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ORIGINAL RESEARCH

Development and Validation of a Risk Prediction Model for 1-Year Readmission Among Young Adults Hospitalized for Acute Myocardial Infarction

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BACKGROUND: Readmission over the first year following hospitalization for acute myocardial infarction (AMI) is common among younger adults (≤55 years). Our aim was to develop/validate a risk prediction model that considered a broad range of factors for readmission within 1 year.

METHODS AND RESULTS: We used data from the VIRGO (Variation in Recovery: Role of Gender on Outcomes of Young AMI Patients) study, which enrolled young adults aged 18 to 55 years hospitalized with AMI across 103 US hospitals (N=2979). The primary outcome was ≥1 all-cause readmissions within 1 year of hospital discharge. Bayesian model averaging was used to select the risk model. The mean age of participants was 47.1 years, 67.4% were women, and 23.2% were Black. Within 1 year of discharge for AMI, 905 (30.4%) of participants were readmitted and were more likely to be female, Black, and nonmarried. The final risk model consisted of 10 predictors: depressive symptoms (odds ratio [OR], 1.03; 95% CI, 1.01–1.05), better physical health (OR, 0.98; 95% CI, 0.97–0.99), in-hospital complication of heart failure (OR, 1.44; 95% CI, 0.99–2.08), chronic obstructive pulmomary disease (OR, 1.29; 95% CI, 0.96–1.74), diabetes mellitus (OR, 1.23; 95% CI, 1.00–1.52), female sex (OR, 1.31; 95% CI, 1.05–1.65), low income (OR, 1.13; 95% CI, 0.89–1.42), prior AMI (OR, 1.47; 95% CI, 1.15–1.87), in-hospital length of stay (OR, 1.13; 95% CI, 1.04–1.23), and being employed (OR, 0.88; 95% CI, 0.69–1.12). The model had excellent calibration and modest discrimination (C statistic=0.67 in development/validation cohorts).

CONCLUSIONS: Women and those with a prior AMI, increased depressive symptoms, longer inpatient length of stay and diabetes may be more likely to be readmitted. Notably, several predictors of readmission were psychosocial characteristics rather than markers of AMI severity. This finding may inform the development of interventions to reduce readmissions in young patients with AMI.

Key Words: acute myocardial infarction ■ Bayesian model averaging ■ psychosocial factors ■ risk prediction model ■ young adults

Readmissions after an acute myocardial infarction (AMI) are common, costly, and represent a marker of suboptimal health care.[1] Each year, nearly 1 in 6 individuals hospitalized with AMI will have an unplanned readmission within 30 days of discharge. Readmissions result in over $1 billion of annual US healthcare costs, of which $365 million is spent on patients under 65 years of age.[2–5] Beyond the burden on the healthcare system, readmissions impose considerable physical, psychological, and financial stress on individuals.[6–8] Despite an overall decrease in cardiovascular disease prevalence and AMI mortality

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CLINICAL PERSPECTIVE

What Is New?

- We present a new risk prediction model for all-cause readmission within 1 year of acute myocardial infarction in younger adults (≤55 years) that considers a broad range of demographic, clinical, and psychosocial factors.

What Are the Clinical Implications?

- Several predictors of readmission were psychosocial characteristics rather than markers of acute myocardial infarction severity including depressive symptoms, better physical health, low income, and being employed.
- These findings may inform the development of interventions to reduce readmissions in young patients hospitalized with acute myocardial infarction.

Nonstandard Abbreviations and Acronyms

BMA	Bayesian model averaging
VIRGO	Variation in Recovery: Role of Gender on Outcomes of Young AMI Patients

in both sexes,[9] rates of AMI hospitalization in younger adults (≤55 years) have increased over the past decade,[10] particularly for younger women.[11,12] Although the risk of post-AMI readmission increases with advancing age, readmissions are also common among younger patients[5]: over 1 in 10 adults with AMI below 65 years of age are readmitted within 30 days,[5] and this risk extends over the first year after AMI.[13]

To reduce rates of readmission, the Centers for Medicare and Medicaid Services publicly reports risk-standardized readmission rates,[14,15] and hospitals are subject to financial penalties for excessive all-cause 30-day AMI readmissions under the Centers for Medicare and Medicaid Services Hospital Readmissions Reduction Program.[14,16–18] Although federal penalties have motivated efforts to develop interventions to reduce 30-day readmissions, to date such efforts have neither been consistently successful nor addressed readmission beyond the first month after discharge in this population.[19–23] Tellingly, there are no available risk prediction models for 1-year post-AMI readmissions among younger adults. Existing risk stratification models for post-AMI readmissions have been developed in predominantly older male patient populations[24] and have demonstrated modest predictive ability and generalizability because of methodological drawbacks including the absence of psychosocial factors.[2,25–27] The few available risk models for 1-year post-AMI readmissions have been intervention specific, were developed in older populations, and did not capture patient-reported outcomes.[28–31] Identifying which young adults hospitalized for AMI are at the highest risk for readmissions can inform the development of interventions that more effectively prevent readmission and improve outcomes in this population.

To address this gap in knowledge, our objective was to develop and validate a global risk prediction model of 1-year post-AMI all-cause readmission in younger adults that considers a broad range of demographic and clinical variables as well as patient-reported outcomes. The purpose of the model is to use information from the in-hospital stay to estimate each individual's probability of readmission. We used data from the VIRGO study (Variation in Recovery: Role of Gender on Outcomes of Young AMI Patients),[32] the largest prospective multicenter longitudinal study of young adults aged ≤55 years hospitalized for AMI.

METHODS

All supporting data are available upon request from the corresponding author.

Participants and Study Design

Between August 21, 2008, and May 1, 2012, we enrolled patients aged 18 to 55 years old hospitalized with AMI from 103 US, 3 Australian, and 24 Spanish hospitals into the VIRGO study, called IMJOVEN (Infarto de Miocardio en la Mujer Joven) in Spain (VIRGO US grant, 5 R01 HL081153-05; VIRGO Spanish grant, 081614) (Figure S1). This was a multicenter observational study designed to investigate factors associated with adverse clinical outcomes in young women (≤55 years) hospitalized for AMI. Patients were prospectively recruited and enrolled in the VIRGO study, which used a 2:1 female-to-male enrollment design to enrich the study inclusion of young women. A total of 6538 patients with AMI were screened at contributing sites, of whom 3572 were eligible and enrolled (N=2397 women; N=1175 men). For the current study only the N=2985 US patients (N=2009 women, N=976 men) hospitalized for AMI were included.[32] After excluding in-hospital deaths (N=6), this resulted in a final cohort of 2979 participants. From this sample we randomly selected 1986 participants to serve as a development cohort with the remaining 993 as the validation cohort. This allocation of the overall sample allowed for sufficient power to both derive and validate our risk prediction model. With our development sample of 1968, an estimated sample C statistic of 0.650, and using the methods of Hanley and McNeil (1982)[33] as well as Kryzanowski and Hand (2009),[34] we are able

to estimate a 2-sided 95.0% CI from 0.62 to 0.68. With regard to validation, it has been suggested by Altman et al (2009)[35] that a validation sample should have a minimum of 100 to 200 outcome events. Our validation sample of 993 includes 300 outcome events, notably higher than the minimum suggested by Altman.

The VIRGO study has been previously described.[32] In brief, AMI was confirmed by increased cardiac biomarkers (with at least 1 cardiac biomarker above the 99th percentile of the upper reference limit) within 24 hours of admission. The study also required additional evidence of acute myocardial ischemia, including at least 1 of the following: symptoms of ischemia, ECG changes indicative of new ischemia (new ST-T changes, new or presumably new left bundle branch block, or the development of pathological Q waves). Patients must have presented directly to the enrolling site or must have been transferred within the first 24 hours of presentation to ensure that primary clinical decision making occurred at the enrolling site. We excluded patients who were incarcerated, did not speak English or Spanish, were unable to provide informed consent or to be contacted for follow-up, developed elevated cardiac markers because of elective coronary revascularization, or had an AMI as the result of physical trauma. Institutional review board approval was obtained at each participating institution, and patients provided informed consent for their study participation, including baseline hospitalization and follow-up interviews.

Study Outcome and Readmission Data Adjudication

The primary outcome of this study was all-cause readmission defined as any hospital or observation stay greater than 24 hours within 1 year of discharge. Readmissions were identified using a 2-stage process. First, when a study participant's 1-year follow-up window closed, the research coordinator at the local site reviewed the records within their hospital network to identify readmission records. In addition, the study participants were also asked to self-report any readmissions during their 1-year post-AMI interviews, including the hospital, date and reason for admission. Second, the Yale Coordinating Center then reconciled the hospital records with the patient self-reported events to ensure that no readmissions were missed. When necessary, the Yale Coordinating Center requested the missing records from hospitals outside of the site networks. Once a readmission had been identified, admission and discharge records were obtained. The major fields collected included number of readmissions, primary admission diagnoses, procedures completed, follow-up visits, and discharge status. For information on principal diagnoses for readmission, emphasis was placed on discerning cardiac versus noncardiac diagnoses.

The VIRGO adjudication process was supported through the use of a custom-developed Research Electronic Data Capture external module.[36] Adjudications were completed by 5 physicians and an advanced practice registered nurse at Yale University who received extensive training and clear guidelines. A data dictionary was created as guidance for each of the major fields, including explicit variable definitions. The data dictionary also included individual cases discussed as a team and provided guidance on future adjudication decisions. The first 253 readmissions were double adjudicated, and subsequent readmissions underwent single adjudication. Discrepancies between adjudicators were resolved by consensus including an additional physician when necessary. Adjudicators could also flag events to be reviewed and discussed by the team. Mortality events were ascertained through interviews with family members and verified with death certificates, hospital records, or obituaries.

Data Collection and Selection of Candidate Predictors

We initially selected a comprehensive list of 65 candidate variables based on our prior work and from existing AMI readmission risk models (Table S1).[2,13,37] Information was collected from medical record abstraction and standardized in-person interviews administered by trained personnel at baseline and before discharge. Variables were classified into categories of sociodemographic factors, cardiac risk factors and medical history, presentation characteristics, in-hospital complications, and psychosocial factors.

