Readmission to intensive care: development of a nomogram for individualising risk

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ABSTRACT

Background: Readmission to intensive care during the same hospital stay has been associated with a greater risk of in-hospital mortality and has been suggested as a marker of quality of care. There is lack of published research attempting to develop clinical prediction tools that individualise the risk of readmission to the intensive care unit during the same hospital stay.

Objective: To develop a prediction model using an inception cohort of patients surviving an initial ICU stay.

Design, setting and participants: The study was conducted at Liverpool Hospital, Sydney. An inception cohort of 14 952 patients aged 15 years or more surviving an initial ICU stay and transferred to general wards in the study hospital between 1 January 1997 and 31 December 2007 was used to develop the model. Binary logistic regression was used to develop the prediction model and a nomogram was derived to individualise the risk of readmission to the ICU during the same hospital stay.

Main outcome measure: Readmission to the ICU during the same hospital stay.

Results: Among members of the study cohort there were 987 readmissions to ICU during the study period. Compared with patients not readmitted to the ICU, patients who were readmitted were more likely to have had ICU stays of at least 7 days (odds ratio [OR], 2.2 [95% CI, 1.85–2.56]); non-elective initial admission to the ICU (OR, 1.7 [95% CI, 1.44–2.08]); and acute renal failure (OR, 1.6 [95% CI, 0.97–2.47]). Patients admitted to the ICU from the operating theatre or recovery ward had a lower risk of readmission to ICU than those admitted from general wards, the emergency department or other hospitals. The maximum error between observed frequencies and predicted probabilities of readmission to ICU was estimated to be 3%. The area under the receiver operating characteristic curve of the final model was 0.66.

Conclusion: We have developed a practical clinical tool to individualise the risk of readmission to the ICU during the same hospital stay in patients who survive an initial episode of intensive care.

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Readmission to the intensive care unit during the same hospital stay has been associated with a greater risk of in-hospital mortality and has been suggested as a marker of quality of care.[1-3] About one in 10 patients surviving an episode of intensive care will be readmitted to the ICU during the same hospitalisation.[2] It is not clear whether the decision to discharge patients from the ICU or the level of care given to these patients on the general wards, or a combination of both, results in readmission to the ICU. Therefore, the ability to identify patients at high risk of readmission to the ICU during the same hospitalisation could allow objective decisions to be made by clinicians regarding the timing of discharge from intensive care, the level of care required by patients on the ward and the need for follow-up by ICU staff. To date, there is a lack of published research on developing clinical prediction tools to individualise the risk of readmission to the ICU during the same hospital stay.[4]

In an attempt to address this problem, we developed a prediction model using an inception cohort of patients surviving an initial ICU stay, as well as a nomogram to individualise risk in patients who survive intensive care and are transferred to the general ward.

Methods

Our study was conducted at Liverpool Hospital, a large teaching hospital in south-western Sydney, Australia, with a 24-bed ICU that has about 2000 admissions per year. The inception cohort used to develop the prediction model consisted of all patients aged 15 years or over who survived an initial ICU stay and were transferred to general ward areas in the study hospital between 1 January 1997 and 31 December 2007. All patients with a decision to limit treatment during an initial ICU stay were excluded from the study. The study was approved by the institutional ethics committee of Liverpool Hospital.

Predictors

In an attempt to avoid over-fitting, potential predictors of ICU readmission were restricted to those identified in previous published literature.[2,5-7] These predictors included increasing age, being male, elective admission status to the

ICU, source of ICU admission, severity of illness at admission to the ICU, length of stay in the ICU, discharge from the ICU after hours, the presence of comorbid conditions on admission to the ICU, and acute renal failure during the ICU stay.

Severity of illness was presented as an APACHE II (Acute Physiology and Chronic Health Evaluation II) score,[8] and comorbid conditions on admission to the ICU were calculated using the Charlson Index.[9] The Charlson Index was calculated using ICD-10 codes suggested by Quan et al[10] and an SAS macro written by one of the authors (S A F). The use of severity of illness on admission to the ICU was justified on two grounds: (i) most ICUs routinely collect these data on admission, but collection of severity of illness data at discharge is less common; and (ii) a meta-analysis has shown that the gradient of risk of readmission to ICU is similar regardless of whether severity of illness is measured at admission or at discharge.[11]

