units in Wales are otherwise consistent with that reported for the wider CMP population. We provide detailed links to publicly available reports and datasets which describe the organisational structure, the changes occurred, and the care processes applied in the Welsh critical care service in the SDC.

Outcomes

The primary outcome was 365-day survival. The secondary outcomes were 30 and 90-day survival and total number of days in hospital per 1000 days in the 365 days following ICU discharge.

Hospital days pre- and post-critical care

Days spent in hospital during the year before and the year after the index ICU admission was measured using the PEDW inpatient dataset for each patient and presented as a proportion of total 365 days pre-ICU and a proportion of time to migration, death or 365 days (whichever was the shortest), respectively. We also reported hospital days per 1000 follow-up days both before and after the index episode. Data errors such as null hospital admission and discharge dates were identified and excluded from the analysis.

Statistical analysis

Statistical analysis was performed in R using the 'Survival' and 'Survminer' packages (19).

Basic demographic data are presented as counts and percentages.

Cox proportional hazards regression models were used to determine risk factors of mortality. Variables were classified as individual patient and care process factors (See Table S1 in the SDC). The Akaike information criterion (AIC) and backward elimination methods were used separately to determine the significant factors associated with mortality. The likelihood ratio test was used in the backward elimination method using a significance level of $p<0.05$. We only considered main effects in this analysis; interaction terms were not included in the models. Proportional hazards were tested by observing the parallel $\ln[-\ln\{S(t)\}]$ curves for each variable and testing the correlation between scaled Schoenfeld residuals and Kaplan Meier survival time. Time dependent coefficients were incorporated in extended Cox models for variables that failed the proportional hazards assumption. Categories were created to denote missing data and we assumed data missing at random.

Results are presented in the form of hazard ratios (HR) with 95% confidence intervals (95% CI) and p-values.

Hospital utilisation is presented as median (IQR) and incident rate ratios were calculated from the ratios of the total days in hospital and the total follow-up time. The Wilcoxon rank-sum test was used to test for differences in the proportion of time spent in hospital between those alive at the end of the study and those who died.

Results

The critical care dataset included 68,577 episodes of care between 1st April 2006 and 31st December 2013. The following flowchart demonstrates how the survival cohort of 40,631 patients and the hospital utilisation cohort of 40,420 patients were obtained (Figure 1.).

Survival Analysis

Of the 40,631 patients discharged alive from critical care, 7,883 (19.4%) died during the 1-year follow-up period. Survival probability at 30 days, 90 days and 1 year following ICU discharge was 0.926 (95% CI 0.923-0.928), 0.885 (0.882-0.888) and 0.805 (0.801-0.809) respectively (Figure 2 and Figure S1 in SDC). This was almost identical throughout the study period (Figure S2 in SDC). Baseline characteristics, organ support and discharge data is shown in SDC Table S2 and Table S3. Comparison of patients who died without leaving the hospital following the index critical care admission vs. those who were discharged alive from the hospital but died later is presented in SDC Table S4.

The geographical distribution of the patients who died during the study period is presented in Figure 3.

In the multivariable Cox regression analysis, we found multiple patient and care process factors associated with higher risk of mortality after 1 year (Figure 4, also see SDC Table S5). Both the AIC and backward elimination methods identified the same variables. Advanced age and comorbidities were significant determinants of long term mortality (Figure S3 and S4 in SDC). Unplanned acute admissions, admissions for medical reasons, admissions from a hospital ward and the provision of basic respiratory, gastrointestinal, liver, neurological or renal support as defined by the CCMDS were associated with increased hazard (more detailed information on organ support definitions can be found in the SDC). Expedited discharge from the ICU due to critical care bed shortage and evening discharges were associated with higher risks of death. Discharges direct to home appear to

reduce the hazard. Details on the variables that failed the proportional hazards assumption are available in the SDC Table S6.

Hospital utilisation

40,420 patients were included in the hospital day utilisation aspect of the analysis, of whom 7,821 had died by the end of the study. The rate of hospitalisation in the year prior to the critical care admission was 28 hospitalised days/1000 days for those who were still alive at the end of the observation period and was 57 hospitalised days/1000 days for those who died by the end of the observation period. The rate during the follow-up period post critical care for those alive and those who died was 88 hospitalised days/1000 days and 412 hospitalised days/1000 days, respectively. The incident rate ratio of hospitalisation for those who were alive and those who died by the end of the study period was 3.19 (95% CI: 3.173, 3.198) and 7.28 (95% CI: 7.233, 7.320), respectively (Table S7 and Figure S5 and S6 in SDC). Of the 32,599 survivors, 17,696 were re-hospitalised during the follow-up period.

In the time period after the critical care admission, the proportion of follow-up time spent in hospital in those who died was significantly higher compared to those who were alive within 1-year of ICU discharge (median= 0.97 IQR= 0.69 for non-survivors vs. median= 0.04, IQR=0.08 for survivors, respectively, p< 0.001.)

Discussion

We found that one in five patients who were discharged alive from critical care died within 1 year, with most events within 90 days of ICU discharge. In a multi-variate analysis, advancing age and multiple comorbidities were associated with adverse outcome, together with need for multiple organ support and length of ICU stay. Importantly, we have discovered several organisational factors which were associated with improved survival, notably, discharge during the morning in office hours and discharge directly to home from the ICU. We found that those who died in the 1-year follow-up period had a higher rate of hospitalisation before and after the critical care admission. Almost half of the patients who died after critical care discharge, died before leaving hospital.

Our study is the first large scale population-based analysis of ICU survivors in the Welsh NHS, encompassing almost a decade. We have confirmed, that 1-year survival is primarily determined by patient factors such as age and chronic comorbidities (20). A contemporary population-based study looking at long-term outcomes over a

10-year period found almost identical 1-year mortality, risk factors and healthcare utilisation of ICU survivors in Canada (21). Similar to our findings age, comorbidity, and primary diagnosis were strongest predictors of 1-year survival in large cohorts of Australian and Dutch patients from point of hospital discharge after critical illness (10, 11). Lone et al. recently reported a 1-year mortality of 10.9% in Scotland (8). Whilst this appears to be half of our 19.5% mortality, their cohort only consisted of ICU survivors who were also alive at hospital discharge. We included all patients, who were discharged alive from the ICU and found that the post-ICU hospital mortality was 9.4%. Thus, our cohort also had a 1-year mortality of 10.8%, when we only look at ICU survivors who were alive at hospital discharge.

Half of the patients who died during our study period did so without leaving the hospital following the critical care index episode. These patients were older, had more comorbidities, had longer ICU stay and received more organ support compared to the ones who died following hospital discharge. It is also possible that these patients had higher illness severity on ICU admission, however we could not quantify this from data available for our analysis. Whilst it is plausible that higher severity of illness on ICU admission results in worse long-term outcomes, it appears to be more important in the short-term, within 30-days of ICU discharge when examined in large, population-based datasets (8, 22, 23). Indeed, investigating determinants of short- and long-term survival in a population-based study set between 1999-2008, Garland and colleagues concluded that short-term mortality was largely determined by acute illness factors, whereas mortality beyond three months was mainly determined by age and comorbidity (7). Our results suggest that despite surviving the acute organ dysfunction and ICU stay, patients older than 80 years of age with comorbidities are at high risk of death within 1-year of ICU discharge. The mortality following ICU discharge in this patient group was worse than the pessimistic prediction model developed in Norway, but similar to the data reported elsewhere on contemporary cohorts (5, 22, 23).

Large percentage of patients who died lived in geographical areas where the over 65 years old population is well above the Welsh average (24). However, in two areas (covered by Cwm Taf and Aneurin Bevan University Health Boards) the number of deaths over the study period seemed to be more closely aligned with high level of deprivation and known concentration of chronic illnesses, primarily due to strong industrial heritage, whilst the over 65 years old population is lower (24). Previously Welch et al. reported that significantly more patients are admitted to critical care in England from areas of high social deprivation, with worse hospital outcomes (25). Our data suggest that lack of critical care capacity may play part in the observed mortality as these are the two health boards that have the least amount of critical care beds per 100.000 population in Wales, whilst according

to the ICNARC data hospital mortality for patients admitted to the critical care units serving these areas was within 1SD of national average (26).

Admissions for medical conditions, patients needing multiple organ support and long ICU stay were independent predictors of death after 1-year of ICU discharge. All these factors have been reported previously as significant determinants of short-term ICU and hospital mortality (7, 10, 21, 27, 28). In line with the recently published analysis of the whole ICNARC dataset, admissions or discharges at night were not associated with adverse outcomes (29). On the other hand, premature discharge, due to lack of critical care bed availability, which happens usually out-of-hours and at times of high nursing and medical workload, is associated with higher mortality. Similar findings have been reported from multiple groups, giving external validity to our data (30, 31). Discharge to home directly from the ICU was associated with better outcome, presumably as patients in this group were younger with fewer comorbidities and reversible single system pathology, in keeping with the findings of Lau et al. (32).

We are the first to provide population-based data on hospital utilisation both before and after the index episode of ICU survivors. Our findings, that the length of hospitalisation in the year prior to ICU admission can be used as a predictor of post-ICU outcome, strengthen our argument on the importance of comorbidities and potentially frailty being key drivers for long-term mortality. The rate and length of hospitalisation associated with ICU survivorship can be used to inform health policy for health care systems similar to the Welsh NHS. Unsurprisingly, hospitalisation was longest amongst the non-survivors, both before and after ICU. This correlates with the high index of comorbidity in this group. Our results will help to inform discussions with patients, family members and healthcare professionals of the consequences of surviving an admission to ICU.

The strengths of this study are the use of a complete national cohort of patients, inclusion of all patients discharged from the ICU, near complete follow-up and use of an integrated data linkage system (14). These factors minimize the risks of selection and loss to follow up biases frequently encountered in prospective observational studies and provide external validity (33). However, there are certain limitations. The national administrative inpatient data lacks detailed information about disease severity and medical treatments, and co-morbidities based on the ICD-10 coding may not be accurate. We could not analyse the impact of illness severity on ICU admission, as this data is not available currently in the SAIL databank. Although this is an important limitation, the currently available evidence suggests following ICU and hospital discharge acute illness severity has diminishing impact on long-term outcomes (7, 8). We did not assess the impact of frailty,

which has been shown to have a significant association with short- and long-term mortality in other regions (34-36). In the current analysis, we were unable to evaluate some important long-term outcomes that are not routinely recorded, such as self-rated health and ability to perform activities of daily living. However, we are working on extending data linkage to primary and social care to evaluate outcomes expected to be related to these factors.

Conclusions

One in five ICU survivors die within one year, with advanced age and comorbidity being significant predictors of outcome. Premature discharge due to unavailability of ICU bed was associated with higher mortality. Hospital use before and after the ICU discharge was high, especially in non-survivors who tended to be older and with significant co-morbidities. While age and co-morbidity are non-modifiable factors, we highlighted potentially adaptable organisational and care process factors to optimise service provision and improve long-term outcomes of the critically ill.

