ORIGINAL RESEARCH

Predicting risk of unplanned hospital readmission in survivors of critical illness: a population-level cohort study

Nazir I Lone ,[1,2] Robert Lee,[2] Lisa Salisbury,[1,3] Eddie Donaghy,[1,4] Pamela Ramsay,[1,5] Janice Rattray,[6] Timothy S Walsh[1,2,4]

► Additional material is published online only. To view please visit the journal online (http://dx.doi.org/10.1136/thoraxjnl-2017-210822).

[1]University Department of Anaesthesia, Critical Care, and Pain Medicine, School of Clinical Sciences, University of Edinburgh, Edinburgh, UK
[2]Usher Institute for Population Health Sciences and Informatics, University of Edinburgh, Edinburgh, UK
[3]Queen Margaret Drive, Queen Margaret University Edinburgh, Musselburgh, UK
[4]MRC Centre for Inflammation Research, University of Edinburgh, Edinburgh, UK
[5]Edinburgh Napier University, Edinburgh, UK
[6]School of Nursing and Health Sciences, University of Dundee, Dundee, UK

Correspondence to
Dr Nazir I Lone, University Department of Anaesthesia, Critical Care, and Pain Medicine, School of Clinical Sciences, University of Edinburgh, Edinburgh, EH16 4SA, UK; nazir.lone@ed.ac.uk

Received 27 July 2017
Revised 7 March 2018
Accepted 19 March 2018
Published Online First
5 April 2018

To cite: Lone NI, Lee R, Salisbury L, *et al*. *Thorax* 2019;**74**:1046–1054.

ABSTRACT

Background Intensive care unit (ICU) survivors experience high levels of morbidity after hospital discharge and are at high risk of unplanned hospital readmission. Identifying those at highest risk before hospital discharge may allow targeting of novel risk reduction strategies. We aimed to identify risk factors for unplanned 90-day readmission, develop a risk prediction model and assess its performance to screen for ICU survivors at highest readmission risk.

Methods Population cohort study linking registry data for patients discharged from general ICUs in Scotland (2005–2013). Independent risk factors for 90-day readmission and discriminant ability (c-index) of groups of variables were identified using multivariable logistic regression. Derivation and validation risk prediction models were constructed using a time-based split.

Results Of 55 975 ICU survivors, 24.1% (95%CI 23.7% to 24.4%) had unplanned 90-day readmission. Pre-existing health factors were fair discriminators of readmission (c-index 0.63, 95% CI 0.63 to 0.64) but better than acute illness factors (0.60) or demographics (0.54). In a subgroup of those with no comorbidity, acute illness factors (0.62) were better discriminators than pre-existing health factors (0.56). Overall model performance and calibration in the validation cohort was fair (0.65, 95% CI 0.64 to 0.66) but did not perform sufficiently well as a screening tool, demonstrating high false-positive/false-negative rates at clinically relevant thresholds.

Conclusions Unplanned 90-day hospital readmission is common. Pre-existing illness indices are better predictors of readmission than acute illness factors. Identifying additional patient-centred drivers of readmission may improve risk prediction models. Improved understanding of risk factors that are amenable to intervention could improve the clinical and cost-effectiveness of post-ICU care and rehabilitation.

Key messages

What is the key question?

► What is the relative importance of risk factors for unplanned 90-day readmission in intensive care unit (ICU) survivors and can those at highest risk of readmission be screened for using risk prediction models?

What is the bottom line?

► 24.1% of ICU survivors had unplanned 90-day readmission. Pre-existing illness indices were better predictors of readmission than acute illness factors, but this was reversed in the subgroup with no recorded comorbidity. Discriminant ability of the overall risk prediction model was fair (c-index 0.65), but the model did not perform sufficiently well as a screening tool at clinically relevant probability thresholds.

Why read on?

► The high unplanned hospital readmission rates we report in ICU survivors are similar to those with chronic diseases. We provide a comprehensive evaluation of drivers for readmission and highlight the importance of preillness health factors in post-ICU morbidity.

INTRODUCTION

Unplanned hospital readmissions within 30 days are estimated to cost the health service in England over £2 billion per year and over $17 billion per year in US Medicare expenditure.[1 2] Reduction strategies targeting readmissions have therefore been a focus for policy makers through quality improvement activities and financial penalties.[2 3] Intensive care unit (ICU) survivors are known to experience increased mortality, use more acute hospital resource and reduced quality of life in the years following hospital discharge.[4–8] This increased morbidity has been termed the 'post-intensive care syndrome' and may leave ICU survivors and their caregivers with less resilience to new acute stressors as well as persisting problems related to the acute critical illness.[9]

Unplanned hospital readmission is a potentially useful outcome measure in ICU survivor populations. It is easy to measure in linked information systems, is associated with increased costs and may reflect the effectiveness of rehabilitation interventions, which are increasingly considered a standard of care following critical illness[10] despite recent conflicting trial evidence.[11] However, the validity of unplanned readmission as an outcome measure requires an understanding of contributing factors, especially those that are potentially modifiable by intervention within survivor populations.

Although statistical models have been developed to predict readmission risk for many hospitalised patient groups,[12–14] none have specifically assessed ICU populations with risk factors related to the critical illness episode, for example, organ dysfunction.

An ICU-specific model could potentially identify survivors at high risk and might enable screening of survivors before hospital discharge in whom to target novel risk reduction strategies.

As part of a mixed methods programme exploring drivers of unplanned readmission following critical illness,[15] we undertook a national cohort study to quantify the proportion of ICU survivors experiencing readmission within 90 days of discharge and identify risk factors for 90-day readmission. We also aimed to develop a risk prediction model and assess its performance as a screening tool to identify ICU survivors at highest readmission risk.

METHODS

Study setting and databases

We used a cohort study design. Data sources were linked registries: Scottish Intensive Care Society Audit Group (SICSAG),[16] Scottish Morbidity Record of acute hospital admissions (SMR01), Scottish death records, acute psychiatric hospital admissions (SMR04), Scottish Cancer Registry and Scottish outpatient registry (SMR00). All data were anonymised and analysed in a safe haven environment. The SICSAG audit registry captures all adult general intensive care activity (24 units in 2013) serving a population of around 5 million (4.2 million aged ≥16 years) within Scotland and is subject to regular validation assessments.[17] See online supplementary data for health service setting details.

