Original Article

SAGE Open Medicine

SAGE Open Medicine
Volume 4: 1–9

DOI: 10.1177/2050312116632426
smo.sagepub.com

Medication regimen complexity and readmissions after hospitalization for heart failure, acute myocardial infarction, pneumonia, and chronic obstructive pulmonary disease

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Abstract

Objectives: Readmission rate is increasingly being viewed as a key indicator of health system performance. Medication regimen complexity index scores may be predictive of readmissions; however, few studies have examined this potential association. The primary objective of this study was to determine whether medication regimen complexity index is associated with all-cause 30-day readmission after admission for heart failure, acute myocardial infarction, pneumonia, or chronic obstructive pulmonary disease.

Methods: This study was an institutional review board–approved, multi-center, case–control study. Patients admitted with a primary diagnosis of heart failure, acute myocardial infarction, pneumonia, or chronic obstructive pulmonary disease were randomly selected for inclusion. Patients were excluded if they discharged against medical advice or expired during their index visit. Block randomization was utilized for equal representation of index diagnosis and site. Discharge medication regimen complexity index scores were compared between subjects with readmission versus those without. Medication regimen complexity index score was then used as a predictor in logistic regression modeling for readmission.

Results: Seven hundred and fifty-six patients were randomly selected for inclusion, and 101 (13.4%) readmitted within 30 days. The readmission group had higher medication regimen complexity index scores than the no-readmission group ($p < 0.01$). However, after controlling for demographics, disease state, length of stay, site, and medication count, medication regimen complexity index was no longer a significant predictor of readmission (odds ratio 0.99, 95% confidence interval 0.97–1.01) or revisit (odds ratio 0.99, 95% confidence interval 0.98–1.02).

Conclusion: There is little evidence to support the use of medication regimen complexity index in readmission prediction when other measures are available. Medication regimen complexity index may lack sufficient sensitivity to capture an effect of medication regimen complexity on all-cause readmission.

Keywords

Medication regimen complexity index, readmission, re-hospitalization, acute care utilization, high-risk disease state

Date received: 26 October 2015; accepted: 13 January 2016

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Introduction

Among Medicare beneficiaries, one in five is re-hospitalized within 30 days of an index hospitalization, and one in three is readmitted within 90 days. Among these re-hospitalizations are unplanned readmissions that account for more than US$17 billion in Medicare health care expenditures annually.[1] Consequently, hospital readmissions have become a national focus for health care systems and health care payers alike. In an effort to reduce unwarranted readmissions, the Center for Medicare and Medicaid Services has subjected hospitals to financial penalties for excess readmissions due to (1) chronic obstructive pulmonary disease (COPD), (2) elective total hip or knee arthroplasty, (3) acute myocardial infarction (AMI), (4) heart failure (HF), and (5) pneumonia (PNA).

Hospitals across the nation are working to identify risk factors for readmissions and searching for tools to aid in the identification of patients who may benefit from targeted interventions. However, few studies have examined medication-related risk factors and hospital readmission, despite the fact that drug-related problems are a known cause of readmission. A study conducted by Ruiz et al.[2] in 2008 found that adverse drug reactions may be the cause of up to 35% of hospital readmissions. In a prospective study of community-dwelling elders, those with post-hospital medication discrepancies had higher 30-day readmission rates compared to those without medication discrepancies (14.3% vs 6.1%, $p = 0.04$).[3] Several medication-related factors have been associated with increased risk of hospitalization including the use of traditional "high-risk" medications (i.e. warfarin, insulin, oral hypoglycemic agents, and sedatives), medication count, and potentially inappropriate medications in elderly individuals.[4–7]