References

1.   Halpern NA, Goldman DA, Tan KS, et al.: Trends in Critical Care Beds and Use Among Population Groups and Medicare and Medicaid Beneficiaries in the United States: 2000-2010. *Crit Care Med* 2016; 44:1490–1499

2.   Cox CE, Martinu T, Sathy SJ, et al.: Expectations and outcomes of prolonged mechanical ventilation. *Crit Care Med* 2009; 37:2888–94

3.   Pugh R, Subbe CP, Thorpe C, et al.: The Baby Boom and later life: is critical care fit for the future? *Anaesthesiol Intensive Ther* 2017; 49:441–444

4.   Angus DC: Admitting Elderly Patients to the Intensive Care Unit-Is it the Right Decision? *JAMA* 2017; 318:1443–1444

5.   Docherty AB, Anderson NH, Walsh TS, et al.: Equity of Access to Critical Care Among Elderly Patients in Scotland: A National Cohort Study. *Crit Care Med* 2016; 44:3–13

6.   Vincent J-L, Marshall JC, Namendys-Silva SA, et al.: Assessment of the worldwide burden of critical illness: the intensive care over nations (ICON) audit. *Lancet Respir Med* 2014; 2:380–386

7.   Garland A, Olafson K, Ramsey CD, et al.: Distinct determinants of long-term and short-term survival in critical illness. *Intensive Care Med* 2014; 40:1097–1105

8.   Lone NI, Gillies MA, Haddow C, et al.: Five-Year Mortality and Hospital Costs Associated with Surviving Intensive Care. *Am J Respir Crit Care Med* 2016; 194:198–208

9.   Ranzani OT, Zampieri FG, Besen BAMP, et al.: One-year survival and resource use after critical illness: impact of organ failure and residual organ dysfunction in a cohort study in Brazil. *Crit Care* 2015; 19:269

10.   Brinkman S, Bakhshi-Raiez F, Abu-Hanna A, et al.: Determinants of mortality after hospital discharge in ICU patients: literature review and Dutch cohort study. *Crit Care Med* 2013; 41:1237–1251

11.   Williams TA, Dobb GJ, Finn JC, et al.: Determinants of long-term survival after intensive care. *Crit Care Med* 2008; 36:1523–1530

12.   Kaarlola A, Tallgren M, Pettilä V: Long-term survival, quality of life, and quality-adjusted life-years among critically ill elderly patients. *Crit Care Med* 2006; 34:2120–2126

13.   Jones KH, Ford DV, Jones C, et al.: A case study of the Secure Anonymous Information Linkage (SAIL) Gateway: a privacy-protecting remote access system for health-related research and evaluation. *J Biomed Inform* 2014; 50:196–204

14.   Ford DV, Jones KH, Verplancke J-P, et al.: The SAIL Databank: building a national architecture for e-health research and evaluation. *BMC Health Serv Res* 2009; 9:157

15.   Lyons RA, Jones KH, John G, et al.: The SAIL databank: linking multiple health and social care datasets. *BMC Med Inform Decis Mak* 2009; 9:3

16.   Lyons RA, Turner S, Lyons J, et al.: All Wales Injury Surveillance System revised: development of a population-based system to evaluate single-level and multilevel interventions. *Inj Prev* 2016; 22 Suppl 1:i50–5

17.   Bottle A, Aylin P: Comorbidity scores for administrative data benefited from adaptation to local coding and diagnostic practices. *J Clin Epidemiol* 2011; 64:1426–1433

18.   Team CI: Summary Hospital-level Mortality Indicator (SHMI). 1st ed. NHS Digital; 2017. https://files.digital.nhs.uk/4E/52CC64/SHMI%20specification.pdf

19.   Crawley MJ: The R Book. Chichester, UK: John Wiley & Sons; 2012.

20.   Orwelius L, Nordlund A, Nordlund P, et al.: Pre-existing disease: the most important factor for health related quality of life long-term after critical illness: a prospective, longitudinal, multicentre trial. *Crit Care* 2010; 14:R67

21.   Hill AD, Fowler RA, Pinto R, et al.: Long-term outcomes and healthcare utilization following critical illness--a population-based study. *Crit Care* 2016; 20:76

22.   Chin-Yee N, D'Egidio G, Thavorn K, et al.: Cost analysis of the very elderly admitted to intensive care units. *Crit Care* 2017; 21:109

23.   Lindemark F, Haaland ØA, Kvåle R, et al.: Age, risk, and life expectancy in Norwegian intensive care: a registry-based population modelling study. *PLoS ONE* 2015; 10:e0125907

24.   Statistics OON: Broad Age Population Estimates in Wales https://www.healthmapswales.wales.nhs.uk/IAS/dataviews/report/multiple?reportId=60&viewId=178& geoTypeId=107,108,109,110,111 (accessed on 05/03/2018)

25.   Welch CA, Harrison DA, Hutchings A, et al.: The association between deprivation and hospital mortality for admissions to critical care units in England. *J Crit Care* 2010; 25:382–390

26.   Rhodes A, Ferdinande P, Flaatten H, et al.: The variability of critical care bed numbers in Europe. *Intensive Care Med* 2012; 38:1647–1653

27.   Garland A, Olafson K, Ramsey CD, et al.: A population-based observational study of intensive care unit-related outcomes. With emphasis on post-hospital outcomes. *Ann Am Thorac Soc* 2015; 12:202–208

28.   Brinkman S, de Jonge E, Abu-Hanna A, et al.: Mortality after hospital discharge in ICU patients. *Crit Care Med* 2013; 41:1229–1236

29.   Arulkumaran N, Harrison DA, Brett SJ: Association between day and time of admission to critical care and acute hospital outcome for unplanned admissions to adult general critical care units: cohort study exploring the 'weekend effect'. *British Journal of Anaesthesia* 2017; 118:112–122

30.   Yang S, Wang Z, Liu Z, et al.: Association between time of discharge from ICU and hospital mortality: a systematic review and meta-analysis. *Crit Care* 2016; 20:390

31.   Neuraz A, Guérin C, Payet C, et al.: Patient Mortality Is Associated With Staff Resources and Workload in the ICU: A Multicenter Observational Study. *Crit Care Med* 2015; 43:1587–1594

32.   Lau VI, Priestap FA, Lam JNH, et al.: Factors Associated With the Increasing Rates of Discharges Directly Home From Intensive Care Units-A Direct From ICU Sent Home Study. *Journal of Intensive Care Medicine* 2018; 33:121–127

33.   Williams TA, Leslie GD: Challenges and possible solutions for long-term follow-up of patients surviving critical illness. *Aust Crit Care* 2011; 24:175–185

34.   Flaatten H, de Lange DW, Morandi A, et al.: The impact of frailty on ICU and 30-day mortality and the level of care in very elderly patients (≥ 80 years). *Intensive Care Med* 2017; 43:1820–1828

35.   Heyland DK, Garland A, Bagshaw SM, et al.: Recovery after critical illness in patients aged 80 years or older: a multi-center prospective observational cohort study. *Intensive Care Med* 2015; 41:1911–1920

36.   Brummel NE, Bell SP, Girard TD, et al.: Frailty and Subsequent Disability and Mortality among Patients with Critical Illness. *Am J Respir Crit Care Med* 2017; 196:64–72

Figure legends

Figure 1. Organisational flowchart of the study

The Welsh Demographic Service dataset was linked with the critical care dataset to determine the week of birth, sex, date of death and anonymised address history	The Patient Episode Database for Wales was linked with the critical care dataset to determine the reason for the hospital admission and to generate the comorbidity index score	The Annual District Death Extract of the Office for National Statistics was linked with the critical care dataset to obtain the date of death

The Welsh Critical Care dataset includes organ support, admission and discharge data

68,577 episodes of care with discharge dates between 01/04/2006 and 31/12/2013

Included episodes from patients with high quality matching, n=67,597 (removed 980 episodes)

Included episodes from Welsh residents, n=61,801 (removed 5796 episodes)

Include episodes from patients aged 16+, n=61,223 (removed 578 episodes)

Include only the first critical care episode per patient, n=50,384 (removed 10,839 episodes)

Include those discharged alive, n=42,583 (removed 7801 episodes/patients)

Exclude those discharged to palliative care, n=42,368 (removed 215 episodes/patients)

Exclude continuing ICU care, n=40,677 (removed 1,691 episodes/patients)

Remove errors, n=40,631 (removed 46 episodes/patients)

Remove those with missing admission and discharge dates, n=40,428 (removed 203 patients)*

Only include those who lived in Wales during the year before the critcal care admission, n=40,420 (removed 8 patients)*

* Extra constraints applied for the health care utilisation aspect of the analysis

High quality matching: using the Matching Algorithm for Consistent Results in Anonymised Linkage (MACRAL) algorithm to apply deterministic record linkage and probabilistic record linkage methods to the set of linked variables (15); First critical care episode: re-admission episodes during the study period were excluded; Discharged alive: patients who died while on the ICU were excluded; Continuing ICU care: patients who were transferred internally within the same critical care unit were excluded.