Participants

The cohort comprised Scottish residents aged ≥16 years admitted to and discharged from general ICUs in Scotland (1 January 2005–31 December 2013) who survived to hospital discharge. For analyses to identify predictors of readmission, the whole cohort was used. For analyses relating to the risk prediction model construction, a time-based partition of the dataset was used to create two groups: discharge from index hospital stay 1 January 2005–17 January 2012, derivation cohort (70%) and 18 January 2012–31 December 2013, validation cohort (30%). For analyses demonstrating the performance of the risk prediction model as a screening tool, the validation cohort was used.

Variables

Outcomes

The primary outcome was first unplanned hospital readmission within 90 days of discharge from index hospitalisation. Second and subsequent readmissions were not included. We chose this time-point as the survivorship literature shows a longer period 'at risk', both for increased mortality and hospital resource use.[4–6] 'Unplanned hospital admission' was defined using 'emergency admission' codes in the 'Admission Type' field in SMR01 database (accuracy >93% in validation reports).[18] We also reported a secondary composite outcome of 90-day death or unplanned readmission. Follow-up was complete, although emigration from Scotland was not recorded. However, emigration in older age groups from Scotland to the remainder of the UK or overseas is known to be low (0.6% of residents aged ≥45 years annually).[19]

Predictors

Factors were classified into three groups: demographics, indices of pre-existing patient health and indices of critical illness severity. See online supplementary data for additional information relating to variables.

Statistical analysis

Data were analysed using SAS Enterprise Guide V.6.1 and Stata V.14. A complete cases analysis was performed for all analyses. Additional information is available in the online supplementary data. We undertook two separate modelling strategies: one to identify independent predictors of readmission risk and one to develop a risk prediction model.

Univariable/multivariable predictors

Individual univariable associations with the outcome were assessed by entering each variable in a logistic regression model and reporting the OR with 95% CI. The c-index was presented to aid interpretation of the predictive ability of each variable. The c-index quantifies the ability of a model to distinguish between patients who experience a readmission and those who do not. A c-index of 0.5 indicates the model performs no better than chance and 1.0 indicates perfect discrimination. However, the c-index may be insensitive when used alone to compare between models. Therefore, to assess the relative importance of the three pre-defined groups of variables (demographics, indices of pre-existing health and indices of critical illness), the c-index of each group was estimated, and observed risk was plotted against equal size deciles of predicted risk. This plot differs from a calibration plot as the deciles of predicted risk are plotted at intervals of equal width on the x-axis rather than at the mean of predicted risk for the decile. Therefore, a steeper upward gradient of observed risk across the x-axis indicates that the group of variables is a better predictor of the outcome than another group. In addition, we presented the classification tables in online supplementary material.[20] This illustrates the change in classification of events and non-events when comparing two models. Multivariable associations with the outcome were assessed using logistic regression with no variable selection procedures.

Risk prediction model

We chose a time-based split as this is a stronger design for internal validation than a random split as the former method allows for random variation.[21] Variable selection for the model derivation was performed using backward elimination with a significance level of 0.05 using 70% of the cohort. We assessed model performance by assessing: discriminant ability, assessed by calculating the concordance index (c-index) and presenting a receiver operating characteristics (ROC) curve; calibration, assessed with a calibration plot of predicted probability against observed proportion with the outcome; and overall model performance by calculating Brier's score. We followed best practice and did not apply a statistical test for calibration (eg, Hosmer-Lemeshow test) nor reported calibration in the derivation dataset.[21] We presented sensitivity and specificity at thresholds of predicted risk to illustrate the ability of the model to be used as a tool to screen patients before hospital discharge.

Subgroup analyses

We repeated multivariable analyses to identify if the relationship between groups of predictors and unplanned readmission differed in two subgroups: patients admitted to ICU on an unplanned basis (excluding those admitted after elective surgery) and patients with no recorded comorbidity. The rationale for this was that patients admitted electively to ICU after planned surgery may follow recognised pathways posthospital discharge. Similarly, patients with no previous comorbidity may have different drivers for unplanned readmission that may be more attributable to acute illness rather than pre-existing ill health.

Sensitivity analysis

We performed the following sensitivity analyses:

1. To evaluate if a shorter follow-up period affected the relative importance of the three predefined groups of variables, we repeated analyses using 30-day unscheduled readmission as the outcome comparing c-indices and ROC curves between groups.
2. To evaluate the effect of death as a competing risk to readmission, we used two approaches. We repeated analyses with the composite outcome of 90-day death or unplanned readmission, inspecting outcome distribution of death without readmission across categories, univariable ORs and risk prediction model performance. However, this approach gives equal value to death and readmission in the outcome. Therefore, we also used Fine and Gray competing risk regression models to identify independent predictors of time to unscheduled readmission within 90 days, which explicitly accounts for the competing risk of death. We evaluated the relative importance of groups of variables by reporting change in Akaike information criterion (AIC), a measure of model fit (lower values indicate better fit).
3. To evaluate the effect of representation of comorbidities, we repeated the multivariable analysis replacing count of comorbidities with individual comorbidities.

RESULTS

In total, 55 975 patients were admitted to ICUs and discharged alive (online supplementary figure 1). Median age was 60 years (IQR 45–71), and patients living in the most deprived regions were over-represented (49.2% resident in two most deprived quintiles, 40% in general population) (table 1; online supplementary table 1). Pre-existing illness and morbidity was prevalent: 31.3% had an unplanned admission during the previous year, while 56.4% had at least one comorbidity. Previous alcohol-related (10.8%) and drug-related morbidity (7.0%) were prevalent (online supplementary table 1). The most common admission diagnosis was pneumonia (8.4%).

