Title

Acute Myocardial Infarction Readmission Risk Prediction Models: A Systematic Review of Model Performance.

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ORIGINAL ARTICLE

Acute Myocardial Infarction Readmission Risk Prediction Models

A Systematic Review of Model Performance

BACKGROUND: Hospitals are subject to federal financial penalties for excessive 30-day hospital readmissions for acute myocardial infarction (AMI). Prospectively identifying patients hospitalized with AMI at high risk for readmission could help prevent 30-day readmissions by enabling targeted interventions. However, the performance of AMI-specific readmission risk prediction models is unknown.

METHODS AND RESULTS: We systematically searched the published literature through March 2017 for studies of risk prediction models for 30-day hospital readmission among adults with AMI. We identified 11 studies of 18 unique risk prediction models across diverse settings primarily in the United States, of which 16 models were specific to AMI. The median overall observed all-cause 30-day readmission rate across studies was 16.3% (range, 10.6%–21.0%). Six models were based on administrative data; 4 on electronic health record data; 3 on clinical hospital data; and 5 on cardiac registry data. Models included 7 to 37 predictors, of which demographics, comorbidities, and utilization metrics were the most frequently included domains. Most models, including the Centers for Medicare and Medicaid Services AMI administrative model, had modest discrimination (median C statistic, 0.65; range, 0.53–0.79). Of the 16 reported AMI-specific models, only 8 models were assessed in a validation cohort, limiting generalizability. Observed risk-stratified readmission rates ranged from 3.0% among the lowest-risk individuals to 43.0% among the highest-risk individuals, suggesting good risk stratification across all models.

CONCLUSIONS: Current AMI-specific readmission risk prediction models have modest predictive ability and uncertain generalizability given methodological limitations. No existing models provide actionable information in real time to enable early identification and risk-stratification of patients with AMI before hospital discharge, a functionality needed to optimize the potential effectiveness of readmission reduction interventions.

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Key Words: Medicaid ■ Medicare ■ myocardial infarction ■ patient readmission ■ risk

WHAT IS KNOWN

- Hospitals are subject to federal financial penalties for excessive 30-day readmissions for acute myocardial infarction (AMI).
- Prospectively identifying patients hospitalized with AMI could help prevent readmissions by enabling targeted interventions, but the performance of AMI-specific readmission risk prediction models is unknown.

WHAT THE STUDY ADDS

- We identified 11 studies of 18 unique readmission risk models, 16 of which were specific to AMI.
- Current AMI-specific readmission risk prediction models have modest predictive ability and uncertain generalizability, given methodological limitations.
- No existing models provide actionable information in real time to enable early identification and risk-stratification of patients with AMI before hospital discharge, a functionality needed to optimize the potential effectiveness of readmission reduction interventions.

Hospital readmissions among patients with acute myocardial infarction (AMI) are frequent, costly, and potentially avoidable.[1–4] Nearly 1 in 6 patients hospitalized with AMI have an unplanned readmission within 30 days of discharge, accounting for over $1 billion of annual US healthcare costs.[1,2] Since 2012, hospitals have been subject to financial penalties for excessive all-cause 30-day readmissions among patients with an index hospitalization for AMI under the Hospital Readmissions Reduction Program (HRRP), implemented by the Centers for Medicare and Medicaid Services (CMS). Although federal readmission penalties have stimulated intense efforts to develop readmissions reduction intervention strategies, these interventions are resource-intensive, are most effective when implemented well before hospital discharge, and have been only modestly successful when applied indiscriminately to all hospital inpatients.[5–8]

Predicting which patients hospitalized for AMI are at highest risk for readmission would enable hospitals to proactively identify and target patients who are the most likely to benefit from more intensive readmission prevention interventions, simultaneously optimizing the allocation of scarce intervention resources and maximizing the potential for successful intervention.[9,10] Head-to-head comparisons of multicondition versus disease-specific readmission risk prediction models suggest that disease-specific models outperform multicondition models.[11] However, the performance and accuracy of AMI-specific readmission risk prediction models are unknown.

Two systematic reviews conducted before the HRRP identified no AMI-specific readmission models nor any all-condition readmission models tested for use in AMI.[12,13] In the 5 years since the implementation of the HRRP, there has been increased interest in preventing readmissions among patients with AMI, with a resulting renewed interest in developing strategies to identify at-risk patients with AMI before hospital discharge. Thus, the objective of this study was to conduct an updated systematic review to include post-HRRP literature on readmission risk prediction models for patients hospitalized with AMI, to assess model performance on identifying patients at risk for 30-day readmission and to assess the methodological quality of available studies.

MATERIALS AND METHODS

Data Sources and Searches

The data, analytic methods, and study materials will not be made available to other researchers for purposes of reproducing the results or replicating the procedure. We searched Ovid MEDLINE, Ovid MEDLINE InProcess, the Cumulative Index to Nursing and Allied Health Literature, the Cochrane Library (including Cochrane Central Register of Controlled Trials, Cochrane Database of Systematic Reviews and the Database of Abstracts of Reviews of Effect), and Embase from database inception through March 2017 for studies of readmission risk prediction models in adults hospitalized with AMI. We used subject headings and text words to identify articles that contained the following 3 concepts (1) readmission (readmi*, readmi*, rehosp*, rehosp*, patient readmission/, readmission/), (2) risk (model*, predict*, risk*, util*, use*, usage, risk/, risk assessment/ risk factors/), and (3) AMI (MI/, anterior wall MI/, inferior wall MI/, acute coronary syndrome/, or myocardial ischemia/). The search strategies are provided in detail in the eAppendix in the Data Supplement.