Variables on sociodemographics collected included age, sex, race/ethnicity, marital status, less than high school education), household primary earner status, low income (defined as personal income ≤30 000 USD), employment status, and current presence of health insurance. Baseline cardiac risk factors and medical history included diabetes mellitus, obesity (body mass index≥30 kg/m^2), hypertension, dyslipidemia, current smoking, family history of cardiovascular disease, physical inactivity, prior MI, renal disease, alcohol abuse, chronic obstructive pulmonary disorder, stroke, heart failure, recreational drug use, and peripheral artery disease.

Presentation characteristics included first health service used, transfer from another institution, late presentation (>6 hours from symptom onset), aspirin at arrival, ejection fraction <40%, peak troponin, estimated glomerular filtration rate, first white blood cell count, first hematocrit, chest pain as primary symptom, Killip class, prior coronary artery bypass grafting, type of AMI, GRACE score, conservative treatment (patient

did not receive percutaneous coronary intervention, thrombolysis or other standard of care procedural interventions in addition to medical therapy [e.g. aspirin, statins, beta blockers]), total length of stay (LOS) in days, discharge to other institutions, and admission to the cardiac or medical intensive care unit. In hospital complications included bleeding, re-infarction, heart failure and cardiac arrhythmias. Discharge instructions included counselling for specific concerns (cardiac, diet, smoking), medication, and exercise. Medications at discharge included clopidogrel/thienopyridines, aspirin, statins, calcium channel blockers, angiotensin converting enzyme inhibitors, angiotensin receptor blockers, and beta blockers.

Psychosocial factors included various items from validated patient reported outcome measures in cardiac populations. Perceived social support was measured using the ENRICHD Social Support ESSI-7 Instrument.[38] For this study we excluded the questions on instrumental support (i.e. household chores) and marital status. The ESSI-5 scale is highly correlated with the full length 7-item scale, with higher scores indicating greater perceived social support.

Depression was measured using the Patient Health Questionnaire-9.[39] This scale quantifies the frequency of depressive symptoms experienced in the prior 2 weeks based on the 9 Diagnostic and Statistical Manual of Mental Disorders (4th edition) criteria for a major depressive disorder, with higher scores indicating higher levels of depression. Perceived stress was measured using the 14-item global Perceived Stress Scale-14.[40] Respondents are evaluated on the degree to which they perceived their life situations over the past month to be unpredictable, uncontrollable, or overloaded, with higher scores indicating greater stress.

Health status was measured using the Seattle Angina Questionnaire and the 12-item Short-Form Health Survey (SF-12). The Seattle Angina Questionnaire is a 19-item, health-related quality-of-life measure specific for patients with coronary artery disease.[41,42] This study used the angina frequency, physical limitation, treatment satisfaction and quality of life domains. Scores range from 0 to 100, with higher scores indicating better functioning. Lastly, the SF-12 instrument measures overall physical and mental health status through 12 items.[43] Both the Physical Component Summary (PCS) and Mental Component Summary (MCS) scores were used for this study and range from 0 to 100, with higher scores indicating a greater level of physical or mental functioning.

Statistical Analysis

We calculated descriptive statistics for the overall population using frequencies for categorical variables and means (SDs) or medians (interquartile ranges) for continuous and count variables. Statistical differences between readmitted and non-readmitted patients were evaluated with χ^2 tests, *t* tests, and Wilcoxon rank-sum tests as appropriate. From the initial list of 65 candidate variables, 20 variables were ineligible based on these criteria: (1) either very low (<0.05) or very high (>0.95) prevalence (e.g., Killip non-reference levels); and (2) not reasonably or consistently measured or available at most hospitals (e.g., troponin). This resulted in 45 candidate variables (Figure 1) with missingness generally <3%, with perceived stress at baseline missing 6.3% and the SF-12 physical and mental measures missing <5% and no missingness in the outcome. The missingness was assumed to be missing-at-random and multiple imputations were generated using fully conditional specifications as implemented in the SAS procedure.
Our development and validation processes followed the practices outlined in the Transparent Reporting of a Multivariable Prediction Model for Individual Prognosis or Diagnosis statement.[44] Selection for the multivariable model used Bayesian model averaging (BMA), a selection approach used in the SILVER-AMI study and described elsewhere.[45–47] A detailed description of the BMA methodology is provided in Data S1. Per our practice in prior studies,[48–50] the final predictors were those exhibiting a positive posterior probability in at least half of the imputations. Because BMA was used for selection rather than the corresponding P values, some model terms may not exhibit *P*-values below 0.05.

Finally, we fit logistic regressions of readmission separately to each of the imputations, with each imputation-specific model using Firth penalized maximum likelihood to estimate the associations. The coefficients from the imputation-specific models were subsequently combined using Rubin's rules.[50,51] The development model was evaluated by assessing area under the curve (AUC) and calibration of the predicted risk. We deemed good fit in each imputation as an AUC ≥65% and good calibration as plots of the mean observed probabilities with CIs that overlap with the diagonal line representing perfect agreement between predicted and observed values, as illustrated in the Transparent Reporting of a Multivariable Prediction Model for Individual Prognosis or Diagnosis materials.

The global model coefficients from the development model then were directly applied to the values of the final predictors for all eligible participants in the validation data, with discrimination and calibration evaluated using the previously mentioned criteria. With the exception of BMA, as implemented in the R package "BMA,"[51,52] all analyses were conducted using SAS Version 9.4 with SAS/STAT 14.3 (SAS Institute Inc, Cary, NC, 2014).[52,53] Statistical significance was defined as a 2 sided *P* value <0.05.

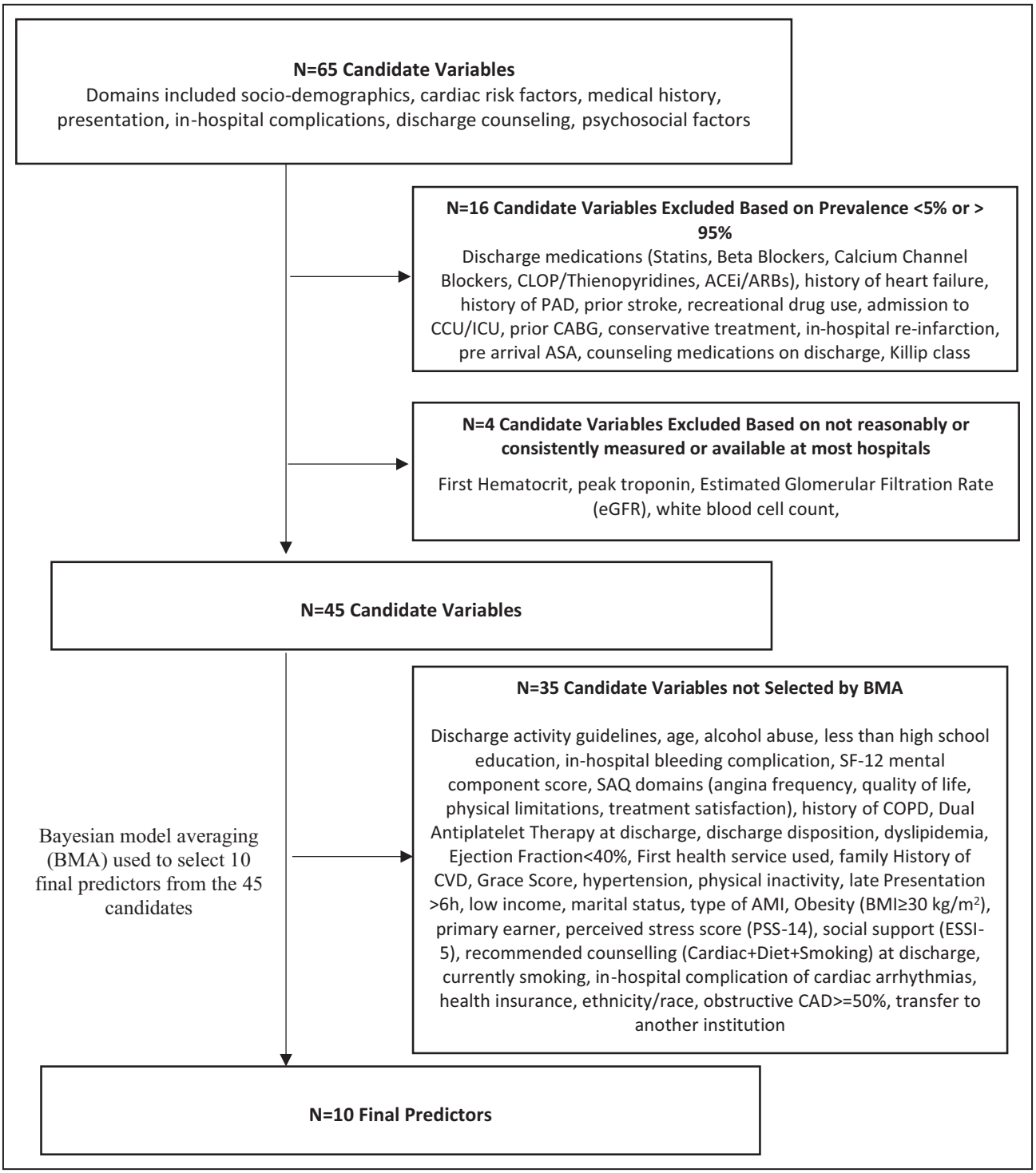

Figure 1. Stages of selection for the final multivariable risk prediction model.
ACEi indicates angiotensin-converting enzyme inhibitors; AMI, acute myocardial infarction; ARBs, angiotensin receptor blockers; ASA, aspirin; BMI, body mass index; CABG, coronary artery bypass grafting; CAD, coronary artery disease; CCU/ICU, cardiac or medical intensive care unit; CLOP, clopidegrel; COPD, chronic obstructive pulmonary disease; CVD, cardiovascular disease; ESSI-7, ENRICHD Social Support Instrument; GRACE, Global Registry of Acute Coronary Events; PAD, peripheral arterial disease; PSS-14, Perceived Stress Scale-14; and SAQ, Seattle Angina Score.

