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Prediction models for hospital readmissions in patients with heart disease: a systematic review and meta-analysis

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ABSTRACT

Objective To describe the discrimination and calibration of clinical prediction models, identify characteristics that contribute to better predictions and investigate predictors that are associated with unplanned hospital readmissions.

Design Systematic review and meta-analysis.

Data source Medline, EMBASE, ICTPR (for study protocols) and Web of Science (for conference proceedings) were searched up to 25 August 2020.

Eligibility criteria for selecting studies Studies were eligible if they reported on (1) hospitalised adult patients with acute heart disease; (2) a clinical presentation of prediction models with c-statistic; (3) unplanned hospital readmission within 6 months.

Primary and secondary outcome measures Model discrimination for unplanned hospital readmission within 6 months measured using concordance (c) statistics and model calibration. Meta-regression and subgroup analyses were performed to investigate predefined sources of heterogeneity. Outcome measures from models reported in multiple independent cohorts and similarly defined risk predictors were pooled.

Results Sixty studies describing 81 models were included: 43 models were newly developed, and 38 were externally validated. Included populations were mainly patients with heart failure (HF) (n=29). The average age ranged between 56.5 and 84 years. The incidence of readmission ranged from 3% to 43%. Risk of bias (RoB) was high in almost all studies. The c-statistic was <0.7 in 72 models, between 0.7 and 0.8 in 16 models and >0.8 in 5 models. The study population, data source and number of predictors were significant moderators for the heterogeneity. Outcome measures from models reported in multiple independent cohorts and similarly defined risk predictors were pooled.

Conclusion Some promising models require updating and validation before use in clinical practice. The lack of independent validation studies, high RoB and low consistency in measured predictors limit their applicability.

PROSPERO registration number CRD42020159839.

Strengths and limitations of this study

► Largest investigation of unplanned hospital readmission risk to date, including 81 unique prediction models in the systematic review.
► Independent and standardised procedures for study selection, data collection and risk of bias (RoB) assessment.
► High RoB in current prediction models and unexplained heterogeneity between models limit recommendations for using prediction model in clinical practice.

INTRODUCTION

Hospital readmissions in patients with acute heart disease are associated with a high burden on patients, healthcare and costs. The identification of high-risk hospitalised patients is important to provide timely interventions. Prediction models guide healthcare providers in daily practice to assess patients’ probability of readmission within a certain time frame and include candidate variables identified by clinical perspectives, literature or data-driven approaches, for example, using machine learning techniques. Data are often collected from observational cohorts of intervention studies and subsequently analysed to examine what set of predictors best predict the risk of readmission. The clinical applicability of risk prediction models in daily practice is currently limited. Statistical models are often not presented in a clinically useful way or models based on administrative data are considered. These models therefore cannot be readily used in daily practice. In addition, prediction models are often developed for a very specific population, which asks from clinicians to be familiar with several models. Furthermore, patients may belong to multiple populations because of cardiac
comorbidities. Numerous systematic reviews have previously investigated the prediction of unplanned hospital readmissions in several populations. While some have included hospitalised patients in general, others have focused specifically on patients with heart failure (HF) or acute myocardial infarction (AMI). The conclusion is generally the same, the discrimination is poor to adequate, and there is little consistency in the type of predictors included in the models.

We believe that the state of the art on risk prediction can be improved if more knowledge is available on the performance of clinical risk prediction models and risk predictors across different populations of patients with heart disease. Although heterogeneity in models and predictors is often considered as a limitation, it can inform effect moderators on how predictions can be improved. For example, perhaps we can identify predictors who demonstrate a consistent association with hospital readmission regardless of the underlying disease. If this can be identified, a more general prediction model could be developed that is relevant for the heterogeneous group of patients on cardiac care units. This might contribute to the early recognition and onset of preventive interventions in patients with heart disease at risk of readmission.

We therefore performed a systematic review and meta-analysis on clinical risk prediction models for the outcome unplanned hospital readmission in patients hospitalised for acute heart disease. Our aims were to describe the discrimination and calibration of clinical prediction models, to identify characteristics that contribute to better predictions, and to investigate predictors that are consistently associated with hospital readmissions.

**METHODS**

A protocol was registered in PROSPERO (registration number: CRD42020159839). The results are reported following the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) statement.

**Eligibility criteria**

Studies were eligible if (1) the study population included hospitalised adult patients with (symptoms of) heart disease; (2) a prediction model with c-statistic was reported; (3) a clinically useful presentation of the model with risk factors was reported; (4) the outcome was unplanned hospital readmissions within 6 months; (5) the study design was appropriate, that is, (nested) case–control study (prospective and retrospective) cohort study, database and registry study, or secondary analysis of a trial; (6) they were reported in English.

**Information sources**

A search strategy was designed with an information specialist (PROSPERO protocol and online supplemental text 1). We searched the Medline, EMBASE, WHO ICTPR search portal (for study protocols) and Web of Science (for conference proceedings) databases up to 25 August 2020 without any restrictions for eligible studies. We searched for full-text manuscripts of the identified protocols. After selecting the full-text manuscripts, we screened references lists and prospective citations (using Google Scholar) for additional eligible studies.

**Study selection**

Three reviewers were involved in the study selection process. Each reviewer independently screened two-thirds of the titles, abstracts and full-text articles of potentially relevant references identified in the literature search. Disagreements were resolved through consensus. Sixteen authors were contacted and six delivered data for readmission when a composite outcome was used. Two authors were also contacted when data were reported combining multiple patient populations. However, no additional data were provided for the population with heart disease and these studies were excluded.

**Data extraction**

Data extraction was performed based on the ‘Critical Appraisal and Data Extraction for Systematic Reviews’ of prediction modelling studies checklist using standardised forms in the Distiller Systematic Review Software (see online supplemental text 2 for the data items). The checklist includes items on 11 relevant domains, including source of data, participants, outcomes, candidate predictors, sample size, missing data, model development, model performance, model evaluation, results and interpretation. One reviewer collected the data and the second reviewer verified the extracted data. Disagreements were resolved through consensus. Eight authors were contacted and two delivered data to resolve uncertainties or missing data.

**Risk of bias**

The Prediction model Risk Of Bias ASsessment Tool (PROBAST) tool was used to assess the risk of bias (RoB) for four ‘quality’ domains, that is, the participants, predictors, outcome and analysis for each model. One author assessed the RoB as low, high or unclear, and the second author verified the extracted data and RoB conclusion. Disagreements were resolved through consensus. In addition, the applicability of the included studies based on our research question was assessed for three domains, that is, participants, predictors and outcome domains and rated as low concerns, high concerns or uncertain concerns regarding applicability.

**Summary measures**

The discrimination of the prediction models was described using the concordance (c)-statistic. Missing SEs were derived from the sample data. The calibration was described using the number of observed and expected events, the calibration slope, calibration in large or the Hosmer-Lemeshow test. A definition of the commonly used measures is described in box 1. The association between risk predictors and hospital readmission was described using regression coefficients.
Box 1 Definitions of commonly used measures

**Discrimination:**
Refers to the ability of a prediction model to discriminate between a patient with and without the outcome, for example, readmission.

**C-statistic:**
Is a measure of discrimination. For binary outcomes, the c-statistic is equivalent to the area under the curve: 1 indicates perfect discrimination, and 0.5 indicates that the models does not perform better than chance. Harrell's c-statistic is often used in survival models.

**Calibration:**
Refers to the agreement between the predicted and the observed probability (or the outcome value for linear models). Calibration is expressed using different measures, for example, calibration slope, calibration in large, Hosmer-Lemeshow test.

**Calibration slope:**
The slope should be 1, a value <1 indicates extreme predictions, and a value of >1 indicates to moderate predictions.