In recent years, there has been interest in defining the "high-risk" medication regimen and understanding how the complexity of a medication regimen may affect various patient outcomes including hospital readmissions. The medication regimen complexity index (MRCI) is a tool developed and validated to measure the complexity of a medication list. The MRCI been shown to have good inter-rater and test-retest reliability and provides a weighted complexity score based on individual component scores for dosage form (Section A), dosing frequency (Section B), and additional directions required for administration (Section C). It is an open-index tool in which higher scores indicate greater regimen complexity. In Section A, higher weights are assigned for medications with less convenient or more difficult to administer dosage forms (e.g. an oral tablet receives 1 point while a metered-dose inhaler receives 4 points). In Section B, medications administered more frequently or at more strict time intervals receive more points (e.g. "twice daily" receives 2 points, while "every 12 h" receives 2.5 points). Finally, in Section C, further points are assigned if the medication regimen indicates any additional instructions such as "break/crush tablet" (1 point) or "taper dose as directed" (2 points).[8]

Studies analyzing MRCI score and readmission have utilized varying methodologies, populations, and outcomes and offer somewhat conflicting findings. While some studies have shown MRCI to have predictive validity with regard to re-hospitalization or acute care utilization (ACU), other studies have shown no significant relationship.[9–12] Therefore, a large study encompassing a wide patient demographic with varying discharge dispositions and index diagnoses was necessary to better understand the impact of MRCI on these outcomes.

The primary objective of this study was to determine the association of MRCI with increased risk of 30-day, all-cause hospital readmission, in patients with index admission for HF, AMI, PNA, or COPD. Secondary objectives were to (1) determine whether medication regimen complexity is associated with increased risk of all-cause, 30-day ACU defined as a composite of readmission, emergency department (ED) visit, or outpatient observation stay and (2) identify demographic, admission, and/or medication-related covariates that are associated with readmission and/or ACU.

Methods

Design and sample

This study was a retrospective chart review that utilized a parallel-group, case–control design. A custom query was completed via Sharp Healthcare's electronic data warehouse to identify study subjects admitted between 1 August 2012 and 1 August 2014 with an index visit for HF, AMI, PNA, or COPD. Block randomization was employed to achieve equal number of subjects by admission diagnosis and study site. Subjects with an all-cause 30-day readmission (inpatient stay) or ACU (inpatient stay, ED visit, or observation stay) were compared to subjects without 30-day readmission or ACU. The study was approved by the Sharp Healthcare institutional review board.

Inclusion and exclusion criteria

Patients were eligible for inclusion if they were 18 years old or older and admitted to one of three study sites with a primary index diagnosis of HF, AMI, PNA, or COPD. *International Classification of Diseases*, 9th Revision (ICD-9) codes corresponding to these disease states were used to identify primary diagnoses. The three study facilities were Sharp Chula Vista Medical Center (SCV), Sharp Grossmont Hospital (SGH), and Sharp Memorial Hospital (SMH), acute care, community hospitals that are part of an integrated regional health care system. Patients who expired during the index visit or left against medical advice were excluded from the study. Patients were also excluded if the complete discharge medication list from their index visit could not be accessed from the medical record.

Variables collected

MRCI scores were calculated for all patients based on the discharge medication list from the index admission. The following additional covariates were collected from the electronic medical record: age, gender, race/ethnicity, marital status, payer type, Charlson comorbidity index score, length of stay (LOS) for the index admission, discharge disposition, and medication count. The Charlson index is a method of categorizing comorbidities that can predict mortality. The Deyo[13] variation of the Charlson index was used, which has been adapted for use with ICD-9 diagnoses codes.

MRCI scoring

MRCI scores were calculated using the University of Colorado's electronic MRC Data Capture Tool and accompanying MRCI Additional Instructions document.[14] If guidelines in the MRCI Additional Instructions appeared to contradict those described in the original MRCI tool, scoring was conducted in accordance with the latter. For situations in which no guidance for scoring was found in either the original MRCI scoring tool or MRCI Additional Instructions, additional scoring guidelines were developed by consensus of authors and MRCI scorers.

Inter-rater reliability

To ensure consistency among individual investigators, MRCI scores for a subset of patients were subjected to inter-rater reliability testing. Block randomization was used to identify 30 patients per disease state, per site, for inter-rater reliability testing. Of the total cohort, 360 patients (47%) were randomly selected. Two separate investigators calculated the MRCI scores for this subgroup, and the Krippendorff's alpha was determined for each index diagnosis.