RESULTS

Baseline Characteristics

Baseline characteristics for the overall sample (N=2979) and for strata by readmission status are presented in Table 1. The mean age of the study population was 47.1±6.2 years, 67.4% were women, and 23.2% were Black. In terms of socio-demographics, patients readmitted within 1 year post AMI were more likely to be female, Black, not married or living with a spouse, and of lower income. They were also less likely to be primary household earners or to be employed, and were also more likely to have diabetes mellitus, hypertension and sedentary lifestyles. In terms of comorbidities and disease severity, patients readmitted within 1-year were more likely to have a prior AMI, history of renal disease, chronic obstructive pulmomary disease, non–ST-segment–elevation myocardial infarction, longer hospitalizations, and in-hospital complications of heart failure. Readmitted patients were more likely to have a higher burden of psychosocial stressors, including higher rates of depression and stress, and poorer physical and mental health. Lastly, readmitted patients reported lower disease specific quality of life as per physical limitations, frequency of angina, and quality of life and treatment satisfaction.

Readmission at 1 Year Post AMI

Within the first year of discharge for AMI, 905 (30.4%) of patients experienced at least 1 all-cause readmission. Overall there were 1658 readmissions: 563 (18.9%) patients were readmitted once, 167 (5.6%) patients were readmitted twice, and 175 (5.9%) patients were readmitted 3 or more than 3 times. Notably, some patients had up to 17 readmissions within this time period. Patients who were readmitted 3 or more times were younger (46.7 years), were mostly female (78.8%) and Black (65.7%), and presented with predominately cardiac complaints. The majority of readmissions were for cardiac related reasons, the most common being either stable or unstable angina (34.08%). Among cardiac readmissions, there were 133 (8.02%) readmissions for AMI recurrence (Table 2). The rate of readmission was relatively constant over the first year with median time to first readmission being 70 days (Figure S2), with 68 deaths (2.3% of sample population).

Multivariable Results: Risk Model for 1-Year Readmission Post AMI

Bayesian model averaging chose 10 predictors in the development cohort (Figure 2): higher level of depression at admission (measured using the Patient Health Questionnaire-9) (OR=1.03, 95% CI 1.01–1.05), better baseline physical health (per the SF-12) (OR=0.98, 95% CI 0.97–0.99), in-hospital complications of heart failure (OR=1.44, 95% CI 0.99–2.08), chronic obstructive pulmomary disease (OR=1.29, 95% CI 0.96–1.74), diabetes mellitus (OR=1.23, 95% CI 1.00–1.52), female sex (OR=1.31, 95% CI 1.05–1.65), low income (OR=1.13, 95% CI 0.89–1.42), prior AMI (OR=1.47, 95% CI 1.15–1.87), greater in-hospital length of stay (OR=1.13, 95% CI 1.04–1.23), and being employed (OR=0.88, 95% CI 0.69–1.12). The strongest predictor was history of a prior AMI, followed by female sex. Of the 10 predictors, only 2 were protective: better physical health and being employed. Variables not selected included medical risk factors and comorbidities, disease severity, discharge counseling, and other in-hospital complications (Figure 1). The model had excellent calibration (calibration plots) and modest discrimination (*C* statistic=0.67 derivation cohort [AUC (95% CI)=0.671 (0.646–0.697)]), (*C* statistic=0.67 validation cohort [AUC (95% CI)=0.673 (0.656–0.689)]) across all multiply imputed data sets. The calibration plots for the development and validation cohorts, as shown in Figure 3A and 3B, exhibit strong overlap of the CIs of the observed probabilities with the diagonal line that represents perfect agreement. Baseline characteristics of young patients with AMI stratified by sex who were readmitted versus not readmitted at 1-year for the 10 final candidate variables are presented in Table S2.

As a sensitivity analysis, we used a single imputation to develop a separate model to examine the predictors of readmission after a first AMI event. The BMA approach chose 9 variables, most of which are also in the model for the full cohort (Table S3). Baseline higher scores for physical health (as per the SF-12), the Global Registry of Acute Coronary Events score, and marital status (ie, being married/living with partner) were protective whereas all other variables such as depression (as per the Patient Health Questionnaire-9), obstructive coronary artery disease (ie, coronary stenosis >=50%), diabetes mellitus, female sex, low income, and length of stay were positively associated with higher likelihood of readmission within 1 year of discharge. As shown in Figure S3, calibration was good whereas discrimination, with a C statistic of 66%, was modest.

DISCUSSION

This study demonstrates that one third of young adults with AMI experience readmission in the first year after their initial hospitalization, with a substantial subset enduring multiple readmissions. Women, individuals with longer hospitalization, a history of prior AMI, and with depression or diabetes mellitus were more likely to be readmitted. Individuals with better physical health and those who were employed were less likely to be readmitted. Unlike traditional cardiac prediction

Table 1. Baseline Characteristics of Young Adults With AMI Who Were Readmitted Versus Not Readmitted at 1 Year (44 Candidate Variables)

	All patients (N=2979)	All patients (Missing)	No readmission (N=2074)	No readmission (Missing)	Readmission within 1 year (N=905)	Readmission within 1 year (Missing)	*P* value
Sociodemographics/socioeconomic status							
Age, mean (SD), y	47.1 (6.18)	0 (0.0%)	47.2 (6.10)	0 (0.0%)	46.9 (6.36)	0 (0.0%)	0.1755
Age, median (interquartile range), y	48.0 (44.0–52.0)	0 (0.0%)	48.0 (44.0–52.0)	0 (0.0%)	48.0 (44.0–52.0)	0 (0.0%)	0.2628
Sex		0 (0.0%)		0 (0.0%)		0 (0.0%)	<0.0001
Female	2007 (67.4%)		1323 (63.8%)		684 (75.6%)		
Male	972 (32.6%)		751 (36.2%)		221 (24.4%)		
Race		0 (0.0%)		0 (0.0%)		0 (0.0%)	0.0001
White	2289 (76.8%)		1631 (78.6%)		658 (72.7%)		
Black	533 (17.9%)		323 (15.6%)		210 (23.2%)		
Married or living with spouse	1658 (55.7%)	0 (0.0%)	1207 (58.2%)	0 (0.0%)	451 (49.8%)	0 (0.0%)	<0.0001
Primary earner	2214 (74.3%)	0 (0.0%)	1578 (76.1%)	0 (0.0%)	636 (70.3%)	0 (0.0%)	0.0008
Low income	1262 (42.4%)	0 (0.0%)	793 (38.2%)	0 (0.0%)	469 (51.8%)	0 (0.0%)	<0.0001
Less than high school education	1280 (43.0%)	0 (0.0%)	864 (41.7%)	0 (0.0%)	416 (46.0%)	0 (0.0%)	0.0319
Currently employed	1828 (61.4%)	0 (0.0%)	1367 (65.9%)	0 (0.0%)	461 (50.9%)	0 (0.0%)	<0.0001
Has health insurance	2294 (77.0%)	0 (0.0%)	1588 (76.6%)	0 (0.0%)	706 (78.0%)	0 (0.0%)	0.4427
Cardiac risk factors							
Diabetes mellitus	1058 (35.5%)	0 (0.0%)	657 (31.7%)	0 (0.0%)	401 (44.3%)	0 (0.0%)	<0.0001
Obesity (body mass index≥30 kg/m^2)	1571 (52.7%)	0 (0.0%)	1069 (51.5%)	0 (0.0%)	502 (55.5%)	0 (0.0%)	0.0528
Hypertension	1974 (66.3%)	0 (0.0%)	1321 (63.7%)	0 (0.0%)	653 (72.2%)	0 (0.0%)	<0.0001
Dyslipidemia	2582 (86.7%)	0 (0.0%)	1781 (85.9%)	0 (0.0%)	801 (88.5%)	0 (0.0%)	0.0516
Current Smoking	891 (29.9%)	0 (0.0%)	635 (30.6%)	0 (0.0%)	256 (28.3%)	0 (0.0%)	0.2015
Family history of cardiovascular disease	2004 (67.3%)	0 (0.0%)	1373 (66.2%)	0 (0.0%)	631 (69.7%)	0 (0.0%)	0.0833
Inactivity	1054 (35.4%)	0 (0.0%)	683 (32.9%)	0 (0.0%)	371 (41.0%)	0 (0.0%)	<0.0001
Medical history							
Prior myocardial infarction	635 (21.3%)	0 (0.0%)	379 (18.3%)	0 (0.0%)	256 (28.3%)	0 (0.0%)	<0.0001
History of renal disease	337 (11.3%)	0 (0.0%)	204 (9.8%)	0 (0.0%)	133 (14.7%)	0 (0.0%)	0.0001
Alcohol abuse	1011 (33.9%)	0 (0.0%)	743 (35.8%)	0 (0.0%)	268 (29.6%)	0 (0.0%)	0.0010
History of chronic obsructive pulmonary disease	346 (11.6%)	0 (0.0%)	198 (9.5%)	0 (0.0%)	148 (16.4%)	0 (0.0%)	<0.0001
History of depression	1212 (40.7%)	0 (0.0%)	766 (36.9%)	0 (0.0%)	446 (49.3%)	0 (0.0%)	<0.0001
Presentation characteristics							
First health service used		0 (0.0%)		0 (0.0%)		0 (0.0%)	0.3395
Directly ER from home	2654 (89.1%)		1852 (89.3%)		802 (88.6%)		
Before ER, Dr office	162 (5.4%)		105 (5.1%)		57 (6.3%)		

(*Continued*)