Figure 2. 1-year survival probability of patients discharged from the Welsh intensive care units during the study period
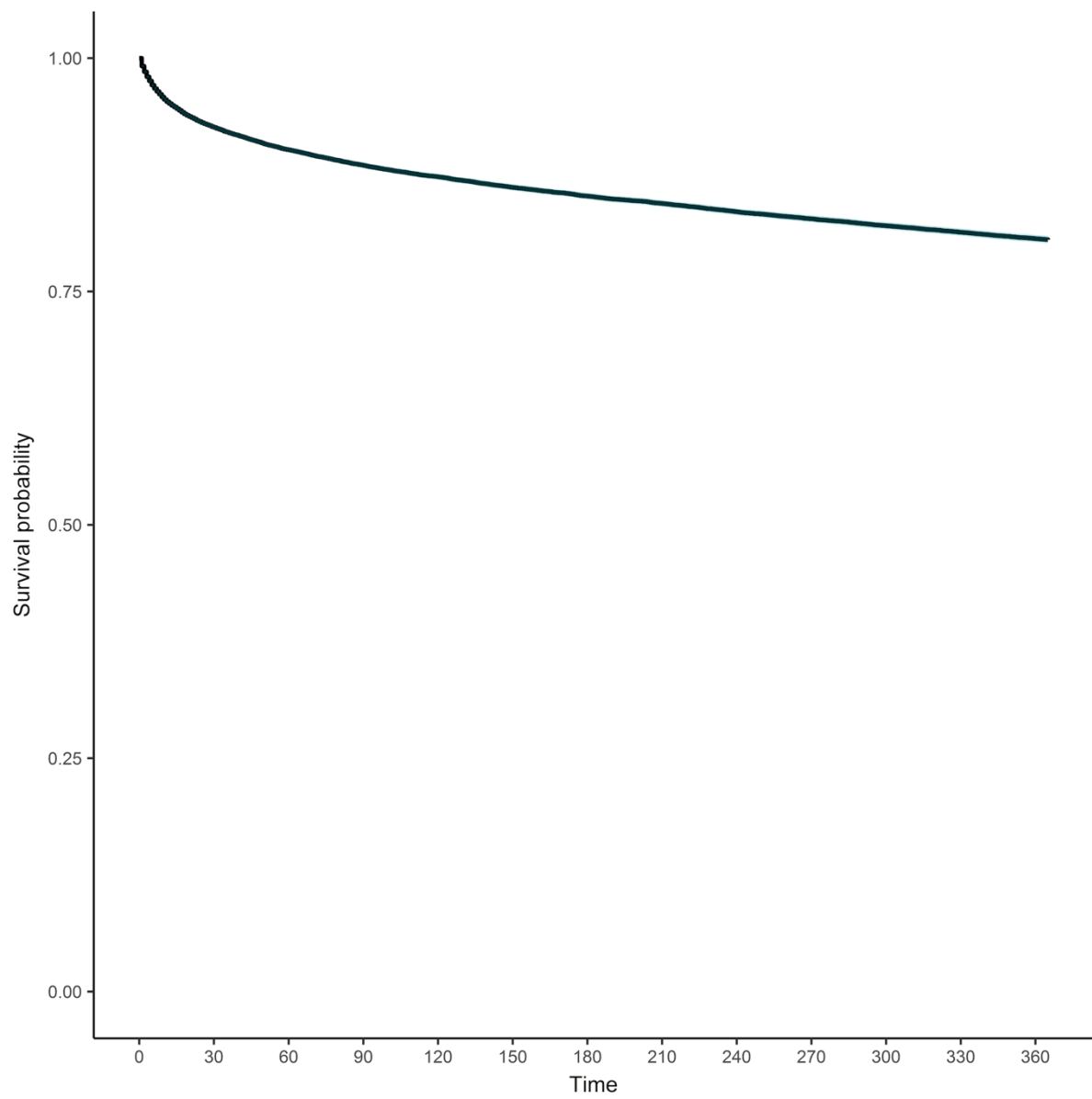
Figure 3. Geographical distribution of deaths during the study period
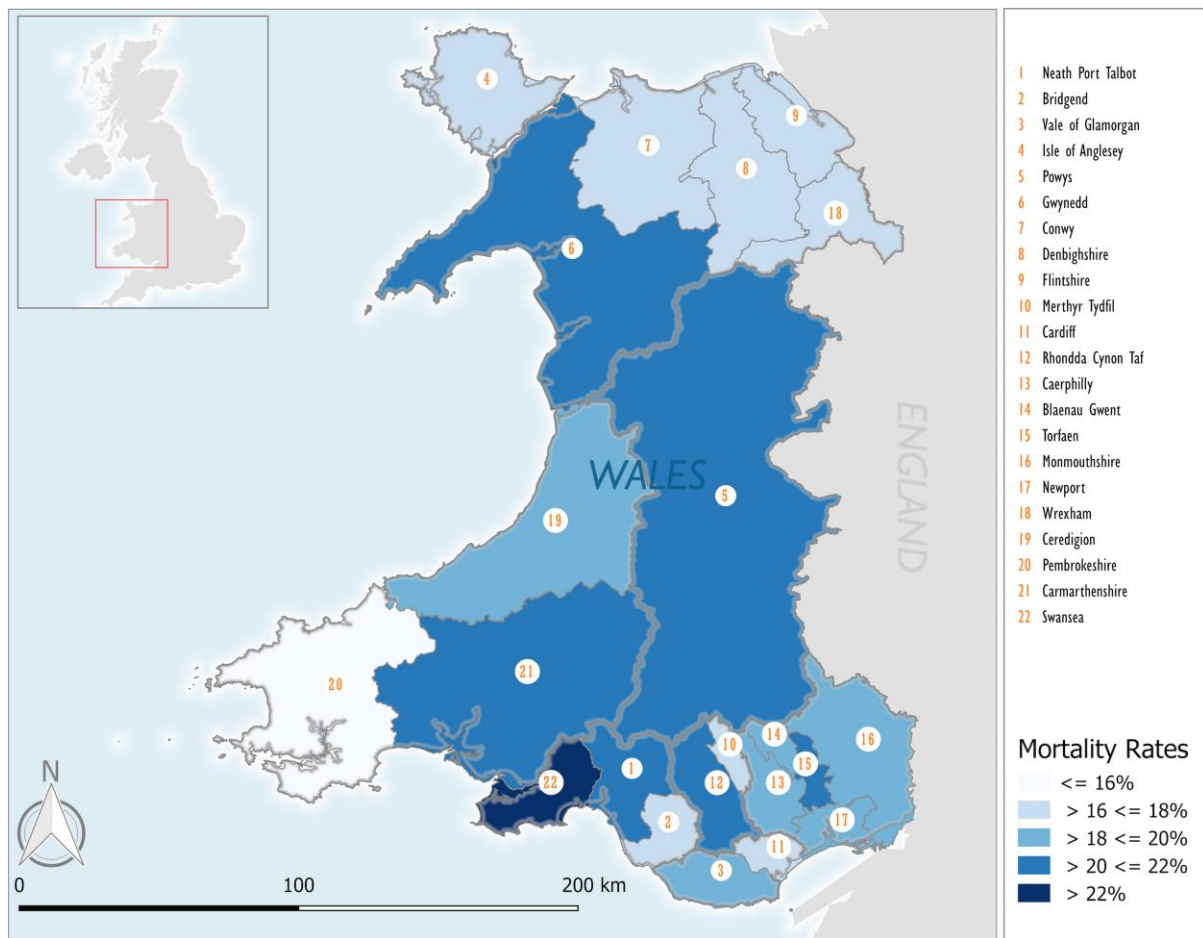
Percentage of death: % of patients who died during the entire study period in a Local Authority area. University Health Board boundaries (consisting of 2 or 3 Local Authorities) are depicted as grey borders. Population details of each Local Authority area is provided in Table S8 in the Supplemental Digital Content.

Figure 4. Factors affecting survival from the multivariate Cox-regression model

Age 50-59 (baseline: age<50)
Age 60-69 (baseline: age<50)
Age 70-79 (baseline: age<50)
Age >=80 (baseline: age<50)
Comorbidity index score: medium, 1-10 (baseline: low, -1-0)
Comorbidity index score: high, score > 10 (baseline: low, -1-0)
Sex: male (baseline: female)
WIMD quintile: most deprived (baseline: middle deprivation)
WIMD quintile: 2 (baseline: middle deprivation)
WIMD quintile: 4 (baseline: middle deprivation)
WIMD quintile: least deprived (baseline: middle deprivation)
Treatment site type: Acute hospital (baseline: major acute hospital)
Treatment speciality: medical (baseline: surgical)
Admission status: unplanned (baseline: planned)
Source location: Accident & Emergency (baseline: theatre and recovery)
Source location: Non-critical care ward (baseline: theatre and recovery)
Source location: HDU (baseline: theatre and recovery)
Source location: other (baseline: theatre and recovery)
Basic cardiovascular support (baseline: no support)
Basic respiratory support (baseline: no support)
Advanced respiratory support (baseline: no support)
Gastrointestinal support (baseline: no support)
Renal support (baseline: no support)
Liver support (baseline: no support)
Neurological support (baseline: no support)
Maximum organ support: 1 (baseline: 0)
Maximum organ support: 2 (baseline: 0)
Maximum organ support: 3-7 (baseline: 0)
LOS in days: 2-4 (baseline: 0-1)
LOS in days: >=5 (baseline: 0-1)
Discharge time: morning, out of hours, 06:00-08:00 (baseline: afternoon, in hours, 12:00-18:00)
Discharge time: morning, in hours, 08:00-12:00 (baseline: afternoon, in hours, 12:00-18:00)
Discharge time: evening, in hours, 18:00-20:00 (baseline: afternoon, in hours, 12:00-18:00)
Discharge time: evening, out of hours, 20:00-00:00 (baseline: afternoon, in hours, 12:00-18:00)
Discharge time: night, out of hours, 00:00-06:00 (baseline: afternoon, in hours, 12:00-18:00)
Discharge location: residence (baseline: ward)
Discharge location: other (baseline: ward)
Discharge location: HDU (baseline: ward)
Discharge status: specialised critical care transfer (baseline: ready)
Discharge status: self (baseline: ready)
Discharge status: early, critical care bed shortage (baseline: ready)
Discharge status: delayed, other bed shortage (baseline: ready)
Discharge status: continued critical care transfer (baseline: ready)

Statistical significance
at 5% level
— No
— Yes

Hazard ratio

WIMD: Welsh Index of Multiple Deprivation; Admission status: unplanned: acute admission from the Emergency Department or the ward; Comorbidity score calculation and organ support definitions are described in the Supplemental Digital Content; Acute hospital: provide a range of acute in-patient and out-patient services, specialist services (including some surgical acute specialties) but not the wide range available in major acute hospitals and may not have 24/7 Emergency Department. LOS: Length of stay; HDU: High dependency unit. Discharge status: specialised critical care transfer: Transferred from critical care unit for tertiary specialist critical care provision; Discharge status: early, critical care bed shortage: Transferred from critical care before deemed clinically ready to lower acuity beds due to ICU capacity reasons; Discharge status: continued critical care transfer: Transferred from critical care unit due to capacity reasons.

Supplementary Digital Content

Risk factors for 1-year mortality and hospital utilisation patterns in critical care survivors: a retrospective, observational, population-based data-linkage study

Tamas Szakmany[*], Angharad M Walters[*], Richard Pugh, Ceri Battle, Damon M Berridge, Ronan A Lyons

Data Sources

Critical Care Dataset

A database providing details of patients' episode of critical care within Welsh units [1]. The dataset includes patient factors such as treatment specialty and care process factors such as the organs supported and discharge time.

Patient Episode Database for Wales (PEDW)

This database contains NHS Wales inpatient and day-case hospital admissions with details of diagnoses recorded using ICD10 codes, procedures recorded using OPCS codes and administrative data such as admission and discharge dates [2].

Annual District Death Extract (ADDE)

This dataset includes death registrations of Welsh residents collected by the Office for National Statistics [3]. The data includes the date of death and underlying cause of death.

Welsh Demographic Service (WDS) Dataset (WDSD)

The WDSD records Welsh NHS patients' **demographic information [4]. The data holds patient address history and GP registrations and can be used to link** people to residences anonymously [5].

Welsh Index of Multiple Deprivation (WIMD) 2011

The Welsh Government creates the official measure of relative deprivation for Lower Super Output Areas (LSOAs) in Wales known as the Welsh Index of Multiple Deprivation (WIMD) [6]. In the current study, we used WIMD 2011. The measure is created using the following different types of deprivation: health, education, employment, income, community safety, geographical access to services, housing, and physical environment [6]. We used deprivation quintiles in this study where quintile 1 corresponds to the most deprived 20% of LSOAs in Wales and quintile 5 represents the least deprived 20% of LSOAs in Wales.

Further information on these datasets can be found at the SAIL databank website [7].

Calculating comorbidity index scores

Weights to calculate the Comorbidity index scores [8]:

Condition	Weight
1. Acute Myocardial Infarction	5
2. Cerebral Vascular Accident	11
3. Congestive Heart Failure	13
4. Connective Tissue disorder	4
5. Dementia	14
6. Diabetes	3
7. Liver disease	8
8. Peptic ulcer	9
9. Peripheral vascular disease	6
10. Pulmonary disease	4
11. Cancer	8
12. Diabetes complications	-1
13. Paraplegia	1
14. Renal disease	10
15. Metastatic cancer	14

| 16. Severe liver disease | 18 |
| 17. HIV* | 2 |

*Note that HIV data is not included in the SAIL databank [7].

