

# **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)<sup>48</sup>. 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<sup>49-50</sup>. 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.

<b>Variable</b>	<b>Label</b>
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  
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
<b>Socio-Demographics/SES</b>							
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
<b>Cardiac risk factors</b>							
Diabetes	1058 ( 35.5%)	0 (0.0%)	657 ( 31.7%)	0 (0.0%)	401 ( 44.3%)	0 (0.0%)	<0.0001
Obesity (BMI $\geq$ 30 kg/m <sup>2</sup> )	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
<b>Medical History</b>							
Prior MI	635 ( 21.3%)	0 (0.0%)	379 ( 18.3%)	0 (0.0%)	256 ( 28.3%)	0 (0.0%)	<0.0001

	<b>All patients (N=2979)</b>	<b>All patients (Missing)</b>	<b>No readmission (N=2074)</b>	<b>No readmission (Missing)</b>	<b>Readmission within 1 year (N=905)</b>	<b>Readmission within 1 year (Missing)</b>	<b>P-Value</b>
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
<b>Presentation Characteristics</b>							
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

	<b>All patients (N=2979)</b>	<b>All patients (Missing)</b>	<b>No readmission (N=2074)</b>	<b>No readmission (Missing)</b>	<b>Readmission within 1 year (N=905)</b>	<b>Readmission within 1 year (Missing)</b>	<b>P-Value</b>
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
<b>Discharge Counseling</b>							
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
<b>In-hospital complications</b>							
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
<b>Psychosocial factors</b> (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 (ENRICH 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)

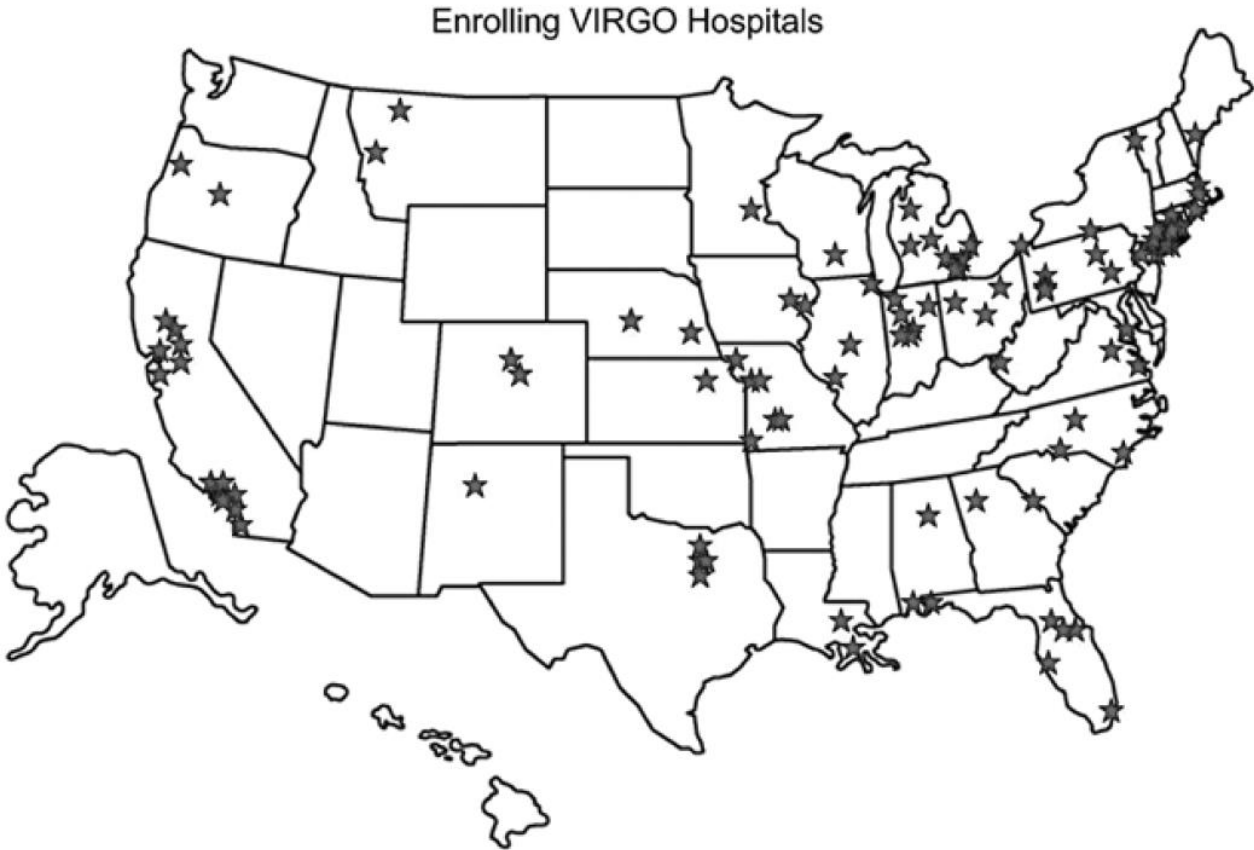
**Table S2. Baseline characteristics of young patients with AMI stratified by sex who were readmitted versus not readmitted at 1-year (10 final candidate variables).**