Table 1. Continued

	All patients (N=2979)	All patients (Missing)	No readmission (N=2074)	No readmission (Missing)	Readmission within 1 year (N=905)	Readmission within 1 year (Missing)	*P* value
Before ER, other health services	163 (5.5%)		117 (5.6%)		46 (5.1%)		
Late presentation >6 h	1319 (44.3%)	0 (0.0%)	894 (43.1%)	0 (0.0%)	425 (47.0%)	0 (0.0%)	0.0538
Ejection fraction >40%	319 (10.7%)	0 (0.0%)	209 (10.1%)	0 (0.0%)	110 (12.2%)	0 (0.0%)	0.0849
Chest pain as primary symptom	2600 (87.3%)	0 (0.0%)	1830 (88.2%)	0 (0.0%)	770 (85.1%)	0 (0.0%)	0.0176
Angiogram		317 (10.6%)		208 (10.0%)		109 (12.0%)	0.0333
Nonobstructive CAD <50%	257 (8.6%)		195 (9.4%)		62 (6.9%)		
Obstructive coronary artery disease ≥50%	2405 (80.7%)		1671 (80.6%)		734 (81.1%)		
Intravenous (cardiogenic shock)	13 (0.4%)		8 (0.4%)		5 (0.6%)		
Type of myocardial infarction		0 (0.0%)		0 (0.0%)		0 (0.0%)	0.0096
ST-segment–elevation myocardial infarction	1483 (49.8%)		1065 (51.4%)		418 (46.2%)		
Non–ST-segment–elevation myocardial infarction	1496 (50.2%)		1009 (48.6%)		487 (53.8%)		
Global Registry of Acute Coronary Events score, mean (SD)	75.2 (19.05)	49 (1.6%)	74.6 (18.00)	23 (1.1%)	76.6 (21.26)	26 (2.9%)	0.0145
Total length of stay, d, mean (SD)	4.2 (3.93)	13 (0.4%)	3.9 (3.41)	8 (0.4%)	4.9 (4.85)	5 (0.6%)	<0.0001
Disposition to other institutions at discharge	2806 (94.2%)	0 (0.0%)	1962 (94.6%)	0 (0.0%)	844 (93.3%)	0 (0.0%)	0.0071
Discharge counseling							
Recommended counseling (cardiac+diet+smoking)	951 (31.9%)	0 (0.0%)	674 (32.5%)	0 (0.0%)	277 (30.6%)	0 (0.0%)	0.3089
Exercise counseling	2751 (92.3%)	0 (0.0%)	1913 (92.2%)	0 (0.0%)	838 (92.6%)	0 (0.0%)	0.7343
Dual antiplatelet therapy	1964 (65.9%)	0 (0.0%)	1389 (67.0%)	0 (0.0%)	575 (63.5%)	0 (0.0%)	0.0688
In-hospital complications							
Bleeding	197 (6.6%)	0 (0.0%)	133 (6.4%)	0 (0.0%)	64 (7.1%)	0 (0.0%)	0.5056
Heart failure	215 (7.2%)	0 (0.0%)	118 (5.7%)	0 (0.0%)	97 (10.7%)	0 (0.0%)	<0.0001
Cardiac arrhythmias	205 (6.9%)	0 (0.0%)	132 (6.4%)	0 (0.0%)	73 (8.1%)	0 (0.0%)	0.0923
Psychosocial factors, mean (SD)							
Social support (ENRICHD Social Support Instrument-7)	21.3 (4.56)	57 (1.9%)	21.5 (4.34)	33 (1.6%)	20.9 (5.01)	24 (2.7%)	0.0058
Depression (Patient Health Questionnaire-9)	7.8 (6.45)	117 (3.9%)	7.2 (6.21)	71 (3.4%)	9.4 (6.73)	46 (5.1%)	<0.0001
Stress (Perceived Stress Scale-14)	26.0 (9.78)	185 (6.2%)	25.3 (9.83)	117 (5.6%)	27.6 (9.48)	68 (7.5%)	<0.0001
Physical limitations (SAQ)	80.6 (25.79)	74 (2.5%)	83.5 (23.83)	48 (2.3%)	73.9 (28.75)	26 (2.9%)	<0.0001
Angina frequency (SAQ)	83.2 (20.77)	9 (0.3%)	84.8 (19.12)	7 (0.3%)	79.4 (23.71)	2 (0.2%)	<0.0001
Treatment satisfaction (SAQ)	91.8 (13.02)	25 (0.8%)	92.4 (12.12)	18 (0.9%)	90.2 (14.76)	7 (0.8%)	<0.0001
Quality of life (SAQ)	57.4 (24.95)	18 (0.6%)	59.6 (24.35)	12 (0.6%)	52.6 (25.63)	6 (0.7%)	<0.0001
General health, SF-12 (physical component score)	43.0 (12.09)	142 (4.8%)	44.6 (11.53)	101 (4.9%)	39.3 (12.53)	41 (4.5%)	<0.0001
General health, SF-12 (mental component score)	45.5 (12.41)	142 (4.8%)	46.2 (12.12)	101 (4.9%)	43.9 (12.94)	41 (4.5%)	<0.0001

ER indicates emergency room; SAQ, Seattle Angina Questionnaire; and SF-12, Short Form-12.

models, several predictors (better physical health, more frequent depressive symptoms, low income, and employment) were psychosocial characteristics rather than markers of cardiac disease severity. Our study is robust in its generalizability, representing data from 103 hospitals across the United States, with adjudicated readmissions confirmed with retroactive chart review in lieu of the more commonly used patient self-reported readmissions.[54] These results can inform the development of psychosocial interventions, particularly those which are sex specific, to reduce readmissions in young patients with AMI.

Our study extends the literature in several important ways. Foremost, this is the first study to develop a risk prediction model for 1-year readmission post AMI among young adults aged 18 to 55 years, while incorporating psychosocial parameters. Prior risk stratification models examining post-AMI readmission have been developed in older populations (aged ≥50 years)[2]: with the few studies that included younger patients having a mean patient age in the 60s. These prior models also did not conduct specific subgroup analyses by age.[2] Beyond the age limitation, prior models, including the Centers for Medicare and Medicaid Services administrative model examining post-AMI readmission, demonstrated modest discrimination (median C statistic, 0.65; range 0.53–0.79), and exhibited methodological limitations.[2,25–27] Overall, there has been a lack of validation and significant reliance on single-center study designs, limiting generalizability, with data obtained exclusively from administrative records, electronic medical records, and clinical databases rather than from patient-reported outcome measures. Lastly, there has been a focus on the 30-day time point, thereby failing to quantify the high risk of readmission in young patients over the entirety of the first year after hospitalization for AMI.

Second, addressing a key draw back in prior models, our risk prediction model included data from the in-hospital stay instead of relying solely on postdischarge variables. This allowed for consideration of predictors that may inform interventions during the acute care episode. Third, our work builds on prior studies by drawing from novel domains such as patient-reported outcome measures and psychosocial factors. In prior models, between 7 and 37 predictors were typically included, among which demographics, comorbidities, and usage metrics were the most frequently included domains,[2] with only 2 models including psychosocial factors.[2] Of note, our model showed that physical health, mental health, and employment status were predictors of readmission, contrasting with findings from prior models largely built around disease severity. Interestingly, the type of myocardial ischemia (ie, obstructive versus nonobstructive coronary artery disease) was considered in our study but was not associated with the outcome or selected for the final model. Furthermore, our final model had fewer clinical factors than previous models, implying that in the young adult population, psychosocial and gender-based variables are potent predictors of readmission in the first year post AMI.

We found that women and individuals with a history of prior AMI, depression, or longer hospital stays were at greater risk for readmission, whereas better physical health and employment were protective. Young women being at higher risk is in line with our previous studies that showed women were more likely to be readmitted at both 30 days and 1 year post AMI.[13,37] There are a host of psychosocial factors, such as poorer health status, more depression and stress, and less social support, contributing to this difference.[55] Also, relative to men with similar cardiac risk, women are less likely to receive preventive treatment such as management of risk factors.[56] Indeed, suboptimal medical management post AMI increases the risk of future events. Women have also been found to be more prone to complications during hospitalization (eg, bleeding events), contributing to longer lengths of stay.[56] These results inform our hypothesis that women may experience more stressful and difficult hospitalizations, in turn creating a higher allostatic load that leads to greater vulnerability to readmission.[37]

In addition, longer length of stay is considered a proxy for poorer overall health. Prior studies have shown that extended hospitalizations are associated with a history of medical comorbidities such as diabetes mellitus and stroke.[57] Depression has also been shown to be associated with readmission, though the mechanism is less clear.[58] Depression itself is a known risk factor for worse cardiac morbidity and mortality, which could explain its positive association with readmission.[59] Other proposed mechanisms include its impact on patients' help-seeking behavior, health behavior, medication adherence, and perception of chest pain.[58]

Lastly, better self-reported physical health status and employment at baseline hospitalization were the only protective factors against readmission. It has been shown that AMI confers significant risk for decline in physical function and that those with worse physical health include the uninsured and those not referred to cardiac rehabilitation.[60] Prior research has also shown that better self-reported physical health status is correlated with less perceived limitations in self-care, improved disease-specific self-care behaviors, and higher levels of health literacy in patients with coronary heart disease. It can also be inferred that these patients benefit from the social determinants of health that contribute to higher levels of health literacy. All of these factors likely enable patients with better self-reported physical

Table 2. Causes of 1-Year Readmission Among Younger Adults Hospitalized for AMI

	Total number of readmissions 1 year post AMI (N=1658)	Percentage of total readmissions at 1 year post AMI
Cardiac readmission	994*	59.95%*
Acute myocardial infarction	133	8.02%
Heart failure	126	7.6%
Stable/unstable angina	565	34.08%
Stroke	10	0.6%
Other cardiac	160	9.65%
Noncardiac readmission	658*	39.69%*
Unknown	6*	0.36%*

AMI indicates acute myocardial infarction.
*<0.0001.

health status to engage in protective health behaviors that decrease the likelihood of readmission.[61,62]

Clinical Implications

Our study has several important clinical implications to improve in-hospital and post-AMI care for young adults with AMI. Based on our findings, a practical intervention at discharge could include solutions to reduce health inequities associated with low income and that are mitigated by reliable employment. For example, social work involvement for coordination of childcare and return to work interventions that support employment may include policy-based interventions promoting more flexible return to work policies to lessen the frequency of joblessness and disability. Such interventions designed to support employment for those at higher risk could also focus on self-management strategies that allow individuals to return to work despite high-risk behaviors.[63] Other interventions at discharge could include digital health applications and wearables that not only track activity but also focus on supporting the psychosocial aspects of care (eg, depression,