The following table illustrates how the scores are calculated. The PEDW inpatients data is used to search for relevant ICD10 codes for the above conditions. Patient A has had an Acute Myocardial Infarction and has a Connective Tissue disorder. These have weights of 5 and 4 respectively therefore the total comorbidity score is 9.

Patient	Condition																	Total
	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	score
A	1	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	9
B	0	0	0	0	0	1	0	0	1	0	0	0	0	0	0	0	0	9

Description of Welsh Critical Care Services 2007-2013

On average, there are 3.2 critical care beds per 100,000 people in Wales.

	Number of critical care beds	Number of critical care consultants	Number of critical care admissions	Number of beds per 100.000 population
2007	175	85	8590	3.1
2013	169 (+11 PACU)	99	9234	3.2

This number varies between health boards, with some sites reporting higher numbers of beds for their local populations than others. In some cases, this difference is easy to explain. Large hospitals providing specialist care are more likely to treat people from outside their local area and therefore require more beds to

accommodate additional patients. In others, a relatively smaller number of beds reflect historical shortages in critical care. More detailed description of the Welsh Critical Care services and the challenges it faced during the study period could be found in the Annual Progress report of the Critical Care Networks [9].

To improve quality and collaborative working, common quality standards were introduced across Wales in 2007 in the Designed for life: Quality requirements for adult critical care services in Wales [10] Welsh Government initiative. This document defined the minimum staffing, monitoring and organ support capabilities for each tier of critical care units. To achieve operational collaboration, since 2008 the Critical Care Networks developed and each unit adopted a number of common guidelines, such as Admission and Discharge [11], Transfer of the critically ill adult patient [12], Tracheostomy care [13], Critical Care Outreach [14], Weaning from mechanical ventilation [15], Sedation [16], Management of severe respiratory failure [17] amongst others. Every critical care unit has been participating in the All Wales Surveillance for central venous catheter related infections and ventilator associated pneumonia. The surveillance data is in the public domain at the Welsh Healthcare Associated Infection Program website [18]. Several local and national quality improvement initiatives have been launched in this area [19, 20].

All Welsh Critical Care units have been participating in the Intensive Care National Audit and Research Centre Case Mix Programme (ICNARC CMP) since 2008. The Annual Quality reports from ICNARC show that all Welsh critical care units were within 2SD of the predicted mortality compared to the whole CMP database, with excellent results on critical care acquired infections and worse than average delays in discharging patients from critical care. The case mix, the acuity, the length of stay and the number of organs supported of the admitted patients was in-line with the CMP average [21].

CCMDS organ support definitions [22]

Basic respiratory support defined as:

• More than 50% oxygen delivered by face mask. (Note: more than 50% has been chosen to identify the more seriously ill patients in a hospital). Short-term increases in the fraction of inspired oxygen (FiO2) to facilitate procedures such as transfers or physiotherapy do not quality.

• Close observation due to the potential for acute deterioration to the point of needing advanced respiratory support. (e.g. severely compromised airway or deteriorating respiratory muscle function).

• Physiotherapy or suction to clear secretions at least two hourly, whether via tracheostomy, minitracheostomy or in the absence of an artificial airway.

• Patients recently (within 24 hours) extubated after a period (greater than 24 hours) of mechanical ventilation via endotracheal tube.

• Mask / hood continuous positive airway pressure (CPAP) or mark / hood Bi-level positive airway pressure ventilation (non-invasive ventilation).

• Patients who are intubated to protect the airway but needing no ventilatory support.

• Continuous positive airway pressure (CPAP) via a tracheostomy. Note. The presence of a tracheostomy used for long term airway access only does not quality for any respiratory support.

Advanced respiratory support defined as:

• Invasive medical ventilatory support applied via a trans-laryngeal tracheal tube or applied via a tracheostomy.

• Bi-level positive airway pressure applied via a trans-laryngeal tracheal tube or applied via a tracheostomy.

• Continuous positive airway pressure via a trans-laryngeal tracheal tube.

• Extracorporeal respiratory support.

Basic cardiovascular support defined as:

• Use of a central venous pressure (CVP) line for monitoring of central venous pressure and / or provision of central venous access to deliver titrated fluids to treat hypovolaemia.

• Use of an arterial line for monitoring of arterial pressure and / or sampling of arterial blood.

• Single intravenous vasoactive drug used to support or control arterial pressure, cardiac output or organ perfusion.

• Single intravenous rhythm controlling drug to support or control cardiac arrhythmias.

Advanced cardiovascular support defined as:

• Multiple intravenous vasoactive and / or rhythm controlling drugs when used simultaneously to support or control arterial pressure, cardiac output or organ perfusion (e.g. inotropes, amiodarone, nitrates). To qualify for advanced support status, at least one drug needs to be vasoactive.

• Continuous observation or cardiac output and derived indices (e.g. pulmonary artery catheter, lithium dilution, pulse contour analyses, oesophageal doppler).

• Intra-aortic balloon pumping and other assist devices.

• Insertion of a temporary cardiac pacemaker (criteria valid for each day of connection to a functioning external pacemaker unit).

Gastrointestinal support defined as:

• Feeding with parenteral or enteral nutrition (implies methods of feeding other than normal oral intake).

Liver support is defined where patients falls into one of the following categories:

• Acute on chronic Hepatocellular failure requiring management of coagulopathy and / or portal hypertension (including liver purification and detoxification techniques).

• Primary Acute Hepatocellular failure patients who are being considered for transplantation and require management of coagulopathy and / or portal hypertension (including liver purification and detoxification techniques)

Neurological support defined as:

• Central nervous system depression sufficient to prejudice the airway and protective reflexes, excepting that caused by sedation prescribed to facilitate mechanical ventilation or poisoning (e.g. deliberate or accidental overdose, alcohol, drugs etc.).

• Invasive neurological monitoring, e.g. intracranial pressure, jugular bulb sampling, external ventricular drain.

• Continuous intravenous medication to control seizures and / or continuous cerebral monitoring.

• Therapeutic hypothermia using coding protocols or devices.

Renal support in the context of critical illness, defined as:

• Acute renal replacement therapy (e.g. haemodialysis, haemofiltration etc.) or the provision of renal replacement therapy to a chronic renal failure patient who is requiring other acute organ support in a critical care situation.

Dermatological support defined as:

• Patients with major skin rashes, exfoliation or burns (e.g. greater than 30% body surface area affected).

• Use of complex dressings (e.g. large skin area greater than 30% body surface area, open abdomen, vacuum dressings or large trauma such as multiple limb or limb and head dressings).

Table S1. Patient, care process and organisational factors examined in Cox proportional hazards model analysis

Patient factors	Care process factors
Age group	Advanced Cardiovascular support
Comorbidity index score group	Basic Cardiovascular support
	Advanced Respiratory support
Sex	Basic Respiratory support
WIMD 2011 quintile	Dermatological support
Treatment speciality	Gastrointestinal support
	Liver support
	Neurological Support
	Renal Support
	Maximum Organ support on any given day
	Trauma/non-trauma patient
	Planned/unplanned admission
	Length of stay in days
	Admission Time
	Admission Source
	Source location
	Treatment site type
	Non-clinical transfer
	Discharge status

	Discharge location
	Discharge Destination
	Discharge Time

Organ support levels, admission and discharge definitions are defined by the Critical Care Minimum Dataset

[22]. WIMD: Welsh Index of Multiple Deprivation

Table S2. Baseline characteristics of the study cohort

Variable	level	All patients (n=40631) n (%)	Survivors (n=32748) n (%)	Non-survivors (n=7883) n (%)	p-value
Age (years)	<50	9398 (23.13%)	8815 (26.92%)	583 (7.40%)	<0.001
	50-59	5629 (13.85%)	4831 (14.75%)	798 (10.12%)	
	60-69	9324 (22.95%)	7585 (23.16%)	1739 (22.06%)	
	70-79	10122 (24.91%)	7633 (23.31%)	2489 (31.57%)	
	>=80	6158 (15.16%)	3884 (11.86%)	2274 (28.85%)	
Comorbidity index score	Low (-1-0)	11857 (29.18%)	11025 (33.67%)	832 (10.55%)	<0.001
	Medium (1-10)	13966 (34.37%)	11972 (36.56%)	1994 (25.30%)	
	High (>10)	14808 (36.45%)	9751 (29.78%)	5057 (64.15%)	
Sex	Female	18965 (46.68%)	15441 (47.15%)	3524 (44.70%)	<0.001
	Male	21666 (53.32%)	17307 (52.85%)	4359 (55.30%)	
Welsh Index of Multiple Deprivation 2011 (quintiles)	1= Most deprived	9755 (24.01%)	7870 (24.03%)	1885 (23.91%)	0.722
	2	8910 (21.93%)	7168 (21.89%)	1742 (22.10%)	
	3	8456 (20.81%)	6783 (20.71%)	1673 (21.22%)	
	4	7082 (17.43%)	5713 (17.45%)	1369 (17.37%)	
	5= Least deprived	6428 (15.82%)	5214 (15.92%)	1214 (15.40%)	
Admission specialty	Surgical	23877 (58.77%)	19817 (60.51%)	4060 (51.50%)	<0.001
	Medical	14461 (35.59%)	11104 (33.91%)	3357 (42.59%)	
	Missing	2293 (5.64%)	1827 (5.58%)	466 (5.91%)	
Admission status	Planned	10649 (26.21%)	9128 (27.87%)	1521 (19.30%)	<0.001
	Unplanned	27445 (67.55%)	21618 (66.01%)	5827 (73.92%)	
	Missing	2537 (6.24%)	2002 (6.11%)	535 (6.79%)	
Admission time	Afternoon	15413 (37.93%)	12534 (38.27%)	2879 (36.52%)	0.005
	Evening	14963 (36.83%)	12054 (36.81%)	2909 (36.90%)	
	Morning	4085 (10.05%)	3221 (9.84%)	864 (10.96%)	
	Night	6113 (15.05%)	4895 (14.95%)	1218 (15.45%)	

	Missing	57 (0.14%)	44 (0.13%)	13 (0.17%)	
Admission source	Same hospital site	38917 (95.78%)	31366 (95.78%)	7551 (95.79%)	0.021
	Other hospital site, same organisation	274 (0.67%)	212 (0.65%)	62 (0.79%)	
	Other hospital site, different organisation	291 (0.72%)	253 (0.77%)	38 (0.48%)	
	Missing	1149 (2.83%)	917 (2.80%)	232 (2.94%)	
Admission location	Theatre & Recovery	20427 (50.27%)	17085 (52.17%)	3342 (42.40%)	<0.001
	Emergency department	8621 (21.22%)	7240 (22.11%)	1381 (17.52%)	
	Ward	9612 (23.66%)	6846 (20.91%)	2766 (35.09%)	
	Other	1548 (3.81%)	1235 (3.77%)	313 (3.97%)	
	Missing	423 (1.04%)	342 (1.04%)	81 (1.03%)	
Trauma preceding critical care admission	No	35745 (87.97%)	28469 (86.93%)	7276 (92.30%)	<0.001
	Yes	4345 (10.69%)	3843 (11.74%)	502 (6.37%)	
	Missing	541 (1.33%)	436 (1.33%)	105 (1.33%)	

Comorbidity index score: Modified Charlson score by Bottle and AylinDifferences between patient characteristic variables in the survivor and non-survivor group were tested with chi-squared test (p<0.05 was considered statistically significant).

