Predicting readmission to intensive care after cardiac surgery within index hospitalization: A systematic review

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Journal of Cardiothoracic and Vascular Anesthesia

Predicting readmission to intensive care after cardiac surgery within index hospitalization: A systematic review

--Manuscript Draft--

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	Stuart W. Grant, PhD, FRCS(cth)
Abstract:	<p>Readmission to the cardiac intensive care unit (CICU) after cardiac surgery has significant implications for both patients and healthcare providers. Identifying patients at risk of readmission could potentially improve outcomes. The objective of this systematic review was to identify risk factors and clinical prediction models for readmission within a single hospitalization to intensive care after cardiac surgery. PubMed, MEDLINE and EMBASE databases were searched to identify candidate articles. Only studies that utilised multivariable analyses to identify independent predictors were included.</p> <p>There were 25 studies and five risk prediction models identified. The overall rate of readmission pooled across the included studies was 4.9%. In all 25 studies, in-hospital mortality and duration of hospital stay were higher in patients who experienced readmission. Recurring predictors for readmission were; preoperative renal failure, age >70, diabetes, chronic obstructive pulmonary disease, preoperative left ventricular ejection fraction <30%, type and urgency of surgery, prolonged cardiopulmonary bypass time, prolonged post-operative ventilation, postoperative anaemia and neurological dysfunction. The majority of readmissions occurred due to respiratory and cardiac complications. Four models were identified for predicting readmission, with one external validation study. As all models developed to date have limitations, further work on larger datasets is required to develop clinically useful models to identify patients at risk of readmission to CICU after cardiac surgery.</p>

Tuesday 31st March 2020

Dear Professor Kaplan,

Re. "Predicting readmission to intensive care after cardiac surgery; a systematic review."

I attach the above manuscript for consideration of publication in the Journal of Cardiothoracic and Vascular Anaesthesia. Readmission to intensive care after cardiac surgery is an important outcome for both patients and health care organisations. Accurately identifying patients who are at high-risk for readmission to ICU is an important step in trying to avoid this event and improve outcomes associated with it.

Research has already been undertaken to this end, but a systematic review of this topic has not previously been performed. This systematic review summarises risk factors for readmission to intensive care and the impact of readmission on outcomes. It includes all published studies that have performed multivariable analyses to identify risk factors for readmission and focusses on developed clinical prediction models.

We think that the information included in this manuscript will be of significant interest to your readership and is likely to be well cited. We would also hope that this review would provide a sound basis for further research into reducing rates of ICU readmission and improving clinical outcomes.

This manuscript has not been published elsewhere or submitted to any other journal. All authors have approved the manuscript for submission and take responsibility for the data presented to the Journal of Cardiothoracic and Vascular Anaesthesia. This work was supported by British Heart Foundation Grant no: PG/16/80/32411 and there are no other conflicts of interest.

Yours sincerely,

Mr Stuart Grant MBChB (Hons), MRCS, PhD

Academic Clinical Lecturer in Cardiothoracic Surgery

Linda Kimani

Samuel Howitt

Charlene Tennyson

Richard Templeton

Charles McCollum

Stuart Grant

4th January 2021

Dear Professor Kaplan,

Re. "Predicting readmission to intensive care after cardiac surgery; a systematic review."

We attach the above revised manuscript for publication in the Journal of Cardiothoracic and Vascular Anaesthesia.

This manuscript has not been published elsewhere or submitted to any other journal. All authors have approved the manuscript for submission to the Journal of Cardiothoracic and Vascular Anaesthesia.

This work was supported by British Heart Foundation Grant no: PG/16/80/32411 and there are no other conflicts of interest.

Yours sincerely,

Linda Kimani

Samuel Howitt

Charlene Tennyson

Richard Templeton

Charles McCollum

Stuart Grant

Manuscript Number: JCVA-D-20-00378R1

Predicting readmission to intensive care after cardiac surgery: A systematic review

Editor and Reviewer comments:

Section Editors

Thank you for this submission.

Please revise - respond to the reviewers in a point-by-point fashion.

Please make clear in the title, abstract, and throughout the revised paper that the focus is readmission to intensive care after cardiac surgery within the same hospitalization.

We thank you for this suggestion, the revised manuscript now clarifies throughout that we are referring to readmission within a single hospitalization.

Reviewer 1:

1. The reviewers have clarified many of my comments and the review is much improved.

We thank the reviewer for this comment.

2. Overall, the results are expected; that older patients, those with renal failure, low EF, DM, etc have a higher risk of re-admission to the CICU.
3. I have two general comments:

The introduction states that the main purpose of the review is to determine predictive variables but in results this is reported last. The intro should be consistent and identify that mortality, length of stay and cause were variables of interest.

We agree that presenting the predictive variables last diminished their importance in the results section. As this is the focus of the review, we have therefore adjusted the results section to present these variables first. Page 2 line 23 now includes mortality, length of stay and readmission causes as variables of interest.

The predictors are the variable most subject to confounding so maybe the main result or focus of the review should be to better characterize causes of readmission and effect on the population?

We agree a review that better characterises the causes for readmission and effect on the population would be useful. However, the primary objective of this review is to identify risk factors associated with readmission to CICU and models that may be useful when aiming to identify those patients who are at risk of readmission. A better understanding of these risk factors and existing models is vital to future risk prediction work which aims to reduce readmissions to CICU following cardiac surgery. It is anticipated that this review forms the basis of such future work.

4. While this has not been done before, these results are not a surprise, in fact they are similar to preoperative predictors of morbidity. The question of why looking at re-admission only - why it

is clinically important should be better addressed.

We thank the reviewer for this suggestion, page 2 line 14 to 16 highlight the key clinical importance of readmissions which include increased mortality in readmitted than non-readmitted patients, (Rosenberg,2000 and Elliot, 2014) and the unexpected strain on resources (Onwochei,2020). These factors are associated with perioperative morbidity but prevention or planning of readmission may contribute to reduced overall mortality and morbidity following cardiac surgery.

5. Is the abstract in JCVA format?

Yes the abstract is unstructured in line with the JCVA online guide for authors

6. This can be shorted to simply say that "a systematic review of studies identifying risk factors for readmission to CICU after cardiac surgery has not previously been published".

"In non-cardiac patients, initial admission to intensive care after elective surgery is much less common. Unplanned admission or readmission to general intensive care in this cohort however occurs in 4- 14% of patients. 6 A systematic review of risk factors for unplanned admission or readmission to general intensive care has been performed."

Thank you for this suggestion. We agree that this section was difficult to follow so we have reworked it on Page 2 line 17 to 24.

Reviewer 3:

Authors addressed Reviewer comments in a comprehensive and thoughtful manner. As a result, the manuscript organization, clarity, and focus has improved. Thank you for this kind comment.

Reviewer 6:

1. The authors revised the manuscript substantially and extensively, clearing out many of the reviewers' comments. Thank you.

We thank the reviewer for this comment.

