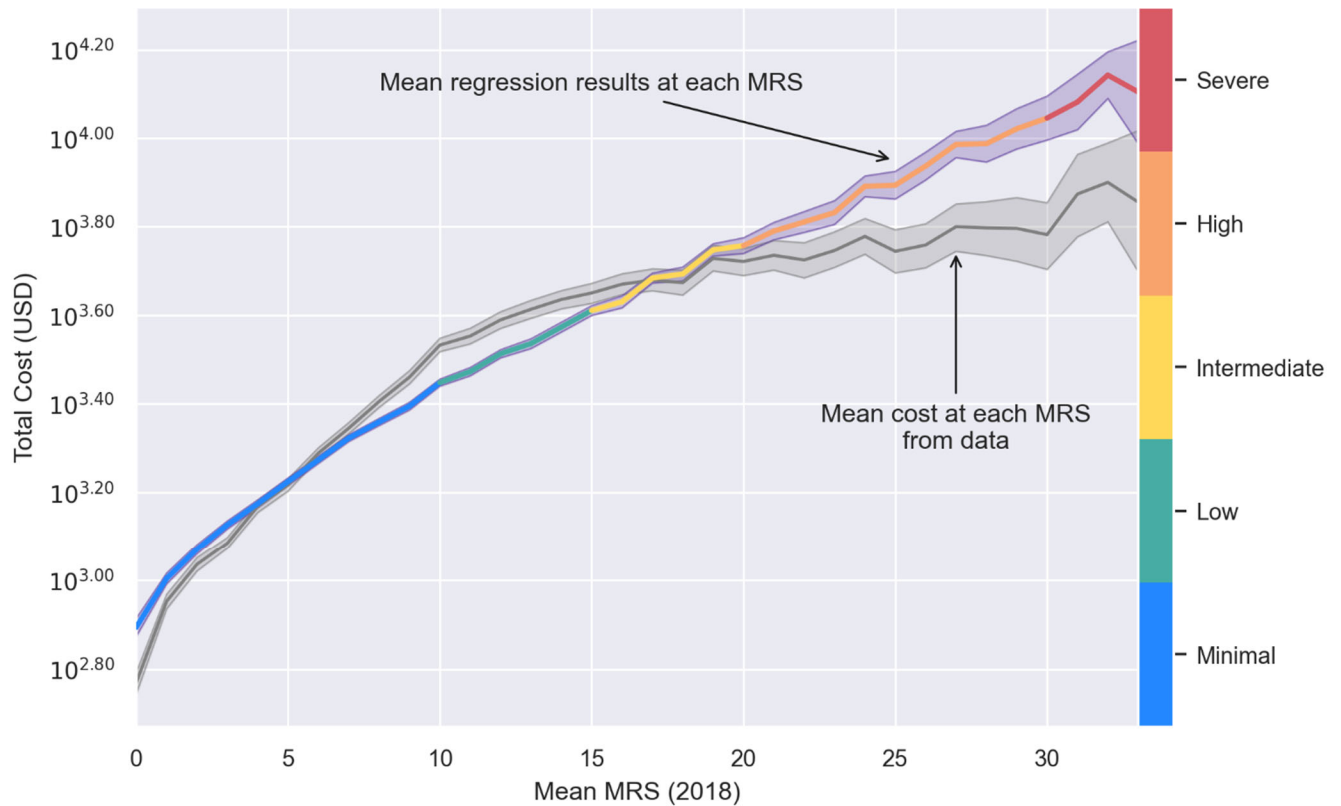


eAppendix: Association of the MedWise Risk Score With Health Care Outcomes

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eAppendix Figure e1. Predicted Total Medical Expenditure vs Observed Costs in 2018 as a Function of Mean MRS^a