Outcome

The main outcome measure of our study was readmission to the ICU during the same hospital stay. The characteristics of early readmissions (occurring < 72 hours after discharge from the ICU) and late readmissions (occurring 72 hours or more after ICU discharge) are presented here. However, in the final prediction model, and therefore nomogram, the outcome of interest was *any* readmission to the ICU during the same hospital stay. A minimum of 10 events during the study period was required to retain a predictor, because the instability of using less than 10 events in developing a predictive model has been well described in the literature.[12,13] As patients who were initially admitted to the ICU from other ICUs (outside the study hospital) had, as a group, less than 10 readmissions to the ICU during the study period, they were added to the "admission from other hospitals" category. For the same reason, patients admitted to the ICU from the coronary care unit were added to the "admitted from ward" category.

Model derivation

A binary logistic regression model was used to develop the multivariate prediction model. Where appropriate, we inspected linearity between continuous predictors and the log odds ratio and assessed potential interaction between predictors, using methods suggested by Harrell et al.[12] Predictors included in the final model were selected using bootstrap methods. In the process, variables were selected using a backward-deletion method, with a generous *P* value for retention (0.2). This procedure was repeated 200 times, and predictors appearing in at least 60% of bootstrap models were included in the final model.[13]

Bootstrap methods were also used to assess over-fitting of predictors and to shrink estimates using a penalised model suggested by Harrell et al.[12,13] Over-fitting occurs when a model performs particularly well on the data set at hand, but subsequent generalisation to external or future hospital populations results in poor performance of predictors. In the process described by Harrell et al, estimates are adjusted using a shrinkage factor derived using repeated bootstrap models (with replacement) to calculate the over-optimism of estimates derived from predictors in the final model. This technique has shown that estimates that are penalised perform much better when applied to populations that are external to that used to derive the prediction model.[14]

To avoid violation of the assumption of independence due to multiple admissions of patients during the study period, bootstrap methods were used to develop the final logistic regression model estimates for the nomogram.[12,15] Both the estimate of effect (odds ratio [OR]) and confidence intervals were derived from repeated bootstrap samples restricted to single admissions in patients admitted more than once during the study period.

Model validation

The ability of the final model to discriminate between patients who were readmitted to the ICU and those who were not was assessed by the area under the receiver operating characteristic curve (AUC).[15] An area of 1.0 reflects a perfect discrimination, and an area of 0.5 reflects discrimination no better than random choice. Internal validation of the final predictive model included bootstrap methods to assess how accurately the model would predict readmission to the ICU in a similar population of patients. In this method, a sub-sample of 50 patients was used to create a training model, which was then applied to the whole data set to estimate biases between the observed and predicted rates of the outcome. This was repeated 200 times to create a distribution of bias between predicted and observed rates, and to estimate the maximum calibration error.[12]

Using the final model, we developed a nomogram for predicting the probability of readmission to the ICU in an individual during the same hospital stay. All analysis was undertaken using the R statistical language.[16] The Design package developed by Harrell[12] was used to create the nomogram. Data management was undertaken using SAS software, version 9.1 (SAS Institute, Inc, Cary, NC, USA).

Results

Model derivation

During the 11-year study period, an inception cohort of 14 952 patients aged 15 years or more survived an initial

Table 1. Characteristics of patients who survived an episode of intensive care and were transferred to general wards, by readmission status*

