

Characterization of the medication regimen complexity index in high-utilizer, adult psychiatric patients

Suzanne C. Harris, PharmD, BCPP¹
Stephanie J. Jean, PharmD, MS, BCPS²

How to cite: Harris SC, Jean SJ. Characterization of the medication regimen complexity index in high-utilizer, adult psychiatric patients. *Ment Health Clin* [Internet]. 2020;10(4):207-14. DOI: 10.9740/mhc.2020.07.207.

Abstract

Introduction: Few studies have examined the role of medication-related factors in psychiatric readmissions. Our objective was to characterize the medication regimen complexity index (MRCI) and assess its association with psychiatric hospital readmission frequency and time to readmission in a high-utilizer psychiatric cohort.

Methods: Adult patients admitted between July 2012 and March 2014 were identified if discharged from an inpatient psychiatry service with greater than or equal to 5 psychiatric readmissions or at least one 30-day readmission. Complexity of the medication regimen was determined using a validated MRCI electronic capture tool.

Results: One hundred sixty-eight patients were included. Average MRCI for all readmissions was 7.09 for psychotropic medications, 5.90 for other prescription medications, 2.98 for over the counter, and 16.00 for total medications. Ages greater than 65 years old and female sex were associated with higher total MRCI scores. Average MRCI for psychotropic medications and average psychotropic medication count, along with depression diagnosis, were found to be significantly associated with average time between each readmission but not with readmission frequency. An average total MRCI score greater than 19.7, when broken down by percentiles, was associated with a shorter time to readmission.

Discussion: Psychotropic regimen complexity, psychotropic medication count, total MRCI greater than 19.7, and a diagnosis of depression may contribute to a shorter time to readmission in adult psychiatric patients with a history of frequent readmissions. Future studies are needed to confirm findings and evaluate clinical significance and impact.

Keywords: medication regimen complexity, MRCI, psychotropic drugs, hospital readmission, patient readmission, transition of care

¹ Clinical Assistant Professor, University of North Carolina Eshelman School of Pharmacy, Chapel Hill, North Carolina; Pharmacy Clinical Specialist, University of North Carolina Medical Center, Chapel Hill, North Carolina, ORCID: <https://orcid.org/0000-0002-1751-4732>; ² (Corresponding author) Clinical Manager, University of North Carolina Medical Center, Chapel Hill, North Carolina, stephanie.jean@unchealth.unc.edu, ORCID: <https://orcid.org/0000-0001-8616-1160>

Disclosures: There are no conflicts of interest to disclose.

Introduction

In recent years, decreasing readmission rates has become a priority for US hospitals.¹⁻⁴ Preventable hospital

readmissions have been estimated to cost more than \$12 billion annually, leading the Centers for Medicare and Medicaid Services to incentivize hospitals to focus on decreasing 30-day readmissions in high-risk disease states, including acute myocardial infarction, heart failure, and pneumonia.^{1,2} In 2012, Centers for Medicare and Medicaid Services began reducing Medicare payments for hospitals with excess readmissions through the Hospital Readmissions Reduction Program, which was created to provide financial incentives to hospitals to reduce readmissions through coordinating transitions of care and improving the quality of patient care.¹ The implementation of these strategies has led to increased



research focusing on measuring the impact that they have on reducing readmissions.

Although several studies have researched the prevention of readmissions for various medical diagnoses, there is little that exists in regards to psychiatric readmissions and even less on the role that medication-related factors may play in the readmissions of psychiatric patients. It has been shown that medication nonadherence is a modifiable risk factor for rehospitalization risk in the severely mentally ill population with 50% becoming nonadherent in the first month following discharge.^{3,5} Medication-related factors, such as number and type of psychotropic medications at discharge, medication changes made within 48 hours of discharge, and the number of medications dispensed without a documented follow-up plan, has been associated with increased hospitalization risk, leading to an interest in understanding how the complexity of a medication regimen may affect patient outcomes, including readmissions.^{3,6} Increasing medication regimen complexity has been found to be directly associated with nonadherence, but the characterization of medication regimen complexity in psychiatric patients has not been extensively investigated.^{4,7}

The medication regimen complexity index (MRCI) is a validated 65-item tool for quantifying drug regimen complexity based on the quantity of medications, dosage form, dosage frequency, and additional or special instructions.^{2,8,9,10} Higher weights are assigned for factors such as dosage forms with less convenient administration, strict time intervals, and additional instructions such as *break/crush tablet*. The MRCI considers disease-specific prescription medications, other prescription medications, and over-the-counter (OTC) medications, and a higher MRCI score indicates higher complexity.

Defining MRCI cutoffs to categorize medication complexity may be dependent upon the studied population, based on previous MRCI studies.^{4,8,10-12} Studies have been conducted in diverse populations, and there are no consistent cutoffs that define low and high complexity in the general population. For instance, 1 study⁸ that evaluated the MRCI in defined populations with chronic disease (geriatric depression, human immunodeficiency virus, diabetes mellitus, and hypertension) found that the MRCI values for meeting complexity thresholds for high and low MRCI scores differed between disease-specific cohorts. For example, low-complexity geriatric depression had a mean of 13 compared with low-complexity hypertension, which had a mean of 7. High-complexity geriatric depression had a mean of 41 compared with high-complexity hypertension, which had a mean of 30.⁸ Additionally, impact of MRCI cutoffs on readmissions were either not reported or findings were not conclusive, limiting associations related to MRCI scores and readmis-

sion risk.^{4,8,10-12} To our knowledge, only 1 study⁴ has looked specifically at utilizing MRCI in psychiatric patients and found average MRCI scores of 17.62 and 19.36. The study focused on adults age 65 years or older with depression and, therefore, did not represent a nonelderly psychiatric population.