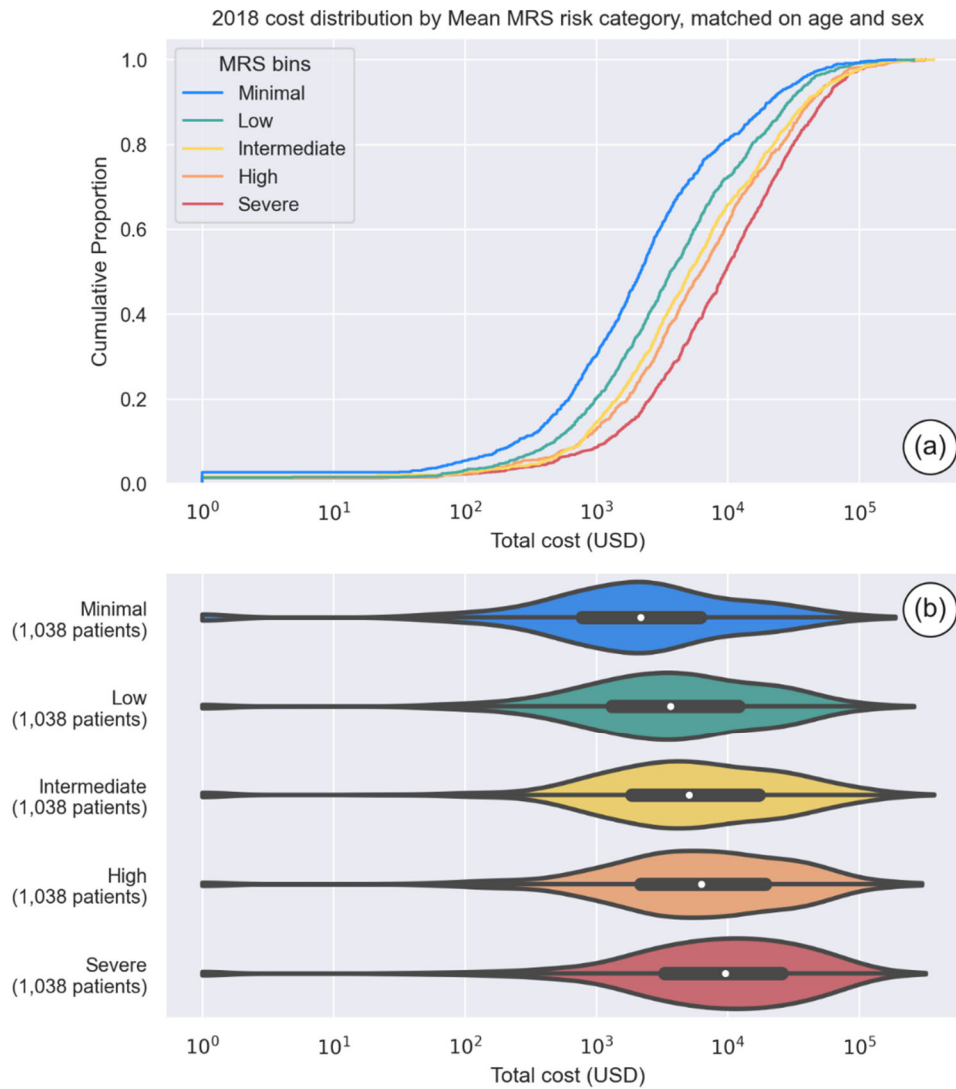
MRS, MedWise Risk Score.

^aPredicted total medical expenditure derived via linear regression. The Mean MRS was associated with total health care expenditure (Medicare Parts A and B) showing independent contribution of the Mean MRS with predictive value of 7.8% cost increase per unit increase in MRS. The model includes Mean MRS, age, and sex as covariates (Mean MRS was capped to values with at least 100 patients). Confidence intervals for the data line were derived from bootstrap sampling.