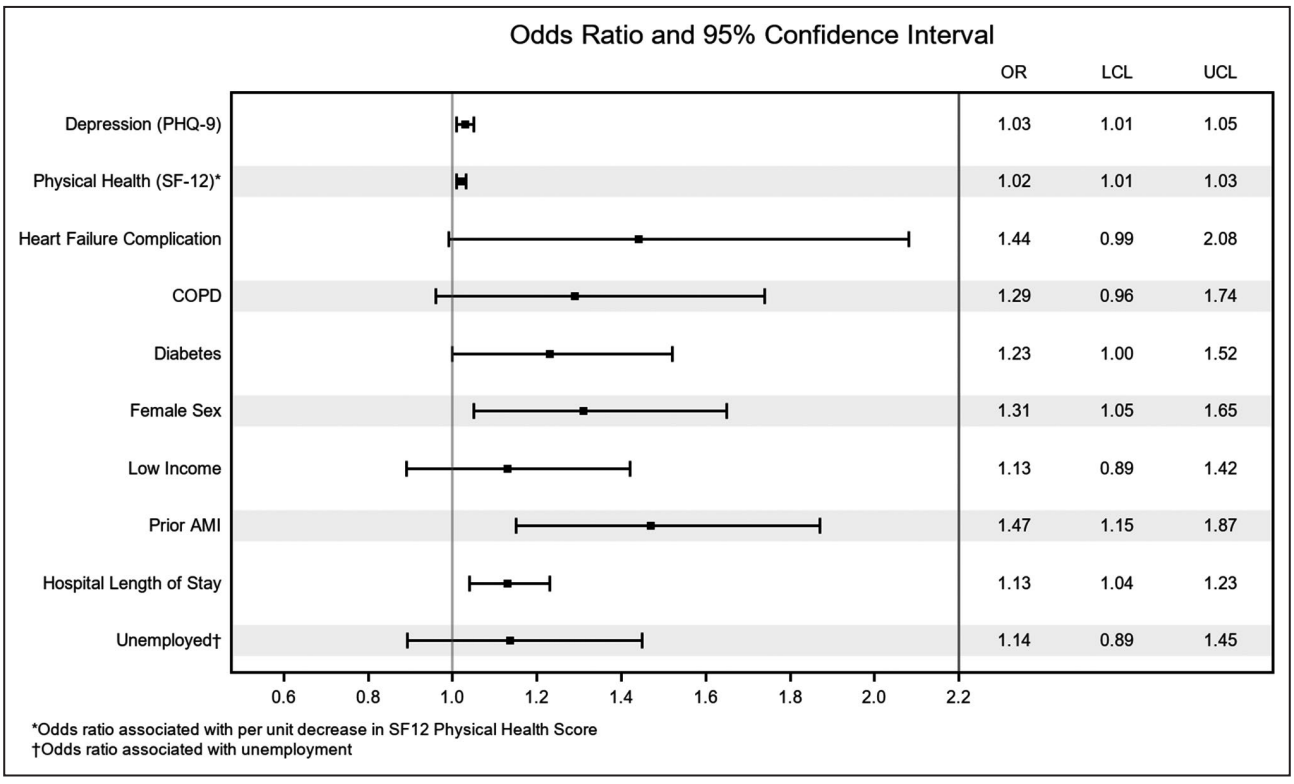

Figure 2. Forest plot showing predictors of 1-year readmission post AMI (odds ratio for readmitted vs not readmitted).
Note that for the purposes of interpretability we have inverted 2 predictors so they align better in the figure (physical health [SF-12], unemployment status). AMI indicates acute myocardial infarction; COPD, chronic obstructive pulmonary disease; LCL, lower control limit; OR, odds ratio; PHQ-9, Patient Health Questionnaire-9; SF-12, Short Form-12; and UCL, upper control limit.

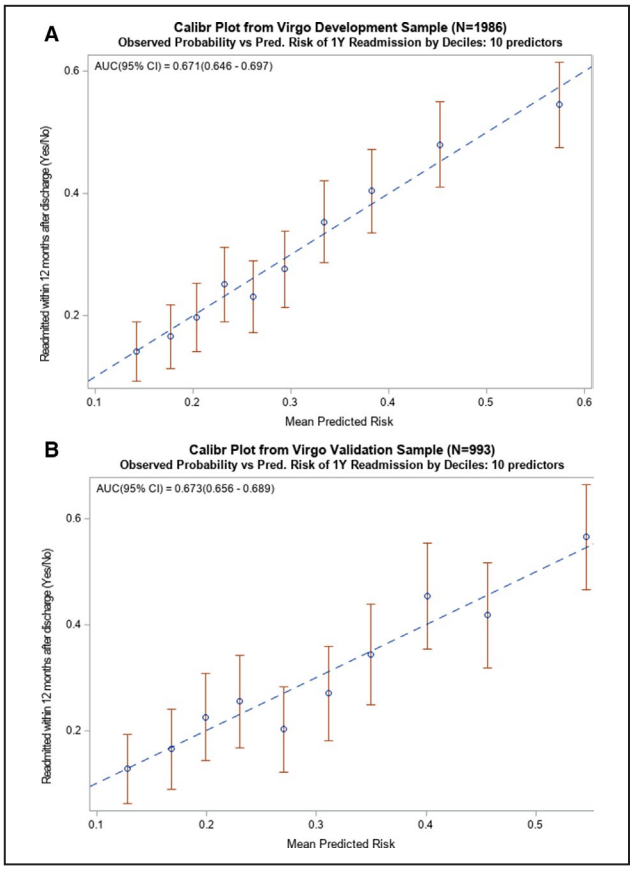

Figure 3. Calibration plots of observed vs predicted risk from the 10-predictor risk model of all-cause readmission within 1-year of hospitalization for AMI among younger adults.

A, Calibration plot from the development sample (N=1986) used to create the 10-predictor risk model that demonstrates how well the deciles of observed and predicted probabilities of 1-year readmission agree over the entire range of predicted risk, where the diagonal line represents perfect agreement. **B**, Calibration plot from the validation sample (N=993) used to exhibit successful application of the 10-predictor model by demonstrating how well the deciles of observed and predicted probabilities of 1-year readmission agree over the entire range of predicted risk, where the diagonal line represents perfect agreement. AMI indicates acute myocardial infarction; and AUC, area under the curve.

social support) and promote adherence to secondary prevention targets. Finally, our findings reaffirm the importance of cardiac rehabilitation counseling at discharge and promoting physical health as a primary prevention strategy to lower risk of readmission among young adults hospitalized for AMI.

Limitations

This study should be interpreted in the context of several limitations. First, some key variables were excluded from the analysis owing to either very high or low prevalence such as the nonreference levels of Killip. Troponin was excluded because of the inconsistency in how it is measured and reported at disparate hospitals. Second, our findings may not be generalizable to other minority groups (ie, American Indian, Alaska Native, Asian, Pacific Islander, East Indian, other race) and Hispanic individuals because of the smaller proportion of these individuals enrolled in our study. Despite this limitation it is important to note that to date this is the largest subset of young patients with AMI in the United States. Future studies need to ensure adequate representation of these ethnic/racial groups. Third, noncardiac causes of readmission could not be obtained owing to time and resource limitations. Finally, although the median C statistic of our study at 0.67 is modest, it lies within the upper part of the range of previously published models for readmission.[2] Of note, readmission, being a complex interaction between the patient, community, environment, and the healthcare system, is a much more difficult outcome to predict than mortality, which is largely driven by disease.[2]

CONCLUSIONS

Among young adults hospitalized for AMI, women and those with a prior AMI, as well as those who had diabetes mellitus, longer hospitalization, or more severe depressive symptoms, were more likely to be readmitted. Only 2 predictors, better physical health at admission and being employed, were protective for readmission in our model. Several predictors were found to be psychosocial characteristics (such as employment, depressive symptoms and self-reported personal health), rather than markers of cardiac disease severity. These results may inform the development of psychosocial interventions to prevent readmission among younger adults hospitalized for AMI.

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Disclosures

None.

Supplementary Material

Data S1
Tables S1–S3
Figures S1–S3

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SUPPLEMENTAL MATERIAL

Data S1.

Model Selection with Bayesian Model Averaging Methodology.

Bayesian model averaging (BMA) examines all the possible combinations of candidate variables and after selecting the best one, retains a subset of others within a performance range known as Occam's window, described in detail in Madigan and Raftery (1994)[48]. For all variables in the subset of best fitting models, BMA subsequently calculates a posterior probability, i.e., the probability the variable is associated with the data generating process of the outcome. The choice of a posterior probability threshold for retention of a predictor in the multivariable model allows flexibility for the myriad scenarios arising from varying sample sizes, differing collections of candidate variables and multiply imputed datasets.

One issue that has not been definitively resolved in the statistical literature is how to select a risk prediction model over multiple imputations. Because missing values result in different subsets of the data at any given stage, they can bias model selection. For this reason, selection needs to take place over the multiply imputed datasets. The question then becomes how to decide on a final set of variables when different "best" models are chosen from different imputations. Having looked at different types of outcomes in a number of studies, our experience with BMA for dichotomous outcomes has consistently resulted in very parsimonious selection where the great majority of predictors receive a posterior probability of zero, with a much smaller number of predictors characterized by posterior probabilities above zero.

Our process has evolved to reviewing those predictors that exhibit a non-zero posterior probability in a majority of the imputations with our clinical experts for face validity, and subsequently accepting those that have some theoretical or mechanistic justification[49-50]. In this study the final predictors were those exhibiting a positive posterior probability in at least half of

the imputations. Because there are many possible ways to implement BMA, and because we wanted to allow the work to be reproducible, we chose to use the BMA package in R using the default of 50% for all priors. This prior assumes that all predictors have an equal chance of being retained in the multivariable model, which we interpret as being relatively non-informative.