Statistical analysis

Initial power analysis required a minimum of 32 patients per group to determine a statistically significant change in readmission with 90% power. A sample size of 63 patients per admission diagnosis per site was utilized.

Mean and standard deviations were calculated for continuous variables along with frequency and percentages for categorical data. Bivariate analyses were conducted utilizing chi-squared test for nominal or categorical variables and Student's *t*-test for continuous variables. A *p* value of less than 0.05 was considered statistically significant. To identify risk factors for 30-day readmission and ACU, a series of multivariate logistic regression models were built in which the individual contributions of covariates were calculated (odds ratio (OR) and 95% confidence interval (95% CI)). Overall model discriminations were determined by the *c*-statistic.

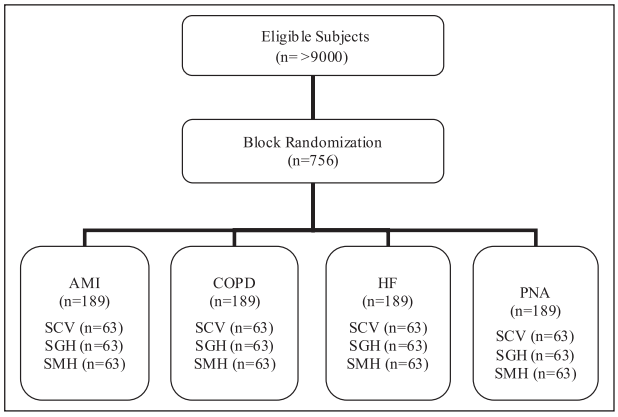

Figure 1. Allocation of subjects.

Results

More than 9000 potentially eligible patients with an index diagnosis of HF, AMI, PNA, or COPD were identified among the study sites. After initial screening, 900 patients meeting inclusion criteria were randomly selected. Following block randomization and application of exclusion criteria, 144 patients (16%) were excluded and 756 patients were identified for MRCI scoring and further analyses. Equal representation of index diagnosis and study site was achieved (Figure 1). Of the 756 patients included in the study, 101 (13%) were readmitted within 30 days of discharge from their index admission. One hundred and sixty-six patients (22%) were found to have ACU within 30 days of discharge.

Bivariate analyses

No statistically significant differences with regard to baseline demographic characteristics were found between those with readmission versus no-readmission, with the exception of Caucasian race (59.4% readmission vs 46.4% no-readmission, $p = 0.02$) and Charlson score (6.0 readmission vs 4.5 no-readmission, $p < 0.01$).

With regard to index admission-related covariates, increased LOS during the index visit (6.32 readmission vs 4.65 no-readmission, $p < 0.01$) as well as discharge to skilled nursing facility (SNF) (18.8% readmission vs 11.8% no-readmission, $p < 0.05$) were associated with an increased risk of 30-day readmission. Those with no 30-day readmission were more likely than their readmitted counterparts to have been discharged to a non-SNF, non-home setting, such as long-term acute care or rehab facility, during their index visit (1.98% readmission vs 8.24% no-readmission, $p = 0.03$) (Table 1).

Medication count was also associated with increased risk of readmission, when examined both as a continuous variable (6.4 readmission vs 6.01 no-readmission, $p < 0.01$) and as a categorical variable with medication count $\geqslant 7$ (93.1%

Table 1. 30-day readmission and acute care utilization demographics and covariates.