eAppendix Figure e2. Cost Distribution in 2018 by Mean MRS Risk Category, Matched on Age and Sex^a

a. Empirical Cumulative Distribution^b

b. Violin Plots^{b,c}



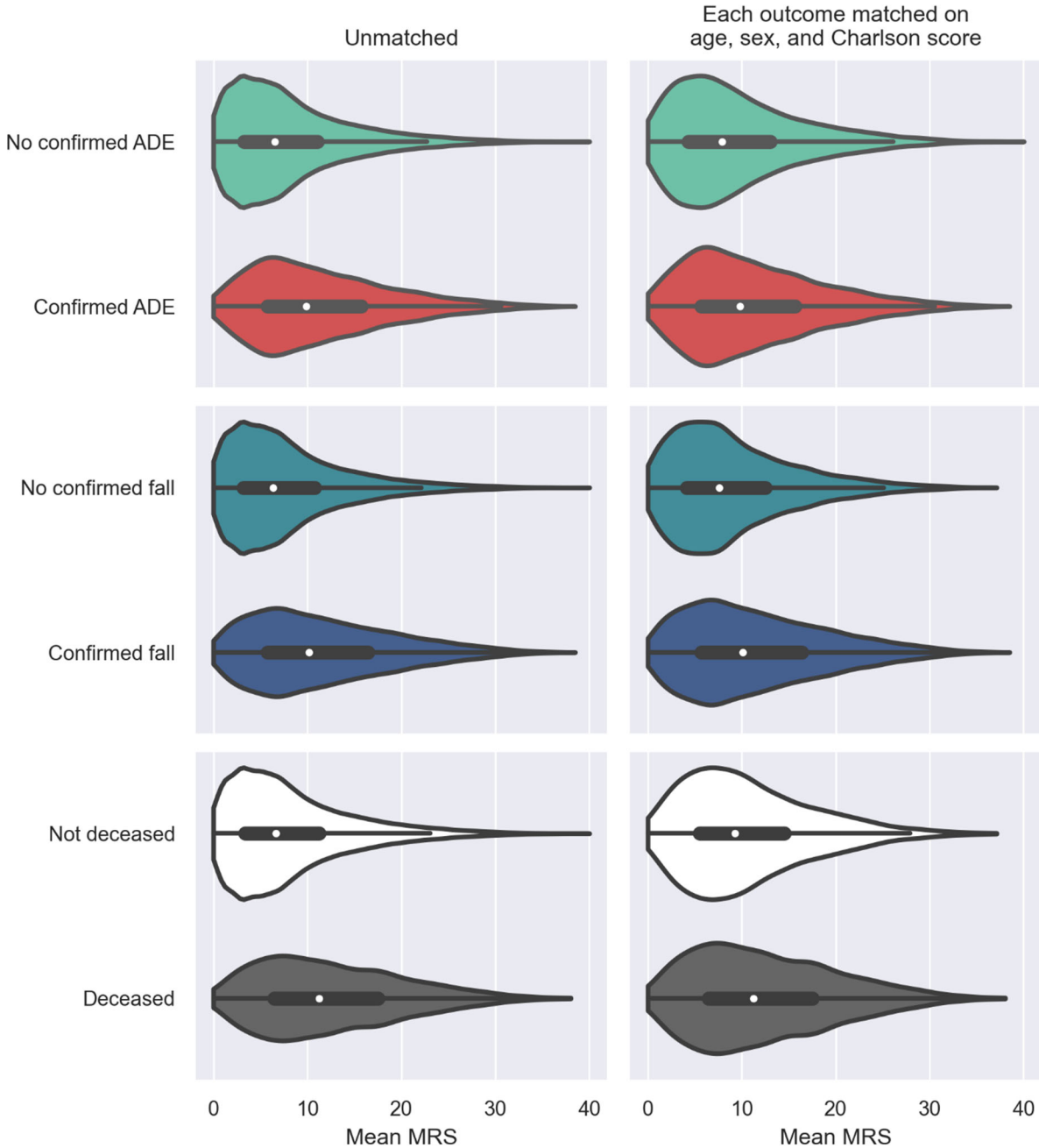
MRS, MedWise Risk Score; USD, US dollars.

^aThis figure illustrates the association between the total medical expenditure and Mean MRS categories.

^bThe blue, green, yellow, orange, and red represent the Minimal (MRS <0-9), Low (MRS 10-14), Intermediate (MRS 15-19), High (MRS 20-29), and Severe (MRS \geq 30) risk categories for their Max MRS, respectively.

^cThe white dots are the medians, and the colored areas are probability density estimates.