2. The fact that so few studies include numbers of enrolled patients is strange and questions the (statistical) validity of these studies.

In the summary of included studies (table 1) the patient population column details the numbers of enrolled patients. This is described in all the studies included in this review.

3. When patients are at risk for readmission, as the authors list up the most important risk factors from the literature, it should also be questioned whether these factors were not yet present at the time of discharge of the patients from the ICU. Was there a checklist before discharge of the patients?

The timing of when risk factors were assessed was inconsistent, which was a limitation of this review however Page 7 line 21 in the manuscript clarifies that physiological risk factors were recorded prior to initial discharge for CICU in 5 studies. We addressed the variable timings of risk factors by grouping the risk factors as preoperative, intraoperative and postoperative. All pre- and intraoperative risk factors were evidently present prior to initial CICU discharge. Post-operative predictors, where included, were for the most part also available prior to CICU discharge. No study described the use of a checklist prior to the discharge of patients from the CICU at the end of their initial stay.

4. A better follow up before discharge could have prevented readmission. Therefore, it could be strongly questioned whether prediction of readmission should not be brought back to a correct estimation of discharge-fitness after cardiac surgery. The latter could be integrated in a discharge-score, including screening of the most important organ systems and presence of some limited acute readmission causes (such as late tamponade, progressive heart failure, sepsis/septic or cardiogenic shock, rhythm disturbances necessitating additional therapy. Additional search in the literature on discharge criteria - a correct discharge is always with the aim of preventing readmission - is therefore an important issue in this respect. Please comment.

We agree wholeheartedly that assessment of fitness for discharge is a vital component for preventing potentially avoidable readmissions. One goal of this review is to identify factors which are present at the time of discharge and which are associated with increased risk of readmission. Future work can focus on the development of tools, similar to those you describe, which aim to recognise potentially unsafe discharges before they are made. During this review we identified many studies which define readmission as any readmission occurring at any time during a single hospitalization. This includes 'late readmissions' which occur beyond 72 hours and are less influenced by discharge fitness and more likely to be related to ward level factors. Therefore, as explored in our discussion we believe it is important to separate admissions according to the time at which they occur. Any tool aimed to ensure "discharge-fitness" should probably be based on risk factors known to be associated with earlier readmission.

5. Another point is the fact that in reality an acute readmission should be differentiated from a non-acute readmission. Also, these issues must be commented and checked in the literature for further details.

Thank you for this point. Again, we agree acute readmission should be separated from planned or delayed readmissions. This distinction is not clear in the studies in this review however it has been looked at in non-cardiac surgery patients readmitted to general ICU. We identify this lack of clarity as a weakness in the literature and as an area to be explored in future research. We have now emphasized this point on Page 15 line 4 to 6.

Renal insufficiency was not defined in terms of the RIFLE criteria (remark 5), which is essential in modern medicine to estimate the degree of failure. Similarly, respiratory complications should be differentiated as not all respiratory failure could result in readmission (remark 5).

We agree that this is a weakness of the studies included in this review. Renal insufficiency was reported in terms of various increases creatinine criteria which may be used to classify the insufficiency by the RIFLE criteria. Unfortunately, the term renal failure also encompassed the requirement for hemofiltration in several studies, therefore we could not group all the definitions by the RIFLE criteria. Similarly, pulmonary dysfunction was variably reported from requirements for intubation/ ventilation to aetiological causes for dysfunction and these groups were not consistently reported independently. We have emphasized the importance of using standardized definitions in future work on this subject. Page 15 line 19-24.

Predicting readmission to intensive care after cardiac surgery within index hospitalization: A systematic review

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Declarations of interest: None

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Predicting readmission to intensive care after cardiac surgery **within index hospitalization**: A systematic review

ABSTRACT

Readmission to the cardiac intensive care unit (CICU) after cardiac surgery has significant implications for both patients and healthcare providers. Identifying patients at risk of readmission could potentially improve outcomes. The objective of this systematic review was to identify risk factors and clinical prediction models for readmission **within a single hospitalization** to intensive care after cardiac surgery. PubMed, MEDLINE and EMBASE databases were searched to identify candidate articles. Only studies that utilised multivariable analyses to identify independent predictors were included.

There were 25 studies and five risk prediction models identified. The overall rate of readmission pooled across the included studies was 4.9%. In all 25 studies, in-hospital mortality and duration of hospital stay were higher in patients who experienced readmission. Recurring predictors for readmission were; preoperative renal failure, age >70, diabetes, chronic obstructive pulmonary disease, preoperative left ventricular ejection fraction <30%, type and urgency of surgery, prolonged cardiopulmonary bypass time, prolonged post-operative ventilation, postoperative anaemia and neurological dysfunction. The majority of readmissions occurred due to respiratory and cardiac complications. Four models were identified for predicting readmission, with one external validation study. As all models developed to date have limitations, further work on larger datasets is required to develop clinically useful models to identify patients at risk of readmission to CICU after cardiac surgery.

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Predicting readmission to intensive care after cardiac surgery **within index hospitalization**: A systematic review

ABSTRACT

Readmission to the cardiac intensive care unit (CICU) after cardiac surgery has significant implications for both patients and healthcare providers. Identifying patients at risk of readmission could potentially improve outcomes. The objective of this systematic review was to identify risk factors and clinical prediction models for readmission **within a single hospitalization** to intensive care after cardiac surgery. PubMed, MEDLINE and EMBASE databases were searched to identify candidate articles. Only studies that utilised multivariable analyses to identify independent predictors were included.

There were 25 studies and five risk prediction models identified. The overall rate of readmission pooled across the included studies was 4.9%. In all 25 studies, in-hospital mortality and duration of hospital stay were higher in patients who experienced readmission. Recurring predictors for readmission were; preoperative renal failure, age >70, diabetes, chronic obstructive pulmonary disease, preoperative left ventricular ejection fraction <30%, type and urgency of surgery, prolonged cardiopulmonary bypass time, prolonged post-operative ventilation, postoperative anaemia and neurological dysfunction. The majority of readmissions occurred due to respiratory and cardiac complications. Four models were identified for predicting readmission, with one external validation study. As all models developed to date have limitations, further work on larger datasets is required to develop clinically useful models to identify patients at risk of readmission to CICU after cardiac surgery.

INTRODUCTION

Over the past two decades the in-hospital mortality rate after cardiac surgery has declined despite an increase in the risk profile of patients undergoing surgery.^{1,2} This is likely to be due to advances in surgical techniques, perioperative management and postoperative care supported by improved clinical governance processes.

Admission to a cardiac intensive care unit (CICU) is routine after cardiac surgery due to the physiological derangement induced by surgery, patient co-morbidities and the relatively high risk of significant early complications.