Table S3. Details of organ support provided on the ICU, length of stay and discharge characteristics of the patients.

Variable	level	All patients (n=40631)	Survivors (n=32748) n (%)	Non-survivors (n=7883) n (%)	p-value
Advanced cardiovascular support (use of two vasoactive agents and/or advanced haemodynamic monitoring)	No	35023 (86.20%)	28490 (87.00%)	6533 (82.88%)	<0.001
	Yes	4043 (9.95%)	3019 (9.22%)	1024 (12.99%)	
	Missing	1565 (3.85%)	1239 (3.78%)	326 (4.14%)	
Basic cardiovascular support (use of single vasoactive agents and/or arterial pressure monitoring)	No	7179 (17.67%)	5885 (17.97%)	1294 (16.42%)	0.005
	Yes	31836 (78.35%)	25567 (78.07%)	6269 (79.53%)	
	Missing	1616 (3.98%)	1296 (3.96%)	320 (4.06%)	

Advanced respiratory support (mechanical ventilation)	No	27203 (66.95%)	21995 (67.16%)	5208 (66.07%)	0.06
	Yes	12045 (29.64%)	9666 (29.52%)	2379 (30.179)	
	Missing	1383 (3.40%)	1087 (3.32%)	296 (3.76%)	
Basic respiratory support (supplemental oxygen, including non-invasive ventilation)	No	15801 (38.89%)	13213 (40.35%)	2588 (32.83%)	<0.001
	Yes	23265 (57.26%)	18305 (55.90%)	4960 (62.92%)	
	Missing	1565 (3.85%)	1230 (3.76%)	335 (4.25%)	
Gastrointestinal support (enteral or parenteral feeding)	No	29632 (72.93%)	24352 (74.36%)	5280 (66.98%)	<0.001
	Yes	9501 (23.38%)	7208 (22.01%)	2293 (29.09%)	
	Missing	1498 (3.69%)	1188 (3.63%)	310 (3.93%)	

Renal support (renal replacement therapy)	No	36093 (88.83%)	29450 (89.93%)	6643 (84.27%)	<0.001
	Yes	2900 (7.14%)	1999 (6.10%)	901 (11.43%)	
	Missing	1638 (4.03%)	1299 (3.97%)	339 (4.30%)	
Liver support	No	37773 (92.97%)	30453 (92.99%)	7320 (92.86%)	0.002
	Yes	121 (0.30%)	82 (0.25%)	39 (0.50%)	
	Missing	2737 (6.74%)	2213 (6.76%)	524 (6.65%)	
Neurological support	No	36082 (88.80%)	29151 (89.02%)	6931 (87.92%)	0.009
	Yes	3529 (8.69%)	2805 (8.56%)	724 (9.18%)	
	Missing	1020 (2.51%)	792 (2.42%)	228 (2.89%)	
Dermatological support	No	37185 (91.52%)	30003 (91.62%)	7182 (91.11%)	0.183
	Yes	2054 (5.06%)	1649 (5.04%)	405 (5.14%)	
	Missing	1392 (3.43%)	1096 (3.35%)	296 (3.76%)	
Maximum organs supported	0	4480 (11.03%)	3761 (11.49%)	719 (9.12%)	<0.001
	1	18228 (44.86%)	15013 (45.84%)	3215 (40.78%)	
	2	8291 (20.41%)	6532 (19.95%)	1759 (22.31%)	
	3-7	8203 (20.19%)	6328 (19.32%)	1875 (23.79%)	
	Missing	1429 (3.52%)	1114 (3.40%)	315 (4.00%)	

LOS (days)	0-1	15765 (38.80%)	13354 (40.78%)	2411 (30.59%)	<0.001
	2-4	14695 (36.17%)	11741 (35.85%)	2954 (37.47%)	
	>=5	10171 (25.03%)	7653 (23.37%)	2518 (31.94%)	
Discharge time	Afternoon, in hours (12:00-18:00)	23521 (57.89%)	19079 (58.26%)	4442 (56.35%)	<0.001
	Evening, in hours (18:00-20:00)	8829 (21.73%)	6880 (21.01%)	1949 (24.72%)	
	Evening, out of hours (20:00-24:00)	1567 (3.86%)	1186 (3.62%)	381 (4.83%)	
	Morning, in hours (08:00-12:00)	5376 (13.23%)	4560 (13.93%)	816 (10.35%)	
	Morning, out of hours (06:00-08:00)	117 (0.29%)	93 (0.28%)	24 (0.30%)	
	Night, out of hours (00:00-06:00)	1121 (2.76%)	869 (2.65%)	252 (3.20%)	
	Missing	100 (0.25%)	81 (0.25%)	19 (0.24%)	
Discharge location	Ward	35386 (87.09%)	28332 (86.52%)	7054 (89.48%)	<0.001
	HDU	1291 (3.18%)	953 (2.91%)	338 (4.29%)	

	Other	775 (1.91%)	661 (2.02%)	114 (1.45%)	
	Home	1875 (4.61%)	1774 (5.42%)	101 (1.28%)	
	Missing	1304 (3.21%)	1028 (3.14%)	276 (3.50%)	
Discharge destination	Same hospital site	37229 (91.63%)	29790 (90.97%)	7439 (94.3%)	<0.001
	Other hospital site in the same organisation	410 (1.01%)	325 (0.99%)	85 (1.08%)	
	Other hospital site in different organisation	530 (1.3%)	405 (1.24%)	125 (1.59%)	
	Non-hospital	1863 (4.59%)	1762 (5.38%)	101 (1.28%)	
	Missing	599 (1.47%)	466 (1.42%)	133 (1.69%)	
Discharge status	Ready for critical care discharge	19323 (47.56%)	15830 (48.34%)	3493 (44.31%)	<0.001
	Transfer for continued critical care	1115 (2.74%)	837 (2.56%)	278 (3.53%)	
	Delayed – ward bed shortage	17923 (44.11%)	14293 (43.65%)	3630 (46.05%)	
	Early - critical care bed shortage	881 (2.17%)	682 (2.08%)	199 (2.52%)	
	Self	117 (0.29%)	110 (0.34%)	7 (0.09%)	
	Specialised critical care transfer	221 (0.54%)	167 (0.51%)	54 (0.69%)	

	Missing	1051 (2.59%)	829 (2.53%)	222 (2.82%)	

Organ support levels are defined by the Critical Care Minimum Dataset [22]. LOS: Length of stay; HDU: High dependency unit. Transfer for continued critical care: Transferred from critical care unit due to capacity reasons; Early – Critical care bed shortage: Transferred from critical care before deemed clinically ready to lower acuity beds due to capacity reasons; Specialised critical care transfer: Transferred from critical care unit for tertiary specialist critical care provision. P-values resulting from chi-squared tests of association between each patient characteristic and mortality.

Table S4. Characteristics of those who died during the index hospitalisation versus those who died following

the index hospitalisation

Variable	level	Died following index hospitalisation (n=4129)	Died during index hospitalisation (n=3754)	p
Age (years)	<50	373 (9.03%)	210 (5.59%)	<0.001
	50-59	478 (11.58%)	320 (8.52%)	
	60-69	1011 (24.49%)	728 (19.39%)	
	70-79	1306 (31.63%)	1183 (31.51%)	
	>=80	961 (23.27%)	1313 (34.98%)	
Comorbidity index score	Low (-1 – 0)	424 (10.27%)	408 (10.87%)	0.034
	Medium (1-10)	1094 (26.50%)	900 (23.97%)	
	High (> 10)	2611 (63.24%)	2446 (65.16%)	
Sex	Male	2352 (56.96%)	2007 (53.46%)	0.002
	Female	1777 (43.04%)	1747 (46.54%)	
Welsh Index of Multiple Deprivation 2011 (quintiles)	1=Most deprived	981 (23.76%)	904 (24.08%)	0.46
	2	913 (22.11%)	829 (22.08%)	
	3	900 (21.80%)	773 (20.59%)	
	4	724 (17.54%)	645 (17.18%)	
	5=Least deprived	611 (14.80%)	603 (16.06%)	
Hospital type	Acute Hospital	603 (14.60%)	542 (14.44%)	0.644
	Major Acute Hospital	3389 (82.08%)	3073 (81.86%)	
	Missing	137 (3.32%)	139 (3.70%)	
Admission speciality	Medical	1589 (38.48%)	1768 (47.10%)	<0.001

	Missing	263 (6.37%)	203 (5.41%)	
	Surgical	2277 (55.15%)	1783 (47.50%)	
Admission status	Unplanned	2782 (67.38%)	3045 (81.113)	<0.001
	Planned	1053 (25.50%)	468 (12.47%)	
	Missing	294 (7.12%)	241 (6.42%)	
Admission source	Other Site Different Trust	16 (0.39%)	22 (0.59%)	0.266
	Other Site Same Trust	35 (0.85%)	27 (0.72%)	
	Missing	132 (3.20%)	100 (2.66%)	
	Same Site	3946 (95.57%)	3605 (96.03%)	
Admission location	Emergency Department	754 (18.26%)	627 (16.70%)	<0.001
	HDU	13 (0.32%)	28 (0.75%)	
	Ward	1176 (28.48%)	1590 (42.36%)	
	Other	131 (3.17%)	141 (3.76%)	
	Theatre & Recovery	2007 (48.61%)	1335 (35.56%)	
	Missing	48 (1.16%)	33 (0.88%)	
Trauma preceding critical care admission	No	3810 (92.27%)	3466 (92.33)	<0.001
	Yes	227 (5.50%)	275 (7.33%)	
	Missing	92 (2.23%)	13 (0.35%)	
Advanced cardiovascular support	No	3547 (85.91%)	2986 (79.54%)	<0.001
	Yes	418 (10.12%)	606 (16.14%)	
	Missing	164 (3.97%)	162 (4.32%)	
Basic cardiovascular support	No	744 (18.02%)	550 (14.65%)	<0.001
	Yes	3229 (78.20%)	3040 (80.98%)	
	Missing	156 (3.78%)	164 (4.37%)	