Of 55 975 patients, 13 471 (24.1%, 95% CI 23.7% to 24.4%) experienced unplanned 90-day readmission (figure 1). A further 712 (1.3%, 95% CI 1.2% to 1.4%) died without being admitted. A total of 14 183 patients (25.3%, 95% CI 25.0% to 25.7%) experienced 90-day readmission/death). An additional 1015 (1.8%, 95% CI 1.7% to 1.9%) died within 90 days, but these deaths occurred after an unplanned readmission.

For full version of baseline characteristics table and missing data, see online supplementary table 1. Unplanned readmission proportions for continuous variables are presented in online supplementary table 2.

Predictors of 90-day unplanned hospital readmission

Patient demographics

In univariable analyses, all demographic factors other than sex had statistically significant associations with readmission risk (older age, social deprivation and remoteness of residence (online supplementary table 2)). As a combined group, the c-index was 0.54 (95% CI 0.54 to 0.55), indicating weak discriminant ability (figure 2).

Indices of pre-existing patient health

Prior health resource use and comorbidities demonstrated better discrimination for readmission risk. The number of previous unplanned inpatient admissions was associated with readmission rates from 19.5% (95% CI 19.1% to 19.9%) (zero admissions) to 70.2% (95% CI 66.6% to 73.6%) (six or more) (online supplementary table 2; c-index 0.60). Pre-existing comorbidities demonstrated moderate discrimination overall (c-index 0.60). In those experiencing an unplanned 90-day readmission, 68.7% (95% CI 67.9% to 69.5%) had at least one comorbidity. All individual comorbidities were associated with increased risk (online supplementary figure 3A, greatest risk: renal disease, moderate/severe liver disease, diabetes with complications with >40% risk). As a combined group, indices of pre-existing health and resource use demonstrated moderate discrimination (c-index 0.63, 95% CI 0.63 to 0.64), which was the highest compared with the other two groups (figure 2, χ^2=389, 2df, P<0.001). This was reflected in improvement in the classification of patients not experiencing a readmission of 31.5% and 10.7% in comparison with demographics and critical illness severity indices, respectively, at the expense of worse reclassification of patients experiencing a readmission (−18.2% and −6.1%, respectively) (online supplementary table 3A, B).

Indices of critical illness severity

Overall, diagnostic category (c-index 0.57) and APACHE II score (c-index 0.55) were weak discriminators (online supplementary table 2). Some specific diagnostic categories were associated with high readmission risk (variceal bleed (45.8%; 95% CI 41.3% to 50.4%) and pancreatitis (40.0%; 95% CI 36.1% to 44.1%)). Organ support variables were weak discriminators of 90-day readmission (c-index range 0.51–0.52). Similarly, length of post-ICU hospital stay and overall length of hospital stay were weak discriminators (c-index 0.52–0.56). As a combined group, the c-index for indices of critical illness severity was 0.60 (95% CI 0.60 to 0.61) (figure 2).

Multivariable analyses

In multivariable analyses, number of previous unplanned admissions was strongly associated with risk of 90-day readmission, with a predicted absolute risk increase from 20.3% (95% CI 19.9% to 20.8%) in those with no previous readmissions to 61.1% (95% CI 57.7% to 65.5%) in those with six or more (OR 6.19, 95% CI 5.12 to 7.49) (online supplementary table 4). Readmission risk increased with comorbidity count, from 19.5% (no comorbidities; 95% CI 18.8% to 20.1%) to 34.5% (5 or more; 95% CI 30.6% to 38.5%). Replacing comorbidity count with individual comorbidities revealed seven individual comorbidities no longer retained statistical significance (online supplementary figure 3B). Several other factors remained statistically significant, but the gradient of readmission risk across categories was less pronounced; these included age, type of admission to ICU and length of post-ICU hospital stay. Several specific diagnoses were independently associated with predicted risk substantially higher than the population mean, namely oesophageal variceal bleed (33.5%, 95% CI 28.8% to 38.1%) and pancreatitis (38.4%, 95% CI 34.0% to 42.7%). Several factors were not significant predictors in multivariable analysis, including socioeconomic status, Acute Physiology Score (APS) and ICU length of stay.

Risk prediction model

In the derivation cohort (n=33 294, online supplementary table 5), the overall discriminant ability of the model was fair (c-index 0.67, 95% CI 0.66 to 0.67) and overall performance was acceptable (Brier's score 0.170). In the validation cohort (online supplementary table 6), discriminant ability and overall performance were similar (c-index 0.65, 95% CI 0.64 to 0.66; Brier's score 0.176; figure 3). Model calibration across the range of predicted risk in the validation cohort was reasonable, although the model slightly underpredicted readmission risk (mean observed risk 25.0%; mean predicted risk 23.6%) (online supplementary figure 4).

Table 1 Baseline characteristics of patients and number experiencing 90-day unplanned hospital readmission