	No-readmission ($n=655$)	Readmission ($n=101$)	p value
Demographic			
Age, years			
Mean (±SD)	69.8 (15.3)	69.0 (16.3)	0.64
Male sex, *n* (%)	348 (53.1)	45 (44.6)	0.11
Race/ethnicity, *n* (%)			
Caucasian	304 (46.4)	60 (59.4)	0.02
African American	41 (6.26)	7 (6.93)	0.79
Hispanic	161 (24.6)	19 (18.8)	0.21
Other race	149 (22.8)	15 (14.9)	0.73
Married, *n* (%)	267 (40.8)	40 (39.6)	0.90
Charlson score, mean (±SD)	4.5 (3.1)	6.0 (3.4)	<0.01
Payer type, *n* (%)			
Medicaid	134 (20.5)	21 (20.8)	0.94
Medicare	398 (60.8)	68 (67.3)	0.21
Commercial	92 (14.1)	10 (9.9)	0.26
Other payer	31 (20.5)	2 (1.98)	0.21
Covariates			
LOS, mean (±SD)	4.7 (5.9)	6.3 (6.5)	<0.01
Discharge disposition, *n* (%)			
Home self-care	413 (63.1)	64 (63.4)	0.95
Home health	111 (17)	16 (15.8)	0.78
Skilled nursing	77 (11.8)	19 (18.8)	<0.05
Other facility, non-SNF	54 (8.24)	2 (1.98)	0.03
Medication count, mean (±SD)	11.5 (6.01)	13.6 (6.4)	<0.01
⩾5 Medications, *n* (%)	599 (91.5)	98 (97)	0.05
⩾7 Medications, *n* (%)	522 (79.7)	94 (93.1)	<0.01
⩾10 Medications, *n* (%)	370 (56.5)	70 (69.3)	0.02
MRCI, mean (±SD)	26.3 (16)	30.8 (15.8)	<0.01
	No-ACU ($n=590$)	ACU ($n=166$)	p value
Demographic			
Age, years			
Mean (±SD)	70 (15.3)	68.2 (15.7)	0.18
Male sex, *n* (%)	309 (52.4)	84 (50.6)	0.69
Race/ethnicity, *n* (%)			
Caucasian	271 (45.9)	93 (56)	0.02
African American	39 (6.61)	9 (5.42)	0.57
Hispanic	143 (24.2)	37 (22.3)	0.60
Other race/ethnicity	137 (23.2)	27 (16.3)	0.05
Married, *n* (%)	238 (40.6)	69 (41.6)	0.83
Charlson score, mean (±SD)	4.45 (3.12)	5.45 (3.4)	<0.01
Payer type, *n* (%)			
Medicaid	110 (18.6)	45 (27.1)	0.02
Medicare	367 (62.2)	99 (59.6)	0.55
Commercial	84 (14.2)	18 (10.8)	0.26
Other payer	29 (4.92)	4 (2.41)	0.16
Covariates			
LOS, mean (±SD)	4.65 (6)	5.66 (5.95)	0.05
Discharge disposition, *n* (%)			
Home self-care	372 (63.1)	105 (63.3)	0.96
Home health	98 (16.6)	29 (17.5)	0.79
Skilled nursing	71 (12)	25 (15.1)	0.30
Other facility, non-SNF	49 (8.31)	7 (4.22)	0.08

Table 1. (Continued)

	No-ACU ($n=590$)	ACU ($n=166$)	p value
Medication count, mean (±SD)	11.5 (6.05)	12.7 (6.2)	0.02
⩾5 Medications, *n* (%)	539 (91.4)	158 (95.2)	0.10
⩾7 Medications, *n* (%)	471 (79.8)	145 (87.4)	0.03
⩾10 Medications, *n* (%)	332 (56.3)	108 (65.1)	0.04
MRCI, mean (±SD)	26.5 (15.9)	28.2 (16.4)	0.22

SD: standard deviation; LOS: length of stay; SNF: skilled nursing facility; MRCI: medication regimen complexity index; ACU: acute care utilization.

readmission vs 79.7% no-readmission, $p<0.01$) and ⩾10 (69.3% readmission vs 56.5% no-readmission, $p=0.02$) (Table 1).

Bivariate comparisons for ACU revealed similar results as for readmission, with statistically significant differences in Caucasian race, Charlson score, and medication count. Those with an acute care revisit were more likely to have had Medicaid as a payer during their index visit (27.1% ACU vs 18.6% no-ACU, $p=0.02$) (Table 1).

MRCI scores

Inter-rater reliability testing revealed a high degree of consistency between MRCI raters, with a Krippendorff's alpha of 0.95 or greater for all disease states (Table 5 in Appendix 1). MRCI score was higher in those who were readmitted than those not readmitted within 30 days (30.8 readmission vs 26.3 no-readmission, $p<0.01$); however, no significant difference was observed with regard to mean MRCI score between those with and without ACU (28.2 ACU vs 26.5 no-ACU, $p=0.22$) (Table 1).