Advanced respiratory support	No	2899 (70.21%)	2309 (61.51%)	<0.001
	Yes	1081 (26.18%)	1298 (34.58%)	
	Missing	149 (3.61%)	147 (3.92%)	
Basic respiratory support	No	1445 (34.99%)	1143 (30.45%)	<0.001
	Yes	2514 (60.89%)	2446 (65.16%)	
	Missing	170 (4.12%)	165 (4.40%)	
Gastrointestinal support	No	3011 (72.92%)	2269 (60.44%)	<0.001
	Yes	962 (23.30%)	1331 (35.46%)	
	Missing	156 (3.78%)	154 (4.10%)	
Renal support	No	3582 (86.75%)	3061 (81.54%)	<0.001
	Yes	376 (9.11%)	525 (13.99%)	
	Missing	171 (4.14%)	168 (4.48%)	
Liver support	No	3853 (93.32%)	3467 (92.36%)	0.149
	Yes	16 (0.39%)	23 (0.61%)	
	Missing	260 (6.30%)	264 (7.03%)	
Neurological support	No	3714 (89.95%)	3217 (85.69%)	<0.001
	Yes	306 (7.41%)	418 (11.14%)	
	Missing	109 (2.64%)	119 (3.17%)	
Dermatological support	No	3817 (92.44%)	3365 (89.64%)	<0.001
	Yes	167 (4.05%)	238 (6.34%)	
	Missing	145 (3.51%)	151 (4.02%)	
Maximum organs supported	0	426 (10.32%)	293 (7.81%)	<0.001
	1	1884 (45.63%)	1331 (35.46%)	
	2	894 (21.65%)	865 (23.04%)	
	3-7	765 (18.53%)	1110 (29.57%)	
	Missing	160 (3.87%)	155 (4.13%)	
LOS (days)	0-1	1447 (35.04%)	964 (25.68%)	<0.001

	2-4	1608 (38.94%)	1346 (35.85%)	
	>=5	1074 (26.01%)	1444 (38.47%)	
Discharge time	Afternoon, in hours (12:00-18:00)	2398 (58.08%)	2044 (54.45%)	<0.001
	Evening, in hours (18:00-20:00)	930 (22.52%)	1019 (27.14%)	
	Evening, out of hours (20:00-24:00)	186 (4.51%)	195 (5.19%)	
	Morning, in hours (08:00-12:00)	466 (11.29%)	350 (9.32%)	
	Morning, out of hours (06:00-08:00)	15 (0.36%)	9 (0.24%)	
	Night, out of hours (00:00-06:00)	125 (3.03%)	127 (3.38%)	
	Missing	9 (0.22%)	10 (0.27%)	
Discharge location	HDU	166 (4.02%)	172 (4.58%)	<0.001
	Other	44 (1.07%)	70 (1.87%)	
	Home	101 (2.45%)	0 (0.00%)	
	Missing	153 (3.70%)	123 (3.28%)	
	Ward	3665 (88.76%)	3389 (90.28%)	
Discharge status	Transfer for continued critical care	128 (3.10%)	150 (3.99%)	0.004

39

	Delayed - ward bed shortage	1889 (45.75%)	1741 (46.38%)	
	Early - critical care bed shortage	89 (2.16%)	110 (2.93%)	
	Ready for critical care discharge	1864 (45.14%)	1629 (43.39%)	
	Self	7 (0.17%)	0 (0.00%)	
	Specialised critical care transfer	26 (0.63%)	28 (0.74%)	
	Missing	126 (3.05%)	96 (2.56%)	

Comorbidity score: modified Charlson score by Bottle and Aylin; Acute hospital: provide a range of acute in-patient and out-patient services, specialist services (including some surgical acute specialties) but not the wide range available in major acute hospitals and may not have 24/7 Emergency Department. Organ support levels are defined by the Critical Care Minimum Dataset [22]. LOS: Length of stay; HDU: High dependency unit.

Transfer for continued critical care: Transferred from critical care unit due to capacity reasons; Early – Critical care bed shortage: Transferred from critical care before deemed clinically ready to lower acuity beds due to capacity reasons; Specialised critical care transfer: Transferred from critical care unit for tertiary specialist critical care provision. P-values resulting from chi-squared tests of association between each patient characteristic and group.

Table S5. Results of the multivariate Cox proportional hazards model analysis

Variable	Level	HR (95%CI)	P-value
Age (baseline: age<50)	50-59	1.77 (1.59, 1.97)	<0.001
	60-69	2.19 (1.99, 2.42)	<0.001
	70-79	2.81 (2.55, 3.09)	<0.001
	Age>=80	4.76 (4.32, 5.25)	<0.001
Comorbidity Index Score (baseline: low -1-0)	Medium (1 - 10)	1.7 (1.56, 1.85)	<0.001
	High (> 10)	3.82 (3.54, 4.13)	<0.001
Sex (baseline: Female)	Male	1.07 (1.02, 1.12)	0.004
WIMD quintile (baseline: middle deprivation)	Most deprived	1.08 (1.01, 1.15)	0.025
	2	1 (0.93, 1.06)	0.892
	4	0.97 (0.91, 1.05)	0.452
	Least deprived	0.94 (0.87, 1.01)	0.116
Treatment site type (baseline: major acute hospital)	Acute hospital	0.93 (0.87, 1)	0.036
	Missing	1.01 (0.86, 1.19)	0.905
Treatment speciality (baseline: surgical)	Medical	1.33 (1.25, 1.41)	<0.001
	Missing	1.15 (1.01, 1.3)	0.029
Admission status (baseline: planned)	Unplanned	1.52 (1.42, 1.63)	<0.001
	Missing	1.24 (1.06, 1.46)	0.008

Source location (baseline: theatre and recovery)	Accident & emergency	0.93 (0.86, 1.01)	0.097
	HDU	1.11 (0.81, 1.52)	0.502
	Non-critical care ward	1.36 (1.27, 1.45)	<0.001
	Other	1.09 (0.95, 1.25)	0.212
	Missing	1.02 (0.78, 1.34)	0.858
Basic cardio support (baseline: no)	Yes	0.85 (0.79, 0.92)	<0.001
	Missing	0.9 (0.69, 1.18)	0.464
Advanced respiratory support (baseline: no)	Yes	0.85 (0.78, 0.92)	<0.001
	Missing	0.97 (0.62, 1.52)	0.895
Basic respiratory support (baseline: no)	Yes	1.07 (1.01, 1.13)	0.015
	Missing	1.41 (0.93, 2.14)	0.110
Gastrointestinal support (baseline: no)	Yes	1.17 (1.07, 1.27)	<0.001
	Missing	0.95 (0.6, 1.52)	0.837
Renal support (baseline: no)	Yes	1.13 (1.04, 1.23)	0.003
	Missing	0.89 (0.57, 1.4)	0.622
Liver support (baseline: no)	Yes	1.45 (1.05, 1.99)	0.023
	Missing	0.88 (0.73, 1.06)	0.177
Neurological support (baseline: no)	Yes	1.2 (1.1, 1.32)	<0.001
	Missing	1.19 (0.69, 2.03)	0.529

Maximum organ support (baseline: 0)	1	1.09 (0.97, 1.23)	0.127
	2	1.28 (1.12, 1.47)	<0.001
	3-7	1.26 (1.06, 1.51)	0.009
	Missing	1.14 (0.77, 1.7)	0.512
LOS in days (baseline: 0-1)	2-4	1.09 (1.03, 1.15)	0.004
	>=5	1.18 (1.1, 1.27)	<0.001
Discharge time (baseline: afternoon, in hours 12:00-18:00)	Evening, in hours (18:00-20:00)	1.07 (1.01, 1.13)	0.018
	Evening, out of hours (20:00-24:00)	1.17 (1.05, 1.3)	0.004
	Morning, in hours (08:00-12:00)	0.88 (0.82, 0.95)	0.001
	Morning, out of hours (06:00-08:00)	0.99 (0.66, 1.48)	0.964
	Night, out of hours (00:00-06:00)	1.08 (0.95, 1.23)	0.260
	Missing	0.78 (0.49, 1.24)	0.292
Discharge location (baseline: ward)	HDU	1.13 (0.97, 1.32)	0.119
	Other	0.8 (0.66, 0.96)	0.019
	Residence	0.44 (0.36, 0.54)	<0.001
	Missing	1.07 (0.86, 1.34)	0.518
Discharge status (baseline: ready)	Continued critical care transfer	1.05 (0.88, 1.26)	0.595
	Delayed, other bed shortage	0.95 (0.9, 1)	0.052
	Early, critical care bed shortage	1.19 (1.02, 1.38)	0.027
	Self	1.99 (0.93, 4.27)	0.076
	Specialised critical care transfer	1.03 (0.77, 1.38)	0.834
	Missing	1.12 (0.84, 1.49)	0.458

Acute hospital: provide a range of acute in-patient and out-patient services, specialist services (including some surgical acute specialties) but not the wide range available in major acute hospitals and may not have 24/7 Emergency Department.

Organ support levels are defined by the Critical Care Minimum Dataset [22]. LOS: Length of stay; HDU: High dependency unit. Transfer for continued critical care: Transferred from critical care unit due to capacity reasons; Early – Critical care bed shortage: Transferred from critical care before deemed clinically ready to lower acuity beds due to capacity reasons; Specialised critical care transfer: Transferred from critical care unit for tertiary specialist critical care provision.

Table S6. Hazard ratios and confidence intervals of time dependent coefficients

Variables and levels	Time (0, 6]	Time (6, 14]	Time (14, 30]	Time (30, 90]	Time (90, 180]	Time (180, 365]
Age (years) 60-69	2.72 (2.11, 3.52)	2.63 (1.89, 3.66)	2.25 (1.65, 3.08)	1.89 (1.53, 2.33)	2.15 (1.7, 2.72)	1.99 (1.65, 2.39)
Age (years) 70-79	3.47 (2.7, 4.45)	3.53 (2.56, 4.87)	3.47 (2.57, 4.68)	2.48 (2.03, 3.04)	2.59 (2.05, 3.26)	2.37 (1.98, 2.84)
Age (years) >=80	7.32 (5.72, 9.38)	6.04 (4.37, 8.34)	5.65 (4.17, 7.65)	4.17 (3.4, 5.12)	4.47 (3.53, 5.65)	3.34 (2.76, 4.03)
Comorbidity score>10	2.9 (2.41, 3.49)	3.43 (2.68, 4.37)	3.57 (2.84, 4.49)	4.26 (3.59, 5.05)	4.56 (3.75, 5.55)	3.95 (3.4, 4.59)
Treatment speciality - medical	1.43 (1.25, 1.64)	1.55 (1.29, 1.85)	1.47 (1.24, 1.74)	1.27 (1.12, 1.44)	1.16 (1, 1.35)	1.22 (1.07, 1.38)
Admission status - unplanned	2.9 (2.32, 3.62)	1.93 (1.52, 2.45)	1.78 (1.44, 2.2)	1.68 (1.45, 1.94)	1.48 (1.28, 1.72)	1.06 (0.94, 1.2)

	(0, 6 days]	(6, 14 days]	(14, 30 days]	(30, 90 days]	(90, 180 days]	(180, 365 days]
Source location - A&E	1.25 (1.03, 1.51)	1.18 (0.93, 1.51)	0.83 (0.65, 1.07)	0.9 (0.76, 1.07)	0.81 (0.67, 0.99)	0.88 (0.74, 1.03)
Source location - non critical care ward	1.9 (1.62, 2.23)	1.68 (1.37, 2.07)	1.71 (1.42, 2.07)	1.28 (1.11, 1.47)	1.04 (0.88, 1.22)	1.1 (0.96, 1.26)
Neurological support - yes	1.89 (1.6, 2.23)	1.07 (0.83, 1.39)	1.07 (0.83, 1.37)	1.07 (0.89, 1.29)	1.07 (0.87, 1.31)	1.07 (0.89, 1.27)
Discharge time – evening, in hours (18:00-20:00)	1.36 (1.2, 1.54)	1.1 (0.93, 1.29)	1.02 (0.87, 1.2)	0.98 (0.87, 1.11)	1.09 (0.95, 1.25)	0.93 (0.83, 1.05)
Discharge location – residence	0.11 (0.04, 0.3)	0.26 (0.11, 0.58)	0.44 (0.23, 0.82)	0.47 (0.31, 0.72)	0.39 (0.24, 0.66)	0.72 (0.52, 0.98)

A&E: Accident and Emergency Department; Organ support levels are defined by the Critical Care Minimum Dataset [22]. Table shows the categories that failed the proportional hazards assumption along with the hazard ratios and 95% confidence intervals for the following 6 time-intervals: (0, 6 days], (6, 14 days], (14, 30 days], (30, 90 days], (90, 180 days] and (180, 365 days].