**Calibration in large:**
The value should be 0, a negative value indicates overestimation of the prediction, and a positive value indicates underestimation of the prediction.

**Hosmer-Lemeshow test:**
This is a goodness-of-fit test for binary outcomes. A significant p value, usually <0.05, indicates poor goodness-of-fit.

**Derivation/development cohort:**
A cohort of patients that is used to estimate the predictor values that are used in a prediction model to estimate a patient's probability for an outcome.

**Validation cohort:**
A cohort of patients that is used to evaluate how well the developed model performs (in terms of discrimination and calibration).

**Internal validation:**
Estimates how well a model will be reproduced in the target population. Several techniques can be used, for example, random-split sample, cross-validation and bootstrapping techniques.

**External validation:**
Evaluates how well a model performs in a new sample and can consist of temporal validation (sample contains more recently treated patients), geographical validation (sample is from a different centre) of a fully independent validation (validation by an independent team).

The c-statistic of the validated model was used if available; otherwise, the c-statistic from the development phase was used.

The c-statistics of specific prediction models that were evaluated in multiple studies were pooled for the endpoint 30-day follow-up.

Coefficients of predictors that were similarly defined in at least five studies were pooled for the endpoint 30-day follow-up. The patient populations were defined as subgroups to explore consistency and heterogeneity ($I^2$, tau) in the effect estimates.

Analyses were performed using the ‘metan’ package in STATA V.15 IC and the ‘metamisc package’ in Rstudio.

**Public and patient involvement**
Because of the design of the study and because we did not collect primary data, we did not involve patients or the public in the design, conduct or reporting of our research.

**RESULTS**
A total of 8588 abstracts were reviewed and 60 studies describing 81 separate models were included (figure 1). Table 1 provides an overview of the included studies and models, which were published between 2001 and 2020. The majority of the studies (n=40) was performed in the USA. The data sources used were mostly retrospective cohort studies (n=15), hospital databases (n=13) and registries (n=13). Included populations were mainly patients with HF (n=29), surgical patients (n=14) and patients with an AMI or acute coronary syndrome (n=10). The average age was between 56.5 and 84 years. The sample size of development cohorts ranged from 182 to 193899 patients and of the validation cohorts between 104 and 321088 patients. The outcome of interest was mostly all-cause readmission (n=41) and measured on 30 days (n=55). The incidence of readmission per study ranged from 3% to 43%.

**Risk of bias**
Figure 2 summarises the RoB and applicability assessment (online supplemental table 1A). The overall RoB was high in 98.9% of the models and only one study showed low RoB in all four domains.

For the domain participants, 82.4% of studies was assessed as high RoB because most studies performed retrospective data analyses or used data from existing sources with large number of candidate predictors that were originally developed for other purposes, for example, administrative databases or registries. The domain predictors were assessed as high RoB in 27.5% of the models, 24.2% as low RoB and 48.4% as unclear RoB. For the domain outcome, 41.8%, 34.1% and 24.2% were assessed as high, low and unclear RoB, respectively.

The domain analysis was assessed as high RoB in 97.8%. Most studies did not use appropriate statistics for the development or validation of prediction models. For example, a
description on how complexities in data were handled (eg, competing risk of death) was often missing and relevant performance measures were incomplete (eg, calibration).

The domain participants and predictors were assessed as low concerns regarding applicability in all studies. For the domain outcome, 70.3% of studies used all-cause readmission as the outcome of interest and were therefore assessed as low concerns regarding applicability.

**Prediction models**

A total of 43 new models were developed for patients with HF (n=15), undergoing surgical procedures (n=12), AMI (n=9), transcatheter aortic valve replacement (TAVR) (n=2), a mixed sample with HF and coronary syndromes (n=2), arrhythmias (n=1), valvular disease (n=1), while one study did not specify the sample (table 1). The c-statistic was lower than 0.6 in 5 models, between 0.6 and 0.7 in 24 models, between 0.7 and 0.8 in 6 models, and between 0.8 and 0.9 in 2 models. In six models, the c-statistic was only reported for a validation cohort (table 2).

A total of 38 separate models were externally validated for patients with HF (n=26), AMI (n=4), surgical patients (n=3), acute coronary syndrome (n=2), arrhythmias (n=2), mixed sample with HF and coronary syndromes (n=1). The discrimination was lower than 0.6 in 16 models, between 0.6 and 0.7 in 24 models, between 0.7 and 0.8 in 5 models, and between 0.8 and 0.9 in 2 models (table 2).

The discrimination of six models was evaluated in multiple independent cohorts and was pooled in meta-analyses (figure 3, online supplemental figures 1–6): the CMS AMI (Centers for Medicare and Medicaid Services Acute Myocardial Infarction) administrative model\(^19\) \(^20\) (0.65, 95% CI 0.56 to 0.73); the CMS HF (Heart Failure) administrative model\(^21\) \(^29\) (0.60, 95% CI 0.58 to 0.62); the CMS HF medical model\(^24\) \(^27\) \(^30\) \(^32\) (0.60, 95% CI 0.58 to 0.62); the HOSPITAL (Hemoglobin level, discharged from Oncology, Sodium level, Procedure during admission, Index admission Type, Admission, Length of stay) score\(^33\) \(^35\) (0.64, 95% CI 0.58 to 0.70); the GRACE (Global Registration of Acute Coronary Events) score\(^36\) \(^37\) (0.78, 95% CI 0.63 to 0.86); and the LACE (Length of stay, acuity of the Admission, Comorbidity of the patient and Emergency department use in the duration of 6 months before admission) score\(^23\) \(^28\) \(^34\) \(^38\) (0.62, 95% CI 0.53 to 0.70).