We present two supplementary sources of information regarding our use of BMA. The first of these is our use of the 50% prior probabilities for each of the candidate variables used in BMA model selection, as illustrated in the following line of R code:

Call: bic.glm.data.frame(x = BMAvirgoAllReadImp1a, y = READ, glm.family = "binomial", strict = FALSE, OR = 20, maxCol = 70, nbest = 5, Prior.param = c(rep(0.5, ncol(x))))

The second supplemental exhibit is the following presentation of the posterior probabilities calculated by BMA (with priors listed above) for each of the candidate variables in one of the imputations. As a reference we have included a table below that defines the final model predictors followed by the posterior probabilities for our candidate predictors (those eligible for BMA) from the first imputation, where the bolded predictors are those with posterior probabilities above zero. We note that the predictor loSES (low income) has a zero posterior probability in this imputation, but because it has a non-zero probability in the majority of the imputations, it was retained.

Variable	**Label**
bPCS	pvm_agg_phys_base
bPHQ9	baseline PHQ_9
comHF	Complication - Heart Failure

Variable	Label
copd	copd_core
dm	pvm_diabetes
fem	female sex
loSES	low income
prMI	pvm_previousMI
tLOStr5	length of stay in hospital truncated at 5 days
workS	PVM_WorkingStatus

Posterior probabilities(%):

actGu	alc2	**bPHQ9**	bleed	bMCS	**bPCS**	bPSS	bSQaf	bSQdp	bSQpl	bSQts
0.0	0.0	**100.0**	0.0	0.0	**100.0**	0.0	0.0	0.0	0.0	0.0

cArrh	cad50	chPain	**comHF**	**copd**	dapt	dispo	**dm**	dyslp	ef40	emArr
0.0	0.0	0.0	**58.5**	**3.4**	0.0	0.0	**51.6**	0.0	0.0	0.0

essi5	**fem**	fhCVD	grace	hisRD	hltIn	htn	inact	lateP	loSES	marit
0.0	**56.0**	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0

obese	nStemi	pEarn	**prMI**	reCsl	smok	**tLOS**	white	**workS**
0.0	0.0	0.0	**93.0**	0.0	0.0	**17.5**	0.0	**3.7**

Table S1. Initial list of 65 candidate variables for risk prediction model of 1-year readmission.

	All patients (N=2979)	All patients (Missing)	No readmission (N=2074)	No readmission (Missing)	Readmission within 1 year (N=905)	Readmission within 1 year (Missing)	P-Value
Socio-Demographics/SES							
Age (Mean ± SD)	47.1 (6.18)	0 (0.0%)	47.2 (6.10)	0 (0.0%)	46.9 (6.36)	0 (0.0%)	0.1755
Age, Median [IQR]	48.0 (44.0, 52.0)	0 (0.0%)	48.0 (44.0, 52.0)	0 (0.0%)	48.0 (44.0, 52.0)	0 (0.0%)	0.2628
Sex		0 (0.0%)		0 (0.0%)		0 (0.0%)	<0.0001
Female	2007 (67.4%)		1323 (63.8%)		684 (75.6%)		
Male	972 (32.6%)		751 (36.2%)		221 (24.4%)		
Race/Ethnicity		0 (0.0%)		0 (0.0%)		0 (0.0%)	0.0001
White	2289 (76.8%)		1631 (78.6%)		658 (72.7%)		
Black	533 (17.9%)		323 (15.6%)		210 (23.2%)		
American Indian/Alaska Native	33 (1.1%)		21 (1.0%)		12 (1.3%)		
Asian/Pacific Islander/East Indian	70 (2.3%)		53 (2.6%)		17 (1.9%)		
Other	51 (1.7%)		44 (2.1%)		7 (0.8%)		
Don’t Know	3 (0.1%)		2 (0.1%)		1 (0.1%)		
Hispanic		0 (0.0%)		0 (0.0%)		0 (0.0%)	0.0355
Yes	235 (7.9%)		183 (8.8%)		52 (5.7%)		
No	2725 (91.5%)		1878 (90.5%)		847 (93.6%)		

	All patients (N=2979)	All patients (Missing)	No readmission (N=2074)	No readmission (Missing)	Readmission within 1 year (N=905)	Readmission within 1 year (Missing)	P-Value
Don’t know	17 (0.6%)		12 (0.6%)		5 (0.6%)		
Patient refused	2 (0.1%)		1 (0.0%)		1 (0.1%)		
Married or Living with spouse	1658 (55.7%)	0 (0.0%)	1207 (58.2%)	0 (0.0%)	451 (49.8%)	0 (0.0%)	<0.0001
Primary earner	2214 (74.3%)	0 (0.0%)	1578 (76.1%)	0 (0.0%)	636 (70.3%)	0 (0.0%)	0.0008
Low income	1262 (42.4%)	0 (0.0%)	793 (38.2%)	0 (0.0%)	469 (51.8%)	0 (0.0%)	<0.0001
Less than high school education	1280 (43.0%)	0 (0.0%)	864 (41.7%)	0 (0.0%)	416 (46.0%)	0 (0.0%)	0.0319
Currently employed	1828 (61.4%)	0 (0.0%)	1367 (65.9%)	0 (0.0%)	461 (50.9%)	0 (0.0%)	<0.0001
Has Health insurance	2294 (77.0%)	0 (0.0%)	1588 (76.6%)	0 (0.0%)	706 (78.0%)	0 (0.0%)	0.4427
Cardiac risk factors							
Diabetes	1058 (35.5%)	0 (0.0%)	657 (31.7%)	0 (0.0%)	401 (44.3%)	0 (0.0%)	<0.0001
Obesity (BMI≥30 kg/m^2)	1571 (52.7%)	0 (0.0%)	1069 (51.5%)	0 (0.0%)	502 (55.5%)	0 (0.0%)	0.0528
Hypertension	1974 (66.3%)	0 (0.0%)	1321 (63.7%)	0 (0.0%)	653 (72.2%)	0 (0.0%)	<0.0001
Dyslipidemia	2582 (86.7%)	0 (0.0%)	1781 (85.9%)	0 (0.0%)	801 (88.5%)	0 (0.0%)	0.0516
Current Smoking	891 (29.9%)	0 (0.0%)	635 (30.6%)	0 (0.0%)	256 (28.3%)	0 (0.0%)	0.2015
Family History of CVD	2004 (67.3%)	0 (0.0%)	1373 (66.2%)	0 (0.0%)	631 (69.7%)	0 (0.0%)	0.0833
Inactivity	1054 (35.4%)	0 (0.0%)	683 (32.9%)	0 (0.0%)	371 (41.0%)	0 (0.0%)	<0.0001
Medical History							
Prior MI	635 (21.3%)	0 (0.0%)	379 (18.3%)	0 (0.0%)	256 (28.3%)	0 (0.0%)	<0.0001

	All patients (N=2979)	All patients (Missing)	No readmission (N=2074)	No readmission (Missing)	Readmission within 1 year (N=905)	Readmission within 1 year (Missing)	P-Value
History of Renal Disease	337 (11.3%)	0 (0.0%)	204 (9.8%)	0 (0.0%)	133 (14.7%)	0 (0.0%)	0.0001
Alcohol Abuse	1011 (33.9%)	0 (0.0%)	743 (35.8%)	0 (0.0%)	268 (29.6%)	0 (0.0%)	0.0010
History of COPD	346 (11.6%)	0 (0.0%)	198 (9.5%)	0 (0.0%)	148 (16.4%)	0 (0.0%)	<0.0001
History of stroke	100 (3.4%)	0 (0.0%)	56 (2.7%)	0 (0.0%)	44 (4.9%)	0 (0.0%)	0.0024
History of heart failure	137 (4.6%)	0 (0.0%)	57 (2.7%)	0 (0.0%)	80 (8.8%)	0 (0.0%)	<0.0001
History of PAD	74 (2.5%)	0 (0.0%)	32 (1.5%)	0 (0.0%)	42 (4.6%)	0 (0.0%)	<0.0001
History of recreational drug use	46 (1.5%)	0 (0.0%)	26 (1.3%)	0 (0.0%)	20 (2.2%)	0 (0.0%)	0.0516
Presentation Characteristics							
Transferred from another institution	1246 (41.8%)	0 (0.0%)	889 (42.9%)	0 (0.0%)	357 (39.4%)	0 (0.0%)	0.0821
First health service used		0 (0.0%)		0 (0.0%)		0 (0.0%)	0.3395
Directly ER from Home	2654 (89.1%)		1852 (89.3%)		802 (88.6%)		
Before ER, Dr Office	162 (5.4%)		105 (5.1%)		57 (6.3%)		
Before ER, other health services	163 (5.5%)		117 (5.6%)		46 (5.1%)		
Late Presentation >6h	1319 (44.3%)	0 (0.0%)	894 (43.1%)	0 (0.0%)	425 (47.0%)	0 (0.0%)	0.0538
ASA at arrival	2857 (95.9%)	0 (0.0%)	2000 (96.4%)	0 (0.0%)	857 (94.7%)	0 (0.0%)	0.2647
Ejection Fraction <40%	319 (10.7%)	0 (0.0%)	209 (10.1%)	0 (0.0%)	110 (12.2%)	0 (0.0%)	0.0849

	All patients (N=2979)	All patients (Missing)	No readmission (N=2074)	No readmission (Missing)	Readmission within 1 year (N=905)	Readmission within 1 year (Missing)	P-Value
Angiogram		317 (10.6%)		208 (10.0%)		109 (12.0%)	0.0333
Non-obstructive CAD <50%	257 (8.6%)		195 (9.4%)		62 (6.9%)		
Obstructive CAD >=50%	2405 (80.7%)		1671 (80.6%)		734 (81.1%)		
Peak Troponin (Mean ± SD)	26.7 (55.50)	33 (1.1%)	27.4 (55.77)	23 (1.1%)	25.2 (54.90)	10 (1.1%)	0.3170
Estimated Glomerular Filtration Rate (eGFR)	88.3 (24.26)	12 (0.4%)	89.3 (22.83)	8 (0.4%)	86.1 (27.14)	4 (0.4%)	0.0023
First White Blood Cell Count	10.8 (3.90)	12 (0.4%)	10.8 (3.87)	6 (0.3%)	10.7 (3.96)	6 (0.7%)	0.2272
First Hematocrit	41.0 (5.23)	13 (0.4%)	41.4 (4.95)	6 (0.3%)	40.2 (5.75)	7 (0.8%)	<0.0001
Chest pain as primary symptom	2600 (87.3%)	0 (0.0%)	1830 (88.2%)	0 (0.0%)	770 (85.1%)	0 (0.0%)	0.0176
Killip class		156 (5.2%)		112 (5.4%)		44 (4.9%)	0.0056
I (no rales)	2705 (90.8%)		1897 (91.5%)		808 (89.3%)		
II (rales in bases / S3)	83 (2.8%)		46 (2.2%)		37 (4.1%)		
III (rales over 1/2 the lungs / Pulmonary edema)	22 (0.7%)		11 (0.5%)		11 (1.2%)		
IV (Cardiogenic shock)	13 (0.4%)		8 (0.4%)		5 (0.6%)		
Prior coronary artery bypass grafting (CABG)	115 (3.9%)	0 (0.0%)	59 (2.8%)	0 (0.0%)	56 (6.2%)	0 (0.0%)	<0.0001
Type of Myocardial Infarction		0 (0.0%)		0 (0.0%)		0 (0.0%)	0.0096