Study Selection

Two authors (Drs Smith and Darden) reviewed the abstracts and full-text articles of potentially relevant references identified from the literature search for eligibility. References of included articles were also hand-searched to identify additional eligible studies. Criteria for inclusion were (1) full text in English; (2) study population included adult patients 18 years or older discharged from the hospital with AMI; (3) article is a primary study that derives or validates a risk prediction model for hospital readmission after an index admission for AMI; (4) the model predicts the risk for the first hospital readmission within 30 days of discharge, not a series or sequence of hospital readmissions; and (5) at least 1 measure of model performance (discrimination or calibration) was reported in the article or made available by contacting the corresponding author.

Data Extraction and Methodological Quality Assessment

Using a standardized abstraction form, 2 reviewers (Drs Smith and Darden) extracted data on the population characteristics,

setting, number of patients and hospitals in the derivation and validation cohorts, definition of AMI, method and time interval of readmission outcome ascertainment, method of derivation and validation, domains of predictors tested, predictors included in the final model, accuracy of risk prediction, and study quality assessment. To facilitate a comparison of the models, we classified predictors into 1 of 9 categories based on prior conceptual frameworks of readmission risk (demographics, socioeconomic status, comorbidities, utilization, laboratory results, vital signs, imaging, procedures, and medications).[13–15] Reviewers resolved disagreements through discussion. If consensus could not be achieved, a third author (Dr Nguyen) resolved discrepancies. Corresponding authors were contacted by e-mail if relevant data were missing, with 3 total attempts.

We assessed the accuracy of risk prediction by evaluating the model's discrimination and overall predictive ability. We assessed discrimination based on the C statistic, which is the probability that given 2 individuals hospitalized with MI (one who was readmitted and the other who was not), the model will predict a higher risk of readmission for the readmitted patient than for the nonreadmitted patient.[16] A C statistic of 0.5 indicates a model performs no better than chance, 0.6 to 0.7 is considered modest discrimination, 0.71 to 0.8 indicates very good discrimination and >0.8 is considered very strong performance.[17] Model calibration is the degree to which predicted rates are similar to those observed in the population.[13] To examine predictive ability, we assessed the range of mean observed risk for readmission for the lowest and highest predicted risk groups.

We qualitatively assessed the quality of included studies using elements from the standards of evidence for evaluating clinical prediction rules[18] and the study quality assessment criteria used by Kansagara et al.[13] Studies were considered to be high quality if they included an adequate description and generalizability of the population, had nonbiased selection of patients, ascertained readmissions within 30 days at any hospital (and not only the index site, because this is aligned with the CMS HRRP policy), and broadly validated the model in external cohorts (versus narrow validation in a single cohort or no validation at all).

Data Synthesis

We were unable to perform a meta-analysis because of the heterogeneity of the included studies. Therefore, we qualitatively synthesized results with a focus on the predictors included in each model, model performance, and methodological quality.

RESULTS

Of 4657 titles identified by our search algorithm, 3831 qualified for abstract review and 42 for full-text review; 11 studies (Figure) describing 18 unique models were ultimately included in the final analysis, of which 16 models were specific to AMI (Table 1).[19–30] The majority of studies were conducted in US populations of hospitalized patients 50 years or age or older (n=7). The median overall observed all-cause 30-day readmission rate across studies was 16.3% (range, 10.6%–21.0%). The objective of most studies (n=7) was to develop models to identify patients hospitalized for MI at high risk for readmission for potential intervention,[19–22,24,27,29] whereas the objective of 3 studies of the CMS AMI administrative model was to estimate hospital-level risk-adjusted 30-day readmission rates for hospital profiling.[23,25,26] One study focused on identifying patient- versus hospital-level predictors for cardiac disease–related readmission.[28] All studies were conducted in the US except for Rana et al,[27] which was conducted at a single community medical center in Australia, and Rodriguez-Padial et al,[28] conducted in Spain using administrative data from the Spanish National Health System.

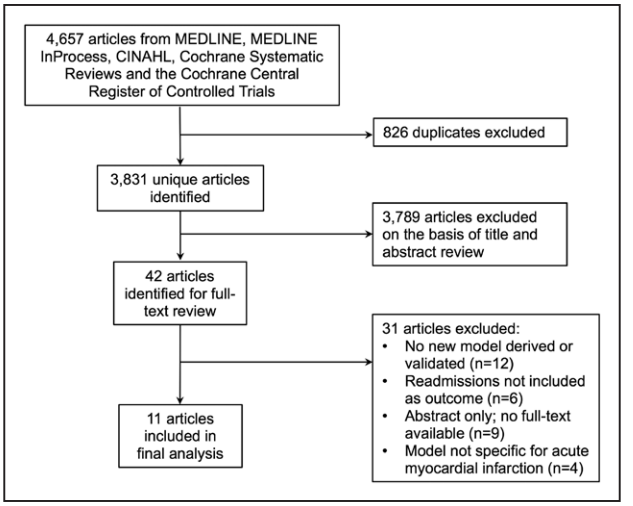

Figure. Article selection.
CINAHL indicates Cumulative Index to Nursing and Allied Health Literature.