On average, models for patients with AMI had the best discrimination (0.67, n=16), followed by patients with TAVR (0.65, n=2), patients with HF (0.64, n=45) and surgical patients (0.63, n=17). The discrimination was highest in studies using secondary analysis (0.70, n=2) and retrospective cohort studies (0.69, n=23), and was lowest
| Study                     | Model                               | Data source                  | Development | Validation | Sample size | Population | Average age | Outcome | Readmission (%) |
|--------------------------|-------------------------------------|------------------------------|-------------|------------|-------------|------------|-------------|---------|----------------|
| Moretti et al[7]         | EuroHeart PCI score                | Hospital database            | NA          | Ext        | –            | 1192       | ACS         | 71 (7)  | 30d            | 4.7      |
| Asche et al[8]           | NR                                  | Retrospective cohort         | Yes         | Split      | 2446        | 612        | AMI         | 66 (15) | 30d            | 8.9      |
| Cediel et al[9]          | TARRACO Risk score                 | Retrospective cohort         | Yes         | No         | 611         | 401        | AMI type 2, ischaemia | D: 78 (17) | V: 60 (21) | 30d      | 2.6      |
| Chotechuang et al[10]    | GRACE                               | Retrospective cohort         | NA          | Ext        | –            | 152        | AMI         | 60.5 (6.3) | 30d             | 5.3      |
| Hilbert et al[11]        | AMI decision tree                  | Registry                     | Yes         | Ext        | 10848       | 10701      | AMI         | NR      | 30d            | 20.6     |
| Dodson et al[12]         | SILVER-AMI 30-day readmission calculator | Prospective cohort     | Yes         | Split      | 2004        | 1002       | AMI         | 81.5 (5.0) | 30d            | 18.2     |
| Kini et al[13]           | NR                                  | Registry                     | Yes         | Split      | 60742       | 26107      | AMI         | 76.5 (8.0) | 90d            | 27.5     |
| Nguyen et al[14]         | AMI READMITS score                 | Retrospective cohort         | Yes         | Split      | 661         | 165        | AMI         | 65.5 (12.8) | 30d            | 13       |
| Full-stay AMI model      | Retrospective cohort               | Yes                          | Split       | –          | 826         | AMI         | 65.5 (12.8) | 30d      | 13             |
| CMS AMI administrative model | Retrospective cohort            | NA                            | Ext         | –          | –           | AMI         | 65.5 (12.8) | 30d      | 13             |
| Krumholz et al[15]       | CMS AMI administrative model       | Registry                     | Yes         | Split, Ext | 100 465     | 321 088    | AMI         | 78.7 (8.0) | 30d            | 18.9     |
| CMS AMI medical model    | Registry                            | Yes                          | Split       | 130 944    | 130 944     | AMI         | 76.2 (7.3) | 30d      | 20             |
| Rana et al[16]           | Elixhauser index                   | Hospital database            | NA          | Ext        | –            | 1660       | AMI         | 67.9     | 30d            | 6.3      |
| HOSPITAL score           | Hospital database                  | NA                            | Ext         | –          | 1660        | AMI         | 67.9     | 30d      | 6.3             |
| Atzema et al[17]         | AFTER Part 2 scoring system        | Retrospective cohort         | Yes         | Split      | 2343        | 1167       | Arrhythmia, AF | D: 68.6 (14.7) | V: 68.3 (15.1) | 30d | 7 | 7.6 |
| Lahewala et al[18]       | CHADS2                              | Administrative               | NA          | Ext        | –            | 116 450    | Arrhythmia, AF | <75     | 30d            | 15.8     |
| CHADS2                   | Administrative                       | NA                            | Ext         | –          | 116 450     | Arrhythmia, AF | <75     | 90d            | 25.1     |
| CHA2DS-VASc              | Administrative                       | NA                            | Ext         | –          | 116 450     | Arrhythmia, AF | 65–74   | 30d            | 15.8     |
| CHA2DS-VASc              | Administrative                       | NA                            | Ext         | –          | 116 450     | Arrhythmia, AF | 65–74   | 90d            | 25.1     |
| Benuzillo et al[19]      | CRSS                                | Hospital database            | Yes         | Boot, Ext  | 2589        | 896 (Ext) | CAGB        | 66.7 (9.9) | 30d            | 9.1      |
| Deo et al[20]            | 30-day CAGB readmission calculator | Administrative               | Yes         | Boot      | 155 054     | 1000       | CAGB        | 65.4 (10.4) | 30d            | 12.5     |
| Engoren et al[21]        | NR                                  | Hospital database            | Yes         | Split     | 2644        | 2711       | CAGB        | NR     | 30d            | 7.6      |
| Lancey et al[22]         | NR                                  | Registry                     | Yes         | Split     | 2341        | 2520       | CAGB        | 64.5 (10.5) | 30d            | 8.8      |
| Rosenblum et al[23]      | The STS PROM score                  | Hospital database            | NA          | Ext        | –            | 21719      | CAGB        | 63.5 (10.7) | 30d            | 9.3      |
| Zitser-Gurevich et al[24]| NR                                  | Prospective cohort           | Yes         | Split     | 2266.5      | 2266.5     | CAGB        | 65–74   | 30d            | 13.3     |
|                         | NR                                  | Prospective cohort           | Yes         | Split     | 2266.5      | 2266.5     | CAGB        | 65–74   | 100d           | 24.1     |

Continued
### Table 1  Continued

| Study              | Model                                | Data source          | Development | Validation | Sample size | Population | Average age | Outcome |
|--------------------|--------------------------------------|----------------------|-------------|------------|-------------|------------|-------------|---------|
|                     |                                      |                      |             |            | Dev         | Val        |             |         |
|                     |                                      |                      |             |            |             |            |             |         |
| Zywot et al,12      | CABG risk scale                      | Administrative       | Yes         | Ext        | 126 519     | 943 18     | CABG        | 30d     | 23       | 21       |
| Ahmad et al,13      | CMS HF administrative model          | Prospective cohort   | NA          | Ext        | –           | 183        | HF          | 30d     | 22.4     |
| Amarasingham et al,12 | ADHERE                              | Hospital database    | NA          | Ext        | –           | 1372       | HF          | 30d     | 24.1     |
| Tabak mortality     | Hospital database                    | NA                   | Ext         | –          | 1372        | HF          | 30d         | 24.1     |
| Au et al,13         | Administrative claims model: HF 30-day mortality | Administrative       | NA          | Ext        | 59 652      | 596 52     | HF          | 30d     | 15.9     |
| Ahmadi et al,14     | Charlson Comorbidity Score           | Administrative       | NA          | Ext        | 59 652      | 596 52     | HF          | 30d     | 15.9     |
| Bardhan et al,15    | LACE                                 | Administrative       | NA          | Ext        | 59 652      | 596 52     | HF          | 30d     | 15.9     |
| Betihavas et al,16  | CMS HF administrative model          | RCT secondary analysis | Yes    | Boot     | 280         | 200        | HF          | 30d     | 15.9     |
| Cox et al,17        | CMS HF medical model                 | Hospital database    | Yes         | No         | –           | 1454       | HF          | 30d     | 21.5     |
| Delgado et al,18    | 15-day CV readmission risk score     | Prospective cohort   | Yes         | Boot      | 1831        | 500        | HF          | 15d     | 7.1      |
| Formiga et al,19    | 30-day CV readmission risk score     | Prospective cohort   | Yes         | Boot      | 1831        | 500        | HF          | 30d     | 13.9     |
| Frizzell et al,20   | CMS HF medical model                 | Hospital database    | NA          | Ext        | –           | 719        | HF          | 30d     | 7.6      |
| Frizzell et al,20   | CMS HF medical model                 | Hospital database    | NA          | Ext        | –           | 719        | HF          | 90d     | 14.4     |
| Hammill et al,21    | HOSPITAL score                       | Registry             | NA          | Ext        | –           | 24163      | HF          | 30d     | 21.2     |
| Hilbert et al,22    | HF decision tree                     | Registry             | Yes         | Ext        | 39 682      | 384 09     | HF          | 30d     | 25.5     | 25.2     |
| Hummel et al,23     | CMS HF medical model                 | Prospective cohort   | NA          | Ext        | –           | 1807       | HF          | 30d     | 27       |
| Huyrin et al,24     | CMS HF medical model                 | Prospective cohort   | Yes         | Ext        | 430         | 1046       | HF          | 30d     | 21       | 24       |
| Huyrin et al,24     | CMS HF medical model                 | Prospective cohort   | Yes         | Ext        | 430         | 1046       | HF          | 90d     | 43       | 42       |
| Ibrahim et al,25    | CMS HF administrative model          | Registry             | NA          | Ext        | –           | 692        | HfEF        | 30d     | 27.3     |
|                     |                                      |                      |             |            |             |            |             |         |         |
|                     |                                      |                      |             |            |             |            |             |         |         |
|                     |                                      |                      |             |            |             |            |             |         |         |
| Study | Model | Data source | Development | Validation | Sample size | Population | Average age | Outcome | Readmission (%) |
|-------|-------|-------------|-------------|------------|-------------|------------|-------------|---------|-----------------|
| Keenan et al | CMS HF administrative model | Registry | Yes | Split, Ext. | 28319 | 845291 | HF | 79.9 (7.8) | 30d | 23.6 |
| | CMS HF medical model | Registry | Yes | Split, Ext. | 64329 | 64329 | HF | 75–84 | 30d | 23.7 |
| Kitamura et al | FIM | Retrospective cohort | NA | Ext | – | 113 | HF | 80.5 (6.7) | 90d | 20.4 |
| Leong et al | 30-day HF readmission risk score | Retrospective cohort | Yes | Split | 888 | 587 | HF | D: 70.0 (12.7) V: 69.1 (12.8) | 30d | 9.9 |
| Li et al | NR | Retrospective cohort | Yes | Split | 51,783 | 25,887 | HF | D: 84 (12) V: 84 (11) | 30d | 24.2 |
| Lim et al | NR | Registry | Yes | No | – | 45,666 | – | HF | 70.5 (12.0) | 30d | 6.6 (car) 13 (all) |
| Reed et al | AH model | Administrative | Yes | Split | – | NR | HF | NR | 30d | NR |
| | CMS HF administrative model | Administrative | NA | Split | – | – | – | – | – | – |
| | Hasen | Administrative | NA | Split | – | – | – | – | – | – |
| | LACE | Administrative | NA | Split | – | – | – | – | – | – |
| | PARR-30 | Administrative | NA | Split | – | – | – | – | – | – |
| Salah et al | ELAN-HF score | Prospective cohort secondary analysis | Yes | No | 1301 | – | HF | 74 (16) | 180d | 36.1 |
| Sudhakar et al | CMS HF medical model | Hospital database | NA | Ext | – | 1046 | HF | 65.2 (16.6) | 30d | 35.3 |
| Tan et al | NR | Hospital database | Yes | Split | 246 | 104 | HF | D: 67.7 (12.3) V: 69.0 (12.9) | 90d | 24.5 11.7 |
| Wang et al | NR | Hospital database | Yes | No | 4548 | – | HF | 68.5 (27.6) | 30d | 25.1 |
| Wang et al | LACE | Retrospective cohort | NA | Ext | – | 253 | HF | 56.6 (11.5) | 30d | 24.5 |
| Yazdan-Ashoori et al | CMS HF administrative model | Prospective cohort | NA | Ext | – | 378 | HF | 73.1 (13.1) | 30d | 26 |
| | LACE | Prospective cohort | NA | Ext | – | 378 | HF | 73.1 (13.1) | 30d | 26 |
| Disdier Moulder et al | NR | Prospective cohort | Yes | No | 258 | HF, ACS, NR | 70.5 (23) | 30d | 17 |
| | NR | Prospective cohort | Yes | No | 258 | HF, ACS, NR | 70.5 (23) | 180d | 38 |
| Raposeiras-Roubin et al | GRACE | Retrospective cohort | NA | Ext | – | 4229 | HF, ACS | 68.2 (18.7) | 30d | 2.6 |
| Burke et al | HOSPITAL score | Retrospective cohort | NA | Ext | – | HF: 3189 AMI: 767 | HF, AMI: 16.8 | 30d | 18.2 AMI: 17.4 |
| Minges et al | NR | Registry | Yes | Split | 193899 | 194179 | HF, PCI | 65+ | 30d | 11.4 |
| Pack et al | Administrative | Yes | Split | 30826 | 7706 | HVD | 64.9 (12.2) | 90d | 12.8 |
| Oliver-McNeil et al | ICD readmission-risk score | Registry Update | Ext | – | 182 | – | ICD | 69 (11) | 30d | 17.6 |
| Wasty et al | Pre-PCI model | Registry | Yes | Split | 24052 | 12008 | NR | 64.8 (12.5) | 30d | 10.4 |
| Study          | Model                      | Data source | Development | Validation | Sample size | Population | Average age | Outcome |
|---------------|----------------------------|-------------|-------------|------------|-------------|------------|-------------|---------|
| Barnett et al | STS augmented clinical model | Registry    | Update      | Ext        | 19964       | Surgical   | 65.3 (12.4) | 30d     |
| Brown et al   | STS 30-day readmission model | Prospective cohort | Update | Boot      | 1046 | Surgical | 65.4 (9.8) | 30d     |
| Espinoza et al| 30-day readmission score after cardiac surgery | Retrospective cohort | Yes | Split | 2529 | Surgical | 65.1 (11.5) | 30d     |
| Ferraris et al| READMIT                    | Prospective cohort | Yes | Split | 2574 | Surgical | 63 (11)    | 30d     |
| Kilic et al   | READMITS                   | Retrospective cohort | Yes | Split | 3898 | Surgical | D:61.9 (14.7) | 30d     |
| Stuebe et al  | Hospital database           | Yes         | No          |            | 4800 | Surgical | 60–69 | 30d     |
| Tam et al     | TAVR 30-Day readmission risk model | Administrative | Yes | Boots, Ext | 39305 | TAVR | D: 81.3 | 30d | 16.2 |
| Khara et al   | TAVR                       | Administrative | Yes | Boots, Ext | 39305 | TAVR | D: 81.3 | 30d | 16.2 |
| Sanchez et al | Registry                   | Yes         | Split       |            | 6903 | TAVR | 81.1 (7.9) | 30d | 9.8 |