The majority of patients have a short stay on CICU, they are then transferred to a ward environment before ultimately being discharged home. The decision to de-escalate care from CICU to the ward setting is usually dependent on clinical judgement but can be facilitated by decision support protocols. Following transfer to the ward from CICU some patients will experience complications that require readmission to CICU within a single hospitalization. These unplanned readmissions place an unexpected strain on resources, reduce system efficiency and are a significant setback to patients.³⁻⁵

Readmission to general critical care units following surgery has been the subject of a systematic review.^{5,6} Although one study included in that review included a subgroup of cardiac surgery patients,⁷ a systematic review of studies identifying risk factors for readmission to CICU after cardiac surgery has not previously been published. The primary objective of this systematic review was therefore to identify risk factors associated with, or models designed to predict, readmission to CICU following cardiac surgery. The secondary objectives were to report common causes for readmission, associated mortality and length of stay.

METHODS

Search Strategy and Data Sources

The Cochrane library database of reviews and PubMed health database were searched using the terms, 'readmission', 'cardiac surgery', 'intensive care' for review articles between 1995 and 2019. We then searched MEDLINE and EMBASE using OVID the online library of databases. The search terms 'cardiac surgery', 'readmission' and terms for risk prediction models as recommended by Geersing et. al were used.⁸ The search strategy is detailed in Appendix 1. Titles in English and including readmission to intensive care were identified and selected. The reference lists of the eligible studies were searched to identify additional studies. The abstracts were then reviewed and assessed against the selection criteria.

Selection Criteria

All studies that reported readmission to intensive care after adult cardiac surgery were assessed for inclusion in the study. The inclusion criteria were: (1) adult patients who underwent cardiac surgery (2) reporting of readmission to CICU after during a single hospitalization as an outcome (3) reporting of multivariable analyses performed to identify risk factors for readmission. The exclusion criteria were: (1) inclusion of medical admissions or other surgical patients in the same cohort as the cardiac surgery patients (2) a lack of identification of factors associated with readmission (3) investigation of readmission to ICU after discharge from hospital (4) exclusion of papers looking at ICU admission following failed fasttrack care in a non ICU setting.

Terms and definitions

Risk factor- any variable assessed for its influence on readmission to intensive care.

The Society of Thoracic Surgeons (STS) database definitions were used by most

1 studies to define risk factors.⁹ Where a study applied a separate definition, this was
2 specified. *Readmission cause*- adverse event that resulted in return to ICU (planned
3 or unplanned) **within a single hospitalization**. *Independent predictor*- a variable
4 identified as significantly associated with readmission to ICU on multivariable
5 analysis.
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11 **Data extraction and Quality Assessment**

12 The articles for inclusion were selected by independent reviewers LK, SH and CT.
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15 Data were extracted using a framework detailed in appendix 2. The review was
16 structured according to the Checklist for critical Appraisal and data extraction for
17 systematic Reviews of prediction Modelling Studies (CHARMS) and the Preferred
18 Reporting Items for Systematic reviews and Meta-Analyses (PRISMA) guidance.^{10,11}
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26 The following elements of each study were reviewed and reported; aim, outcome
27 definition, follow-up, loss to follow-up, data collection (consecutive, prospective),
28 prospective calculation of study size, inclusion criteria, control group and statistical
29 analyses. The level of bias was reported using the QUIPS (Quality in Prognostic
30 Studies) tool for risk factor analysis studies whereas for studies that included a risk
31 prediction model, the PROBAST (Prediction model Risk Of Bias ASsessment Tool)
32 was used.^{12,13}
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44 Patient-level readmission data from each study were summarized to provide the total
45 readmission rate across all studies. The causes for readmission were grouped into
46 organ-specific classes; respiratory, cardiac, renal, gastrointestinal, neurological,
47 sepsis and return to theatre. "Return to theatre" was used as an umbrella term to
48 categorise all causes for readmission that required further surgical intervention such
49 as bleeding, cardiac tamponade or sternal re-suturing. The raw data on causes for
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readmission were extracted from each study. Mortality and length of stay data were presented as median and interquartile ranges.

Model analysis

Where a clinical prediction model was identified, the CHARMS checklist was used to extract data from the manuscript.¹⁰ Data on independent predictors including method of selection, events per variable (EPV) ratio, development and validation population, methods, statistical performance, model evaluation and model delivery methods (clinical risk scores/ risk indexes) were extracted. The adherence of the model publication to TRIPOD guidelines was also assessed.¹⁴ Statistical performance related to discrimination was assessed using area under the receiver operating characteristic curve (AUC) with an AUC value of >0.7 defined as acceptable. Measures of calibration extracted included the Hosmer-Lemeshow (HL) test result,¹⁵ calibration plot performance and R² score.^{16,17}

RESULTS

Selected Studies

There were no existing Cochrane, Centre for Reviews or PubMed Health registered reviews summarising risk factors or prediction models for readmission to intensive care after cardiac surgery. The process detailing the selection of studies is outlined in Figure 1.

Study quality and population characteristics

Twenty-five studies met the inclusion criteria. Details regarding these studies and the population characteristics are summarized in Table 1 and Table 2. Most studies were performed in academic institutions (86%). The studies identified were carried out in Europe (48%), North America (28%) and Asia (24%). All studies included were

1 observational. The majority (86%) were cohort studies with the rest performed using
2 case-control methodology. Of the included studies, 83% were performed
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4 retrospectively. Data were collected consecutively in 13 studies with this information
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6 not provided in the other 12 studies. The majority (60%) of studies recruited patients
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8 who were operated on within the most recent decade (2010-2020) with the rest
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10 performed prior to 2010. The handling of missing data was only reported in five
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12 studies. The study size varied from 80 to 10,992. Sample size calculation was
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14 included in one study.¹⁸ All studies described preoperative patient demographics.
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16 The overall risk of bias was low in 21 (72%) of the included studies.
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22 **Outcome definitions**

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24 **All readmissions during a single hospitalization** were considered irrespective of
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26 timing. No study defined a time period in which readmission to the CICU needed to
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28 occur in order to be classified as “Readmission to CICU”. The period spent on the
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30 ward was reported in 6/25 studies and one study grouped readmission time by
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32 period from discharge.^{18–24} Given that the same patient can potentially be readmitted
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34 to ICU on more than one occasion, eight studies also reported the number of unique
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36 patients who experienced readmission.
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42 **Readmission rates and causes**