When results were stratified with regard to index diagnosis and index site of admission, significant differences were noted between demographic, index admission-related, and medication-related covariates. Significant differences were also noted with regard to 30-day readmission and ACU rates between index site of admission (Tables 6 and 7 in Appendix 1).

Multivariate logistic regression modeling

A number of multivariate logistic regression models for readmission and ACU were examined. Model I utilized the following demographics and covariates: (1) age, (2) gender, (3) race/ethnicity, (4) marital status, (5) payer type, (6) discharge disposition, (7) index diagnosis, (8) LOS, and (9) medication count ⩾10. Moderate discriminative ability was demonstrated for readmission and ACU (Model I: *c*-statistic 0.69 and 0.67). Each subsequent model was developed in sequence as a composite including Model I and Charlson score (Model II), or MRCI (Model III), or Charlson score plus MRCI (Model IV).

The addition of Charlson score to Model I increased discriminative ability for both readmission and ACU, respectively (Model II: *c*-statistic 0.73 and 0.69). The addition of MRCI to Model I slightly increased the discriminative ability for readmission; however, no such effect was seen with ACU (Model III: *c*-statistic 0.70 and 0.67). The addition of both Charlson score and MRCI to Model I resulted in the same discriminative ability for readmission and ACU as the addition of Charlson score alone (Model IV: *c*-statistic 0.73 and 0.69) (Table 2).

Table 2. Stepwise multivariate regression for readmission and acute care utilization.

	Variables	Readmission *c*-statistic	ACU *c*-statistic
Model I	Demographic/covariates[a]	0.69	0.67
Model II	Model I + Charlson	0.73	0.69
Model III	Model I + MRCI	0.70	0.67
Model IV	Model I + Charlson + MRCI	0.73	0.69

MRCI: medication regimen complexity index; ACU: acute care utilization; LOS: length of stay.
[a]Demographics and covariates: age, gender, race/ethnicity, marital status, payer type, site, discharge disposition, index diagnosis, LOS, and medication count ⩾10.

ORs for individual variables in the multivariate models that were found to be significant are shown in Tables 3 and 4 along with their referent categories. When controlling for demographics and other patient covariates, MRCI did not significantly affect the odds of readmission (OR 0.99, 95% CI 0.97–1.01) or ACU (OR 0.99, 95% CI 0.98–1.02). Charlson score and discharge from index site B significantly increased the odds of both readmission and ACU. Female gender increased the odds of readmission, while Medicaid as a payer increased the odds of ACU. Discharge to non-home, non-SNF facility decreased the odds of readmission, and "other race" (non-Caucasian, non-African American, and non-Hispanic) significantly decreased the odds of ACU.

Discussion

A review of MRCI-related literature found four studies prior to this analysis that examined the relationship between MRCI score and readmission. A wide variety of methodologies, patient populations, and outcomes were employed in these studies, and somewhat conflicting results have emerged. A prospective study by Wimmer et al.[9] in patients aged 70 years

Table 3. Multivariate regression significant odds ratios for readmission.[a]

	Odds ratio	95% CI
Model I		
LOS	1.04	(1.01–1.08)
Discharge to other facility, non-SNF	0.21	(0.05–0.91)
Index site B	2.39	(1.31–4.38)
Model II		
Female gender	1.75	(1.07–2.86)
LOS	1.04	(1.001–1.08)
Charlson score	1.17	(1.09–1.26)
Discharge to other facility, non-SNF	0.19	(0.04–0.85)
Index site B	2.56	(1.39–4.74)
Model III		
LOS	1.04	(1.01–1.08)
Discharge to other facility, non-SNF	0.19	(0.04–0.84)
Index site B	2.40	(1.31–4.40)
Model IV		
Female gender	1.75	(1.07–2.85)
LOS	1.04	(1.01–1.08)
Charlson score	1.17	(1.09–1.26)
Discharge to other facility, non-SNF	0.18	(0.04–0.82)
Index site B	2.40	(1.31–4.40)

CI: confidence interval; LOS: length of stay; SNF: skilled nursing facility.
[a]Referent categories: male for gender, site A for index site, and home self-care for discharge disposition.