Characteristic	Readmission to ICU status			Combined	*P*
	No readmission to ICU	Early readmission to ICU (< 72 hours)	Late readmission to ICU (⩾ 72 hours)		
Admissions	13 965	404	583	14 952	
Number of patients	12 534	374	522	13 430	
Mean age in years (SD)	57 (18)	59 (18)	60 (17)	57 (18)	< 0.001
Male *n* (%)	8 448 (61%)	257 (64%)	349 (60%)	9 054 (61%)	0.400
Elective admission to ICU *n* (%)	4 390 (31%)	82 (20%)	166 (20%)	4 588 (31%)	< 0.001
Source of ICU admission *n* (%)					< 0.001
Emergency department	7 140 (51%)	190 (47%)	254 (44%)	7 584 (51%)	
Operating theatre/recovery ward	4 229 (30%)	95 (24%)	140 (24%)	4 464 (30%)	
General ward	1 639 (12%)	83 (21%)	117 (20%)	1 839 (12%)	
Another hospital	914 (7%)	32 (8%)	70 (12%)	1 016 (7%)	
Another ICU	22 (< 1%)	1 (< 1%)	2 (< 1%)	25 (< 1%)	
Coronary care unit	19 (< 1%)	3 (1%)	0	22 (< 1%)	
Mean APACHE II score (SD)	13 (7)	15 (8)	16 (7)	13 (7)	< 0.001
Median ICU length of stay (IQR)	2 (1–4)	2 (1–6)	3 (1–7)	2 (1–4)	< 0.001
ICU stay ⩾ 7 days *n* (%)	1 782 (13%)	108 (27%)	174 (30%)	2 064 (14%)	< 0.001
Discharged from ICU after hours† *n* (%)	6 965 (50%)	211 (52%)	348 (60%)	7 524 (50%)	< 0.001
Charlson Index *n* (%)					
No comorbidity	11 475 (82%)	331 (82%)	463 (79%)	12 269 (82%)	0.040
1	706 (5%)	17 (4%)	22 (4%)	745 (5%)	
2	537 (4%)	21 (5%)	25 (4%)	583 (4%)	
⩾ 3	1 245 (9%)	35 (9%)	73 (13%)	1 353 (9%)	
Acute renal failure in ICU *n* (%)	145 (1%)	6 (1%)	17 (3%)	168 (1%)	< 0.001
In-hospital mortality *n* (%)	637 (5%)	91 (23%)	141 (24%)	869 (6%)	< 0.001

APACHE = Acute Physiology and Chronic Health Evaluation. ICU = intensive care unit. IQR = interquartile range. * Categorical data were compared using a Pearson χ^2 test, and continuous data using a Wilcoxon or Kruskal-Wallis test. † Discharged from ICU outside the hours of 08:00–16:00.

ICU stay and were transferred to general wards in the study hospital. Among members of this cohort, 987 readmissions to the ICU (involving 896 patients) occurred during the same hospital stay. Characteristics of patients admitted to the ICU then discharged to a general ward, by readmission status, are presented in Table 1. Patients readmitted to the ICU tended to be older and had a higher proportion of non-elective initial admissions to the ICU; they also tended to have greater severity of illness (APACHE II score) on initial admission to the ICU and were more likely to stay in the ICU for at least 7 days. The frequency of discharges from the ICU after hours (outside 08:00–16:00 hrs) and acute renal failure during the initial ICU stay were higher among patients who were readmitted to the ICU, and their mortality rate was 4–5 times higher than that of patients discharged to the ward after an initial ICU stay and not readmitted.

Estimates of effect (ORs) of predictors retained in the final model and risk of readmission to the ICU during the same hospitalisation are presented in Table 2. Patients with ICU stays of at least 7 days were at the highest relative risk of readmission to the ICU (OR, 2.2 [95% CI, 1.85–2.56]), followed by those with non-elective initial admission to the ICU (OR, 1.7 [95% CI, 1.44–2.08]) and those with acute renal failure (OR, 1.6 [95% CI, 0.97–2.47]). Also, compared with admissions to the ICU from the operating theatre or recovery ward, patients initially admitted from other sources (the ward, emergency department or other hospital hospitals) had a higher risk of readmission to the ICU (Table 2).

Model fit

Internal validation of the model using bootstrap methods resulted in an estimated maximum calibration error of 3%

between predicted probabilities and observed frequencies of readmission to the ICU. The AUC was 0.66, and the correlation between observed frequencies and predicted probability was 0.32 (Figure 1).

Model application

The final model to individualise the risk of readmission during the same hospitalisation in patients discharged to the ward from the ICU is presented as a nomogram in Figure 2. For example, a 70-year old male non-electively admitted to the ICU from the emergency department, with an APACHE II score of 20, with acute renal failure, who stayed in the ICU for at least 7 days and was discharged after hours would have a one in four (25%) risk of readmission to the ICU during the same hospital stay.