Study Populations and Definitions of AMI

Study populations ranged from cohorts at single academic medical centers (n=4)[19,21,27,29]; to statewide,[22,26] multistate,[24,25] or multisite cohorts (n=5)[20]; to national cohorts using Medicare[23,25] or national health system data[28] (n=3). Nine studies defined AMI as the primary discharge diagnosis using *International Classification of Diseases*, Ninth Revision (ICD-9) codes, ICD-10 codes, or diagnosis-related group codes.[20–23,25–29] Two studies used clinical criteria ascertained from registry data to define AMI.[22,24]

Model Characteristics

Among the 18 unique models identified, the CMS AMI administrative model was the most commonly studied model—it was validated in 7 separate cohorts across 4 studies[23–26] though 1 study[24] used a modified version of the CMS model that included fewer predictors

Table 1. Details of AMI Readmission Risk Prediction Model Studies

Study	Model	Purpose of Model	Setting and Study Dates	Population Age, y	Definition of AMI	Derivation Cohort, n	Validation Cohort, n	Observed 30-d Readmit Rates, % (n)*
Brown et al[19]	AMI registry model	Identify high-risk patients	1 AMC in New Hampshire, 1/2006–12/2011	≥50	Registry diagnosis	1271	None	10.6 (135)†
Burke et al[20]	HOSPITAL score‡	Identify high-risk patients	6 AMCs in United States, 1/2011–12/2011	≥18	ICD-9	N/A	767	AMI-related§: 12.7 (97); all-cause: 17.4 (134)
Hebert et al[21]	AMI EHR model	Identify high-risk patients	1 AMC in Ohio, 8/2008–7/2011	≥50	ICD-9	1047	Split‖: 230; historical‖: 594	13.0 (30); 15.5 (92)
Hilbert et al[22]	California statewide AMI administrative model	Identify high-risk patients	Statewide hospital administrative data from California¶; 1/2010–11/2010; 1/2011–11/2011	≥18	DRGs	10848	10701	19.7 (2108)
Krumholz et al[23]	CMS AMI administrative model	Risk-adjustment to profile hospitals	Nationwide Medicare hospital data, 1/2005–12/2006	≥65	ICD-9	100465	Split: 100285#	18.9 (18954)†
							Historical: 220803**	
							CCP cohort: 130944††	20.0 (26136)
	CMS AMI CCP medical record model	Validation of CMS AMI admin model	Medical record data from 4178 hospitals in the United States and Puerto Rico, 1994–1995		Chart review	130944	None	20.0 (26136)†
McManus et al[24]	CMS-like registry model‡‡ (CMS base model)	Identify high-risk patients	6 hospitals in Georgia and Massachusetts, 4/2011–5/2013	≥65	Registry diagnosis	804	None	13.2 (106)†
	CMS base model+clinical							
	CMS base model+clinical+mental health							
	CMS base model+clinical+mental health+SES							
Meddings et al[25]	CMS AMI administrative model in HRS-CMS cohort	Risk-adjustment to profile hospitals	HRS-CMS linked data, 1995–2012§§	≥65	ICD-9	N/A	833	16.3 (136)†
	Disability/SES-enriched CMS AMI administrative model (HRS-CMS)§§					833	None	
	CMS AMI administrative model in ACS-HCUP cohort		ACS-HCUP linked data, 2009–2012‖‖			N/A	17496	14.0 (2452)†
	Disability/SES-enriched CMS AMI administrative model (ACS-HCUP)‖‖					17496	None	
Nagasako et al[26]	CMS AMI administrative model	Risk-adjustment to profile hospitals	Statewide Missouri Medicare data, 6/2009–5/2012	≥65	ICD-9	N/A	11392	16.4 (1869)¶¶
	SES-enriched CMS AMI administrative model		Statewide Missouri Medicare data linked to census-tract data from Truven Analytics and Nielsen, 6/2009–5/2012			11392	11392	16.3 (1856)¶¶
Rana et al[27]	AMI EHR model##	Identify high-risk patients	1 community hospital in Australia, 1/2009–12/2011	≥18	ICD-10***	1107	533	IHD-related##: 6.3 (105); all-cause: 12.7 (212)
	HOSPITAL score‡					N/A		
	Comorbidities model†††					N/A		

(*Continued*)

Table 1. Continued

Study	Model	Purpose of Model	Setting and Study Dates	Population Age, y	Definition of AMI	Derivation Cohort, n	Validation Cohort, n	Observed 30-d Readmit Rates, % (n)*
Rodriguez-Padial et al[28]	Spanish National Health System AMI administrative model‡‡‡	Identify predictors associated with cardiac disease–related readmission	Spanish National Health System, 2012	≥35	ICD-9	22 359§§§	11 179§§§	Cardiac disease–related‡‡‡: 5.4 (1811)
Yu et al[29]‖‖	AMI hospital 2 model	Identify high-risk patients	1 hospital in Midwest United States; dates not reported	≥65	ICD-9	844	169###	21.0 (177)
	LACE model at hospital 2¶¶¶							
	AMI hospital 3 model		1 hospital in Northeast United States; dates not reported			1506	301###	16.0 (241)
	LACE model at hospital 3¶¶¶							

ACS indicates American Community Survey; AMC, academic medical center; AMI, acute myocardial infarction; CMS, Centers for Medicare & Medicaid Services; CCP, Cooperative Cardiovascular Project; DRG, diagnosis-related group; EHR, electronic health record; HCUP, Healthcare Cost and Utilization Project; HRS, Health and Retirement Study; ICD, International Classification of Disease; IHD, ischemic heart disease; N/A, not applicable; and SES, socioeconomic status.