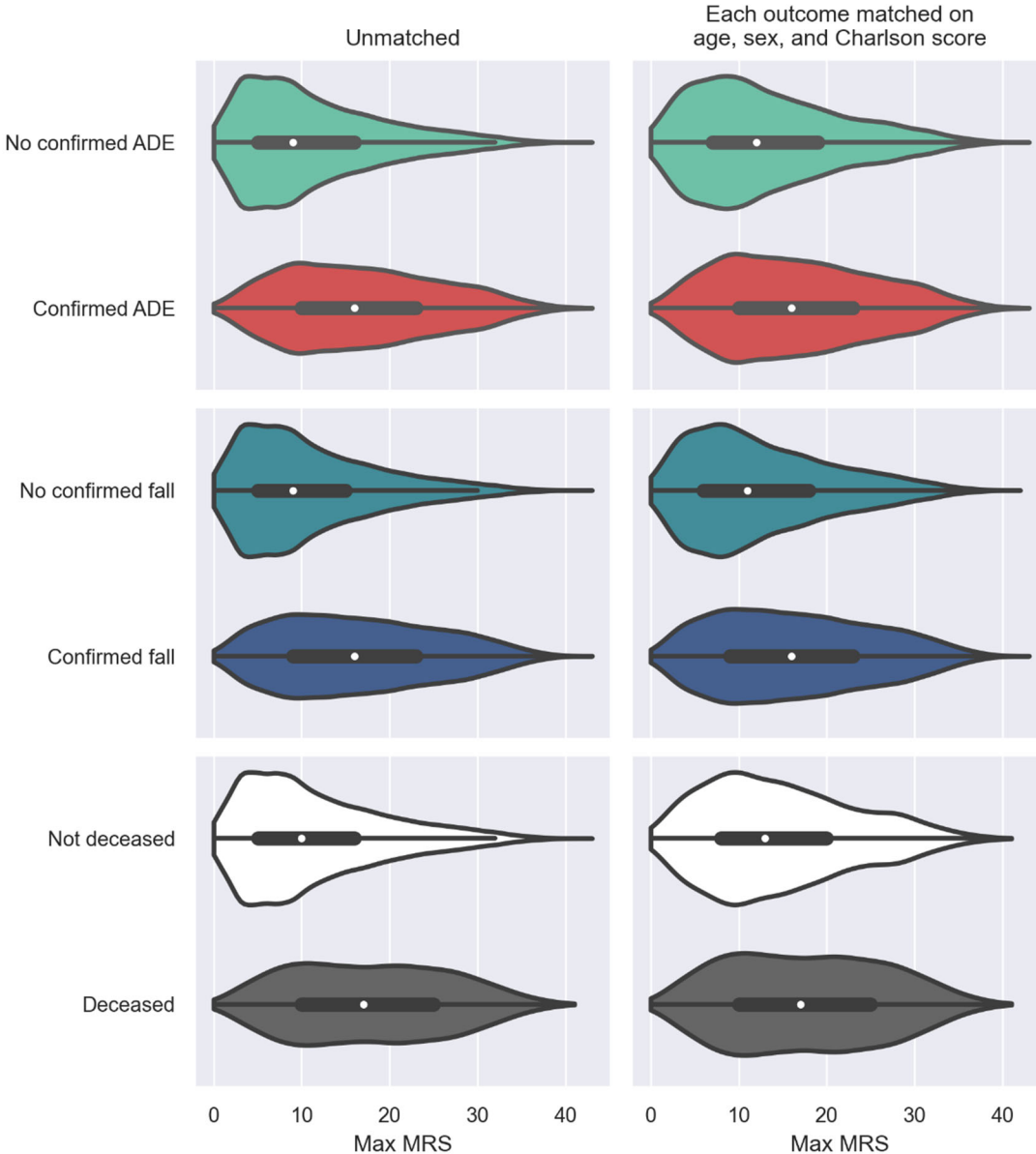
eAppendix Figure e3. Violin Plots Illustrating Mean MRS Distributions Among Patients Without or With Experiencing the Following Binary Outcomes: ADE (1st row), Fall (2nd row), and Death (3rd row)



ADE, adverse drug event; MRS, MedWise Risk Score.