Age is reported as mean (SD); median (IQR) or average age as reported in the study.
ACS, acute coronary syndrome; ADHERE, Acute Decompensated Heart Failure Registry; AF, atrial fibrillation; AH, Adventist Health Off-the-shelf model; AMI, acute myocardial infarction; Boot, bootstrapping; CABG, coronary artery bypass grafting; Car, cardiac-related; CHA2DS2-VASc, congestive heart failure, hypertension, age ≥ 75 years, diabetes mellitus, stroke or transient ischemic attack (TIA), vascular disease, age 65 to 74 years, sex category; CMS, Centers for Medicare and Medicaid Services; CRSS, CABG Readmission Risk Score; d, days; Dev, development; ELAN-HF, European Collaboration on Acute Decompensated Heart Failure; Ext, external validation; FIM, motor and cognitive Functional Independence Measure; GRACE, Global Registration of Acute Coronary Events; HF, heart failure; HFpEF, heart failure with preserved ejection fraction; HVD, heart valve disease; ICD, implantable cardioverter defibrillator; LACE, Length of stay, acuity of the Admission, Comorbidity of the patient and Emergency department use in the duration of 6 months before admission; NA, not applicable; NR, not reported; PARR-30, Patients at Risk of Re-admission within 30 days; PCI, percutaneous coronary intervention; READMITS, Renal Function, Elevated Brain Natriuretic Peptide, Age, Diabetes Mellitus, Nonmale Sex, Intervention with TIMely Percutaneous Coronary Intervention, and Low Systolic Blood Pressure; SILVER-AMI, Comprehensive Evaluation of Risk Factors in Older Patients with AMI; Split, random split; STS PROM, Society of Thoracic Surgeons Predicted Risk of Mortality; TARRACO, Troponin Assessment for Risk stRatification of patients without Acute CoRonal atherothrombosis; TAVR, transcatheter aortic valve replacement; Val, validation.
in studies using registries (0.61, n=17) and hospital databases (0.61, n=18). The discrimination decreased when the number of predictors increased (beta −0.002, n=90). There were no moderation effects based on the average age of the sample, outcome definition and endpoint of the prediction (online supplemental figures 7–8 and online supplemental table 1B).

The calibration was reported for 27 models using multiple measures and could not be pooled (table 2).