Demographics	Category	Number with characteristic n (%) or median (IQR)	Number with 90-day unplanned readmission n (%)
Sex	Female	24 466 (43.7)	5952 (24.3)
Age at admission to ICU (years)	Median and quartiles	60 (45–71)	–
Scottish Index of Multiple Deprivation	First quintile (most deprived)	14 809 (26.5)	3810 (25.7)
	Second quintile	12 907 (23.1)	3182 (24.7)
	Third quintile	11 269 (20.1)	2645 (23.5)
	Fourth quintile	9631 (17.2)	2129 (22.1)
	Fifth quintile (least deprived)	7328 (13.1)	1699 (23.2)
Remoteness of residence	Urban area	37 469 (68.1)	9321 (24.9)
	Accessible	13 271 (24.1)	2974 (22.4)
	Remote or very remote	4294 (7.8)	965 (22.5)
Indices of pre-existing patient health			
Admissions/attendances in year prior to index hospital stay			
Number of unplanned inpatient admissions	0	38 429 (68.7)	7494 (19.5)
	1	10 582 (18.9)	2968 (28)
	2 or more	6964 (12.5)	3009 (43.2)
Number of elective inpatient and day case admissions	0	37 770 (67.5)	8395 (22.2)
	1	4286 (7.7)	1203 (28.1)
	2 or more	13 919 (24.9)	3873 (27.8)
Number of new outpatient attendances	0	27 134 (48.5)	5889 (21.7)
	1 or more	28 841 (51.5)	7582 (26.3)
Number of acute psychiatric admissions	0	54 703 (97.7)	13 079 (23.9)
	1 or more	1272 (2.3)	392 (30.8)
Number of comorbidities present	0	24 420 (43.6)	4214 (17.3)
	1	17 490 (31.2)	4419 (25.3)
	2 or more	14 065 (25.1)	4838 (34.4)
Indices of critical illness severity			
Type of admission to ICU	Elective surgery	15 553 (28)	3480 (22.4)
	Emergency surgery	13 222 (23.8)	3323 (25.1)
	Non-operative	26 798 (48.2)	6576 (24.5)
APACHE II score at admission to ICU	Median and Quartiles	15 (11, 20)	–
Mechanical ventilation during ICU stay	Yes	33 447 (60.2)	8116 (24.3)
Renal replacement therapy during ICU stay	Yes	3925 (7.1)	1170 (29.8)
Cardiovascular system support during ICU stay	Yes	20 101 (36.2)	5174 (25.7)
Maximum number of organs supported on any day during ICU stay	0	17 877 (32.2)	4070 (22.8)
	1	20 969 (37.8)	5032 (24)
	2	14 277 (25.7)	3638 (25.5)
	3	2407 (4.3)	649 (27)
Length of ICU stay (days)	Median and quartiles	2 (1–4)	–
Length of index hospital stay (days)	Median and quartiles	15 (8–31)	–

ICU, intensive care unit.

Performance of risk prediction model as a screening tool

The model's performance as a screening tool is illustrated using the validation cohort in table 2 (see online supplementary table 7 for 95% CI). Assigning ≥20% predicted probability of the outcome as the threshold to 'screen positive' would lead to the majority (54.2%, 95% CI 53.4% to 55.0%) of patients screening positive with a 30.7% (95% CI 29.2% to 32.3%) false-negative rate and a 49.2% (95% CI 48.2% to 50.1%) false-positive rate. Increasing the threshold to ≥50% improves the probability of identifying a patient who will subsequently experience a readmission but a substantially smaller proportion of the population screen positive (decreasing to 1.6%, 95% CI 1.4% to 1.8%). Online supplementary table 8 illustrates the patient characteristics and outcomes of those who would screen positive compared with those who would screen negative at two probability thresholds (≥20% and ≥50%).

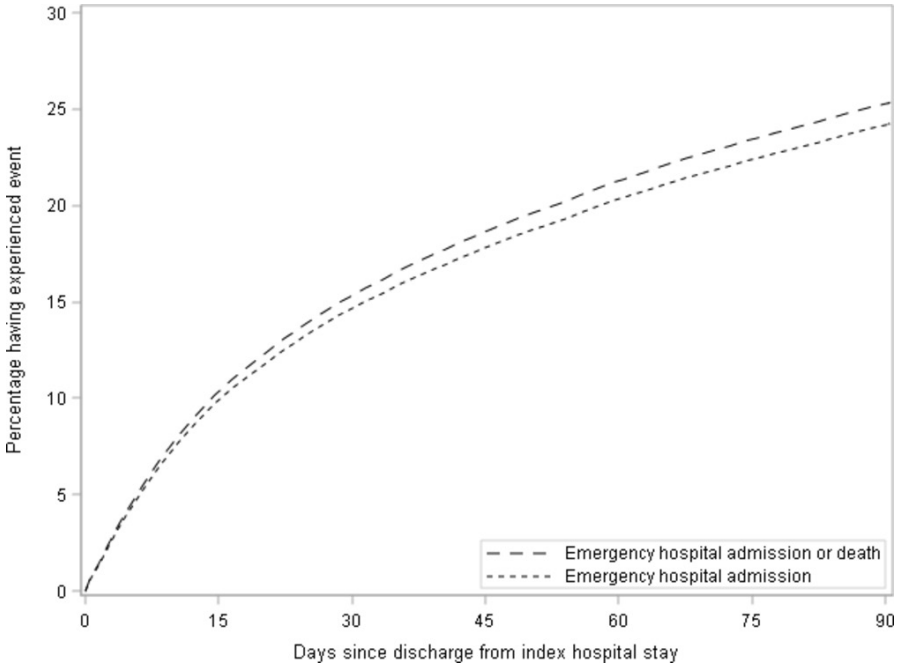

Figure 1 Cumulative incidence within 90 days of discharge from index hospital stay of (A) unplanned hospital admission and (B) unplanned hospital admission or death.

Subgroup analyses

In the subgroup of patients admitted to ICU on an unplanned basis (n=40 020; unplanned hospital readmissions n=9899, 24.7%, 95% CI 24.3% to 25.2%), results were similar to the full cohort. The three groups of variables had similar patterns of association compared with the full cohort (online supplementary figures 5A and 6A, table 9). In the subgroup of patients with no previous comorbidity (n=24 420; unplanned readmissions n=4214, 170.3%, 95% CI 16.8% to 17.7%), indices of critical illness severity had the greatest discriminant ability (c-index 0.622) (online supplementary figures 5B and 6B, table 9).

Sensitivity analysis

Similar results were found using 30-day unscheduled readmission as the outcome: indices of pre-existing patient health retained the highest discriminant ability (c-index 0.617 vs 0.601 critical illness indices vs 0.535 demographics; χ^2=304, 2 df, P<0.001) (online supplementary figure 2 and table 9).

The small proportion of deaths without a preceding unplanned readmission that occurred in individuals was relatively balanced across covariates in the derivation cohort (online supplementary table 2). Both sensitivity analyses using logistic regression models of combined outcome of 90-day death or readmission and time to first unplanned readmission (Fine and Gray regression model) accounting for the competing risk of death (online supplementary table 4) did not substantially differ from the findings of the primary multivariable analysis. Model performance for the combined outcome of 90-day death or readmission was similar (c-index 0.66, 95% CI 0.65 to 0.67; Brier's score 0.179). The relative importance of the three groups of covariates was similar for both analyses comparing c-indices of the combined outcome (90-day death/readmission) (online supplementary figure 2 and table 9) and analyses comparing AIC for time to first unplanned readmission (AIC 244 863 pre-existing health vs 246 039 critical illness indices vs 246 909 demographics; full model 244 238).