Discussion

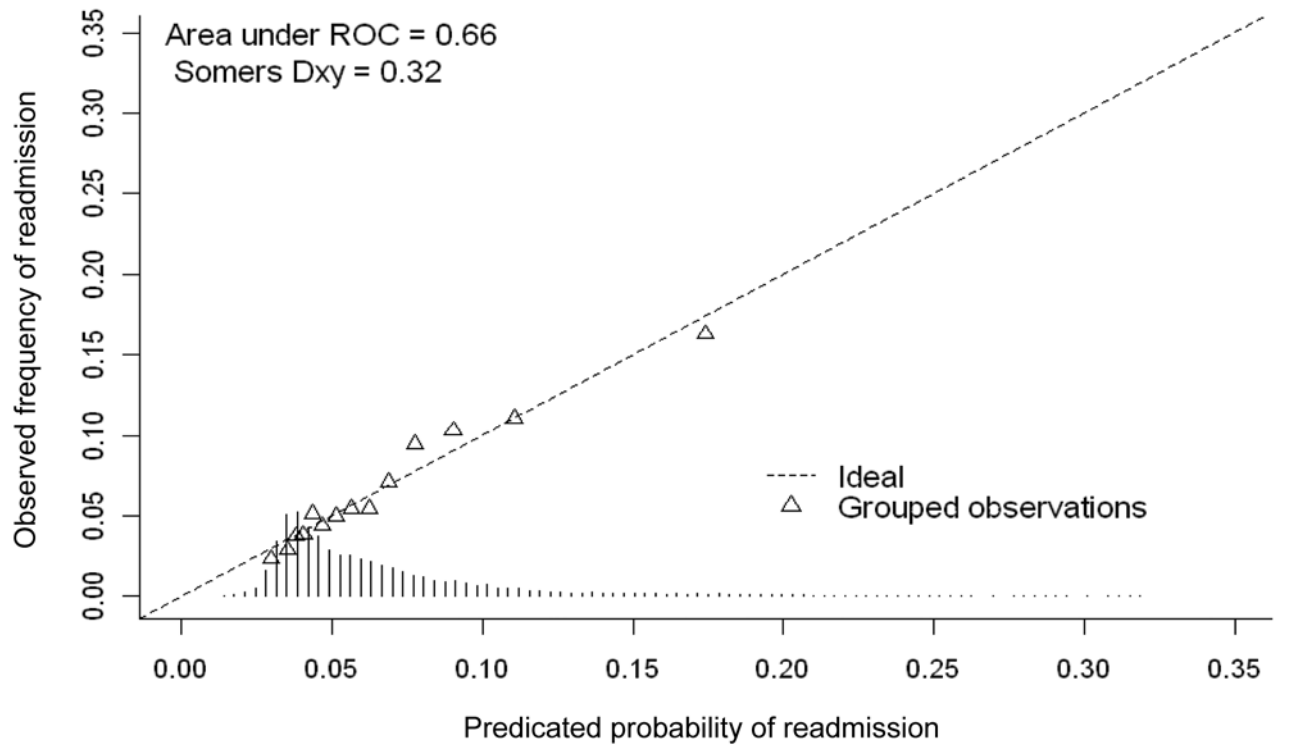
We were able to develop a practical clinical tool to individualise the risk of readmission to the ICU during the same hospital stay. This tool is targeted at patients who survive an

Table 2. Final logistic regression model estimates

Characteristic	Odds ratio (95% CI)	*P*
Age (per each 10 years)	1.1 (1.01–1.09)	0.02
Male	1.1 (0.95–1.25)	0.21
Non-elective admission*	1.7 (1.44–2.08)	< 0.01
Source of admission to ICU		
Operating theatre/recovery ward	1.0†	< 0.01
Emergency department	1.5 (1.27–1.83)	< 0.01
General ward	1.9 (1.58–2.36)	< 0.01
Other hospital	1.6 (1.24–2.03)	< 0.01
APACHE II score (per each SD)	1.2 (1.07–1.23)	< 0.01
ICU stay ⩾ 7 days	2.2 (1.85–2.56)	< 0.01
Discharged from ICU after hours‡	1.2 (1.04–1.36)	0.01
Acute renal failure in ICU	1.6 (0.97–2.47)	0.06