Table 4. Multivariate regression significant odds ratios for acute care utilization.[a]

	Odds ratio	95% CI
Model I		
Race other	0.50	(0.30–0.85)
Payer Medicaid	2.16	(1.08–4.30)
Index site B	2.54	(1.55–4.17)
Model II		
Race other	0.50	(0.29–0.84)
Charlson score	1.12	(1.06–1.19)
Index site B	2.54	(1.55–4.17)
Model III		
Race other	0.50	(0.29–0.85)
Payer Medicaid	2.16	(1.09–4.30)
Index site B	2.54	(1.55–4.17)
Model IV		
Race other	0.49	(0.29–0.83)
Charlson score	1.12	(1.06–1.18)
Index site B	2.66	(1.61–4.38)

CI: confidence interval.
[a]Referent categories: Caucasian for race/ethnicity, commercial for payer, and site A for index site.

or older found that MRCI score was not associated with unplanned hospital readmissions. Willson et al.[10] conducted a retrospective parallel-group case–control study that found MRCI scores were predictive of re-hospitalizations for adverse drug events (ADEs). In an analysis of medication records from 15 home care agencies, Dierich et al. concluded that high-risk medication regimens were composed of polypharmacy, potentially inappropriate medication use, and medication regimen complexity. In another study focusing on home health, Schoonover et al. looked more broadly at the effects of medication regimen complexity and examined the association between MRCI score and health care utilization. Schoonover et al.[12] concluded that higher MRCI scores increased the odds for a potential ADE and for 30-day hospital readmission; however, higher scores did not significantly elevate the odds for ED use.

To our knowledge, this was the first study to examine the predictive ability of MRCI for all-cause readmission in key high-risk disease states (HF, AMI, PNA, and COPD) that are currently the focus of nation-wide readmission reduction efforts, in a diverse patient population with regard to patient age and discharge disposition. Additionally, few other studies have examined ACU more broadly as opposed to readmission exclusively. A more complete picture of unplanned care is important to examine, and there is concern that efforts to avoid readmission penalties may result in increased utilization of outpatient observation stays in inpatient facilities. A retrospective study of Medicare Part A claims for Rhode Island Medicare beneficiaries from 2009 through 2011 found that ED and inpatient admissions rates decreased, while corresponding observation stay rates increased.[15]

The primary finding of this study was that when controlling for demographics and other patient variables, MRCI does not significantly affect the odds of readmission. Nor does MRCI appear to improve the discriminative ability of prediction models beyond what can be obtained utilizing patient demographics along with basic index admission information and a common measure of comorbidity (Charlson score). This is consistent with the results of a prospective study by Wimmer et al.,[9] which utilized Cox proportional hazards regression to control for similar covariates, and concluded that MRCI was not associated with readmission. Unlike Wimmer et al., however, we did find MRCI to be significantly related to readmission in unadjusted bivariate analyses. Unadjusted MRCI scores in our study were significantly higher in the readmitted subjects than in those not readmitted within 30 days, as was the case in the studies by Willson et al.,[10] Dierich et al.,[11] and Schoonover et al.[12] Nevertheless, given the limited utility of MRCI as a predictor in the context of other covariates, there does not appear to be sufficient evidence for the use of MRCI, in its current form, in all-cause readmission risk prediction. Furthermore, Charlson score appears to be a much stronger readmission predictor in our models and is much more easily calculated than MRCI score.