*Reported 30-d all-cause readmission rate for the respective validation cohort unless otherwise specified.

†Reported 30-d all-cause readmission rate for derivation cohort.

‡The HOSPITAL score is a previously validated readmission risk prediction model that includes the following predictors, ascertained at discharge: hemoglobin, discharge from an oncology service, sodium level, procedure during index hospitalization, index hospitalization type classified as urgent, number of admissions during the last 12 mo, and length of stay.[31]

§Authors assessed HOSPITAL score performance for prediction of both potentially preventable readmissions (ie, readmissions related to same diagnosis as for index hospitalization, in this case, for AMI) as defined by an automated algorithm[30] and all-cause readmission.

‖Primary study cohort consisted of data from 2009–2011; derivation sample was 80% and split validation sample consisted of a 20% randomly selected cohort from these 2 years of data. Historical validation cohort consisted of all observations from 2008–2009. Both validation cohorts were separate and distinct from derivation cohort.

¶Used administrative data from the Healthcare Cost and Utilization Project State Inpatient Databases for the state of California.

#Cohort comprised of claims data from second half of 2006, whereas first half was used for derivation.

**Cohort comprised of data from the full year of 2005.

††The authors derived a separate model based on hospital medical record data from the Cooperative Cardiovascular Project (CCP), a database with records from acute care hospitals in the United States and Puerto Rico from 1994–1995. Patients with CCP data who were matched to the Medicare enrollment database were included in the cohort. The purpose of the CCP model was primarily for comparison to the CMS AMI administrative model for validation purposes.

‡‡The authors used fewer than the total number of predictors included in the original CMS AMI model because of unavailability of certain data. The final CMS-like registry model included 19 of the 31 factors used in the original CMS model; domains of predictors that were not included were predictors related to brain disorders, urinary tract infection, specific hematologic disorders, and other lung disorders.

§§Model created using linked data on index hospitalizations from 6/1996–6/2012 CMS Medicare Inpatient Standard Analytic Files and most recent prehospitalization survey available in 1995–2010 HRS data. HRS data included patient-level measures of disability (limitations in activities of daily living, nursing home status, or use of home health services) and social determinants of health (marital status, presence of children, receipt of Medicaid, household wealth, race). Final model included only nursing home status as an additional predictor to enhance CMS AMI administrative model.

‖‖Model created using linked data from the ACS and HCUP State Inpatient Databases for the states of Florida and Washington because of the availability of ZIP codes in HCUP data for these states. ACS data included community-level (ie, ZIP code level) measures of disability (proportion of adults ≥65 y with difficulty dressing or bathing) and social determinants (proportion of married adults ≥65 y, proportion in the highest income quartile, and proportion with Medicaid). Final model included only race as an additional predictor to enhance CMS AMI administrative model.

¶¶Data obtained from contacting study author.

##Model designed to predict only IHD-related 30-d readmissions, not all-cause 30-d readmissions. IHD-related readmissions were defined as those with primary or secondary ICD-10 discharge diagnoses of angina pectoris (I20), AMI (I21), subsequent myocardial infarction (I22), complications after AMI (I23), other acute ischemic heart diseases (I24), or chronic IHD (I25).

***Included individuals with a diagnosis of AMI listed as either a primary or secondary discharge diagnosis, unlike other studies which limited inclusion to only those with AMI as a primary discharge diagnosis. AMI was defined by ICD-10 codes I21 (AMI) or I22 (subsequent myocardial infarction).

†††The comorbidities model was initially based on the Elixhauser comorbidity index and adapted to include only comorbidities highly predictive of readmissions in the study cohort.

‡‡‡Model designed to predict only cardiac disease–related 30-d readmissions, not all-cause 30-d readmissions. Cardiac disease–related readmissions were defined as those with a primary discharge diagnosis of rheumatic heart disease (ICD-9 codes 390–398), hypertensive heart disease (401–405), ischemic heart disease (410–414), disease of pulmonary circulation (415–417), other forms of heart disease (420–429), and aortic aneurysm and dissection (441.01, 441.1, 441.2, 444.1).

§§§Size of derivation and validation cohorts calculated based on reported total cohort size of 33 538 patients and report that the model was developed with 2/3 of the data set and validated with remaining 1/3.

‖‖This study reported the development of hospital-specific models derived at 3 US hospitals; AMI models were only developed at 2 of the 3 hospitals. The LACE model was tested in the AMI population at each of these 2 hospitals.

¶¶¶The LACE model includes the following predictors, ascertained at discharge, length of stay, acuity (ie, hospitalization type classified as emergent or urgent), Charlson comorbidity score, and emergency department visits in the past 6 mo.[32]

###The size of the validation cohort was calculated based on the authors' report that 20% of samples were used for testing.