DISCUSSION

In a large, complete population study, we have demonstrated that 1 in 4 ICU survivors experience an unplanned readmission within 90 days of hospital discharge. Indices of pre-existing ill health were more strongly predictive of readmission than indices of critical illness severity in the whole cohort, but this was reversed in subgroup analyses of patients with no recorded comorbidity. A risk prediction model derived from multiple data sources had, at best, only moderate discriminant ability. A screening tool derived from this model is unlikely to perform sufficiently well in isolation to identify cases in whom to target high intensity interventions aimed at reducing readmissions among ICU survivors.

Our data indicate unplanned readmission rates among ICU survivors are substantially higher than the general hospital population (30-day readmission 14.7% in ICU survivors vs 7.0% in all hospital inpatients[22]). Unplanned readmission rates are increasingly used as a quality indicator and target for improvement.[23 24] Although many variables had statistically significant associations with readmission risk, almost all had limited discriminant power as individual factors. A key finding was that ICU-related factors such as organ support are not independently associated with readmission risk among survivors. In contrast, pre-existing health factors had the greatest predictive power of all variables. However, in the subgroup of patients with no pre-existing comorbidity, indices of critical illness had greater discriminant power than pre-existing health factors. These findings are consistent with precritical illness chronic health being the dominant factor *at a population level* in general critical care survivors in determining post-ICU health trajectories, whereas new impairments that follow an ICU admission may be more dominant in subgroups with no comorbidity.[25–27]

Addressing recovery from critical illness from this perspective has important implications for research, policy and service design given the high prevalence of older patients with comorbidity in critical care populations.[4 6] For example, it may explain the lack

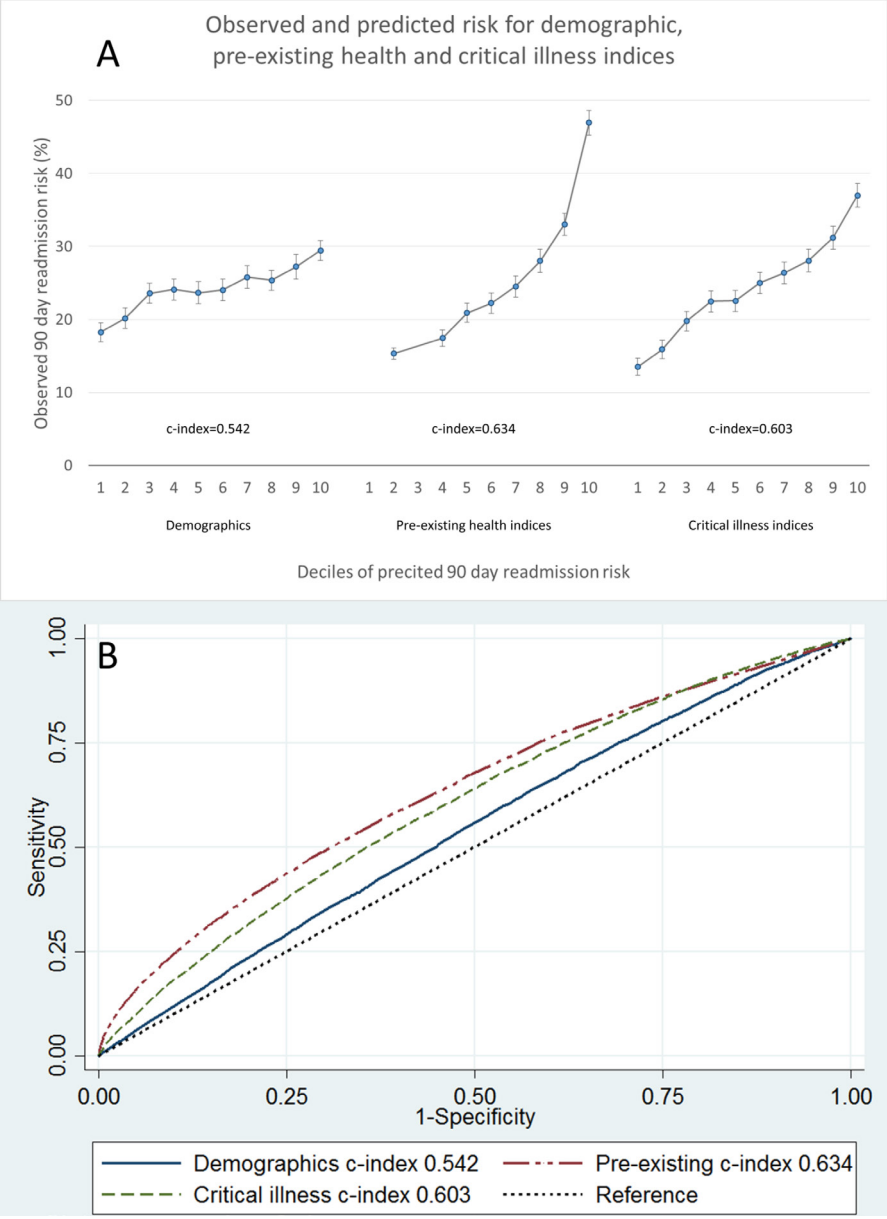

Figure 2 (A) Observed risk of 90-day unplanned hospital readmission by deciles of predicted risk and (B) receiver operator characteristics for three groups: patient demographics, indices of pre-existing patient health and indices of critical illness severity. Within each panel, each point represents 10% of the cohort grouped by their predicted risk of 90-day readmission derived from the group of characteristics labelled by the panel axis label. The observed risk for 'Demographics' variables ranges from 18.2% in the lowest predicted risk decile to 29.4% in the highest. The observed risk for the 'pre-existing health indices' group of variables ranges from 15.3% in the lowest predicted risk decile to 46.9% in the highest. The gradient of the line is therefore steeper. The steeper positive gradient observed for 'Pre-existing health indices' compared with 'Demographics' indicates that there is a greater increase in observed readmission risk for each increment in decile of predicted risk for the group of characteristics, and therefore this group is a better predictor of readmission across the range of predicted risk.

of effect on clinical outcomes from rehabilitation interventions focused mostly on physical therapy alone[7] and also questions the rationale for using outcomes such as longer term hospital costs and health-related quality of life in critical care trials without accounting for preillness health status.