**Predictors**

A total of 766 predictor values were estimated in the included models. The median number of predictors per model was 15 (IQR=9–28). The predictors were mostly situated in the domains medical comorbidities (n=211),

![Figure 2](PROBAST (Prediction model Risk Of Bias ASsseessment Tool) risk of bias and applicability. The PROBAST tool\(^{16}\) was used to assess the risk of bias for the participants, predictors, outcome and analysis for each model. Only one study demonstrated low risk of bias on all domains.)
### Table 2: Model discrimination and calibration

| Study | Model                                    | Setting     | Predictors; n | Cohort                | Discrimination | Type calibration | Calibration |
|-------|------------------------------------------|-------------|---------------|-----------------------|----------------|------------------|-------------|
| Moretti et al<sup>77</sup> | EuroHeart PCI score                       | ACS         | 16            | External              | 0.59 (0.48–0.71) | NA               |             |
| Asche et al<sup>46</sup> | NR                                       | AMI         | 19            | Development; random split | 0.74; NR       | NA               |             |
| Cediel et al<sup>64</sup> | TARRACO risk score                        | AMI type 2; ischaemia | 7            | Development (30d)     | 0.71 (0.61–0.82) | NA               |             |
| Burke et al<sup>15</sup> | HOSPITAL score                            | AMI         | 7             | External              | 0.66 (0.61–0.71) | HLT p=0.49      |             |
| Chotechuang et al<sup>36</sup> | GRACE                                    | AMI         | 9             | External (30d)        | 0.77 (0.65–0.88) | NA               |             |
| Cediel et al<sup>64</sup> | TARRACO risk score                        | AMI type 2; ischaemia | 7            | Development (180d)    | 0.71 (0.64–0.78) | NA               |             |
| Hilbert et al<sup>59</sup> | AMI decision tree                         | AMI         | 44            | Development; External | 0.65 (0.64–0.66) | HLT p=0.05; p=0.05 | NA          |
| Dodson et al<sup>36</sup> | SILVER-AMI 30-day readmission calculator  | AMI         | 10            | Development; random split | 0.65; 0.63     | HLT             |             |
| Kini et al<sup>60</sup> | NR                                       | AMI         | 12            | Development; random split | NR; 0.66       | Slope; in large; plot | 0.973 (p=0.330); −0.038 (p=0.221) |
| Nguyen et al<sup>19</sup> | AMI READMITS score                        | AMI         | 7             | Development; random split | 0.75 (0.70–0.80) | Plot; plot       |             |
| Full-stay AMI model        | AMI                                      | 10          | Development; random split | 0.78 (0.74–0.83) | Plot            |             |
| CMS AMI administrative model | AMI                                      | 32          | External      | 0.74 (0.69–0.74)     | Plot            |             |
| Krumholz et al<sup>20</sup> | CMS AMI administrative model              | AMI         | 32            | Development; external; random split | 0.63; 0.63; 0.62 | In large; slope |             |
| CMS AMI medical model      | AMI                                      | 45          | Development; random split | 0.58; 0.59    | NA              | 0, 1/0.015; 0.997/0.015; 0.983 |
| Rana et al<sup>33</sup> | Elixhauser index                          | AMI         | 30            | External              | 0.53 (0.42–0.65) | NA               |             |
| HOSPITAL core              | AMI                                      | 7           | External      | 0.60 (0.47–0.73)     | NA              |             |
| Atzema et al<sup>17</sup> | AFTER Part 2 scoring system              | Arrhythmia; AF | 12            | Development           | 0.69; NR       | NA               |             |
| Lahewala et al<sup>80</sup> | CHADS2                                   | Arrhythmia; AF | 5             | External (30d)       | 0.64           | NA               |             |
| CHADS2                     | Arrhythmia; AF                           | 5           | External (90d) | 0.63           | NA               |             |
| CHADS-VASc                 | Arrhythmia; AF                           | 9           | External (30d) | 0.65           | NA               |             |
| CHADS-VASc                 | Arrhythmia; AF                           | 9           | External (90d) | 0.63           | NA               |             |
| Benuzillo et al<sup>81</sup> | CRSS                                     | CABG        | 5             | Development; bootstrapping | 0.63; 0.63     | HLT            | 7.13 (p=0.52); 9.31 (p=0.32) |
| Deo et al<sup>62</sup> | 30-days CABG readmission calculator      | CABG        | 20            | Development           | 0.65           | NA               |             |
| Engoren et al<sup>16</sup> | NR                                       | CABG        | 6             | Development; random split | 0.68 (0.64–0.72) | 0.68 (0.64–0.68) | NA          |

Continued
| Study            | Model                        | Setting | Predictors; n | Cohort                  | Discrimination       | Type | Calibration |
|------------------|------------------------------|---------|---------------|-------------------------|----------------------|------|-------------|
| Lancey et al.    | NR                           | CABG    | 8             | Development; random split | 0.64; 0.57           | NA   |             |
| Rosenblum et al. | The STS PROM score          | CABG    | 40            | External                | 0.59 (0.57–0.60)     | NA   |             |
| Zitser-Gurevich et al. | NR                      | CABG    | 17            | Development; external (30d) | 0.63; 0.66/0.63       | HLT  | 7.91 (p=0.44) |
|                 | NR                           | CABG    | 13            | Development (100d)      | 0.65                 | HLT  | 6.76 (p=0.56) |
| Zywat et al.     | CABG risk scale              | CABG    | 27            | Development; external   | NR; 0.70             | Plot |             |
| Ahmad et al.     | CMS HF administrative model  | HF      | 37            | External                | 0.66 (0.57–0.76)     | HLT  | p=0.19      |
| Amarasingham et al. | ADHERE administrative model | HF      | 3             | External                | 0.56 (0.54–0.59)     | NA   |             |
| Au et al.        | Administrative claims model  | HF      | 17            | External                | 0.58 (0.58–0.59)     | NA   |             |
|                  | Charlson Comorbidity Score   | HF      | 32            | External                | 0.55 (0.55–0.56)     | NA   |             |
|                  | CMS HF administrative model  | HF      | 37            | External                | 0.59 (0.59–0.60)     | NA   |             |
|                  | LACE                         | HF      | 18            | External                | 0.58 (0.58–0.59)     | NA   |             |
|                  | Bardhan et al.               | NR      | 30            | Development             | 0.56                 | NA   |             |
|                  | Betihavas et al.             | NR      | 7             | Development; bootstrapping | NR; 0.80            | NA   |             |
| Burke et al.     | HOSPITAL score               | HF      | 7             | External                | 0.67 (0.65–0.70)     | HLT  | p=0.10      |
| Cox et al.       | CMS HF administrative model  | HF      | 37            | External                | 0.61                 | NA   |             |
|                  | CMS HF medical model         | HF      | 20            | External                | 0.60                 | NA   |             |
| Delgado et al.   | 15-day CV readmission risk score | HF | 5             | Development; bootstrapping | 0.65; 0.63         | Plot |             |
|                  | 30-day CV readmission risk score | HF | 11           | Development; bootstrapping | 0.66; 0.64         | Plot |             |
| Formiga et al.   | CMS HF medical model         | HF      | 19            | External (30d)          | 0.65 (0.57–0.72)     | NA   |             |
|                  | CMS HF medical model         | HF      | 19            | External (60d)          | 0.62 (0.56–0.68)     | NA   |             |
| Frizzell et al.  | CMS HF administrative model  | HF      | 37            | External                | 0.60                 | NA   |             |
| Hammill et al.   | CMS HF administrative model  | HF      | 37            | External                | 0.59                 | Plot |             |
| Hilbert et al.   | HF decision tree             | HF      | 44            | Development; External   | 0.59 (0.58–0.60)     | NA   |             |