Table 2. Domains of Predictors and Performance of AMI Readmission Risk Prediction Models

Study	Model	Domains of Predictors Evaluated*	Domains of Predictors Included in Final Model*	Discrimination (C statistic)†	Predictive Ability: Range of Mean Observed Readmission Rates‡	
					Lowest Predicted Risk Group	Highest Predicted Risk Group
Brown et al[19]	AMI registry model	D, C, MI, P, V, M, HC	D, C, MI, P, M, HC	0.71 (derivation)	Not reported	Not reported
Burke et al[20]	HOSPITAL score	N/A	U, L, P	0.67 (for AMI)§	8.9%‖	22.2%‖
				0.66 (all-cause)	8.6%‖	33.3%‖
Hebert et al[21]	AMI EHR model	D, C, U, L, P, M, SES	D, C, U, L, M	0.76 (random); 0.66 (historical)	3.0%¶	27.0%¶
Hilbert et al[22]	California statewide AMI administrative model	D, C, U, P	D, C, U, P	0.61	9.6%#	35.7%#
Krumholz et al[23]	CMS AMI administrative model	D, C	D, C	0.63 (split); 0.62 (historical); 0.59 (CCP)	8.0%; 8.0%; 13.0%	33.0%; 32.0%; 31.0%
	CMS AMI CCP medical record model	Not reported	D, C, MI, L, V	0.58 (derivation)	13.0%	29.0%
McManus et al[24]	CMS-like registry model (CMS base model)	N/A	D, C	0.63 (derivation)	6.0%	19.0%
	CMS base model+clinical	D, C, MI, L, V	D, C, MI, L, V	0.65 (derivation)	Not reported	Not reported
	CMS base model+clinical+mental health	D, C, MI, L, V, MH	D, C, MI, L, V, MH	0.65 (derivation)	Not reported	Not reported
	CMS base model+clinical+mental health+SES	D, C, MI, L, V, MH, SES	D, C, MI, L, V, MH, SES	0.65 (derivation)	5.0%	27.0%
Meddings et al[25]	CMS AMI administrative model in HRS-CMS cohort	N/A	D, C	0.64	Not reported	Not reported
	Disability/SES-enriched CMS AMI administrative model (HRS-CMS)	D, C, SES, F	D, C, SES, F	0.79 (derivation)		
	CMS AMI administrative model in ACS-HCUP cohort	N/A	D, C	0.64		
	Disability/SES-enriched CMS AMI administrative model (ACS-HCUP)	D, C, SES, F	D, C, SES	0.63 (derivation)		
Nagasako et al[26]	CMS AMI administrative model	N/A	D, C	0.76	0.2%**	40.5%**
	SES-enriched CMS AMI administrative model	D, C, SES	D, C SES	0.76	0.2%**	43.0%**
Rana et al[27]	AMI EHR model	D, C, U, L, P	D, C, U, L, P	0.78 (for IHD)	Not reported	Not reported
	HOSPITAL score	N/A	U, L, P	0.60 (for IHD)		
	Comorbidities model	C	C	0.53 (for IHD)		
Rodriguez-Padial et al[28]	Spanish National Health System AMI administrative model	D, C, P, S††	D, C, P, S††	0.74 (for cardiac disease)	4.4%‡‡	8.2%‡‡

(*Continued*)

Table 2. Continued

Study	Model	Domains of Predictors Evaluated*	Domains of Predictors Included in Final Model*	Discrimination (C statistic)†	Predictive Ability: Range of Mean Observed Readmission Rates‡	
					Lowest Predicted Risk Group	Highest Predicted Risk Group
Yu et al[29]	AMI hospital 2 model	D, C, U	D, C, U	0.66§§	Not reported	Not reported
	LACE model at hospital 2	N/A	C, U	0.57		
	AMI hospital 3 model	D, C, U	D, C, U	0.64§§		
	LACE model at hospital 3	N/A	C, U	0.63		

ACS indicates American Community Survey; AMC, academic medical center; AMI, acute myocardial infarction; CMS, Centers for Medicare & Medicaid Services; SES, socioeconomic status; DRG, diagnosis-related group; EHR, electronic health record; HCUP, Healthcare Cost and Utilization Project; HRS, Health and Retirement Study; ICD, International Classification of Disease; IHD, ischemic heart disease; N/A, not applicable; and SES, socioeconomic status.

*C indicates comorbidities; D, demographics; F, functional status/disabilities; HC, hospital complications; I, imaging; L, laboratory results; M, medications; MH, mental health; MI, AMI characteristics (ie, location, ST elevation, AMI symptoms); P, procedures; S, system factors (hospital or cardiac unit type); SES, socioeconomic status; U, utilization; and V, vital signs.

†Discrimination reported is for predicting all-cause 30-d readmission in the validation cohort, unless otherwise specified.

‡Range of mean observed risk for 30-d readmission is reported for lowest predicted and highest predicted risk groups as defined by each study. We abstracted data for the lowest and highest risk decile groups when possible. When this was not possible, alternate definitions of risk groups are identified as per the relevant footnotes.

§C statistic for predicting AMI-related readmissions was 0.68 when cohort was restricted to only adults ≥65 y of age.

‖There were 3 overall risk groups, defined by number of points using the HOSPITAL score: low risk=0–4 points; intermediate risk=5–6 points, and high risk ≥7 points. Here, lowest predicted risk group was defined as those with 0–4 points and highest predicted risk group was defined as those with ≥7 points.

¶Predicted risk was defined as 3 categories: low, medium, and high. No additional information was given on how these categories were defined. Data presented here are for observed readmission rates in the low and high-risk groups.

#This was a recursive partitioning (decision tree) model. We reported here the minimum and maximum overall observed risk in the nodes corresponding to the lowest and highest risk partitions.

**Data obtained from contacting study author.

††Neither procedure or system factors were included in the logistic regression model but the authors conducted subgroup analysis of readmission rates stratified by procedure factors (ie, type of AMI treatment received); and by system factors (hospital/cardiac unit type and place of discharge) and found significant differences in risk-adjusted 30-d readmission rates.