One possible explanation for why MRCI may not be a useful predictor for readmission when controlling for other variables is that perhaps this tool is missing important measures of complexity that may contribute to readmission risk. While more complex dosage forms, frequencies, and additional administration directions likely increase the risk of non-adherence and medication misadventures such as ADEs, perhaps other factors are more likely to increase this risk sufficiently in order to translate into re-hospitalizations. These factors may include the knowledge and abilities of the individual carrying out the regimen, level of health literacy, as well as clinical comorbidities and high-risk medications with particular comorbidities (e.g. chronic kidney disease). These additional factors may be particularly important to take into consideration in the regimens of patients with the high-risk disease states examined in our study. In the AMI and HF population, for example, patients are very likely to be prescribed high-risk medications known to cause ADEs, such as antithrombotics and diuretics. In PNA and COPD, a lack of understanding or inability to adhere strictly to instructions, for example, inability to complete an antibiotic regimen or demonstrate proper inhaler technique, may contribute significantly to readmissions. Perhaps the creation of a modified regimen complexity index which takes into consideration these additional clinical and patient-specific factors would prove more valuable in readmission prediction.

Interestingly, discharge to other non-SNF facilities (relative to home self-care) appeared to be a protective factor against readmission in our study. Those discharged to non-SNF facilities such as rehab facilities or long-term acute care were much less likely to be readmitted within 30 days than those sent to home with self-care. One possible explanation for this is that some of these patients, particularly those sent to acute long-term care, may have expired during the 30-day period after their discharge.

Another surprising finding was that a significantly higher proportion of readmitted and ACU patients were Caucasian in the bivariate analyses. Some studies have identified socioeconomic factors, such as race/ethnicity, income, and payer status, to be significant predictors in readmission. However, those of minority racial groups have generally been associated with increased risk of readmission. A recent study by Vivo et al. compared 30-day and 1-year re-hospitalization for >47,000 HF patients among racial/ethnic groups. When controlling for clinical, hospital, and other socioeconomic status variables, relative to Caucasians, African Americans and Hispanics had higher 30-day and 1-year readmission rates.[16] In multivariate analyses, "other race/ethnicity" (non-Caucasian, non-African American, and non-Hispanic) appeared to be protective against ACU; however, it is difficult to draw conclusions regarding this finding as greater than 50% of individuals in this group were of unidentified race/ethnicity.

With regard to income and payer status, no significant differences were found with regard to readmission; however, those with a Medicaid payer had significantly higher rates of ACU relative to those with a commercial payer when controlling for other variables.

Limitations

Although this study was limited due to a retrospective design, the authors utilized a large sample size and block randomization to increase the internal validity. Only readmissions and ACU within Sharp Healthcare could be assessed; therefore, the possibility exists that some individuals in the no-readmission and no-ACU groups did indeed readmit/revisit elsewhere. Likewise, the Charlson score may have been underestimated as these scores were calculated based on diagnoses documented only within the Sharp Healthcare network. Inconsistent methods with regard to documentation of prior-to-admission and discharge medications may have affected the accuracy of MRCI scores. However, no significant changes were made to these processes within the health system during the study time period, and it is unlikely that the documentation methods were different between study groups. Additionally, a high inter-rater reliability ensured that MRCI scoring was consistent among disease states and study sites.

Conclusion

The addition of MRCI to a multivariate regression model with more traditional readmission predictors does not appear to improve discriminative ability. Therefore, there is little evidence to support the use of MRCI, in its current format, in all-cause readmission risk prediction. Comorbidity, however, does improve readmission models, which suggests that Charlson score or another validated comorbidity measure should be included when developing readmission risk prediction tools. Significant disease state and study site differences were identified, thus supporting the need for disease-specific and institution-specific identifiers in prediction models.

MRCI may be useful in the prediction of drug-related readmissions, such as those due to ADEs and adherence problems, as opposed to all-cause readmissions. MRCI may also prove useful in long-term or short-term prediction models, such as 7-day or 90-day readmission/ACU. Further research is needed to validate these hypotheses.

Additional studies are also needed to better understand the impact of medication-related predictor variables, such as potentially inappropriate medications[17] in the elderly and high-risk medication use, on readmission and ACU. Finally, the development of a more sensitive tool than the MRCI, perhaps one that incorporates clinical and/or patient-specific factors, may prove useful for capturing an effect of regimen complexity on readmission or ACU.

Acknowledgements

This work was presented as a platform presentation at the Western States Conference in San Diego, CA, 20 May 2015.