Continued
| Study          | Model                                      | Setting             | Predictors; n | Cohort                  | Discrimination | Type calibration | Calibration |
|---------------|--------------------------------------------|---------------------|---------------|-------------------------|----------------|------------------|-------------|
| Hummel et al  | CMS HF medical model                       | HF                  | 28            | External                | 0.61           | NA               |             |
| Huynh et al   | NR                                         | HF                  | 12            | Development; external   | 0.82 (0.76–0.87) | 0.73 (0.69–0.77) | NA          |
| Ibrahim et al | HOSPITAL score                             | HfEF                | 7             | External                | 0.60 (0.55–0.64) | NA               |             |
| LACE + index  | HfEF                                       | External            | 24            | External                | 0.57 (0.52–0.62) | NA               |             |
| Keenan et al  | CMS HF administrative model                 | HF                  | 37            | Development; external; random split | 0.60; 0.60; 0.61 | In large; slope 0, 1/0.02; 1.01/ 0.09; 1.05 |             |
|               | CMS HF medical model                       | HF                  | 30            | Development; random split | 0.58; 0.61     | In large; slope 0, 1/0, 1 |             |
| Kitamura et al| FIM                                        | HF                  | 13            | External                | 0.78           | NA               |             |
| Leong et al   | 30-day HF readmission risk score           | HF                  | 7             | Development; random split | 0.76; 0.76     | NA               |             |
| Li et al      | NR                                         | HF                  | 10            | Development; random split | 0.63 (0.62–0.63) | HLT; plot 0.15 (p=0.005) |             |
| Lim et al     | NR                                         | HF                  | 13            | Development              | 0.68 (car); 0.62 (all) | HLT 27.5 (p=0.001) (car) 8.0 (p=0.429) (all) |             |
| Reed et al    | AH model                                   | HF                  | 14            | Development; random split | 0.86 (0.85–0.86) | 0.85 (0.84–0.86) | NA          |
|               | CMS HF administrative model                 | HF                  | 37            | Random split            | 0.55 (0.54–0.56) | 0.55 (0.54–0.57) | NA          |
|               | Hasan                                       | HF                  | 9             | Random split            | 0.80 (0.79–0.81) | 0.80 (0.80–0.82) | NA          |
|               | LACE                                        | HF                  | 18            | Random split            | 0.75 (0.74–0.81) | 0.74 (0.73–0.76) | NA          |
| Reed et al    | (continued)                                | PARR-30             | HF            | Random split            | 0.82 (0.81–0.83) | 0.81 (0.80–0.82) | NA          |
| Salah et al   | ELAN-HF Score                              | HF                  | 10            | Development              | 0.60 (0.56–0.64) | NA               |             |
| Sudhakar et al| CMS HF medical model                       | HF                  | 20            | External                | 0.61 (0.57–0.64) | Random patient-level, 0.58 (0.50–0.65) | NA          |
| Tan et al     | NR                                         | HF                  | 3             | Random split            | 0.73           | HLT; plot p=0.62 |             |
| Wang et al    | NR                                         | HF                  | 12            | Development              | 0.65           | NA               |             |
| Wang et al    | LACE                                        | HF                  | 18            | External                | 0.56 (0.48–0.64) | NA               |             |
| Yazdan-Ashoori et al | CMS HF administrative model | HF | 37 | External | 0.61 (0.55–0.67) | NA |             |
|               | LACE                                        | HF                  | 18            | External                | 0.59 (0.52–0.65) | HLT p=0.73 |             |
## Table 2  Continued

| Study                | Model            | Setting                             | Predictors; n | Cohort               | Discrimination | Type calibration | Calibration |
|----------------------|------------------|-------------------------------------|---------------|----------------------|----------------|------------------|-------------|
| Disdier Moulder et al\textsuperscript{73} | NR               | HF; ACS; NR                         | 4             | Development (30d)     | 0.68           |                  | NA          |
|                      |                  |                                     |               |                      |                |                  | NA          |
| Raposeiras-Roubin et al\textsuperscript{77} | GRACE            | HF; ACS                             | 9             | External             | 0.74 (0.73–0.80) | HLT p=0.14       |             |
| Minges et al\textsuperscript{74} | NR               | HF; PCI                             | 35            | Development; random split | 0.67; 0.66     |                  | NA          |
| Pack et al\textsuperscript{75} | NR               | HVD                                | 28            | Development; random split | 0.67 (full dev)/ 0.65 (nomogram); 0.67 (full val) | Harrell’s E; O; E; Harrell’s E; plot | 0.1%; 1.9%; 1.6% |
| Oliver-McNeil et al\textsuperscript{76} | ICD readmission-risk score | ICD | 4          | Update; External     | 0.69 (0.58–0.79) | HLT; plot | 3.44 (p=0.49) |
| Wasfy et al\textsuperscript{72} | Pre-PCI model    | NR                                 | 23            | Development; random split | 0.68; 0.67     | HLT; plot | p=0.59 |
| Barnett et al\textsuperscript{77} | NR validation   | Surgical                            | 15            | External             | 0.59           |                  | NA          |
|                      | NR update        | Surgical                            | 18            | Update               | 0.60 (0.59–0.62) |                  | NA          |
| Brown et al\textsuperscript{43} | STS augmented clinical model | Surgical          | 27            | Update (bootstrap); random split; external (bootstrap) | 0.66 (0.61–0.72); 0.56; 0.47 (0.42–0.53) | HLT | p=1.0 |
| Espinoza et al\textsuperscript{78} | 30-day readmission score after cardiac surgery | Surgical | 5         | Development; random split | 0.66 (0.63–0.70) 0.64 (0.61–0.67) |                  | NA          |
| Ferraris et al\textsuperscript{44} | READMIT         | Surgical                            | 9             | Development           | 0.70           |                  | HLT 5.966 (p=0.651) |
| Klic et al\textsuperscript{79} | NR               | Surgical                            | 15            | Development; random split | NR; 0.64       | HLT; plot | p=0.45; p=0.57 |
| Stuebe et al\textsuperscript{80} | NR               | Surgical                            | 7             | Development           | 0.63           |                  | NA          |
| Tam et al\textsuperscript{44} | NR               | Surgical                            | 29            | Development; bootstrapping | 0.63; 0.65     |                  | Plot        |
| Khera et al\textsuperscript{85} | TAVR 30-Day readmission risk model | TAVR | 11      | Development; random split; external | NR; 0.63; 0.69 | HLT; RMSE; RMSE; Plot | p=0.33; 0.978; 0.928 |
| Sanchez et al\textsuperscript{70} | NR               | TAVR                               | 10            | Development; random split | 0.61; 0.60     |                  | HLT p=0.749; p=0.403 |

ACS, acute coronary syndrome; ADHERE, Acute Decompensated Heart Failure Registry; AF, atrial fibrillation; AH, Adventist Health Off-the-shelf model; AMI, acute myocardial infarction; CABG, coronary artery bypass grafting; Car, cardiac-related; CHADS2, Congestive heart failure, Hypertension, Age, Diabetes, previous Stroke/transient ischemic attack attack; CHADS2-VASC, congestive heart failure, hypertension, age ≥ 75 years, diabetes mellitus, stroke or transient ischemic attack (TIA), vascular disease, age 65 to 74 years, sex category; CMS, Centers for Medicare and Medicaid Services; CRSS, CABG Readmission Risk Score; d, days; dev, development; FIM, motor and cognitive Funcional Independence Measure; GRACE, Global Registry of Acute Coronary Events; HF, heart failure; HFpEF, heart failure with preserved ejection fraction; HLT, Hosmer-Lemeshow test; HOSPITAL, Hemoglobin level, discharged from Oncology; Sodium level, Procedure during admission, Index admission Type, Admission, Length of stay; HVD, heart failure; ICD, implantable cardioverter defibrillator; LACE, Length of stay, acuity of the Admission, Comorbidity of the patient and Emergency department use in the duration of 6 months before admission; NA, not applicable; NR, not reported; O, E, observed, expected; PARR-30, Patients at Risk of Re-admission within 30 days; PCI, percutaneous coronary intervention; plot, calibration plot; READMITS, Renal Function, Elevated Brain Natriuretic Peptide, Age, Diabetes Mellitus, Nonmale Sex, Intervention with Timely Percutaneous Coronary Intervention, and Low Systolic Blood Pressure; SILVER-AMI, Comprehensive Evaluation of Risk Factors in Older Patients with AMI; STS, Society of Thoracic; STS PROM, Society of Thoracic Surgeons Predicted Risk of Mortality; TAVR, transcatheter aortic valve replacement; val, validation.
admission and infection, but this was not consistent across the samples and the prediction intervals were not significant. The effect of these predictors was mostly smaller in the HF samples.