^aThe left panel represents unmatched data and the right panel represents patient-matched analyses for age, sex, and Charlson Comorbidity Index score. The white dots are the medians, and the colored areas are probability density estimates.

eAppendix Figure e4. Violin Plots Illustrating Max MRS Distributions Among Patients Without or With Experiencing the Following Binary Outcome: ADE (1st row), Fall (2nd row), and Death (3rd row)^a



ADE, adverse drug event; MRS, MedWise Risk Score.

^aThe left panel represents unmatched data and the right panel represents patient-matched analyses for age, sex, and Charlson Comorbidity Index score. The white dots are the medians, and the colored areas are probability density estimates.

eAppendix Table e1. Odds Ratios: Association Between the Mean MRS With Health Outcomes Including ADE, Fall, and Mortality

Model	Parameter	OR of ADE (95% CI)	OR of fall (95% CI)	OR of death (95% CI)
1 (not adjusted)	MRS per unit Minimal MRS (reference)	1.067 (1.064-1.070) 1	1.078 (1.076-1.080) 1	1.082 (1.077-1.087) 1
	Low MRS	1.984 (1.883-2.090)	2.094 (2.016-2.176)	2.201 (1.996-2.428)
	Intermediate MRS	2.460 (2.313-2.617)	2.851 (2.725-2.982)	3.321 (2.986-3.694)
	High MRS	2.956 (2.767-3.158)	3.842 (3.664-4.029)	4.134 (3.700-4.620)
	Severe MRS	4.843 (4.090-5.735)	5.223 (4.565-5.976)	5.178 (3.857, 6.952)
2	MRS per unit Minimal MRS (reference)	1.067 (1.064-1.070) 1	1.075 (1.073-1.077) 1	1.073 (1.068-1.078) 1
	Low MRS	1.982 (1.882-2.089)	1.902 (1.830-1.978)	1.833 (1.661-2.023)
	Intermediate MRS	2.459 (2.312-2.615)	2.630 (2.512-2.753)	2.772 (2.490-3.087)
	High MRS	2.956 (2.767-3.158)	3.680 (3.505-3.864)	3.49 (3.119-3.906)
	Severe MRS	4.847 (4.093-5.739)	5.734 (4.982-6.600)	4.916 (3.64-6.639)
3	MRS per unit Minimal MRS (reference)	1.067 (1.064-1.070) 1	1.077 (1.075-1.079) 1	1.082 (1.077-1.087) 1
	Low MRS	1.984 (1.884-2.090)	2.104 (2.024-2.186)	2.202 (1.996-2.428)
	Intermediate MRS	2.459 (2.312-2.615)	2.839 (2.714-2.970)	3.321 (2.986-3.694)
	High MRS	2.949 (2.760-3.151)	3.739 (3.565-3.922)	4.131 (3.696-4.617)
	Severe MRS	4.825 (4.075-5.714)	5.017 (4.383-5.743)	5.171 (3.851-6.943)
4	MRS per unit Minimal MRS (reference)	1.049 (1.046-1.052) 1	1.070 (1.068-1.072) 1	1.062 (1.057-1.067) 1
	Low MRS	1.627 (1.542-1.716)	1.911 (1.839-1.987)	1.758 (1.591-1.942)
	Intermediate MRS	1.903 (1.786-2.028)	2.535 (2.422-2.654)	2.485 (2.229-2.771)
	High MRS	2.197 (2.052-2.353)	3.356 (3.198-3.523)	2.949 (2.631-3.305)
	Severe MRS	3.232 (2.707-3.859)	4.311 (3.760-4.944)	3.162 (2.335-4.281)
5	MRS per unit Minimal MRS (reference)	1.067 (1.064-1.070) 1	1.074 (1.072-1.076) 1	1.074 (1.068-1.079) 1
	Low MRS	1.983 (1.882-2.090)	1.916 (1.842-1.992)	1.821 (1.650-2.010)
	Intermediate MRS	2.458 (2.311-2.615)	2.633 (2.515-2.756)	2.768 (2.486-3.082)
	High MRS	2.949 (2.760-3.150)	3.621 (3.448-3.802)	3.54 (3.162-3.962)

eAppendix: Association of the MedWise Risk Score With Health Care Outcomes
 From a supplement to *The American Journal of Managed Care*[®]: “Innovative Enhanced Medication Therapy Management
 Model: MedWise Risk Score, Medication Safety Review, and Health Care Outcomes”