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44 The readmission rate pooled across all studies was 4.9%. Two studies compared
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46 readmission rates between specific procedure groups; Boeken et al reported
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48 readmission rates of 4.0% following off-pump coronary artery bypass (OPCAB)
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50 compared to 4.80% following minimally invasive procedures and Hui et al reported a
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52 readmission rate of 18.4% following LVAD insertion.^{18,25} In contrast, for the three
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54 studies that only studied readmission after CABG procedures the rate of readmission
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1 ranged from 3.6% to 6.6%.The remaining studies assessed readmission following
2 mixed adult cardiac surgery.
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4 Causes for readmission were reported in 16 studies and grouped into organ-specific
5 classes; respiratory, cardiac, renal, gastrointestinal, neurological, sepsis and return
6 to theatre. Table 1 shows the most frequent cause documented in each study and
7 Figure 2 details the overall frequency of causes across all studies. Respiratory
8 complications were the most frequent cause of readmission (n= 11). The proportion
9 of readmissions for which respiratory complications were responsible ranged from
10 18.0% to 53.3%. The proportion of readmissions that were due to cardiac
11 complications ranged from 22.9% to 35.6% in the 6 studies that reported this
12 information. Similarly, return to theatre was associated with 6.4% to 15.9% of
13 readmissions. Across the studies the proportions of readmissions due to other casues
14 were; neurological 2.2% to 15.2%, renal 2.4% to 23.0%, gastrointestinal 2.4%-7.9%
15 and sepsis 1.4% to 15.6%. One study assessed differences in mortality rates based
16 on reason for readmission and demonstrated that patients readmitted due to renal
17 complications had a higher mortality (46%) than patients readmitted with
18 cardiovascular (31%) or respiratory complications (22%).²⁶
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42 **Risk factors and predictors of readmission**

43 All studies investigated pre and post-operative risk factors associated with
44 readmission. Intra-operative risk factors were investigated in 24 studies. The
45 identified risk factors for readmission are detailed in Figure 3. **Physiological**
46 **variables recorded prior to initial CICU discharge were included in five studies; these**
47 **variables were measured at a single time-point in four studies and one study**
48 **included continuous variables with temporal trends.**^{21,27–30} Nurse staffing levels, time
49 of discharge from ICU and bed availability were each investigated in two separate
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studies and were not found to be significant predictors for readmission.^{31,32}

Preoperative variables found to be associated with readmission in four or more studies were (in order of frequency); preoperative renal failure, chronic obstructive pulmonary disease, age >70, New York Heart Association classification (NYHA) >III, ejection fraction <40% and procedure urgency. Postoperative respiratory complications including prolonged mechanical ventilation and pneumonia prior to initial discharge from ICU were the most frequent postoperative variables identified as a risk factor in six studies. In the 11 studies that reported the median initial length of ICU stay, readmitted patients has initially stayed in ICU for 2 to 9 days and non-readmitted patients for 1 to 4 days and prolonged initial ICU stay was a predictor of readmission.

Models to predict readmission to ICU after cardiac surgery

Five risk prediction models developed to predict readmission to ICU were identified. The models are described in detail using the CHARMS criteria in Table 2 and summarized below.

BAT model³¹

The BAT (Bounce back After Transfer) model was developed to predict unplanned cardiac surgery readmissions. The BAT score includes the following variables; female, NHYA III/V, urgent or emergent operative status and postoperative renal failure during index CICU admission, allowing it to be calculated at the end of the CICU stay. It was developed using data from 421 adult cardiac surgery patients who underwent coronary artery bypass grafting or aortic valve replacement in the USA. The rate of unplanned readmission following discharge from CICU to the ward was 6.6%. The model showed good discrimination (AUC 0.81), and had an R² of 0.86 in the development population. The model has not been externally validated to date.

APPROACH model^{28,29}

The APPROACH (Alberta Provincial Project for Outcomes Assessment in Coronary Heart Disease) model, was developed from data for all adult patients undergoing cardiac surgery in a single province in Canada between 2004 and 2012. The risk score is designed to be calculated at the time of initial discharge from CICU and includes postoperative events (deep sternal wound infection, gastrointestinal bleed, cardiac arrest, pneumonia, pleural effusion, neurological complications and leg graft harvest site infection) alongside measured variables (ejection fraction <20%, 20-34%, age >90, 80-89, 70-79, chronic lung disease, single valve/non-CABG surgery, multiple valve surgery). There were 10,799 patients included in the dataset used for development and validation of the model. The readmission rate in the study population was 4.4%. Following internal validation using bootstrapping, the model showed good discrimination (AUC = 0.80) and adequate calibration according to the H-L test. The model was validated externally in a cohort of 805 patients with a readmission rate of 4.6%.²⁹ The APPROACH model demonstrated good discrimination (AUC = 0.75) but poor calibration according to the H-L test.

Refined APPROACH model²⁹

The APPROACH model was refitted by verma et al to include the following additional variables; re-intubation, tracheostomy, oxygen at discharge, inotropes at discharge, heart rate and systolic blood pressure. The refitted model including all the additional variables resulted in a slight improvement in discrimination (AUC 0.77) compared to the development set. The addition of systolic blood pressure at the time of discharge resulted in the largest improvement in discrimination (AUC = 0.78) and adequate calibration according to the H-L test. The refined model has not been externally validated.

Thomson model 2018 ³⁰

The study comprised of 4,869 patients, who had undergone cardiac surgery procedures at a single centre in the United Kingdom. The final score included the following risk factors; operative urgency, diabetes, chronic kidney disease stage 3-5, hypertension, logistic EuroSCORE, the Intensive Care National Audit and Research Centre (ICNARC) score, preoperative neurological disease, aortic valve surgery and postoperative anaemia. The risk of readmission can be calculated at any point during the CICU stay. The readmission rate was 3.2%. The authors reported that bootstrapped model was well calibrated with good discrimination but details on statistical performance were not provided. This model has not been externally validated to date.

Li model 2019 ³³

This model was developed to predict the risk of CICU readmission after valve surgery in China. The derived risk score includes age >65, chronic lung disease, previous cardiac surgery, LVEF <50%, LVEF <40%, NYHA III/IV, multiple valve repair/replacement, cardiopulmonary bypass time >180 minutes, cardiac arrest, ARDS, pneumonia, deep sternal wound infection and postoperative renal failure. All variables are collected during the index admission to CICU allowing the score to be calculated prior to ward transfer. The model was developed and internally validated in 1216 patients. The rate of readmission was higher than in other studies at 13.4%. The model demonstrated good discrimination (AUC =0.88) in the same institution in a cohort of patients observed at a different time (n=382) and was adequately calibrated according to the H-L test. This model has not been externally validated to date.

Mortality and length of stay following readmission

The mortality rate for patients who experienced readmission was reported in all studies. Patients who were readmitted to CICU had a higher in-hospital mortality rate (median 15.4%, IQR 12.10-19.30), than those who were not (median 1.4%, IQR 0.3-3.1). A single study reported 1-year mortality which was also higher in the readmitted group (21.0% vs 4.2%).²⁸ In-hospital length of stay was reported in 11 studies and was longer in the readmitted group for all studies. The median time between initial discharge from ICU and readmission was reported in 6/25 studies and ranged from 3-7 days. In the one study that reported readmissions grouped by time, the majority were readmitted within the first 24 hours of discharge from CICU (47.2%).¹⁹ The duration of the second ICU stay following readmission after standard care was reported in five studies and ranged from 6 to 13 days.

DISCUSSION

Approximately 5% of patients in the studies identified in this review experienced readmission to CICU. The most common causes of readmission were respiratory or cardiac complications. Readmission to CICU was consistently associated with prolonged in-hospital length of stay and an increased risk of in-hospital mortality.

This review has identified the important risk factors related to CICU readmission and five models designed to predict readmission. Of the five models identified, only one has been externally validated.