The coefficients for most predictors could not be pooled because they had different definitions, cut-off values or reference categories. However, renal disease, including dialysis, a longer length of stay, creatinine, NT-proBNP (N-Terminal-PRO hormone Brain Natriuretic Peptide) and previous hospital admissions demonstrated a consistent association with readmissions.

**DISCUSSION**

In this systematic review, we included 60 studies that reported the results from 81 separate clinical risk prediction models and 766 risk predictors for unplanned readmission in patients with acute heart disease. We found some promising prediction models, however, no clinical model demonstrated good discrimination (ie, c-statistic >0.8) in independently externally validated cohorts, regardless of the underlying patient populations. GRACE was the only model that demonstrated adequate discrimination in multiple cohorts in patients with acute coronary syndromes and HF. There was little consistency in the measurement of risk predictors.

The results of our review are in line with previous systematic reviews which have mainly focused on samples of patients with HF, AMI or focused on generic prediction models. All reviews confirm that the discrimination is generally low. Our review confirms the importance of previous HF and previous hospital admissions as consistent predictors of the risk of readmission. In addition, two prevalent comorbidities, COPD and valvular disease, were also consistent predictors across the different populations. Other reviews also identified the importance of age, gender, comorbidities and certain laboratory values. These were also significant in our review but the association was not always consistent across the different populations or heterogeneously measured making comparisons difficult. As a result, no clinical risk prediction model or set of predictors that is relevant for different populations of heart disease could be identified.

Our review focused specifically on prediction models with a clinical presentation that can be used in daily practice, for example, risk scores or nomograms. These simple models do not consider interactions between predictor values or non-linear link functions in their predictions. This may partially explain the poor discrimination. Using web applications or electronic patient records to run more complex prediction algorithms can likely offer a solution for future models. A recent systematic review observed an average c-statistic of 0.74 for models using electronic patient records and machine learning algorithms. Our review included 11 studies that developed or validated electronic tools for risk prediction and their discrimination ranged between 0.59 and 0.77.
However, these electronic tools were mostly derived from score charts and nomograms.

There are also concerns about the generalisability of the prediction models. The median age of patients included in the samples was 68 years (IQR=65–75). However, older and frail patients suffer more multimorbidity and geriatric syndromes, and the distribution of predictor and outcome values will also be different than in younger samples. It is therefore unlikely that the majority of the current models will hold their value in daily clinical practice where there is a high prevalence of older patients. Only eight studies included one or more geriatric risk factors (e.g., physical performance, dementia) as predictors for readmission. The performance of models including geriatric conditions was similar to models without these conditions. This might be explained by the relative young mean age of the samples in our review. Mahmoudi et al. reported that functional and frailty status are important predictors, but were only included in a small number of studies. Frailty was not identified in any of the models in our review. It might be valuable to examine the additive value of these predictors in prediction models for patients with heart disease.

We observed high RoB in almost all clinical risk prediction models (98.8%). This was mainly because the calibration was lacking or not fully reported (e.g., only p value of Hosmer-Lemeshow test). Furthermore, most studies performed retrospective data analyses or used data from existing sources. However, our results demonstrate that studies using these data sources had the lowest c-statistic, and that the c-statistic decreased when more predictors were tested. Databases often have missing data, misclassification bias and random measurement error, which likely explains their average poor performance. Only the SILVER-AMI (Comprehensive Evaluation of Risk Factors in Older Patients with AMI) study demonstrated low RoB on all domains. However, their readmission risk calculator for older patients with AMI only discriminated modestly (c-statistic=0.65).

Our review shows the current state-of-the-art of risk prediction in patients with acute heart disease. The timely identification of patients with acute heart disease at risk of readmission remains challenging with the prediction models identified in this systematic review. Therefore, further research in risk prediction remains important and some recommendations for further research can be derived from this review. First, consistency is needed in the definition and measurement of predictors. More homogeneity might improve the identification of important predictors and their effect on readmission. Based on our insights, we believe that models could be improved by incorporating some key predictors, that is, age, gender, comorbidity scores (or at least heart failure, COPD, cardiovascular disease, diabetes mellitus), admission status, readmission history and the geriatric profile (e.g., functional status, cognitive

### Figure 4
Predictors of unplanned hospital readmission. The plot provides an overview of the random-effects meta-analyses that were performed for predictors who were similarly defined for the outcome unplanned hospital readmission at 30-day follow-up. See online supplemental table 2A and online supplemental figures 9–26 for more details. CABG, coronary artery bypass grafting; COPD, chronic obstructive pulmonary disease; PCI, percutaneous coronary intervention.
status). Because there are a still a large number of potential predictors, a large sample size is needed to estimate the coefficients with sufficient precision, and to prevent against overfitting the models. Some selection of predictors may still be warranted, and penalised techniques (eg, lasso regression) should be preferred over traditional selection based on p values. Second, the results suggest that multiple predictors are associated with readmissions regardless of the underlying population. Therefore, attention might be shifted from developing new risk prediction models to updating and externally validating existing prediction models in different populations with heart disease. For example, the Adventist Health Off-the-shelf model\cite{1} showed high discrimination rates in both the development (0.86) and the validation cohorts (0.85). External validation is recommended to examine the generalisability of this model in other settings. In addition, the AMI READMITS (Acute Myocardial Infarction Renal Function, Elevated Brain Natriuretic Peptide, Age, Diabetes Mellitus, Nonmale Sex, Intervention with Timely Percutaneous Coronary Intervention, and Low Systolic Blood Pressure) score\cite{2}, full-stay AMI readmission model\cite{3} pre-PCI model\cite{4}, motor and cognitive Functional Independence Measure (FIM)\cite{5}, READMIT\cite{6}, 30-day readmission model of Huynh et al\cite{7} and the model of Engoren et al\cite{8} were examined in one study and showed reasonable c-statistics in the development (0.68–0.82) and validation cohorts (0.64–0.78). For these studies, model updating recalibration and external validation is recommended to improve the predictive performance and generalisability of these prediction models. Third, the applicability of current prediction models in daily practice is an important concern as most models had poor performance, were not replicated and had high RoB. More high-quality studies are needed that evaluate the discrimination, calibration and clinical usefulness. To limit the RoB as much as possible, future studies should adhere to the relevant reporting guidelines\cite{9} and could use PROBAST\cite{10} as a guidance to plan their study. Fourth, more complex models integrated in electronic patient records may result in better predictions.

**Limitations**

Although we performed an extensive literature search, we might have missed some eligible studies, particularly those published in non-English languages. We were able to perform meta-analysis for predictors that were often (≥5 models) reported. However, it might be possible that some less frequently mentioned predictors (eg, geriatric predictors) are a valuable addition in clinical practice. The review included a large number of results and statistical tests which may result in an inflated alpha error. The meta-regression identified that models with less predictors had a better discrimination, but this could also be explained by overfitting models; this could not be tested.

**CONCLUSION**

A large number of clinical models have recently been developed. Although some models are promising as they demonstrated adequate to good discrimination, no model can currently be recommended for clinical practice. The lack of independently validated studies, high RoB and low consistency in measured predictors limit their applicability. Model updating and external validation is urgently needed.

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**Data availability statement** All data relevant to the study are included in the article or uploaded as supplementary information.

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REFERENCES

1. Virani SS, Alonso A, Benjamin EJ, et al. Heart disease and stroke statistics—2020 update: a report from the American heart association. *Circulation* 2020;141:e139–56.

2. Shippe ME, Deppen SA, Farjah F, et al. Developing prediction models for clinical use using logistic regression: an overview. *J Thorac Dis* 2019;11:S574–84.

3. Smith LN, Makam AN, Darden D, et al. Acute myocardial infarction risk prediction models: a systematic review of model performance. *Circ Cardiovasc Qual Outcomes* 2018;11:e003885.

4. Di Tanna GL, Wirtz H, Burrows KL, et al. Evaluating prediction models for adults with heart failure: a systematic literature review. *PLoS One* 2020;15:e0224135.