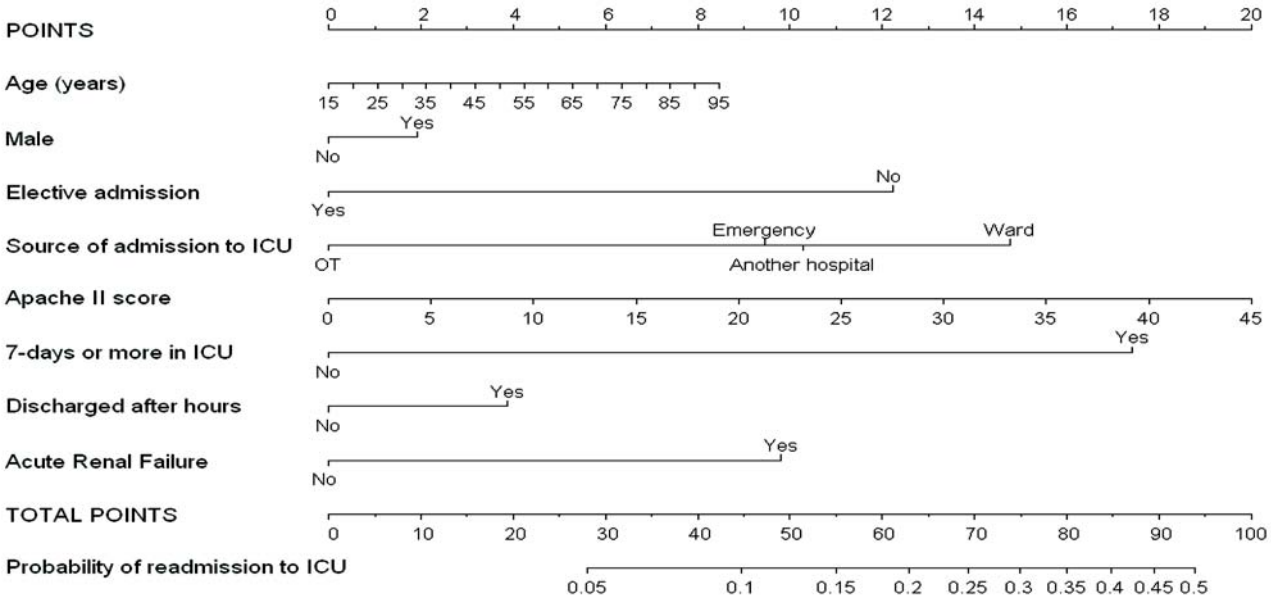
APACHE = Acute Physiology and Chronic Health Evaluation. ICU = intentive care unit. * Source of data: Australian and New Zealand Intensive Care Society database. † Reference value. ‡ Discharged from ICU outside the hours of 08:00–16:00.

Figure 1. Predicted probability versus observed frequencies of readmission to the ICU during the same hospitalisation*



ICU = intensive care unit. ROC = receiver operating characteristic. Somers Dxy = Somers rank correlation. * Model calibration — observed frequencies and predicted probability of groups (of at least 100). Area under the ROC curve and Somers rank correlation among observed frequencies and predicted probabilities have been added to the plot, as well as an ideal line of agreement. The distribution of predicted probabilities of readmission to ICU is presented as vertical bars.

Figure 2. Nomogram for predicting the probability of readmission to the ICU during the same hospitalisation*



APACHE = Acute Physiology and Chronic Health Evaluation. ICU = intensive care unit. OT = operating theatre. * Instructions: For each characteristic, locate the individual's profile on the appropriate axis. Using a pencil and ruler, draw a line vertically up to the top "points" axis. Sum the points for individual characteristics to create a total score. Using the total score, draw a line vertically down from the "total points" axis through the "probability of readmission to ICU" axis to obtain risk. For example, a 70-year-old (6 points) male (2 points) non-electively admitted to ICU (12 points) from the emergency department (9 points), with an APACHE II score of 20 (9 points), with acute renal failure (10 points), who stayed in the ICU for at least 7 days (17 points) and was discharged after hours (4 points) has a total point score of 69, corresponding to a 25% risk of readmission to ICU during the same hospital stay.

initial episode of intensive care and are then discharged to general wards. Potential predictors of readmission to the ICU were obtained from previous literature. Data on these predictors are commonly collected in the ICU setting. Model parameters were penalised by a shrinkage factor to avoid over-fitting, and the maximum error between observed frequencies and predicted probabilities of readmission to the ICU was estimated to be 3%. The final model was shown to have modest discriminatory ability to separate individuals who would or would not be readmitted to the ICU during the same hospitalisation (AUC, 0.66).