‡‡Readmission risk was stratified by 4 hospital types, those with (1) no structured cardiac unit; (2) cardiac unit without angioplasty laboratory; (3) structured cardiac unit with angioplasty laboratory but without cardiac surgery; (4) structured cardiac unit with angioplasty laboratory and cardiac surgery. Hospital type 1 was considered the highest risk, whereas hospital type 4 was the lowest risk.

§§We reported the highest available C statistic, selecting from results reported for linear support vector machine, polynomial kernel support vector machine, and Cox proportional hazards regression modeling approaches for the AMI model.

because of lack of data availability. The utility of 2 previously validated all-condition readmission risk prediction models[31,32] when applied specifically to AMI populations was assessed in 3 studies[20,27,29]: the HOSPITAL score (low hemoglobin <12 g/dL at discharge, discharge from an oncology service, low sodium <135 mEq/L at discharge, procedure during hospitalization, non-elective index admission type, number of admissions during previous year, length of stay ≥5 days)[20,27] and the LACE model (length of stay, acuity of admission, Charlson comorbidity index, number of emergency department visits in preceding 6 months).[29] The remaining 15 models were a mix of de novo models and significantly modified or enhanced versions of existing models.

Data Sources

Models were derived from and tested in several types of data sources, including administrative data (n=6 models)[22,23,25,26,28]; electronic health record data (n=4 models)[20,21,27]; medical record data (n=1 model)[23]; unspecified clinical hospital data (n=3 models)[29]; and cardiac registry data (n=5 models, including a registry version of the CMS model).[19,24]

Types of 30-Day Readmission Outcomes

Of the 18 different models, 15 were designed to predict all-cause readmissions[19–26,29]; and 4 were designed to predict cardiac-specific readmissions, including ischemic heart disease–related readmissions[27] (defined as readmissions with primary discharge diagnosis ICD-10 codes I20-I25; n=2 models); and cardiac disease–related readmissions[28] (defined as readmissions with primary discharge diagnosis ICD-9 codes 390-398, 401-405, 410-414, 415-417, 420-429, 441.01, 441.1, 441.2, 444.1; n=1 model). These categorizations were not mutually exclusive because one model, the HOSPITAL score, was used to predict both all-cause readmissions[20] and cardiac-specific readmissions, defined as potentially preventable (ie, AMI-related) readmissions[20] and ischemic heart disease–related readmissions.[27]

Predictors of Readmission

The 18 different models included between 5 to 37 predictors across a variety of domains (Table 2). All models except for the HOSPITAL score included medical comorbidities. All models except for the HOSPITAL score,[20,27] LACE model,[29] and a comorbidities model[27] included demographics. Prior healthcare utilization was included in 10 models,[20–23,27,29] laboratory values in 7,[20,21,23,24,27] procedures in 5,[20,22,27,28] socioeconomic status in 4,[24–26] medications in 2,[19,21] and vital signs in 4.[23,24] The 6 models based on medical record or registry data[19,23,24] included detailed clinical data related to AMI characteristics and severity of illness at presentation (ie, cardiac arrest, shock, multivessel disease, cardiac biomarker elevation), and AMI process of care quality measures (ie, time to procedure, medications given during percutaneous coronary intervention, and discharge medications). One model included measures of in-hospital complications (ie, new onset heart failure).[19] Two models included detailed information on psychosocial/mental health factors (social support, health literacy/numeracy, severe depression/anxiety, and perceived stress).[24] One model included a surrogate measure of functional status (nursing home residency).[25] The complete list of included predictors and their reported effect sizes are shown in eTable I in the Data Supplement. Additional information on model development, including details on modeling approach, assumptions, prediction selection, etc are described in eTable II in the Data Supplement.

Model Performance

Among the 15 models predicting all-cause readmissions, model discrimination (C statistic) ranged from 0.57 to 0.79 (median, 0.65; Table 2). The CMS AMI administrative model, the most commonly tested risk prediction model, had a median C statistic of 0.63 across the 7 cohorts in which it was tested,[23–26] though the C statistic was notably 0.76 when validated in a cohort using state-level Medicare data from Missouri,[26] (E. Nagasako, MD, PhD; e-mail communication, January 31, 2017). Enhanced versions of the CMS AMI administrative model with more clinically granular data,[24] or additional data on socioeconomic status[24–26] or functional status[25] had generally modest improvements in discrimination compared with the base CMS AMI model. In 1 cohort using registry data,[24] enhancing a CMS-like base model with more detailed clinical, mental health, and socioeconomic data in a stepwise fashion resulted in a marginal increase in the C statistic from 0.63 to 0.65 (*P* value not reported), with the largest improvement driven by the initial addition of detailed clinical data on AMI type, presenting vital signs, and selected laboratory values including maximum troponin value. In another study,[25] the addition of nursing home status as a surrogate for functional status to the CMS model resulted in an increase in the C statistic from 0.64 to 0.79 but the change was not statistically significant (*P*=0.24; 95% CI not reported), likely because of the relatively small cohort (n=833) and extremely low prevalence of nursing home residence (n=18). One model incorporating a single ZIP code level proxy of socioeconomic status (race) to the CMS AMI model had a slight decrease in C statistic from 0.64 to 0.63[25]; another that incorporated ZIP code level data on race and income had no change in C statistic (0.76 versus 0.76).[26]

Aside from variations of the CMS model, other AMI-specific models using more clinically granular electronic health record data[21] or registry data[19] did not have better discrimination for all-cause readmissions compared with a model derived from administrative claims data,[22] though this comparison is limited by the small number of identified studies (n=3), discordant C statistics across

validation cohorts in 1 study,[21] and unreported model validation in 1 study.[19]