Our model had a similar discriminant ability compared with other published risk prediction scores used in general hospitalised populations (c-indices of studies using retrospective administrative data 0.55–0.72).[28] This was despite inclusion of ICU-related/acute factors. These findings may be explained by our datasets not including important factors associated with readmission risk, such as social and organisational factors identified in a systematic review.[28] Research in other populations highlights the importance of these factors, which have not previously been well addressed in ICU survivor populations. For example, family stress,[29] lack of information [30] and frailty[31] could all be important during the early posthospital period. Furthermore, some patients will experience readmissions due to unpredictable factors that would not be present in exhaustively comprehensive datasets. Analysis of PROFILE's qualitative component, comprising interviews and focus groups with ICU survivors and their carers, may reveal additional insights.[15] Our study clearly shows that additional research is needed to understand other factors driving

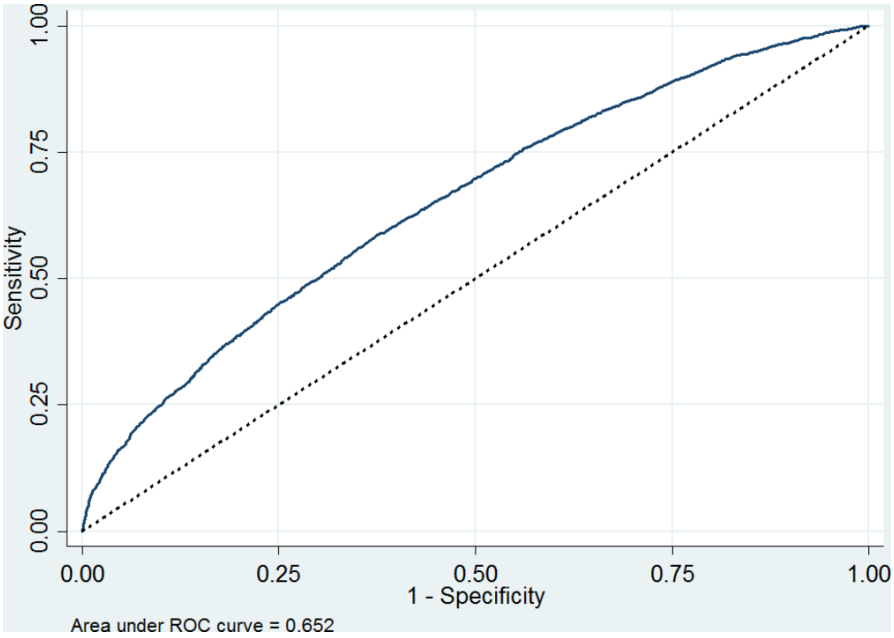

Figure 3 Receiver operator characteristics (ROC) curve for model predicting unplanned hospital readmission within 90 days of discharge from index hospital stay in the validation cohort (n=14 273).

readmission risk in this population to improve the discriminant value of a clinical decision support tool.

We used 90-day unplanned readmission as our primary outcome, whereas 30-day readmission is widely used in other patient groups.[12 27 28 32] We believe the longer time period is justified, because the ICU survivorship literature shows a longer period 'at risk', both for increased mortality and hospital resource use.[4–6] In addition, a sensitivity analysis using 30-day readmission as the outcome was similar to the primary outcome. Furthermore, HRQoL typically starts to plateau in ICU survivors after 3 months,[7 31] and this time point is widely used for primary outcome measurement in critical care trials.[7 33] Extending the period of interest further risks including readmissions that are less causally related to the critical illness hospitalisation.

Our study has a number of strengths. The database had complete population coverage, included a diverse range of data sources that undergo regular validation and contained a large number of events, resulting in unbiased, precise estimates. We undertook sensitivity analyses to explore the effect of death as a competing risk. We reported our risk prediction model using current best practice and undertook internal validation using a recommended time-based split.[21] Other risk prediction scores for readmission have minimised the number of variables to ensure ease of clinical use.[12 34 35] We decided a priori to pursue a non-parsimonious approach to model building with the intention of electronic implementation.

There are potential limitations to our study. We were unable to access measurements of preadmission functional status, frailty trajectories or biomarkers relating to inflammation, which have been associated with poorer health outcomes following critical illness.[31 32 36 37] Furthermore, we had no data on social care or other non-clinical variables that have been shown to influence readmission risk, for example, polypharmacy,[14] or low health literacy.[38] These are not routinely considered in critical care recovery pathways.

Our study has a number of methodological limitations. While a time-based split is a robust method of model

Table 2 Performance of risk prediction model as a screening tool to identify patients at risk of unplanned hospital readmission

Threshold of predicted risk for screening positive	Number (%) screening positive	Sensitivity and false-negative rate (%)	Specificity and false-positive rate (%)	Positive predictive value (%)	Negative predictive value (%)	Positive likelihood ratio	Negative likelihood ratio
≥20%	7734 (54.2)	69.3/30.7	50.8/49.2	31.9	83.3	1.41	0.60
≥30%	2806 (19.7)	32.6/67.4	84.7/15.3	41.4	79.1	2.13	0.80
≥40%	1129 (7.9)	16.7/83.3	95.0/5.0	52.7	77.4	3.35	0.88
≥50%	484 (3.4)	8.6/91.4	98.3/1.7	63.2	76.4	5.17	0.93
≥60%	226 (1.6)	4.4/95.6	99.4/0.6	69.0	75.8	6.74	0.96