5. Mahajan SM, Heidenreich P, Abbott B, et al. Predictive models for identifying risk in meta-analyses. *BMJ* 2014;4:240–6.

6. Bethavas V, Davidson PM, Newton PJ, et al. What are the factors in risk prediction models for rehospitalization for adults with chronic heart failure? *Circ Cardiovasc Qual Outcomes* 2012;5:39–46.

7. Rahimi K, Bennett D, Conrad N, et al. Risk prediction in patients with heart failure: a systematic review and analysis. *JACC Heart Fail* 2014;2:406–6.

8. Moreh N, Sheldon TA, Sutton AJ, et al. Use of electronic medical records in development and validation of risk prediction models of 30-day mortality after hospitalization for heart failure: a systematic review. *Eur J Cardiovasc Nurs* 2018;17:675–89.

9. O’Connor M, Murtagh CM, Shah S, et al. Patient characteristics predicting readmission among individuals hospitalized for heart failure. *Med Care Res Rev* 2016;73:34–50.

10. Mahmoudi E, Kamdar N, Kim N, et al. Use of electronic medical records in development and validation of risk prediction models of performance. *Circ Cardiovasc Qual Outcomes* 2020;13:396–404.

11. Desai MM, Stauffer BD, Feringa HH, et al. Statistical models and patient predictors of readmission for acute myocardial infarction: a systematic review. *Circ Cardiovasc Qual Outcomes* 2009;2:500–7.

12. Ross JS, Mulvey GK, Stauf B, et al. Risk of readmission after hospital discharge among heart failure patients at risk for 30-day readmission using an administrative dataset and “off the shelf” readmission models. *Internet J Cardiovasc Res* 2014:9:07–15.

13. Hummel SL, Katrapati P, Gillespie BW, et al. Application of the heart failure readmission risk score: a first European study. *Int J Cardiol* 2017;236:304–9.

14. Sudhakar S, Zhang W, Kuo Y-F, et al. Validation of the readmission risk score in heart failure patients at a tertiary hospital. *J Card Fail* 2015;21:885–91.

15. Choteuchang Y, Phrommintikul A, Muenpa R, et al. The prognostic utility of grace risk score in predictive cardiovascular event rate in STEMI patients with successful fibrinolysis and delay intervention in non PCI-capable Hospital: a retrospective cohort study. *BMC Cardiovascular Disorders* 2016;16:1212.

16. Raposeiras-Roubin S, Abou-Assi E, Cambeiro-González C, et al. Mortality and cardiovascular morbidity within 30 days of discharge following acute coronary syndrome in a contemporary European cohort of patients: how can early risk prediction be improved? *Eur J Intern Med* 2013;24:383–91.

17. Wagner H, Robinson RD, Johnson C, et al. Using the lasso index to predict hospital readmissions in congestive heart failure patients. *BMC Cardiovascular Disorders* 2014;14:97.

18. Deakin BB, Pepe MS. Joint modeling, covariate adjustment, and interaction: contrasting inferences in risk prediction models and risk prediction performance. *Epidemiology* 2011;22:805–12.

19. Lee SW, Park J, Kim S, et al. Use of electronic medical records in development and validation of risk prediction models of performance. *Circ Cardiovasc Qual Outcomes* 2020;13:396–404.

20. Deakin BB, Pepe MS. Joint modeling, covariate adjustment, and interaction: contrasting inferences in risk prediction models and risk prediction performance. *Epidemiology* 2011;22:805–12.

21. Deakin BB, Pepe MS. Joint modeling, covariate adjustment, and interaction: contrasting inferences in risk prediction models and risk prediction performance. *Epidemiology* 2011;22:805–12.

22. Deakin BB, Pepe MS. Joint modeling, covariate adjustment, and interaction: contrasting inferences in risk prediction models and risk prediction performance. *Epidemiology* 2011;22:805–12.

23. Deakin BB, Pepe MS. Joint modeling, covariate adjustment, and interaction: contrasting inferences in risk prediction models and risk prediction performance. *Epidemiology* 2011;22:805–12.

24. Deakin BB, Pepe MS. Joint modeling, covariate adjustment, and interaction: contrasting inferences in risk prediction models and risk prediction performance. *Epidemiology* 2011;22:805–12.
fibrillation in the emergency room, part 2 (AFTER2) study. Am Heart J 2018;203:85–92.

48 Huynh Q, Negishi K, De Pasquale CG, et al. Validation of predictive score of 30-day hospital readmission or death in patients with heart failure. Am J Cardiol 2018;122:278–86.

49 Li L, Baek J, Jesdale BM, et al. Predicting 30-day mortality and 30-day re-hospitalization risks in Medicare patients with heart failure discharged to skilled nursing facilities: development and validation of models using administrative data. J Nurs Home Res Sci 2019;5:60–7.

50 Sanchez CE, Espinoza J, Camporr et al. Development and validation of a simple risk score to predict 30-day readmission after coronary artery bypass. J Thorac Cardiovasc Surg 2015;149:e1:850–7.

51 Jordan K, Moons K. Electronic healthcare records and prognosis research. In: Prognosis research in healthcare. concepts, methods and impact. Oxford: Oxford University press, 2019.

52 Wasty JH, Rosenfeld K, Zelevinsky K, et al. Prediction model to identify patients at high risk for 30-day readmission after percutaneous coronary intervention. Circ Cardiovasc Qual Outcomes 2013;6:429–35.

53 Kitamura M, Izawa KP, Taniue H, et al. Relationship between activities of daily living and readmission within 90 days in hospitalized elderly patients with heart failure. Biomed Res Int 2017;2017:7420738.

54 Ferraris VA, Ferraris SP, Harmon RC, et al. Risk factors for early Hospital readmission after cardiac operations. J Thorac Cardiovasc Surg 2001;122:278–86.

55 Engoren M, Habib RH, Dooner JJ, et al. Use of genetic programming, logistic regression, and artificial neural nets to predict readmission after coronary artery bypass surgery. J Clin Monit Comput 2013;27:455–64.

56 et al Collings G, Reitsma J, Altman D. Transparent reporting of a multivariable prediction model for individual prognosis or diagnosis (TRIPOD): the TRIPOD statement. 2019. Available: https://www.equator-network.org/reporting-guidelines/tripod-statement/ [Accessed 20 Aug 2020].

57 Moretti C, D’Ascenzo F, Omede P, et al. Thirty-day readmission rates after PCI in a metropolitan center in Europe: incidence and impact on prognosis. J Cardiovasc Med 2015;16:239–45.

58 Cediel G, Sandoval Y, Sexter A, et al. Risk estimation in type 2 myocardial infarction and myocardial injury: the tarraco risk score, Am J Med 2019;132:171–7.

59 Hilbert JP, Zasaadi S, Keyser DJ, et al. Using decision trees to manage Hospital readmission risk for acute myocardial infarction, heart failure, and pneumonia. Appl Health Econ Health Policy 2014;12:573–85.

60 Kini V, Peterson PN, Spurtus JA, et al. Clinical model to predict 90-day risk of readmission after acute myocardial infarction. Circ Cardiovasc Qual Outcomes 2018;11:e004788.

61 Benuzzillo J, Caine W, Evans RS, et al. Predicting readmission risk shortly after admission for CABG surgery. J Card Surg 2018;33:163–70.

62 Deo SV, Plaza S, Altarabsheh SE, et al. Risk calculator to predict 30-day readmission after coronary artery bypass: a strategic decision support tool. Heart Lung Circ 2019;28:1896–903.

63 Lansey R, Kurlansky P, Argenziano M, et al. Uniform standards do not apply to readmission following coronary artery bypass surgery: a multi-institutional study. J Thorac Cardiovasc Surg 2015;149:e1:850–7.