Table S7. Incident rates and ratios of hospital admission in survivors and non-survivors after 1 year following ICU discharge

	Total hospital days before index critical care admission	Total follow-up days before index critical care admission	Total hospital days post ICU discharge	Total follow-up days post ICU discharge	Incident rate before index critical care admission per 1000 days	Incident rate post ICU discharge per 1000 days	Incident rate ratio (95% CI)
Survivors	327,625	11,898,635	1,037,270	11,825,343	28	88	3.1857 (3.1732, 3.1982)
Non-survivors	161,517	2,854,665	329,010	799,126	57	412	7.2766 (7.2334, 7.3201)

Incident rate before index critical care admission: Total hospital days before index critical care admission divided by Total follow-up days before index critical care admission multiplied by a thousand.

Incident rate post ICU discharge: Total hospital days post ICU discharge divided by Total follow-up days post ICU discharge multiplied by a thousand

Incident rate ratio: Incident rate post ICU discharge divided by Incident rate before index critical care admission

Table S8. Demographic details of Welsh Counties pictured in Figure 3.

Name of Local Authority	Population in 2013 (n)	Percentage of population >65 years	Number of people above the age 65 (n)
Isle of Anglesey	70091	23.7	16579
Gwynedd	121911	21.9	26672
Conwy	115835	25.7	29757
Denbighshire	94510	22.4	21189
Flintshire	153240	19.2	29341
Wrexham	136399	18.2	24824
Powys	132705	24.7	32718
Ceredigion	75964	22.0	16726
Pembrokeshire	123261	23.3	28750
Carmarthenshire	184681	22.0	40572
Swansea	240332	18.9	45361
Neath Port Talbot	139898	19.7	27544
Bridgend	140480	18.9	26606
The Vale of Glamorgan	127159	19.6	24967
Rhondda Cynon Taf	236114	18.1	42842
Merthyr Tydfil	59021	17.5	10332
Caerphilly	179247	17.8	31831
Blaenau Gwent	69789	18.8	13086
Torfaen	91407	19.0	17355
Monmouthshire	92100	22.5	20675
Newport	146558	17.1	25077
Cardiff	351710	13.6	47826

Data obtained from https://www.healthmapswales.wales.nhs.uk/IAS/dataviews/view?viewId=178 (accessed 06/22/18)

Fig S1. Magnified Kaplan-Meier curve with 95% CI of the patients discharged alive from the Welsh ICUs
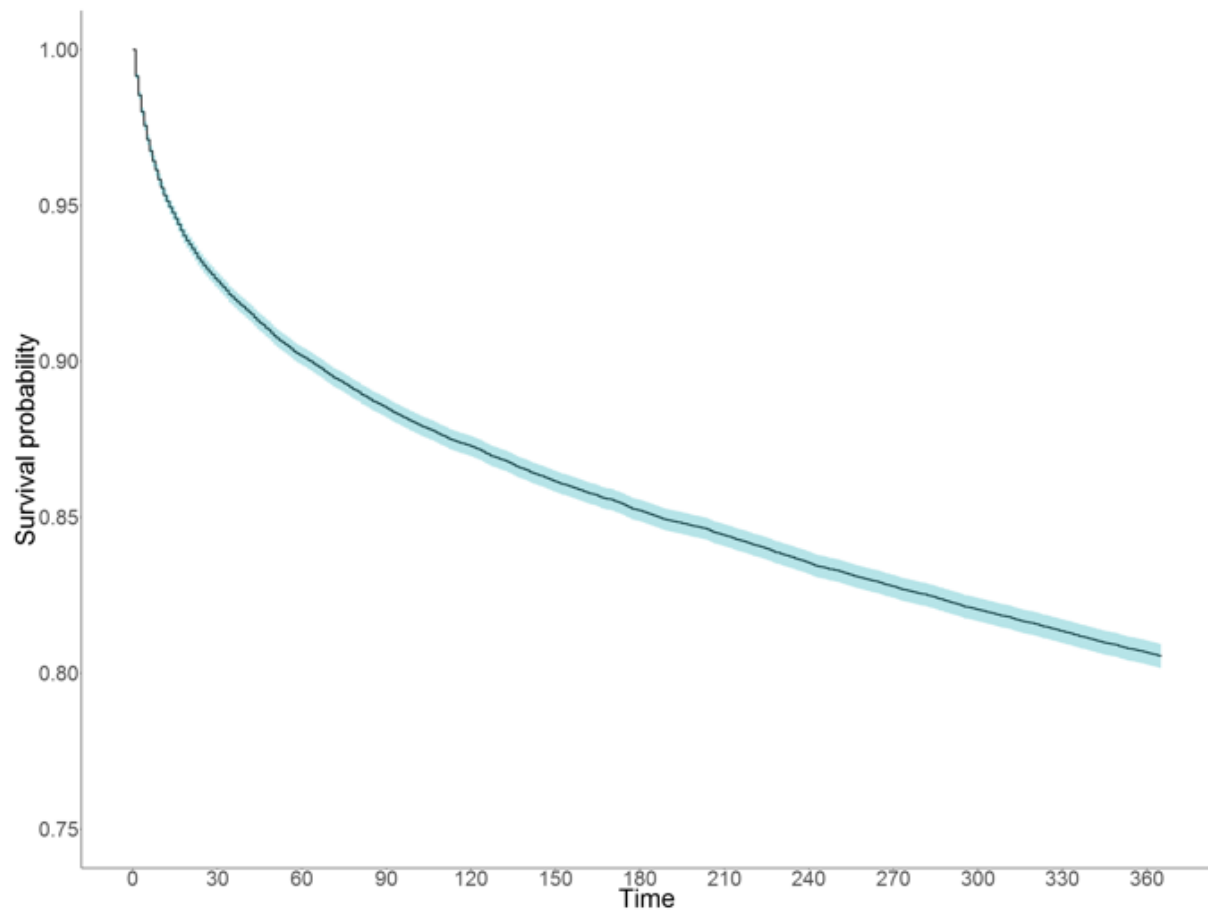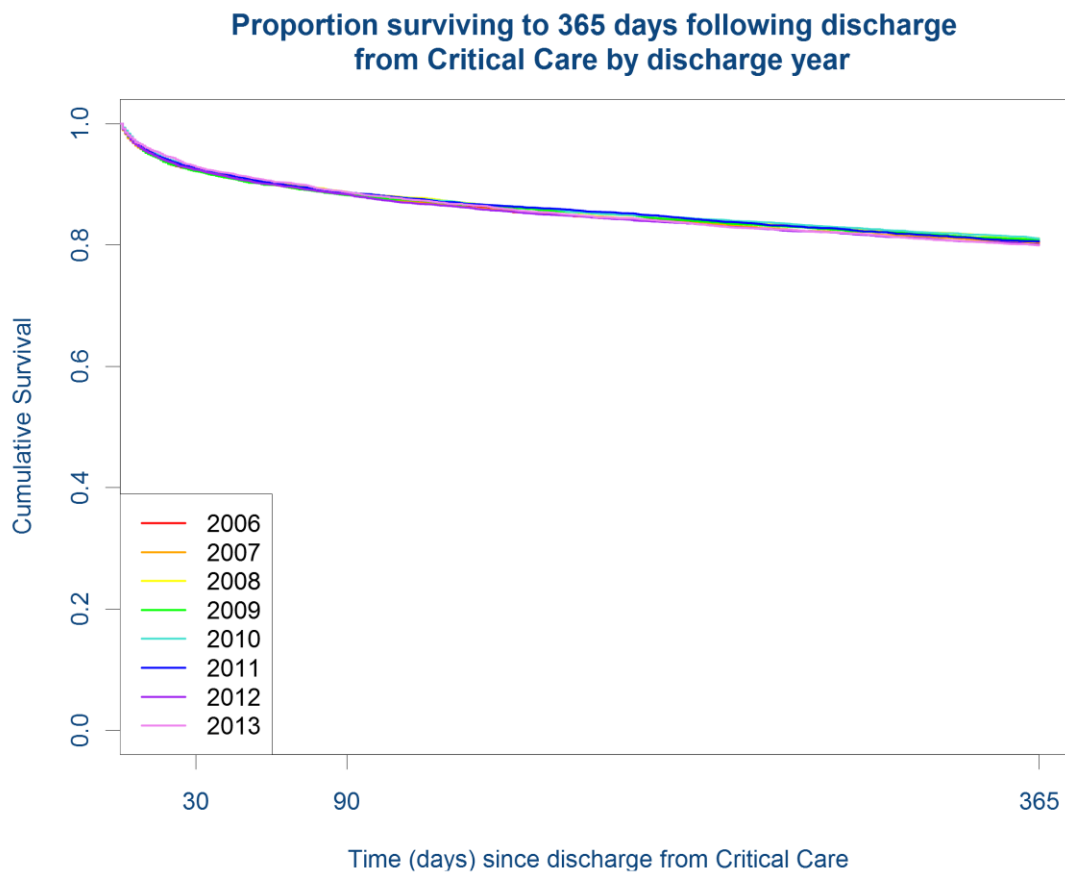
Figure S2. Kaplan-Meier curve of the patients discharged alive from the Welsh ICUs stratified by year

**Proportion surviving to 365 days following discharge from Critical Care by discharge year**

Year	At-risk (n)	Died (n)
2006	1684	329
2007	5469	1079
2008	6076	1148
2009	5557	1063
2010	5718	1082
2011	5138	994
2012	5752	1142
2013	5237	1046