See online supplementary table 7 for 95% CIs

The likelihood ratio for a positive screening test result is the ratio of the true positive rate to the false positive rate. Larger values of the positive likelihood ratio (greater than 1) indicate better performance of the screening test at obtaining positive screening test results in patients who experience a readmission in comparison with those who do not experience a readmission. The likelihood ratio for a negative screening test result is the ratio of the false negative rate to the true negative rate. Smaller values of the negative likelihood ratio (less than 1) indicate better performance of the screening test at obtaining negative screening test results in patients who do not experience a readmission in comparison with those who do experience a readmission. Equations: sensitivity=true positive rate; 1 – sensitivity=false negative rate; specificity=true negative rate; 1 – specificity=false positive rate; positive likelihood ratio=true positive rate/false positive rate=sensitivity/(1 – specificity); negative likelihood ratio=false negative rate/true negative rate = (1 – sensitivity)/specificity.

validation, secular trends in demographics, clinical practice and healthcare organisation can bias model performance. This may mean time-based validation methods perform worse than methods in which derivation and validation cohorts are drawn from the same time period. In addition, using statistical significance to select variables may have resulted in more complex models than, for example, using change in Bayesian information criterion. Furthermore, 12.8% were missing APACHE II scores. This is due to specific APACHE II model exclusions, rather than being 'missing', and these values cannot therefore be imputed. This means our model cannot be generalised to those patients excluded from APACHE II scoring.

Our design did not enable an assessment of the proportion of readmissions that might be avoided through interventions. A recent systematic review estimated the median proportion of avoidable readmissions was 27%.[39] This research question may be better investigated using qualitative methodology, which was the approach used in a parallel part of our research programme.[15] Understanding the modifiable factors that cause readmissions in critical care survivors is essential for designing effective anticipatory interventions. Developing and testing such interventions requires detailed understanding of the factors that may be important.[40] While we could only report presence of comorbidity, our study suggests optimising chronic disease management is at least as important as strategies specific to the complications of critical illness.

Our results have important implications for future research and policy. The unplanned readmission rates we report in ICU survivors are similar to those with chronic disease currently targeted with specific discharge pathways and community support.[41 42] Although guidelines promote rehabilitation after critical illness,[10 43] the most clinically and cost-effective way to deliver these are unknown and evidence-based care pathways do not yet exist, in contrast with other conditions such as myocardial infarction[42] and stroke.[44] Our data support the need for clear pathways with appropriate support for ICU survivors during care transitions, especially from secondary into primary care.

CONCLUSION

We have demonstrated that 1 in 4 patients experience an unplanned hospital readmission within 90 days of discharge following an episode of critical illness. Pre-existing illness indices are better predictors of readmission risk than acute illness factors at a whole cohort level. In a subgroup of those with no comorbidity, acute illness factors predominate. Identifying additional patient-centred drivers of readmission may improve risk prediction models. Improving our understanding of patient groups and risk factors that are amenable to intervention could improve the clinical and cost-effectiveness of post-ICU care and rehabilitation.

Acknowledgements We are grateful to clinicians in ICUs in Scotland who contribute data to the Scottish Intensive Care Society Audit Group registry and Information Services Division (ISD Scotland) for providing data and undertaking linkage.

Contributors All contributed to conception and design of the work. NIL and RL contributed to data acquisition and analysis. All authors contributed to interpretation of data for the work. NIL and TSW drafted the work. All authors revised it critically for important intellectual content. All authors gave final approval of the version to be published. All authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

Funding The project was funded through a research grant from the Chief Scientist Office for Scotland (reference CZH/401026). The corresponding author had full access to all the data in the study and had final responsibility for the decision to submit for publication.

Competing interests None declared.

Ethics approval All data relating to patients were anonymised and analysed in a safe haven environment. This study gained approval from the Privacy Advisory Committee of NHS National Services Scotland (Reference PAC 12/14). South East Scotland Research Ethics Committee granted a waiver (Reference NR/1403AB5).

Provenance and peer review Not commissioned; externally peer reviewed.

ORCID iD

Nazir I Lone http://orcid.org/0000-0003-2707-2779

REFERENCES

1 Jencks SF, Williams MV, Coleman EA. Rehospitalizations among patients in the Medicare fee-for-service program. *N Engl J Med* 2009;360:1418–28.
2 NHS Confederation FTN. Briefing: the impact of non-payment for acute readmissions. 2011 http://www.chks.co.uk/userfiles/files/The%20impact%20of%20non-payment%20for%20acute%20readmissions%20FINAL%20FOR%20WEB.pdf
3 Zuckerman RB, Sheingold SH, Orav EJ, *et al*. Readmissions, observation, and the hospital readmissions reduction program. *N Engl J Med* 2016;374:1543–51.
4 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.
5 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.
6 Wunsch H, Guerra C, Barnato AE, *et al*. Three-year outcomes for medicare beneficiaries who survive intensive care. *JAMA* 2010;303:849–56.
7 Walsh TS, Salisbury LG, Merriweather JL, *et al*. Increased hospital-based physical rehabilitation and information provision after intensive care unit discharge: The RECOVER randomized clinical trial. *JAMA Intern Med* 2015;175:901–10.
8 Oeyen SG, Vandijck DM, Benoit DD, *et al*. Quality of life after intensive care: a systematic review of the literature. *Crit Care Med* 2010;38:2386–400.
9 Needham DM, Davidson J, Cohen H, *et al*. Improving long-term outcomes after discharge from intensive care unit: report from a stakeholders' conference. *Crit Care Med* 2012;40:502–9.
10 Tan T, Brett SJ, Stokes T. Rehabilitation after critical illness: summary of NICE guidance. *BMJ* 2009;338:b822.
11 Connolly B, Salisbury L, O'Neill B, *et al*. Exercise rehabilitation following intensive care unit discharge for recovery from critical illness. *Cochrane Database Syst Rev* 2015;113:Cd008632.
12 Donzé JD, Williams MV, Robinson EJ, *et al*. International validity of the HOSPITAL score to predict 30-day potentially avoidable hospital readmissions. *JAMA Intern Med* 2016;176:496–502.
13 Wallace E, Stuart E, Vaughan N, *et al*. Risk prediction models to predict emergency hospital admission in community-dwelling adults: a systematic review. *Med Care* 2014;52:751–65.
14 Donnan PT, Dorward DW, Mutch B, *et al*. Development and validation of a model for predicting emergency admissions over the next year (PEONY): a UK historical cohort study. *Arch Intern Med* 2008;168:1416–22.
15 Walsh TS, Salisbury L, Donaghy E, *et al*. PReventing early unplanned hOspital readmission aFter critical ILlnEss (PROFILE): protocol and analysis framework for a mixed methods study. *BMJ Open* 2016;6:e012590.
16 SICSAG. Scottish intensive care society audit group annual report: audit of intensive care units in Scotland 2016 Reporting on 2015. 2016 http://www.sicsag.scot.nhs.uk/docs/2016-08-09-SICSAG-Publication-Report.pdf (cited 04 Oct 2016).
17 SICSAG. Scottish intensive care society audit group annual report: data quality. 2017 http://www.sicsag.scot.nhs.uk/quality/data.html (cited 06 Apr 2017).
18 NSS. Assessment of SMR01 Data Scotland 2014-2015. 2015 http://www.isdscotland.org/Health-Topics/Hospital-Care/Publications/2012-05-08/Assessment-of-SMR01Data-2010-2011-ScotlandReport.pdf (cited 06 Apr 2017).
19 Scotland NRo. Migration between Scotland and Overseas. 2017 http://www.nrscotland.gov.uk/statistics-and-data/statistics/statistics-by-theme/migration/migration-statistics/migration-between-scotland-and-overseas (cited 01 May 2017).
20 Kerr KF, Wang Z, Janes H, *et al*. Net reclassification indices for evaluating risk prediction instruments: a critical review. *Epidemiology* 2014;25:114–21.
21 Moons KG, Altman DG, Reitsma JB, *et al*. Transparent Reporting of a multivariable prediction model for Individual Prognosis or Diagnosis (TRIPOD): explanation and elaboration. *Ann Intern Med* 2015;162:W1–73.
22 Blunt I, Bardsley M, Grove A, *et al*. Classifying emergency 30-day readmissions in England using routine hospital data 2004-2010: what is the scope for reduction? *Emerg Med J* 2015;32:44–50.