	All patients (N=2979)	All patients (Missing)	No readmission (N=2074)	No readmission (Missing)	Readmission within 1 year (N=905)	Readmission within 1 year (Missing)	P-Value
STEMI	1483 (49.8%)		1065 (51.4%)		418 (46.2%)		
NSTEMI	1496 (50.2%)		1009 (48.6%)		487 (53.8%)		
Grace Score (Mean ± SD)	75.2 (19.05)	49 (1.6%)	74.6 (18.00)	23 (1.1%)	76.6 (21.26)	26 (2.9%)	0.0145
Conservative treatment	89 (3.0%)	0 (0.0%)	51 (2.5%)	0 (0.0%)	38 (4.2%)	0 (0.0%)	0.0103
Total length of stay in Days, Mean (SD)	4.2 (3.93)	13 (0.4%)	3.9 (3.41)	8 (0.4%)	4.9 (4.85)	5 (0.6%)	<0.0001
Disposition to other institutions at discharge	2806 (94.2%)	0 (0.0%)	1962 (94.6%)	0 (0.0%)	844 (93.3%)	0 (0.0%)	0.0071
Admitted to CCU/ICU	130 (4.4%)	0 (0.0%)	90 (4.3%)	0 (0.0%)	40 (4.4%)	0 (0.0%)	0.9213
Discharge Counseling							
Recommended Counselling (Cardiac+Diet+Smoking)	951 (31.9%)	0 (0.0%)	674 (32.5%)	0 (0.0%)	277 (30.6%)	0 (0.0%)	0.3089
Medication Counselling	2937 (98.6%)	0 (0.0%)	2047 (98.7%)	0 (0.0%)	890 (98.3%)	0 (0.0%)	0.4490
Exercise Counselling	2751 (92.3%)	0 (0.0%)	1913 (92.2%)	0 (0.0%)	838 (92.6%)	0 (0.0%)	0.7343
CLOP/Thienopyridines	2052 (68.9%)	0 (0.0%)	1442 (69.5%)	0 (0.0%)	610 (67.4%)	0 (0.0%)	0.2495
Statins	2739 (91.9%)	0 (0.0%)	1903 (91.8%)	0 (0.0%)	836 (92.4%)	0 (0.0%)	0.5671
Dual Antiplatelet Therapy	1964 (65.9%)	0 (0.0%)	1389 (67.0%)	0 (0.0%)	575 (63.5%)	0 (0.0%)	0.0688
ACEi/ARBs	1915 (64.3%)	0 (0.0%)	1331 (64.2%)	0 (0.0%)	584 (64.5%)	0 (0.0%)	0.8525
Beta Blockers	2713 (91.1%)	0 (0.0%)	1895 (91.4%)	0 (0.0%)	818 (90.4%)	0 (0.0%)	0.3871

	All patients (N=2979)	All patients (Missing)	No readmission (N=2074)	No readmission (Missing)	Readmission within 1 year (N=905)	Readmission within 1 year (Missing)	P-Value
Calcium Channel Blocker	148 (5.0%)	0 (0.0%)	97 (4.7%)	0 (0.0%)	51 (5.6%)	0 (0.0%)	0.2682
In-hospital complications							
Bleeding	197 (6.6%)	0 (0.0%)	133 (6.4%)	0 (0.0%)	64 (7.1%)	0 (0.0%)	0.5056
Re-infarction	28 (0.9%)	0 (0.0%)	15 (0.7%)	0 (0.0%)	13 (1.4%)	0 (0.0%)	0.0641
Heart failure	215 (7.2%)	0 (0.0%)	118 (5.7%)	0 (0.0%)	97 (10.7%)	0 (0.0%)	<0.0001
Cardiac arrhythmias	205 (6.9%)	0 (0.0%)	132 (6.4%)	0 (0.0%)	73 (8.1%)	0 (0.0%)	0.0923
Psychosocial factors (Mean ± SD)							
Social Support (ESSI-5)	21.3 (4.56)	57 (1.9%)	21.5 (4.34)	33 (1.6%)	20.9 (5.01)	24 (2.7%)	0.0058
Depression (PHQ-9)	7.8 (6.45)	117 (3.9%)	7.2 (6.21)	71 (3.4%)	9.4 (6.73)	46 (5.1%)	<0.0001
Stress (PSS-14)	26.0 (9.78)	185 (6.2%)	25.3 (9.83)	117 (5.6%)	27.6 (9.48)	68 (7.5%)	<0.0001
Physical Limitation (SAQ)	80.6 (25.79)	74 (2.5%)	83.5 (23.83)	48 (2.3%)	73.9 (28.75)	26 (2.9%)	<0.0001
Anginal Frequency (SAQ)	83.2 (20.77)	9 (0.3%)	84.8 (19.12)	7 (0.3%)	79.4 (23.71)	2 (0.2%)	<0.0001
Treatment satisfaction (SAQ)	91.8 (13.02)	25 (0.8%)	92.4 (12.12)	18 (0.9%)	90.2 (14.76)	7 (0.8%)	<0.0001
Quality of Life (SAQ)	57.4 (24.95)	18 (0.6%)	59.6 (24.35)	12 (0.6%)	52.6 (25.63)	6 (0.7%)	<0.0001
General health, SF-12 (PCS)	43.0 (12.09)	142 (4.8%)	44.6 (11.53)	101 (4.9%)	39.3 (12.53)	41 (4.5%)	<0.0001
General health, SF-12 (MCS)	45.5 (12.41)	142 (4.8%)	46.2 (12.12)	101 (4.9%)	43.9 (12.94)	41 (4.5%)	<0.0001

BMI (body mass index); CVD (cardiovascular disease); MI (myocardial infarction); COPD (chronic obstructive pulmonary disease); PAD (peripheral artery disease); ASA (aspirin at arrival); CAD (coronary artery disease); STEMI (ST-Elevation MI); NSTEMI (Non-

ST Elevation MI); CCU/ICU (coronary care unit / intensive care unit); ACEi/ARBs (angiotensin converting enzyme inhibitors / angiotensin receptor blockers); ESSI-5 (ENRICHD Social Support instrument); PHQ-9 (Patient Health Questionnaire-9); PSS-14 (Perceived Stress Scale), SAQ (Seattle Angina Questionnaire); SF-12 PCS (Short Form-12 physical component score); SF-12 MCS (Short Form-12 mental component score)

Table S2. **Baseline characteristics of young patients with AMI stratified by sex who were readmitted versus not readmitted at 1-year (10 final candidate variables).**

	All patients (N=2979)	Women (N=2007; 67.3%)	Men (N=972; 32.6%)	P-Value
PHQ-9 (Depression), Mean (SD)	7.8 (6.45)	8.7 (6.62)	6.0 (5.69)	<0.0001
SF-12 (PCS), Mean (SD)	43.0 (12.09)	41.9 (12.19)	45.3 (11.54)	<0.0001
Complication - Heart failure	215 (7.2%)	160 (8.0%)	55 (5.7%)	0.0212
History of COPD	346 (11.6%)	284 (14.2%)	62 (6.4%)	<0.0001
Diabetes	1058 (35.5%)	799 (39.8%)	259 (26.6%)	<0.0001
Low income	1262 (42.4%)	956 (47.6%)	306 (31.5%)	<0.0001
Prior MI	635 (21.3%)	413 (20.6%)	222 (22.8%)	0.1576
Hospital length of stay in Days, Mean (SD)	4.2 (3.93)	4.4 (4.20)	3.9 (3.31)	0.0019
Unemployed	1151 (38.6%)	879 (43.8%)	272 (28.0%)	<0.0001

Table S3. **BMA preliminary results showing predictors of 1-year readmission post AMI (among the subset of admissions with no history of prior AMI from a single imputation) (Odds ratio for readmitted vs. not readmitted).**

Obs	Variable	Estimate	StdErr	ProbChiSq	OR	LCLor	UCLor
1	Intercept	-0.5853	0.4617	0.2049	0.56	0.23	1.38
2	Depression (PHQ-9)	0.0313	0.00981	0.0014	1.03	1.01	1.05
3	Physical health (SF-12)	-0.0210	0.00525	<.0001	0.98	0.97	0.99
4	Obstructive CAD >=50%	0.3330	0.2061	0.1062	1.40	0.93	2.09
5	Diabetes	0.2931	0.1255	0.0195	1.34	1.05	1.71
6	Female sex	0.3123	0.1372	0.0228	1.37	1.04	1.79
7	GRACE score	-0.00707	0.00350	0.0434	0.99	0.99	1.00
8	Low Income	0.2053	0.1298	0.1137	1.23	0.95	1.58
9	Marital status	-0.1208	0.1252	0.3347	0.89	0.69	1.13
10	Hospital length of stay (Days)	0.0348	0.0153	0.0228	1.04	1.00	1.07