In the 4 models predicting cardiac-specific readmissions, model discrimination ranged from 0.53 to 0.78 (median, 0.67), though this comparison is limited by varying definitions of cardiac-specific readmissions as described above. Two models were all-condition risk prediction models applied to an AMI cohort to predict cardiac-specific readmissions: a comorbidities model,[27] and the HOSPITAL score.[20,27] Both all-condition models had poor to modest discrimination across studies (range, 0.53–0.67). The 2 AMI-specific models[27,28] had very good discrimination for cardiac-specific readmissions (range, 0.74–0.78) though generalizability is uncertain given that one model was derived and validated within a single center[27]; the other study was conducted outside of the United States.[28]

The range of observed risk across risk groups for included models is shown in Table 2. The models were able to adequately risk stratify patients, with observed mean readmission rates ranging from ≈3-fold to 9-fold difference between the lowest and highest predicted risk groups (range from 3.0% among the lowest risk individuals to 43.0% among the highest risk individuals). Measures of model performance other than C statistic were inconsistently reported across studies (eTable II in the Data Supplement). Measures of calibration (including predicted or observed mean readmission rates by risk group, or other statistical measures of calibration) were also inconsistently reported across studies (eTable III in the Data Supplement), precluding a systematic assessment of model calibration.

Quality Assessment of Study Methods

Model quality was variable across studies (Table 3). All studies included an adequate description of the population and had nonbiased selection of patients. However, 9 newly developed models across 4 studies did not report any type of model validation.[19,24,25,27] Four newly developed models from data in a single academic medical center across 3 studies were internally, but not externally validated, limiting generalizability.[21,27,29] Additionally, these 3 studies only captured readmissions to the index hospital, and therefore underestimated true readmission rates.[21,27,29] The CMS AMI administrative model had the highest level of evidence for model validation as it was broadly validated in 7 distinct cohorts spanning different populations and time periods.[23–26]

DISCUSSION

In this systematic review, we identified 11 studies of 18 unique readmission risk prediction models, 16 of which were specific to AMI. The median reported all-cause 30-day readmission rate after AMI was 16.3%, consistent with estimated national rates.[33,34] Overall, current AMI-specific models had modest discrimination with a median C statistic of 0.65, and were of uncertain generalizability because of methodological limitations. Most studies were low to moderate quality because of lack of model validation or being a single-center study. No existing models have the potential to provide actionable information in real time, given that current models are based on data not available until well after hospital discharge (ie, administrative claims data), or require burdensome data collection beyond what is readily available from routine electronic health record data (ie, registries).

The overall modest predictive ability of identified models is likely because hospital readmissions are more challenging to predict compared with mortality. Mortality risk is largely predicated on illness severity, comorbidity burden, and prior utilization patterns.[9,35] In patients hospitalized with AMI, the use of clinically granular data from registries has enabled accurate risk prediction of AMI mortality up to 1 year or longer after index hospitalization.[35–37] Clinical severity measures such as AMI location, type (ie, non–ST-segment–elevation myocardial infarction versus ST-segment–elevation myocardial infarction), troponin value, adequacy of revascularization, and severity of underlying coronary artery disease could also be potentially helpful to predict readmissions in AMI. However, the few studies included in our review that incorporated detailed clinical data were of modest quality, limiting inferences about the utility of these data in predicting readmissions in AMI.

Additionally, hospital readmissions may depend more on complex interactions between patient, hospital, community, and environment rather than on clinical severity of illness alone.[9,38–45] In certain conditions such as heart failure and pneumonia, including more data on socioeconomic and psychosocial factors improved prediction of 30-day readmission risk.[9,11,13] The studies in this review that included detailed data on socioeconomic status, functional status, mental health and psychosocial factors at either an individual- or community (ZIP code)-level found inconsistent effects of the inclusion of these data on model performance but had certain methodological limitations precluding definitive inferences about the utility of such data in predicting readmissions. Further investigation is needed to better understand whether including socioeconomic, functional, and psychosocial factors improve readmission risk prediction in AMI.

Predicting 30-day risk specifically for cardiac-specific readmissions may be easier than predicting all-cause readmissions given that 2 of the 4 models focused only on cardiac-specific readmissions had very good discrimination.[27,28] Both models included detailed clinical information on recent cardiovascular symptoms, diagnoses, procedures, and complications suggesting that the presence of cardiovascular comorbidities may be more predictive of cardiac-specific versus all-cause readmissions. However, the usefulness of this approach is limited because hospitals are penalized for inappropriately