23 Fischer C, Lingsma HF, Marang-van de Mheen PJ, *et al*. Is the readmission rate a valid quality indicator? A review of the evidence. *PLoS One* 2014;9:e112282.
24 Press MJ, Scanlon DP, Ryan AM, *et al*. Limits of readmission rates in measuring hospital quality suggest the need for added metrics. *Health Aff* 2013;32:1083–91.
25 Iwashyna TJ. Trajectories of recovery and dysfunction after acute illness, with implications for clinical trial design. *Am J Respir Crit Care Med* 2012;186:302–4.
26 Iwashyna TJ, Netzer G, Langa KM, *et al*. Spurious inferences about long-term outcomes. *Am J Respir Crit Care Med* 2012;185:835–41.
27 Hua M, Gong MN, Brady J, *et al*. Early and late unplanned rehospitalizations for survivors of critical illness*. *Crit Care Med* 2015;43:430–8.
28 Kansagara D, Englander H, Salanitro A, *et al*. Risk prediction models for hospital readmission a systematic review. *JAMA* 2011;306:1688–98.
29 Cameron JI, Chu LM, Matte A, *et al*. One-year outcomes in caregivers of critically Ill patients. *N Engl J Med* 2016;374:1831–41.
30 Deacon KS. Re-building life after ICU: a qualitative study of the patients' perspective. *Intensive Crit Care Nurs* 2012;28:114–22.
31 Bagshaw SM, Stelfox HT, Johnson JA, *et al*. Long-term association between frailty and health-related quality of life among survivors of critical illness: a prospective multicenter cohort study. *Crit Care Med* 2015;43:973–82.
32 Greysen SR, Stijacic Cenzer I, Auerbach AD, *et al*. Functional impairment and hospital readmission in Medicare seniors. *JAMA Intern Med* 2015;175:559–65.
33 Lacroix J, Hébert PC, Fergusson DA, *et al*. Age of transfused blood in critically ill adults. *N Engl J Med* 2015;372:1410–8.
34 Hasan O, Meltzer DO, Shaykevich SA, *et al*. Hospital readmission in general medicine patients: a prediction model. *J Gen Intern Med* 2010;25:211–9.
35 van Walraven C, Dhalla IA, Bell C, *et al*. Derivation and validation of an index to predict early death or unplanned readmission after discharge from hospital to the community. *CMAJ* 2010;182:551–7.
36 Ferrante LE, Pisani MA, Murphy TE, *et al*. Functional trajectories among older persons before and after critical illness. *JAMA Intern Med* 2015;175:523–9.
37 Griffith DM, Lewis S, Rossi AG, *et al*. Systemic inflammation after critical illness: relationship with physical recovery and exploration of potential mechanisms. *Thorax* 2016;71:820–9.
38 Bailey SC, Fang G, Annis IE, *et al*. Health literacy and 30-day hospital readmission after acute myocardial infarction. *BMJ Open* 2015;5:e006975.
39 van Walraven C, Bennett C, Jennings A, *et al*. Proportion of hospital readmissions deemed avoidable: a systematic review. *CMAJ* 2011;183:E391–402.
40 Craig P, Dieppe P, Macintyre S, *et al*. Developing and evaluating complex interventions: the new Medical Research Council guidance. *BMJ* 2008;337:a1655.
41 Hartl S, Lopez-Campos JL, Pozo-Rodriguez F, *et al*. Risk of death and readmission of hospital-admitted COPD exacerbations: European COPD Audit. *Eur Respir J* 2016;47:113–21.
42 Jones K, Saxon L, Cunningham W, *et al*. Secondary prevention for patients after a myocardial infarction: summary of updated NICE guidance. *BMJ* 2013;347:f6544.
43 Faculty of Intensive Care Medicine. Guidelines for the Provision of Intensive Care Services. 2015 https://www.ficm.ac.uk/standards-and-guidelines/gpics (cited 14 Oct 2016).
44 Dworzynski K, Ritchie G, Fenu E, *et al*. Rehabilitation after stroke: summary of NICE guidance. *BMJ* 2013;346:f3615.