Previous prediction tools to identify patients at risk of readmission to the ICU during the same hospital stay have been limited to measures of workload or severity of illness. The Stability and Workload Index for Transfer (SWIFT) score[4] out-performed models based on APACHE II score plus characteristics of ICU stay (such as length of stay, mechanical ventilation days and days to ICU admission) in its ability to discriminate between readmission and non-readmission (SWIFT AUC, 0.75, v APACHE II + stay characteristics AUC, 0.69). The SWIFT score was also validated in the same North American ICU in which its was developed on a later prospective cohort and in a mixed medical–surgical European ICU population (AUCs, 0.74 and 0.70, respectively).[4]

A limitation to previous attempts to identify patients at risk of readmission to the ICU has been the absence of tools for individualising risk. Our study offers a clinically useful tool for identifying patients at risk of readmission to intensive care at the time of discharge from the ICU to general wards. Variation between the specific predictors of readmission identified in our study and those identified by other authors highlights the need for hospitals to develop local risk models. For instance, patients in our cohort who survived an initial ICU stay or were admitted to the ICU from the operating theatre had a lower risk of readmission than patients admitted from the emergency department or general ward. In contrast, Metnitz et al[17] found no difference between admission categories in rates of readmission and non-readmission to the ICU. And, in extreme contrast, Ho et al[6] found that patients who were initially admitted to the ICU from the operating theatre had a higher risk of readmission to the ICU than patients admitted to the ICU from the emergency department or ward.

Nomograms to individualise patient risk are widely reported in cancer research[18-24] and sporadically in other clinical settings.[25-28] However, to our knowledge, they have not been applied to individualise risk of readmission to the ICU during the same hospitalisation. Our investi-

gation therefore offers an important innovation for identifying patients who survive an episode of intensive care, are transferred to a general ward, and are at risk of readmission to the ICU. However, the utility of a prediction model depends on two important components of accuracy:

- How well the model is calibrated. For example, if the average predicted proportion of readmissions to the ICU was 0.15 and the actual observed proportion was 0.15, the model would be considered to be well calibrated.
- The discriminatory ability of the model. In predicting a binary outcome, this is reduced to the proportion of all pairs of patients surviving an episode of intensive care and transferred to the general ward (one with the outcome of readmission to ICU and one without), and the probability of the final model to assign higher risk in individuals with the outcome of interest. This probability is reported as the AUC.

In addressing these two important issues of prognostic model performance, we were able to develop a prognostic model with moderate discriminatory ability (AUC = 0.66) and good calibration (maximum calibration bias of 3%) to individualise risk of readmission to the ICU during the same hospitalisation.[13]

Limitations of our study should be highlighted. For instance, any tools used to identify patients at risk of readmission to the ICU will have difficulty predicting acute events that occur on wards, such as gastrointestinal bleeds, cardiovascular ischaemia, cardiac arrhythmias and new episodes of sepsis.[3] Furthermore, by using administrative data, we may have underestimated the effects of some factors (eg, comorbid status, which relies on the use of hospital ICD codes to calculate a Charlson Index). What we have done is to use data that are routinely collected on ICU patients to develop a tool that can identify patients at risk of readmission once discharged to the ward. A potential limitation of our study was that data used to develop our model were limited to those routinely collected by our ICU. On the other hand, development of such a tool by any ICU would in most cases require no new data collection.

Although the prediction model was shown to perform well on the population of patients used to develop it, historically the clinical usefulness of any prediction model has been assessed on its external validation. Perhaps novel in health services research, but common in such areas as econometrics, external validation of results is not the aim of model development, and we would encourage hospitals to develop their own specific models to identify patients at risk of readmission to intensive care during the same hospital stay. In other words, a potential strength of our study is that the methods (rather than the results) can be generalised to other hospitals.

The clinical application of our prediction model would be the specific follow-up of high-risk patients by critical-care outreach teams. This has already been proposed as a way of reducing readmission rates.[29] What our tool adds is the ability to individualise risk and therefore target high-risk patients, who would then remain under surveillance by ICU outreach staff in an attempt to prevent readmission to intensive care.

Conclusion

We developed a practical clinical tool to individualise the risk of readmission to the ICU during the same hospital stay in patients who survive an initial episode of intensive care. Using a pencil and ruler, and routinely collected ICU data, clinicians can identify, at the time of discharge from the ICU, patients who should be followed up to help prevent readmission to the ICU.

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