Figure S3. Distribution of age and comorbidity score groups of the 32,748 patients alive at the end of follow-up.
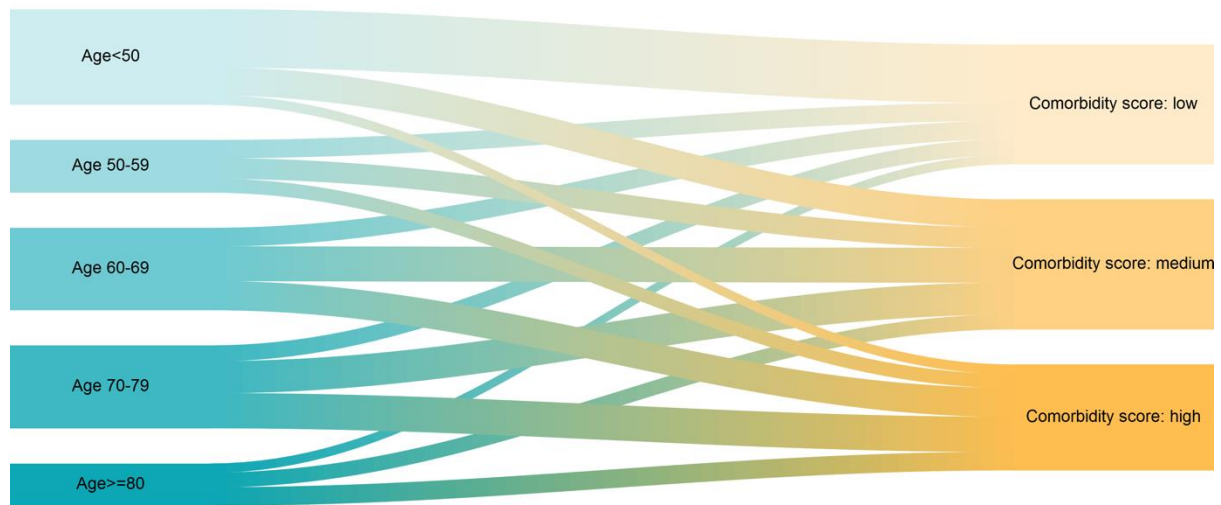
Age: years; Comorbidity score low: comorbidity score -1 to 0; Comorbidity score medium: comorbidity score 1 to 10; Comorbidity score high: comorbidity score above 10

Figure S4. Distribution of age and comorbidity score group of the 7883 patients who died during follow-up.
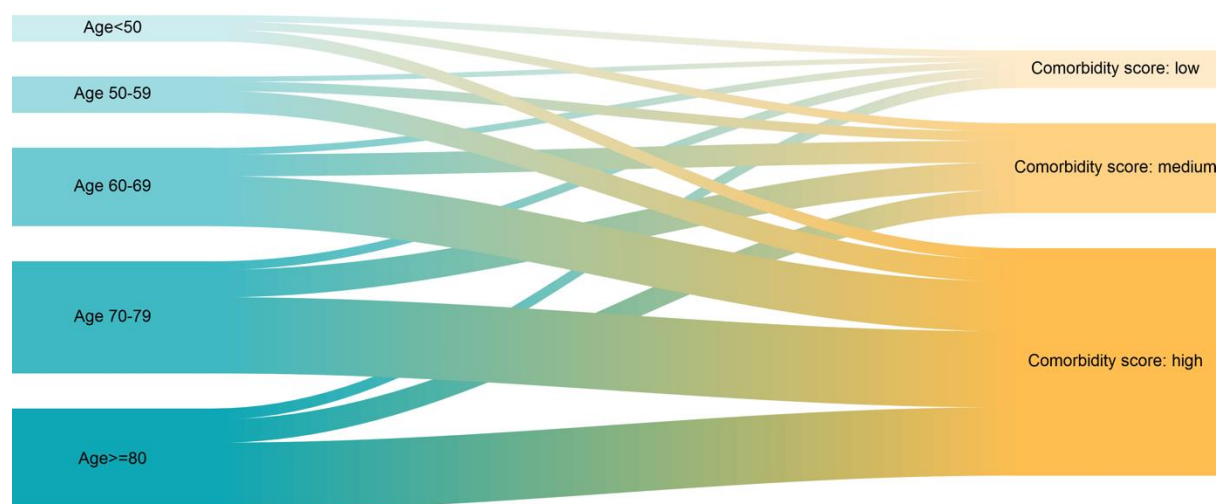
Age: years; Comorbidity score low: comorbidity score -1 to 0; Comorbidity score medium: comorbidity score 1 to 10; Comorbidity score high: comorbidity score above 10

Figure S5. Distribution of the proportion of follow-up time spent in hospital post critical care for those who were still alive at the end of the follow-up period
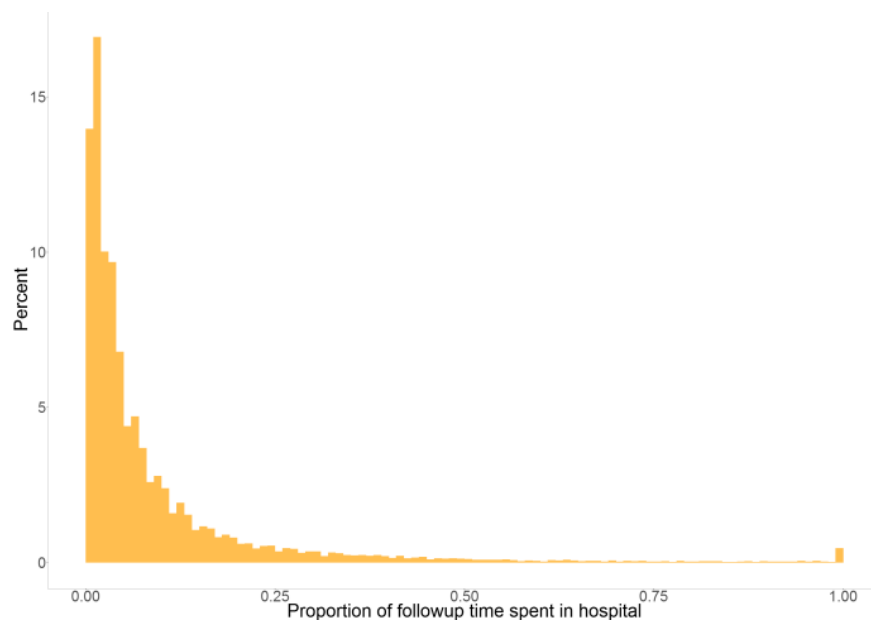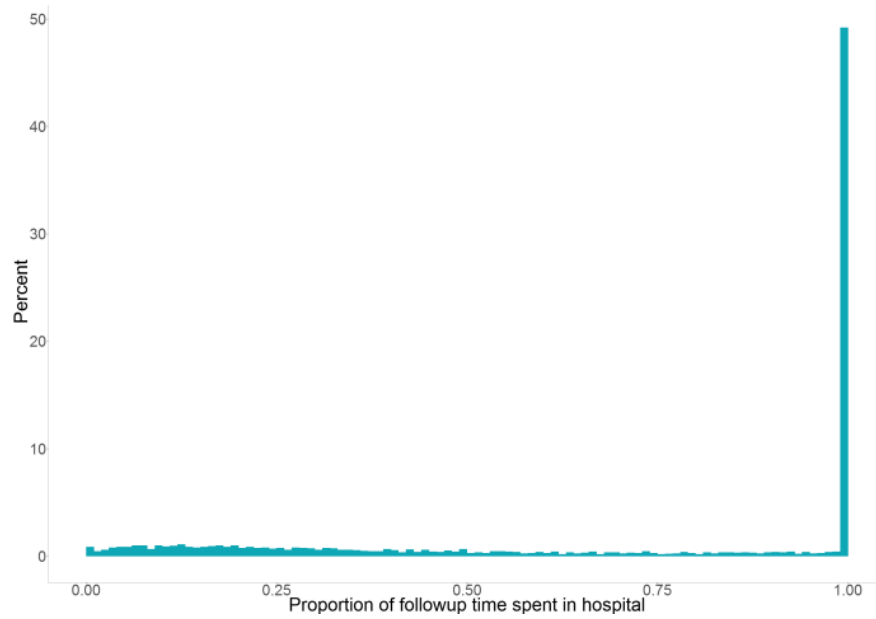
Figure S6. Distribution of the proportion of follow-up time spent in hospital post critical care for those who died by the end of the follow-up period

References

1. https://saildatabank.com/saildata/sail-datasets/critical-care-dataset/ (accessed 29th Nov 2017)

2. https://saildatabank.com/saildata/sail-datasets/patient-episode-database-for-wales-pedw/ (accessed 29th Nov 2017)

3. https://saildatabank.com/saildata/sail-datasets/annual-district-death-extract-adde/ (accessed 29th Nov 2017)

4. http://www.wales.nhs.uk/nwis/page/52552 (accessed 29th Nov 2017)

5. https://saildatabank.com/saildata/sail-datasets/welsh-demographic-service-wds/ (accessed 29th Nov 2017)

6. http://gov.wales/docs/statistics/2011/110831wimd11summaryen.pdf (accessed 29th Nov 2017)

7. https://saildatabank.com/saildata/sail-datasets/ (accessed 29th Nov 2017)

8. Team CI (2017) Summary Hospital-level Mortality Indicator (SHMI), 1st ed. 1–37.

9. http://www.wcctn.wales.nhs.uk/sitesplus/documents/1210/Annual%20Report_English_FINAL%20WEB.pdf (accessed 14th January 2018)

10. http://www.wales.nhs.uk/sites3/Documents/768/Quality%20requirements%20for%20critical%20care.pdf (accessed 14th January 2018)

11. http://www.wcctn.wales.nhs.uk/sitesplus/documents/1210/Admission%20Discharge%20Guideline_Revised%20June%20%2716_APPROVED.pdf (accessed 14th January 2018)

12. http://www.wcctn.wales.nhs.uk/sitesplus/documents/1210/Guidelines%20for%20the%20transfer%20of%20the%20critically%20ill%20adult_Approved_2017.pdf (accessed 14th January 2018)

13. http://www.wcctn.wales.nhs.uk/sitesplus/documents/1210/SEWCCN%20Tracheostomy%20Guidelines.pdf (accessed 14th January 2018)

14. http://www.wcctn.wales.nhs.uk/sitesplus/documents/1210/Service%20specifications%20for%20Outreach%20Services%20-%20Final.pdf (accessed 14th January 2018)

15. http://www.wcctn.wales.nhs.uk/sitesplus/documents/1210/Guideline%20for%20Weaning%20from%20Ventilation_FINAL%20Approved.pdf (accessed 14th January 2018)

16. http://www.wcctn.wales.nhs.uk/sitesplus/documents/1210/Sedation%20guidelines%20for%20intensive%20care%20-%20approved.pdf (accessed 14th January 2018)

17. http://www.wcctn.wales.nhs.uk/sitesplus/documents/1210/Management%20of%20Severe%20Resp%20Failure%20APPROVED_Revised%20Oct%202013_AMMENDED%20FORMATTED%20JUNE%202014.pdf (accessed 14th January 2018)

18. http://www.wales.nhs.uk/sites3/page.cfm?orgId=379&pid=23910 (accessed 14th January 2018)

19. Hermon A, Pain T, Beckett P, Jerrett H, Llewellyn N, Lawrence P, et al. Improving compliance with central venous catheter care bundles using electronic records. Nurs Crit Care 2015; 20:196–203.

20. Pugh R, Harrison W, Harris S, Roberts H, Scholey G, Szakmany T, et al. Is HELICS the Right Way? Lack of Chest Radiography Limits Ventilator-Associated Pneumonia Surveillance in Wales. Front Microbiol 2016;7:1271.

21. https://onlinereports.icnarc.org/Reports/Index (accessed 14th January 2018)

22. http://content.digital.nhs.uk/media/1362/HES-Hospital-Episode-Statistics-Adult-Critical-Care-Data-Dictionary/pdf/CC_DataDictionary.pdf (accessed 29th Nov 2017)