	Severe MRS	4.828 (4.076-5.717)	5.587 (4.854-6.431)	5.018 (3.715-6.779)
6	MRS per unit	1.049 (1.046-1.052)	1.066 (1.064-1.069)	1.056 (1.050-1.061)
	Minimal MRS (reference)	1	1	1
	Low MRS	1.639 (1.554-1.730)	1.766 (1.698-1.837)	1.497 (1.354-1.655)
	Intermediate MRS	1.908 (1.790-2.034)	2.364 (2.257-2.477)	2.142 (1.919-2.391)
	High MRS	2.171 (2.027-2.325)	3.183 (3.029-3.344)	2.636 (2.349-2.958)
	Severe MRS	3.122 (2.613-3.729)	4.646 (4.031-5.354)	3.306 (2.428-4.503)

ADE, adverse drug event; MRS, MedWise Risk Score; OR, odds ratio.

^aORs derived from binary logistic regression models. The ORs for MRS categories are relative to the Minimal category. Unadjusted models and models controlling for covariates were tested as follows: Model 1, MRS; Model 2, MRS plus age; Model 3, MRS plus sex; Model 4, MRS plus Charlson Comorbidity Index score; Model 5, MRS plus age and sex; Model 6, MRS plus age, sex, and Charlson Comorbidity Index score.

eAppendix Table e2. Performance of Binary Outcome Logistic Regression Models With Max MRS and the Mean MRS (2018)

MRS type	Model	Model type	ADE			Fall			Mortality		
			AUC	Sensitivity	Specificity	AUC	Sensitivity	Specificity	AUC	Sensitivity	Specificity
Max MRS	1	MRS unit	0.68	0.67	0.60	0.68	0.62	0.65	0.70	0.63	0.67
		MRS categories	0.67	0.76	0.51	0.67	0.54	0.72	0.69	0.60	0.70
	2	MRS unit	0.68	0.66	0.62	0.73	0.68	0.66	0.79	0.75	0.70
		MRS categories	0.67	0.56	0.70	0.72	0.66	0.68	0.79	0.75	0.70
	3	MRS unit	0.68	0.67	0.60	0.69	0.64	0.64	0.70	0.62	0.68
		MRS categories	0.67	0.76	0.51	0.68	0.67	0.61	0.69	0.60	0.70
4	MRS unit	0.73	0.64	0.70	0.69	0.63	0.64	0.77	0.74	0.66	
	MRS categories	0.73	0.66	0.68	0.68	0.68	0.60	0.76	0.74	0.67	
5	MRS unit	0.68	0.64	0.63	0.73	0.68	0.67	0.79	0.77	0.69	
	MRS categories	0.67	0.74	0.53	0.72	0.71	0.64	0.79	0.76	0.69	
6	MRS unit	0.74	0.67	0.67	0.73	0.69	0.66	0.83	0.79	0.74	
	MRS categories	0.73	0.65	0.69	0.73	0.65	0.71	0.83	0.79	0.74	
Mean MRS	1	MRS unit	0.64	0.57	0.64	0.65	0.54	0.69	0.68	0.65	0.61
		MRS categories	0.61	0.49	0.71	0.62	0.51	0.72	0.64	0.56	0.70
	2	MRS unit	0.64	0.57	0.64	0.71	0.65	0.68	0.78	0.70	0.72
		MRS categories	0.62	0.49	0.71	0.70	0.65	0.67	0.77	0.75	0.68
	3	MRS unit	0.64	0.56	0.65	0.66	0.58	0.66	0.68	0.66	0.61
		MRS categories	0.61	0.49	0.71	0.64	0.51	0.72	0.64	0.56	0.70
4	MRS unit	0.72	0.68	0.63	0.67	0.60	0.66	0.77	0.71	0.69	
	MRS categories	0.71	0.58	0.73	0.66	0.59	0.65	0.76	0.70	0.69	
5	MRS unit	0.64	0.56	0.65	0.71	0.65	0.68	0.78	0.69	0.73	
	MRS categories	0.62	0.49	0.71	0.71	0.67	0.65	0.77	0.78	0.65	
6	MRS unit	0.72	0.67	0.65	0.72	0.67	0.66	0.83	0.78	0.74	
	MRS categories	0.71	0.67	0.64	0.72	0.67	0.66	0.83	0.77	0.75	