Figure S1. **VIRGO enrollment sites in United States (N=103 hospitals).**

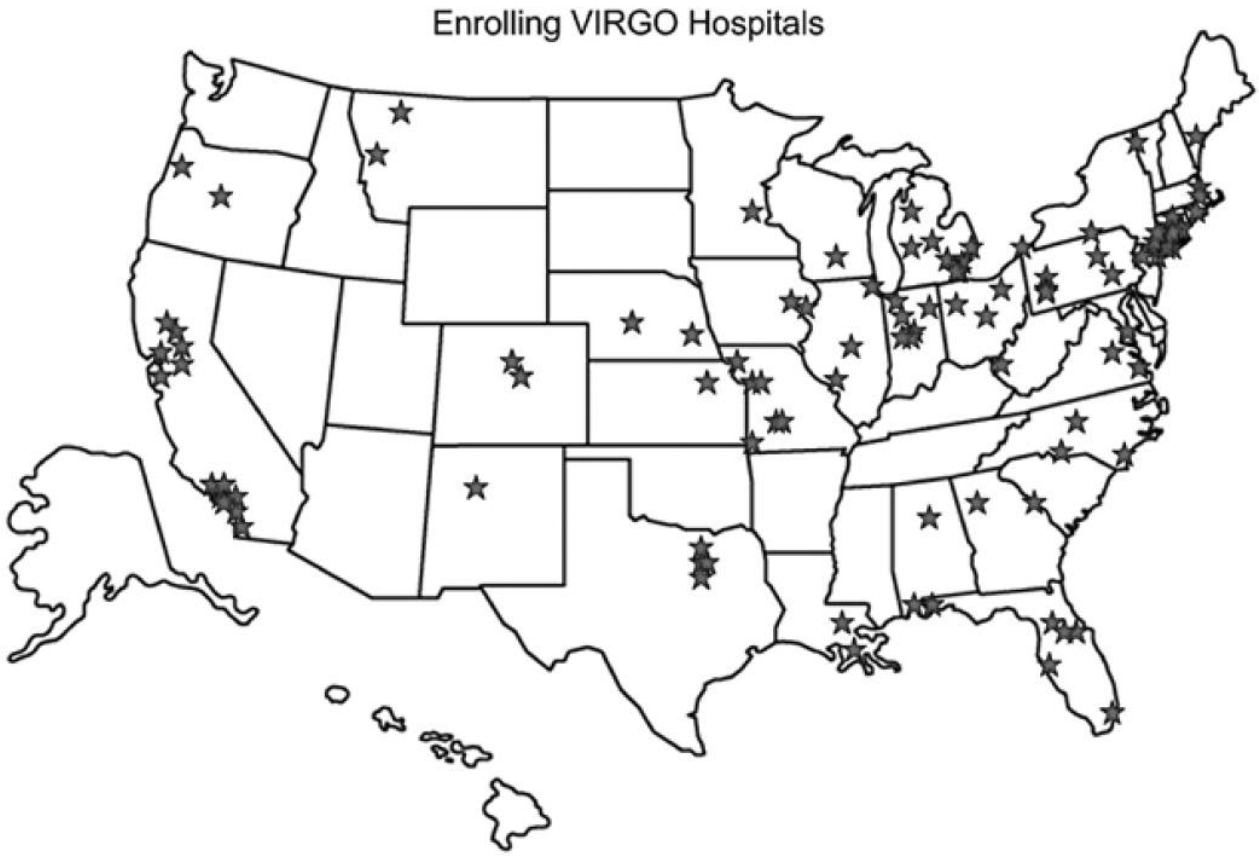


Figure S2. Timing of 1-year readmissions: Kaplan-Meier curve for survival free from hospital readmission within 1-year of discharge among patient readmitted.

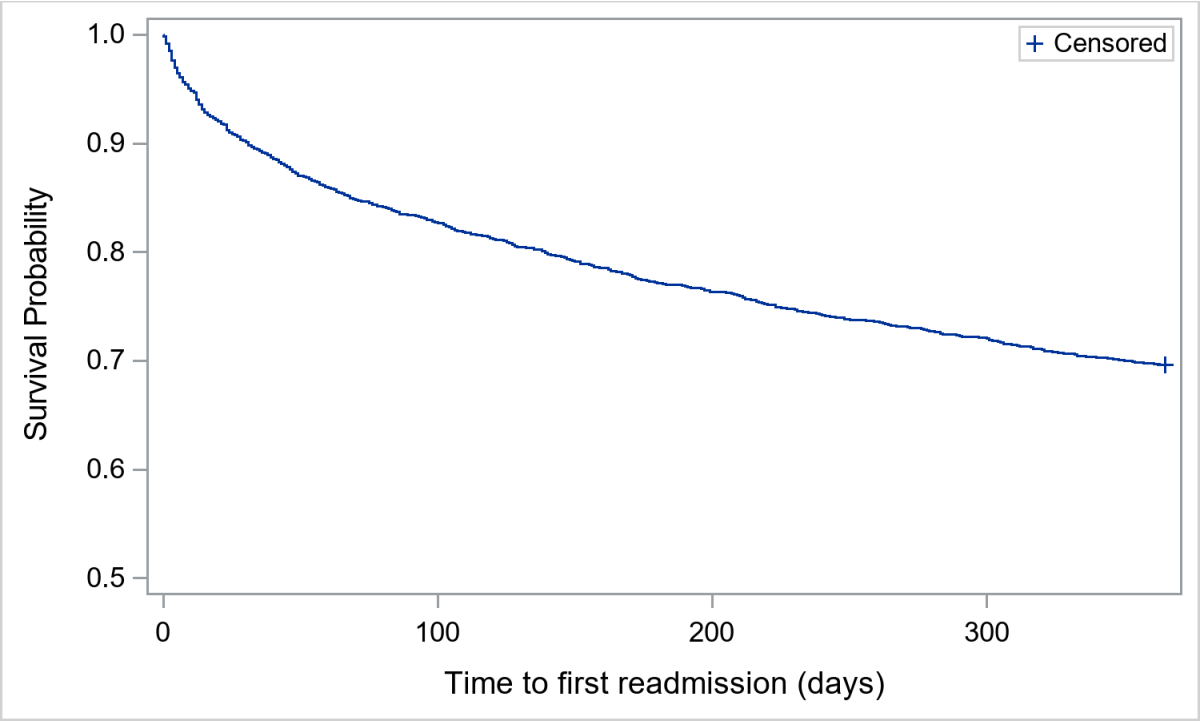
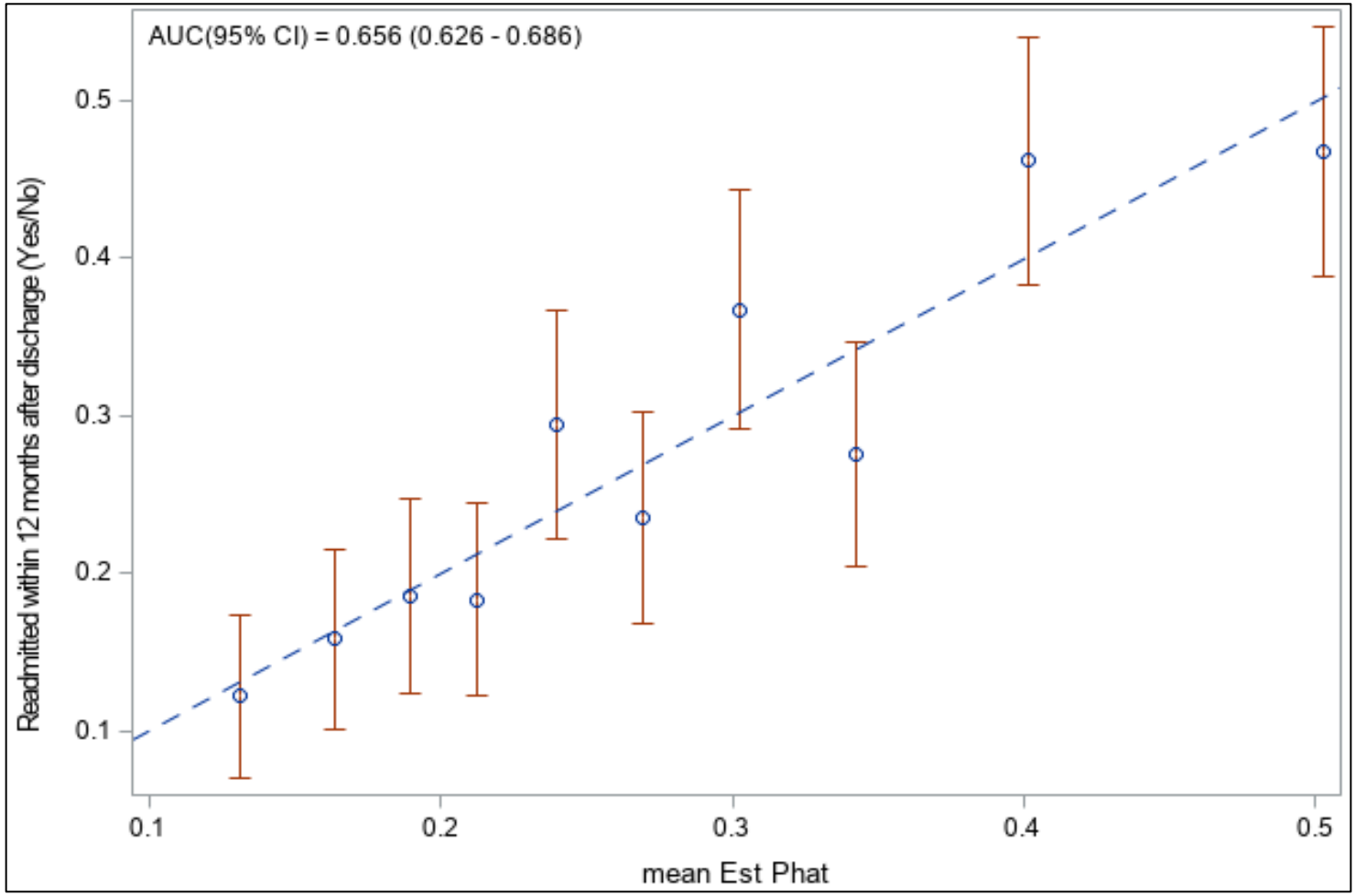


Figure S3. Calibration plots for the development and validation cohorts of predictors of readmission after a first AMI event.



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