Readmission to CICU was uniformly defined as a second admission to CICU during a single hospitalization in all studies. However, the timing of readmission relative to the initial discharge from CICU was only reported in six studies. The benchmark of unplanned readmission to CICU within 48 hours of discharge which is used as a marker of quality of care, could therefore not be evaluated in this review.⁴ The timing

of readmission and variation in risk factors associated with readmission at different times relative to initial CICU discharge has been evaluated by a number of authors.

Brown et.al suggested two full calendar days is the optimal time interval for attributing readmission to ICU rather than ward related factors.³⁴ Later readmission (>72hours after ICU discharge) has been suggested to be more closely related to patient factors such as baseline comorbidities and ward care.³⁵

Although there was a lack of distinction in timing of readmission, independent risk factors were common across studies. Of the pre-operative risk factors, renal failure was the most common risk factor with other common risk factors including age>65, hypertension, raised body mass index >27, aortic valve surgery. However, overall, post-operative factors tended to demonstrate more significant influence on the risk of readmission to ICU. The largest study included found that postoperative events contributed to the majority of the readmission risk in comparison to intraoperative and preoperative factors.²⁸ Postoperative renal failure (defined variably as use of renal replacement therapy or raised serum creatinine concentration) was included as a risk factor in four of the models included in this review.

Post-operative physiological data were included in two models. The model by Thompson et al, includes the ICNARC postoperative physiology score.³⁰ Post-operative physiological variables have also been shown to be useful for predicting other complications after cardiac surgery.³⁶ Xue et. al demonstrated that inclusion of temporal trends in post-operative physiological measurements improved model performance compared with models solely based on snapshots of physiological values.²⁷

Although not included in the identified models, the effect of the duration of the initial CICU admission on the risk of subsequent readmission has also been investigated.

1 Some studies suggested that 'premature' discharges were associated with increased
2 risk of adverse outcomes.^{6,34} However in a study of on-pump CABG patients, those
3 who were discharged on post-operative day zero or day one did not have an
4 increased risk of adverse outcomes or mortality at 30-days compared to those
5 discharged on post-operative day two.³² In this review we identified three studies that
6 demonstrated prolonged initial CICU stay was an independent risk factor for
7 readmission to CICU.^{24,37,38}

8 Risk factors for readmission are related to but different from causes for readmission
9 and we have assessed both in this review. The most common causes for
10 readmission were respiratory or cardiac complications. Readmission to CICU is
11 normally deployed in patients who experience severe complications to facilitate more
12 intensive monitoring and treatments. As such, failure to rescue (FTR) which is
13 defined as the inability to prevent death after the development of a complication is
14 intimately related to readmission to CICU.³⁹

15 Patients who deteriorate on the ward can either be readmitted to CICU in an attempt
16 to avoid FTR or may experience FTR without readmission to CICU. Accurate
17 models designed to be applied prior to a patient's discharge from CICU could
18 potentially reduce the incidence of FTR as patients who experience complications in
19 a CICU environment are more likely to be rescued than those who deteriorate in a
20 ward environment.⁴⁰ Models based on data collected after discharge from CICU,
21 such as early warning scores are likely to be better suited to identifying patients at
22 risk of FTR late after CICU discharge. However, all models identified in this review
23 were based on data up to the point of discharge from CICU with none including ward
24 level factors.

Of the five models identified, only a single model has been externally validated to date and no examples of model application in a clinical trial or impact study were identified. The lack of clinical translation may be related to statistical challenges. Firstly, readmission to CICU after cardiac surgery is a rare event. To maximize the chance that any model to predict readmission will transfer well to other institutions, the model design cohort should have an appropriate sample size and ratio of events per variable (EPV) value of 10 or greater.⁴¹ Only two of the five studies included a sample size calculation and three of the included models had an EPV of less than five.⁴² Most models identified were internally validated using a random split approach in the same population, which rarely achieved the suggested number of events (>100 outcomes) and limited the analysis of variable shrinkage in the development datasets.^{30,31,33} Another consideration given the low incidence of the outcome is that the datasets used for model development and validation are inherently unbalanced. As a result discrimination may potentially appear excellent solely due to a model correctly identifying a high number of patients as being at low-risk of readmission.⁴³ Going forward, precision recall curve analysis is likely to be a more appropriate tool to assess model performance in this setting .

Limitations of this review

There are a number of methodological limitations that have prevented a meta-analysis of the studies included in this review. All the included studies were of an observational design, the majority were retrospective with variable outcome reporting which distorted the baseline risks to readmission and increased the chances of missing data. Secondly, a number of the included studies did not report how missing

1 data was handled. This limited the statistical conclusions and prevented pooling of
2 the outcomes across studies.
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4 The definition of “readmission to CICU” encompasses a relatively heterogenous
5 groups of patients. As mentioned previously, those admitted within 48 hours of
6 discharge are likely to have different reasons for readmission and different outcomes
7 to those readmitted after a longer period on the ward. Further in-depth analysis of
8 risk factors in patients re-admitted at different time points after initial discharge to the
9 wards was not possible in this review. However, although re-admission to CICU is a
10 relatively heterogenous outcome influenced by patient and institution level factors, it
11 is clearly an important outcome associated with both morbidity and mortality.
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23 *Evidence gaps and key questions for future clinical trials*

24 The definition of readmission used in this study ensured inclusion of patients who
25 experienced this complication at any time but also resulted in the aggregation of a
26 number of potentially diverse groups. A time-specific definition of readmission will
27 improve research into prediction of readmission to CICU. Future studies that explore
28 risk factors related specifically to ‘early readmissions’, ‘late readmissions’ or
29 ‘recurrent readmissions’ may also highlight key differences in these groups. For
30 example models to prevent “unsafe” discharges from CICU may perform better if
31 designed to focus on risk factors associated with early readmission. Risk factor
32 analysis would also be improved by the use of standardized definitions for
33 independent variables and clear time-points for recording them. This may be
34 particularly important when evaluating the importance of renal and respiratory
35 dysfunction which were defined inconsistently throughout the studies identified in this
36 review.
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1 FTR rates in postoperative patients have been shown to be influenced by
2 institutional level factors such as hospital teaching status, hospital technology level,
3 nurse-patient ratios and ICU bed capacity rates.⁴⁴ These hospital-level variables are
4 challenging to measure and an unobserved source of confounding around the act of
5 readmitting a patient to CICU. Although not explored in the studies in this review,
6 research into FTR rates and CICU readmission may offer insights into differences
7 between rates and outcomes of readmission to CICU after cardiac surgery that are
8 related to institutional level differences.^{39,45–47}

9 Most studies identified in this review excluded those who died during the index ICU
10 admission or on the ward without being readmitted to CICU, without adjustment for
11 the competing risk to mortality. This means that a patient who died on a ward without
12 readmission to CICU in one institution (as so was excluded from a study) might have
13 been readmitted to CICU and included in a similar study in a different institution.
14 Investigating this concept in future studies would improve the understanding of
15 mortality associated with readmission to ICU⁴⁸

16 **CONCLUSIONS**

17 Approximately 1 in 20 cardiac surgery patients will experience readmission to CICU.
18 Readmission to CICU is associated with an increased risk of mortality, prolonged
19 length of stay and poorer outcomes in these patients. Respiratory deterioration was
20 the most frequent cause for readmission in the studies included. Renal dysfunction
21 (both pre-operative and post-operative) was the most consistent predictor of
22 readmission. The models identified in this review may be useful in benchmarking
23 institutions, however further research is required on external validation and to
24 establish their utility in clinical practice.