ADE, adverse drug event; AUC, area under the curve; MRS, MedWise Risk Score.

^aPerformance tracked using AUC, sensitivity, and specificity. The sensitivity and specificity were determined using the Youden method: Model 1, MRS; Model 2, MRS plus age; Model 3, MRS plus sex; Model 4, MRS plus Charlson Comorbidity Index score; Model 5, MRS plus age and sex; Model 6, MRS plus age, sex, and Charlson Comorbidity Index score. The MRS categories refer to Minimal (MRS <0-9), Low (MRS 10-14), Intermediate (MRS 15-19), High (MRS 20-29), and Severe (MRS ≥30) risk levels.

eAppendix Table e3. Performance of Emergency Department (ED) Admission Negative Binomial Regression Models With Max MRS and Mean MRS (2018)^a

MRS type	Model ^b	RMSE	MAE	AIC
Max MRS^c	1	1.154	0.525	337689
	2	1.150	0.526	335634
	3	1.153	0.532	337669
	4	1.143	0.516	333212
	5	1.149	0.525	335540
	6	1.138	0.513	331433
Mean MRS	1	1.178	0.535	344468
	2	1.173	0.537	342764
	3	1.178	0.535	344466
	4	1.164	0.523	338567
	5	1.172	0.537	342723
	6	1.159	0.521	337107

AIC, Akaike information criterion; MAE, mean absolute error; MRS, MedWise Risk Score; RMSE, root-mean-square error

^aMetrics are root-mean-square error (RMSE) after rounding, mean absolute error (MAE) after rounding, and Akaike information criterion (AIC)

^bModel 1, MRS; Model 2, MRS plus age; Model 3, MRS plus sex; Model 4, MRS plus Charlson Comorbidity Index score; Model 5, MRS plus age and sex; Model 6, MRS plus age, sex, and Charlson Comorbidity Index score.

^cThe best scores on RSME, MAE and AIC metric performance indicators were obtained with the MaxMRS

eAppendix Table e4. Performance of Hospital Admission and Average Length of Stay Zero-Inflated Poisson Regression Models with Max and Mean MRS (2018)^a

MRS type	Model	Hospitalization ^b		LOS ^c	
		RMSE	MAE	RMSE	MAE
MaxMRS	1	0.661	0.256	2.328	1.141
	2	0.659	0.252	2.322	1.128
	3	0.660	0.254	2.327	1.137
	4	0.633	0.240	2.277	1.069
	5	0.656	0.250	2.320	1.126
	6	0.639	0.238	2.273	1.056
MeanMRS	1	0.677	0.246	2.368	1.300
	2	0.675	0.245	2.362	1.259
	3	0.676	0.246	2.369	1.294
	4	0.644	0.239	2.309	1.125
	5	0.674	0.244	2.359	1.255
	6	0.642	0.238	2.304	1.121

AIC, Akaike information criterion; LOS, length of stay; MAE, mean absolute error; MRS, MedWise Risk Score; RMSE, root-mean-square error

^aMetrics are root-mean-square error (RMSE) after rounding, mean absolute error (MAE) after rounding, and Akaike information criterion (AIC)

^bThe best scores on RSME metric performance indicator were obtained with the Max MRS

^cThe best scores on RSME and MAE metric performance indicators were obtained with the Max MRS

^dModel 1, MRS; Model 2, MRS plus age; Model 3, MRS plus sex; Model 4, MRS plus Charlson Comorbidity Index score; Model 5, MRS plus age and sex; Model 6, MRS plus age, sex, and Charlson Comorbidity Index score.