	<b>All patients (N=2979)</b>	<b>Women (N=2007; 67.3%)</b>	<b>Men (N=972; 32.6%)</b>	<b>P-Value</b>
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).**

<b>Obs</b>	<b>Variable</b>	<b>Estimate</b>	<b>StdErr</b>	<b>ProbChiSq</b>	<b>OR</b>	<b>LCLor</b>	<b>UCLor</b>
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.**

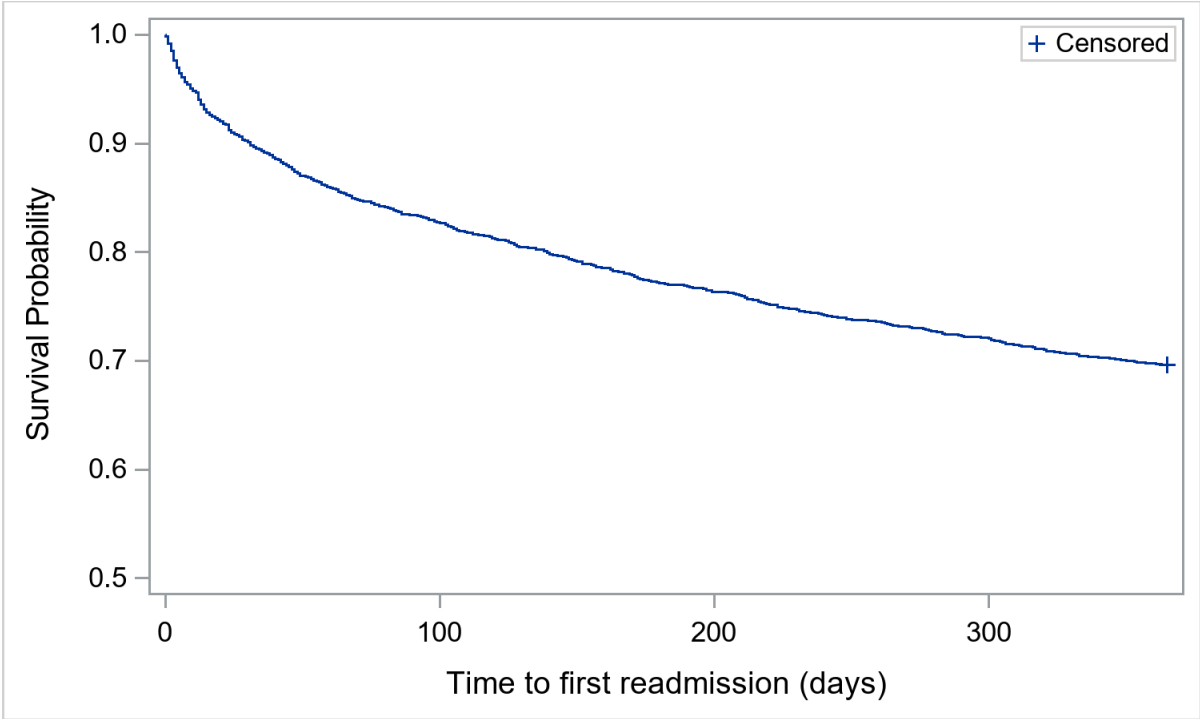


Figure S3. Calibration plots for the development and validation cohorts of predictors of readmission after a first AMI event.