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7 **Figure Legends**
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10 **Figure 1: Study selection flow diagram**
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12 **Figure 2: Median percentage of readmissions due to specific causes (when**
13 **specified) across included studies.**
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17 **Figure 3: Number of studies identifying specific risk factors readmission to**
18 **CICU on multivariable analysis.**
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27 **Supplementary material**
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29 **Appendix 1: Readmission to ICU after cardiac surgery- Online databases search**
30 **terms**
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36 **Appendix 2: Data Extraction form**
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39 **Appendix 3: PRISMA checklist**
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Appendix 1

ICU READMISSION- Online databases search terms

Cochrane search- no results

1. MeSH descriptor: [Coronary Artery Bypass] explode all trees or MeSH descriptor: [Heart Valve Prosthesis] explode all trees or MeSH descriptor: [Cardiac Surgical Procedures] explode all trees
2. MeSH descriptor: [Readmission] explode all trees or MeSH descriptor: [Recidivism] explode all trees.
3. MeSH descriptor: [Decision Making] explode all trees or MeSH descriptor: [Decision Support Techniques] explode all trees or MeSH descriptor: [Bayes Theorem] explode all trees

Medline and EMBASE Search: 810

1. (Heart surg* or Cardi* surg or Coronary artery bypass or Coronary bypass or CABG or Coronary Graft or coronary or OPCAB).
2. (Valve or Tricuspid or Mitral or Aortic or or valve prosth*)
3. aorta, thoracic/ or "sinus of valsalva"/ or aortic aneurysm, thoracic/ or aortic rupture/ or aortic arch syndromes/
4. Cardiac surgery.mp. or Thoracic Surgery/(Limit to human and adult)
5. (Readmission* or Recidivism*).af.
6. (Intensive care or HDU or ICU or CVICU or CICU).af.
7. "analytical, diagnostic and therapeutic techniques and equipment (non mesh)"/ or treatment outcome/ or patient care/ or therapy, computer-assisted/ or anesthesia/ or cardiovascular surgical procedures/ or monitoring, intraoperative/ or perioperative care/ or decision support techniques/ or models, theoretical/ or "health care (non mesh)"/ or outcome reporting.mp. or database.mp. or prognostication.mp. or algorithm.mp. or prediction model.mp. or risk stratification.mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]
8. 1 or 2 or 3 and 4 and 5 and 6 and 7 = 4210
9. Reviews=810
10. After title review=59

Data extraction template (Adapted from the CHARMS checklist and TRIPOD checklist)

Domain	Contents	Descriptor examples
Authors	First Author Surname, Year of publication, Country of study	
Source of data	Study design Number of Centers	Cohort, case-control, RCT, Registry data Single/ Multi-center. University or tertiary hospital
Participants	Recruitment (Period and sequence) Inclusion and exclusion criteria	No. of years, consecutive.
Outcome predicted	Definition, frequency, blinding of outcome assessment, timing of outcome	Readmission rate within 48hours of ICU, blinded researcher
Predictors	Type. Univariate selection and retention in model	P value <0.05, forward/Backward stepwise analysis
Sample size	Calculation Events per variable	Number of outcomes/events in relation to the number of candidate predictors
Missing data	Number of participants with missing data/ overall percentage of missing data. Handling of missing data	Complete case analysis (Exclusion of all records with missing values) Imputation/Other methods.
Model development	Modelling technique	Logistic regression, Bayes, Machine learning
Model performance	Calibration Discrimination Classification Prior cut points	-Calibration plot, Calibration slope, Hosmer-Lemeshow test. - AUC(C-statistic/index), D-statistic, log-rank - Sensitivity, specificity, predictive values, net reclassification improvement.
Model Evaluation	Validation techniques Adjustments for poor validation	Internal: random split of data, resampling methods, e.g., bootstrap or cross-validation, none External: temporal, geographical, different setting, different investigators) Adjustments: intercept recalibrated, predictor effects adjusted, or new predictors added
Results	Models presented Alternative model presentations and how they were derived	Equation , including predictor weights or regression coefficients, intercept, baseline survival, model performance measures (with standard errors or confidence intervals Sum score, nomogram, score chart, predictions for specific risk subgroups with performance

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PRISMA Checklist

Section/topic	#	Checklist item	Reported on page #
TITLE			
Title	1	Identify the report as a systematic review, meta-analysis, or both.	1
ABSTRACT			
Structured summary	2	Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number.	1
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of what is already known.	1-2
Objectives	4	Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).	2
METHODS			
Protocol and registration	5	Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number.	Appendix 3
Eligibility criteria	6	Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale.	3
Information sources	7	Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched.	3
Search	8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.	Appendix 2
Study selection	9	State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis).	3 Figure 1
Data collection process	10	Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators.	3-4
Data items	11	List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made.	Appendix 2
Risk of bias in individual studies	12	Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis.	PROBAST and QUIPS tool 3
Summary measures	13	State the principal summary measures (e.g., risk ratio, difference in means).	Difference in means
Synthesis of results	14	Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., I ²) for each meta-analysis.	Not done due to Heterogeneity in studies

PRISMA Checklist

Section/topic	#	Checklist item	Reported on page #
Risk of bias across studies	15	Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies).	Selection bias- procedure subgroups
Additional analyses	16	Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified.	Not done
RESULTS			
Study selection	17	Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram.	Figure 1
Study characteristics	18	For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations.	Table 1
Risk of bias within studies	19	Present data on risk of bias of each study and, if available, any outcome level assessment (see item 12).	Table 2
Results of individual studies	20	For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally with a forest plot.	Not done
Synthesis of results	21	Present results of each meta-analysis done, including confidence intervals and measures of consistency.	Not done
Risk of bias across studies	22	Present results of any assessment of risk of bias across studies (see Item 15).	Table 2
Additional analysis	23	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]).	Not done
DISCUSSION			
Summary of evidence	24	Summarize the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., healthcare providers, users, and policy makers).	11-14
Limitations	25	Discuss limitations at study and outcome level (e.g., risk of bias), and at review-level (e.g., incomplete retrieval of identified research, reporting bias).	15
Conclusions	26	Provide a general interpretation of the results in the context of other evidence, and implications for future research.	16
FUNDING			
Funding	27	Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review.	Title page

From: Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group (2009). Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. PLoS Med 6(7): e1000097.
doi:10.1371/journal.pmed1000097