Table 3. Assessment of Study Quality

Study	Model	Generalizability of Population?	Nonbiased Selection?	Readmission Adequately Ascertained?	Level of Evidence for Model Validation?
Brown et al[19]	AMI registry model	No (single center)*	Yes†	Partly, only index hospital‡	No validation performed*
Burke et al[20]	HOSPITAL score	Partial (6 centers across 6 states)‡	Yes†	Partly, only index hospitals‡	N/A, previously validated model
Hebert et al[21]	AMI EHR model	No (single center)*	Yes†	Partly, only index hospital‡	Narrow validation (split cohort, historical cohort)‡
Hilbert et al[22]	California statewide AMI administrative model	Partial (statewide California)‡	Yes†	Yes†	Narrow validation (historical cohort)‡
Krumholz et al[23]	CMS AMI administrative model	Yes (nationwide Medicare data)†	Yes†	Yes†	BROAD VALIDATION (separate cohorts)†
	CMS AMI CCP medical record model	Yes (nationwide hospital data)†	Yes†	Yes†	No validation performed*
McManus et al[24]	CMS-like registry model (CMS base model)	Partial (2 states: Massachusetts and Georgia) ‡	Yes†	Yes†	No validation performed*
	CMS base model clinical				
	CMS base model+clinical+mental health				
	CMS base model+clinical+mental health+SES				
Meddings et al[25]	CMS AMI administrative model in HRS-CMS cohort	Partial (nationwide data but small sample size due to limited availability of HRS data)‡	Yes†	Yes†	N/A, previously validated model
	Disability/SES-enriched CMS AMI administrative model (HRS-CMS)				No validation performed?*
	CMS AMI administrative model in ACS-HCUP cohort	Partial (2 states: Florida and Washington)‡			N/A, previously validated model
	Disability/SES-enriched CMS AMI administrative model (ACS-HCUP)				No validation performed?*
Nagasako et al[26]	CMS AMI administrative model	Partial (statewide Medicare data in Missouri)‡	Yes†	Yes†	Narrow validation (bootstrapping)‡
	SES-enriched CMS AMI administrative model				
Rana et al[27]	AMI EHR model	No (single center)*	Yes†	Partly, only index hospital and only IHD-related readmissions, not all cause‡	Narrow validation (split cohort)‡
	HOSPITAL score				N/A, previously validated model
	Comorbidities model				No validation performed*
Rodriguez-Padial et al[28]	Spanish National Health System AMI administrative model	Partial (national data in Spain)‡	Yes†	Partly, national data but only cardiac disease–related readmissions, not all-cause‡	Narrow validation (split cohort)‡
Yu et al[29]	AMI hospital 2 model	No (single center, 1 Midwest hospital)*	Yes†	Partly, only index hospital‡	Narrow validation (split cohort)
	LACE model at hospital 2				N/A, previously validated model
	AMI hospital 3 model	No (single center, 1 Northeast hospital)*	Yes†	Partly, only index hospital‡	Narrow validation (split cohort)‡
	LACE model at hospital 3				N/A, previously validated model

ACS indicates American Community Survey; AMC, academic medical center; AMI, acute myocardial infarction; CMS, Centers for Medicare & Medicaid Services; SES, socioeconomic status; DRG, diagnosis-related group; EHR, electronic health record; HCUP, Healthcare Cost and Utilization Project; HRS, Health and Retirement Study; ICD, International Classification of Disease; IHD, ischemic heart disease; N/A, not applicable; and SES, socioeconomic status.

*Low methodologic quality.

†Characteristics consistent with higher methodologic quality.

‡Characteristics consistent with fair/moderate methodologic quality.

high all-cause 30-day readmissions under the CMS HRRP, and not just cardiac-specific 30-day readmissions.

Two models predicting all-cause 30-day readmissions had notably high C statistics of 0.79[25] and 0.76[26] though the significance of these findings is uncertain. Meddings et al[25] found that adding social determinants ascertained from the Health and Retirement Study to the CMS AMI model resulted in substantial improvement in model discrimination, with a change in C statistic from 0.64 to 0.79 for the enhanced model. However, the difference was not statistically significant, likely because of the small cohort (n=833), low number of readmissions (n=136), and low number of subjects with the presence of highly predictive social determinants such as nursing home residence (n=18) resulting in a less precise estimate of discrimination. Nagasako et al[26] found that the unenhanced CMS AMI model performed exceptionally well in a statewide cohort of Missouri Medicare beneficiaries from 2009 to 2012 with a C statistic of 0.76, far higher than that observed in both the index and any other study of the CMS AMI model. The reasons for improved discrimination of the CMS model in this cohort are unclear.

Although we found overall modest discrimination for all-cause 30-day readmissions, the range of predicted risk among current models is adequate for stratifying patients into high, intermediate, and low risk groups to target readmission prevention interventions. However, most models were based on data (ie, administrative claims or registry) not readily available at the time of hospitalization, limiting the usefulness of these models in clinical practice for prospective risk stratification to enable targeted intervention to reduce readmissions. Because interventions to reduce readmissions have the most potential to be effective when they are initiated during hospitalization well before discharge,[5,8] future research should also focus on developing models that are easy to implement at bedside and provide clinically actionable information as early as possible in a patient's hospital course.

Our review has certain limitations. First, despite a comprehensive literature search strategy, we may have overlooked studies published in non-English languages or nonindexed studies. Second, few studies directly compared models within the same population so caution should be used when directly comparing model performance across different populations. Third, because most studies defined AMI using ICD-9, ICD-10, and diagnosis-related group discharge codes, it is unclear whether defining AMI prospectively on admission would meaningfully influence risk prediction modeling.

In conclusion, current AMI-specific readmission risk prediction models have modest predictive ability and uncertain generalizability given methodological limitations. The utility of including additional data on clinical AMI characteristics and nonclinical risk factors such as socioeconomic, functional, and psychosocial factors on improving model performance currently remains unclear. No existing models have the potential to provide actionable data in real time, given that all current models are based on data that are not available until discharge or well afterward, or require additional information beyond that collected as a part of routine clinical care. Future studies should focus on developing models with improved accuracy that provide clinically actionable information in real time as early in the hospital course as possible, to target high-risk individuals with a multicomponent transitional care intervention.

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DISCLOSURES

None.

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FOOTNOTES

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Acute Myocardial Infarction Readmission Risk Prediction Models: A Systematic Review of Model Performance

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