Declaration of Conflicting Interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Ethical approval

Ethical approval for this study was obtained from the Sharp HealthCare IRB.

Funding

The author(s) received no financial support for the research, authorship, and/or publication of this article.

Informed consent

Informed consent was not sought for this study because an informed consent waiver was obtained from the Sharp HealthCare IRB.

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Appendix 1

Table 5. MRCI inter-rater reliability by index disease.[a]

	AMI (*n* = 180)	COPD (*n* = 180)	HF (*n* = 180)	PNA (*n* = 180)
Krippendorff's alpha	0.95	0.97	0.98	0.98

AMI: acute myocardial infarction; COPD: chronic obstructive pulmonary disease; HF: heart failure; PNA: pneumonia.

Table 6. Significant differences in covariates between index diagnoses.

	AMI (*n* = 189)	COPD (*n* = 189)	HF (*n* = 189)	PNA (*n* = 189)	*p* value
Age, years					
Mean (±SD)	65.5 (13.4)	71.5 (12.0)	72.4 (15.8)	69.2 (18.4)	<0.01
Male sex, *n* (%)	124 (65.6)	75 (39.7)	102 (53.9)	92 (48.7)	<0.01
Race					
Caucasian	74 (39.2)	110 (58.2)	89 (47.1)	91 (48.2)	0.03
Other	61 (32.3)	35 (18.5)	37 (19.6)	31 (16.4)	<0.01
Married, *n* (%)	97 (51.3)	65 (34.4)	66 (34.9)	79 (41.8)	0.02
Divorced	24 (12.7)	44 (23.2)	28 (14.8)	24 (12.7)	0.013
Married	97 (51.3)	65 (34.4)	66 (34.9)	79 (41.8)	0.002
Widowed	29 (15.3)	47 (24.9)	54 (28.6)	51 (26.9)	0.011
Charlson score, mean (±SD)	3.9 (3.50)	4.7 (2.9)	5.7 (3.1)	4.4 (3.5)	<0.01
MRCI, mean (±SD)	20.7 (16.0)	35.3 (14.4)	25.3 (15.3)	26.3 (16.2)	<0.01
Payer type					
Medicare	88 (46.6)	139 (73.5)	116 (61.4)	123 (65.1)	<0.01
Commercial	55 (29.1)	13 (6.9)	15 (7.9)	19 (10.1)	<0.01
Discharge disposition					
Home health	29 (15.3)	30 (15.9)	44 (23.3)	24 (12.7)	0.039

AMI: acute myocardial infarction; COPD: chronic obstructive pulmonary disease; HF: heart failure; PNA: pneumonia; SD: standard deviation; MRCI: medication regimen complexity index.

Table 7. Significant differences in covariates, readmission, and ACU between index sites.

	Site A (*n* = 252)	Site B (*n* = 252)	Site C (*n* = 252)	*p* value
Age, years				
Mean (±SD)	70.1 (14.7)	67.6 (15.6)	71.3 (15.7)	0.02
Race/ethnicity, *n* (%)				
Caucasian	71 (28.2)	157 (62.3)	136 (53.9)	<0.01
Hispanic	117 (46.4)	23 (9.13)	40 (15.9)	<0.01
Divorced, *n* (%)	32 (12.8)	53 (21.0)	35 (14.1)	0.02
Payer type, *n* (%)				
Commercial	24 (9.52)	29 (11.5)	49 (19.4)	<0.01
LOS, mean (±SD)	5.42 (4.45)	3.71 (3.50)	5.47 (8.60)	<0.01
Discharge disposition, *n* (%)				
Home self-care	160 (63.5)	173 (68.7)	144 (57.1)	0.02
Home health	45 (17.9)	24 (9.52)	58 (23.0)	<0.01
Readmission in 30 days, *n* (%)	22 (8.73)	50 (19.8)	29 (11.5)	<0.01
ACU in 30 days, *n* (%)	40 (15.9)	78 (31.0)	48 (19.1)	<0.01

ACU: acute care utilization; SD: standard deviation; LOS: length of stay.