Table 1: Summary of included studies

[Click here to access/download;Table;Table 1-summary of included studies.docx](#)

Table 1: Summary of studies included in review										
Author Year Country	Study: Centre, Institution Design	Data Collection Recruitment period (Years)	Patient population (No, Cases)	Study inclusion criteria	Study exclusion criteria	Primary Outcome	Secondary Outcomes	Primary cause of readmission	Readmission rate	
Cohn ²⁰ 1999 USA	Single centre Academic Cohort	Retrospective 1999-1998 (4)	2228	All cardiac procedures Survival to primary ICU discharge	Intraop /ICU death Incomplete ICU stay data	Readmission to ICU after index surgical admission (Episodes NR)	Mortality LOS (Hospital)	Respiratory	8.4%	
Bardell ⁴⁸ 2002 Canada	Single centre Academic Cohort	Prospective 1998-2001 (2)	2117	CABG only	NR	Readmission to ICU after index surgical admission (Episodes NR)	Mortality	Respiratory	3.6%	
Chung ²¹ 2002 UK	Single centre Academic Case control	Retrospective 1998 (1)	130-(65:65)	All cardiac procedures Single hospitalization	Transplant Preoperative admission to ICU	Readmission to ICU after index surgical admission (Episodes NR)		Cardiac	NR	
Vohra ⁴⁹ 2005 UK	Single centre Academic Cohort	Retrospective 1996-2003 (7)	7717	CABG or valve Survival to primary ICU discharge	Intraop/ICU death OPCAB	Readmission to ICU after index surgical admission (Episodes NR)	Mortality Mean LOS (CICU and Hospital)	Respiratory	2.3%	
Litmathe ²² 2009 Germany	Single centre Academic Cohort	Retrospective 2004-2007 (3)	3374	All cardiac procedures		Readmission to ICU (Episodes reported)	Mortality LOS (Hospital)	Respiratory	5.9%	
Toraman ⁵⁰ 2010 Turkey	Single centre Non-academic Cohort	Prospective 1998-2008 (9)	4270	All cardiac procedures	NR	Readmission to ICU after index surgical admission (Episodes NR)		Respiratory	2.2%	
Joskowiak ³⁷ 2012 Germany	Single centre Academic Cohort	Retrospective 2007-2010 (3)	7105	All cardiac procedures Survival to primary ICU discharge		Readmission to ICU after index surgical admission (Episodes NR)	Mortality LOS (Hospital)	Respiratory	7.8%	
Benetis ²³ 2013 Lithuania	Single centre Academic Case control	Retrospective 2009-2010 (1)	169 (54: 115)	Single hospitalization CABG patients	NR	Readmission to ICU after index surgical admission (Episodes NR)	Mortality	Cardiac arrhythmias (Atrial fibrillation)	5.0%	

<i>Boeken²⁵</i>	Single centre Academic Cohort	Retrospective 2005-2010 (5)	5132	CABG, Valve or combined	NR	Readmission to ICU after index surgical admission (Episodes reported)	Subgroup analysis	Respiratory	Overall 5.7% On-pump4.4% OPCAB 4.0%
<i>Van Diepen²⁷</i>	Single centre Academic Cohort	Prospective 2004-2012 (8)	10,799	CABG, Valve or combined Survival to primary ICU discharge	Non-cardiovascular procedures, Transplant, VAD or ECMO insertion	Readmission to ICU after index surgical admission (Episodes reported)	Mortality LOS (Hospital)	NR	4.4%
<i>Giakoumidakis⁵¹</i>	Single centre Academic Cohort	Retrospective 2011-2012 (1)	595	All cardiac procedures	<18 years Off-pump	Readmission to ICU after index surgical admission due to cause directly related to primary admission to ICU	Mortality	Respiratory	3.7%
<i>Gumus³⁶</i>	Single centre Academic Cohort	Retrospective 2010-2013 (3)	679	CABG	NR	Readmission to ICU after index surgical admission (Episodes NR)	Mortality	Respiratory	5.3%
<i>Jarzabek²⁴</i>	Single centre NR Case control	Retrospective 2008-2010 (2.7)	2076 (56:2020)	All cardiac procedures Survival to primary ICU discharge	Aortic aneurysm, Acute aortic dissection, Cardiac aneurysm, Other rate diseases of health and great vessels	Readmission to ICU after index surgical admission (Episodes NR)	Mortality LOS (Hospital)	Haemodynamic instability	2.7%
<i>Litwinowicz²⁶</i>	Single centre Academic Cohort	Retrospective 2009-2013 (5)	10992	All cardiac procedures Survival to primary ICU discharge	Heart transplant	Readmission to ICU after index surgical admission due to cause directly related to primary admission to ICU (Episodes reported)	Mortality LOS (Hospital)	Cardiac	1.8%
<i>Litzenberger⁵²</i>	Single centre Academic Cohort	Retrospective 2013-2014 (2)	1167	All cardiac procedures	NR	Readmission to ICU after index surgical admission (Episodes reported)	Mortality	NR	4.5%
<i>Magruder³¹</i>	Single centre Academic Cohort	Prospective 2013-2014 (1)	532	CABG	Incomplete ICU stay data	Readmission to ICU after index surgical admission (Episodes NR, Timing reported)	Mortality	Respiratory	6.6%
<i>Kang⁵³</i>	Single centre Academic	Retrospective 2012-2013	1368	All cardiac procedures	Planned readmissions due	Readmission to ICU after index surgical admission	Mortality	Cardiac	5.9%

Table 2: Study heterogeneity

	Categories	Sub-group	Studies	Authors
Clinical diversity				
Participants	Selection criteria	All cardiac surgery	13	Cohn 1999, Chung 2002, Litmathe 2009, Toraman 2010, Joskowiak 2012, Giakoumidakis 2014, Jarzabek 2014, Litwinowicz 2015, Litzenberger 2015, Kang 2016, Kolat 2018, Thomson 2018, Roumani 2018
		Procedure sub-groups	12	Bardell 2002, Vohra 2005, Benetis 2013, Boeken 2014, Van diepen 2014, Gumus 2014, Magruder 2015, Hui 2018, Li 2019, Verma 2019, Calafiore 2001, Kogan 2003
	Recruitment period	<2010	7	Cohn 1999, Bardell 2002, Vohra 2005, Toraman 2010, Calafiore 2001, Chung 2002, Litmathe 2009
		2010-2015	10	Joskowiak 2012, Benetis 2013, Boeken, 2014, Jarzabek 2014, Van diepen 2014, Giakoumidakis 2014, Gumus 2014, Litwinowicz 2015, Litzenberger 2015, Magruder 2015
		2015-2020	6	Kang 2016, Kolat 2018, Thomson 2018, Hui 2018, Li 2019, Verma 2019
		Not specified	2	Kogan 2003, Roumani 2018
Outcomes	Readmission to ICU defined	Yes	ALL	Cohn 1999, Bardell 2002, Vohra 2005, Toraman 2010, Joskowiak 2012, Benetis 2013, Van diepen 2014, Giakoumidakis 2014, Jarzabek 2014, Gumus 2014, Litwinowicz 2015, Magruder 2015, Thomson 2018, Hui 2018, Li 2019, Verma 2019, Litzenberger 2015, Litmathe 2009, Roumani 2018, Calafiore 2001, Kogan 2003, Chung 2002, Boeken 2014, Jarzabek 2014, Kolat 2018
		Episodes reported	8	Litmathe 2009, Boeken 2014, Van diepen 2014, Litwinowicz 2015, Li 2019, Verma 2019, Litzengberger 2015, Thomson 2018
		Timing reported	2	Kogan 2003, Magruder 2015
Institution		Academic	23	Cohn 1999, Bardell 2002, Vohra 2005, Joskowiak 2012, Benetis 2013, Van diepen 2014, Giakoumidakis 2014, Gumus 2014, Litwinowicz 2015, Magruder 2015, Litmathe 2009, Thomson 2018, Hui 2018, Li 2019, Verma 2019, Calafiore 2001, Kogan 2003, Chung 2002, Boeken 2014, Jarzabek 2014, Kolat 2018, Litzenberger 2015, Roumani 2018
		Non-Academic	1	Toraman 2010
		Not specified	1	Jarzabek 2014,
Centres	Single centre	Asia	5	Toraman 2010, Kang 2016, Li 2019, Kogan 2003, Gumus 2014
		Europe	12	Chung 2002, Litmathe 2009, Vohra 2005, Joskowiak 2012, Boeken 2014 Benetis 2013, Giakoumidakis 2014, Jarzabek 2014, Litwinowicz 2015, Thomson 2018, Calafiore 2001,,Kolats 2018
		North America	8	Cohn 1999, Bardell 2002, Van diepen 2014, Magruder 2015, Verma 2019, Litzenberger 2015, Roumani 2018, Hui 2018
Methodological diversity				
Study	Design	Cohort	21	Cohn 1999, Bardell 2002, Vohra 2005, Toraman 2010, Joskowiak 2012, Benetis 2013, Van diepen 2014, Giakoumidakis 2014, Jarzabek 2014, Gumus 2014, Litwinowicz 2015, Magruder 2015, Thomson 2018, Hui 2018, Li 2019, Verma 2019, Litzenberger 2015, Litmathe 2009, Roumani 2018, Calafiore 2001, Kogan 2003
		Case-control	4	Chung 2002, Boeken, 2014, Jarzabek 2014, Kolat 2018
	Missing data handling	Complete case	3	Cohn 1999, Magruder 2015, Li 2019
		Imputation	1	Thomson 2018
		Not reported	21	Bardell 2002, Vohra 2005, Toraman 2010, Joskowiak 2012, Benetis 2013, Van diepen 2014, Giakoumidakis 2014, Jarzabek 2014, Gumus 2014, Litwinowicz 2015, Hui 2018, Verma 2019, Litzenberger 2015, Litmathe 2009, Roumani 2018, Calafiore 2001, Kogan 2003, Chung 2002, Boeken 2014, Jarzabek 2014, Kolat 2018
Model development	Method	Logistic Regression	6	Lee 2013, Van Diepen 2014, Magruder 2015, Thomson 2018, Verma 2019, Li 2019
		Not performed	19	Cohn 1999, Bardell 2002, Vohra 2005, Toraman 2010, Joskowiak 2012, Benetis 2013, Giakoumidakis 2014, Jarzabek 2014, Litwinowicz 2015, Magruder 2015, Hui 2018, Kang 2016, Calafiore 2001, Kogan 2003
Overall Risk of bias				
	Within studies (overall PROBAST /QUIPS rating)	Low	18	Cohn 1999, Bardell 2002, Vohra 2005, Toraman 2010, Joskowiak 2012, Benetis 2013, Van diepen 2014, Giakoumidakis 2014, Jarzabek 2014, Litwinowicz 2015, Magruder 2015, Kolat 2018, Thomson 2018, Hui 2018, Li 2019, Verma 2019, Calafiore 2001, Kogan 2003
		High	4	Chung 2002, Boeken, 2014, Gumus 2014, Roumani 2018
		Unclear	3	Litmathe 2009, Litzenberger 2015, Kang 2016
	Across studies	Selection bias	10	Bardell 2002, Vohra 2005, Benetis 2013, Boeken 2014, Van diepen 2014, Gumus 2014, Magruder 2015, Hui 2018, Li 2019, Verma 2019
		Inclusion of causes for readmission as candidate variable	2	Van diepen 2014, Verma 2019

Model	Author	Predictor selection univariate (p value < 0.05)	Validation technique	Development				Validation			
				Cohort (n)	Events per variable	Measure of Calibration	Measure of Discrimination	Cohort (n)	Events per variable	Measure of Calibration	Measure of Discrimination
BATS model	<i>Magruder USA 2015</i>	Akaike Information Criterion	NR	Prospective CABG or AVR (421)	3.1 (31/10)	R ² =0.86	AUC = 0.81	NR	NR	NR	NR
APPROACH model	<i>Van Diepen Canada 2014</i>	Forward stepwise	Internal Bootstrap (1000 rep)	Prospective CABG or Valvular (10799)	40 (479/12)	HL chi-square p = 0.19	AUC = 0.80	Prospective CABG or Valvular (10799)	40 (479/12)	NR	NR
APPROACH model refined	<i>Verma Canada 2019</i>	Forward stepwise	Internal Bootstrap (1000 rep)	NR	NR	NR	NR	Prospective CABG Or Valvular (805)	1.9 (37/19)	HL chi-square p=0.01	AUC = 0.75
	<i>Verma Canada 2019</i>	Forward stepwise	NR	Prospective CABG Or Valvular (805)	1.85 (37/20)	HL chi-square p = 0.75	AUC=0.78	NR	NR	NR	NR
Thomson	<i>Thomson UK 2018</i>	Backward stepwise	Internal Bootstrap (2000 rep)	Retrospective Mixed Cardiac (4869)	17.3 (56/9)	Good correlation	Good discrimination	Retrospective Mixed Cardiac (4869)	17.3 (56/9)	NR	NR
Li	<i>Li China 2019</i>	Forward stepwise	Temporal Split sample	Retrospective Valve surgery (824)	4 (52/13)	HL chi-square p=0.30	AUC = 0.89	Retrospective Valve surgery (392)	2 (28/13)	HL chi-square p=0.29	AUC = 0.88

Abbreviations: **rep**-replications, **NR**-Not Reported, **AUC**- Area Under Curve, **HL**-Hosmer-Lemenshow

Figure 1: Study selection flow diagram

Figure 2: Median percentage of readmissions due to specific causes (when specified) across included studies

Figure 3: Number of studies identifying specific risk factors readmission to CICU on multivariable analysis

Figure 3: Abbreviations; ICNARC-Intensive care national audit and research centre, NYHA-New York Heart Association