Our study sought to utilize the MRCI tool to characterize regimen complexity in a high-utilizer psychiatric cohort specific to a large academic medical center that serves as the second largest of 4 inpatient psychiatric facilities in the surrounding area of the study state. Our aim is to better elucidate the MRCI scores that are common in this cohort and how they are related to readmissions. Study findings may aid in informing avenues for future research and the development of targeted clinical pharmacy interventions to reduce medication complexity and with the hope to reduce the risk for readmissions.

Methods

Study Design

This study was a single-site, retrospective study approved by the University of North Carolina's Institutional Review Board. Patients admitted between July 2012 and March 2014 were included if they were age 18 years or older and were identified as a high-utilizer of inpatient psychiatric services, defined as having been discharged from an adult inpatient psychiatry service with greater than or equal to 5 psychiatric readmissions or at least one 30-day psychiatric readmission in this time frame. This criteria was selected based on previous literature defining high utilization of psychiatric patients as well as the study institution's utilization data provided from the institution's quality management team.¹³ Patients were excluded if they were younger than 18 years of age and/or were discharged from and readmitted to facilities other than the institution's psychiatric services.

Patient data was collected through the electronic hospital and pharmacy databases and the electronic medical record system. Demographics, number of readmissions, and number and type of medications for each hospital discharge and readmission were collected. Dosage form, frequency of dosing, and additional usage directions for each medication on each discharge were collected from the electronic pharmacy database to determine the complexity of the medication regimen, which was computed using the 65-item validated Microsoft Access version 1.0 (Redmond, WA) medication regimen complexity electronic data capture tool by the University of Colorado Skaggs School of Pharmacy and Pharmaceutical Sciences. The tool used for coding is publically available online.⁸

For each hospital discharge, an MRCI was computed for 3 separate medication categories (psychotropic medications, other prescription medications, OTC medications) based on the discharge medication list. Any medication that had been prescribed for a psychiatric indication or side effect, regardless of Food and Drug Administration-approved indication (eg, propranolol for akathisia), was categorized as a psychotropic medication. The 3 scores were then combined to calculate the total MRCI score for that discharge. An average total MRCI score was computed for each patient by averaging the total MRCI scores from each discharge, and an average MRCI score for each of the 3 medication categories was also computed by averaging the MRCI scores for each medication category from each discharge.

The medication count for each of the 3 medication categories at first discharge and the total medication count at first discharge were recorded. The average total medication count for each patient and the average medication count for each medication category were also computed and recorded. To determine the time to readmission, the number of days between first hospital discharge and first hospital readmission was calculated for each patient, and the average time to readmission for each patient was determined by averaging the number of days between each hospital discharge and readmission. The number of hospital readmissions was totaled for each patient to determine the patient's readmission frequency.

Data Analysis

Data was recorded without patient identifiers, and confidentiality was maintained. Descriptive statistics were utilized to analyze baseline characteristics. Student *t* test and ANOVA were used for comparing means, and Pearson's correlation was utilized to calculate correlations using statistical software Stata, version 16.0 (College Station, TX).

Results

A total of 174 patients were identified, and 168 patients were included in data analysis. Six patients were excluded due to not fully meeting inclusion criteria. Table 1 provides demographic information. The mean age was 41.3 years (range 18 to 94), and the majority were female (56%) and unemployed (51%). All patients had only 1 primary diagnosis recorded, and the average number of comorbid psychiatric diagnoses per person was 0.69 (range 0 to 3). Length of stay ranged from 2 to 84 days, and time between readmissions ranged from 1 to 504 days. Total number of readmissions ranged from 2 to 9. Ninety percent had psychiatric readmissions within 30 days. Eight percent had both 5 or more psychiatric admissions and

readmissions within 30 days, and 2% had 5 or more psychiatric admissions only.

MRCI Score and Readmission Risk by Demographics

There were some demographics with significant differences in MRCI (Table 2). Specifically, age 65 years or older and female sex were associated with a higher average MRCI ($P=.0001$, $P=.0032$, respectively). A diagnosis of schizophrenia was found to be associated with a lower average MRCI ($P=.046$). When evaluating readmissions, those with major depressive disorder had a shorter time to readmission (18 days) compared to other diagnoses (31 to 67 days; $P=.0185$). No demographic variables were associated with readmission frequency.

MRCI Score: Psychotropic Medications

The MRCI scores for psychotropic medications are in Table 3. At first hospital discharge, the MRCI for psychotropic medications was unrelated to the days between first discharge and first readmission. However, the average MRCI for psychotropic medications for all readmissions was 7.09 and was significantly associated with time between each readmission ($P=.044$). There was no significant association between the average MRCI for psychotropic medications and readmission frequency (Table 3).

MRCI Score: Other Prescription Medications

The MRCI scores for other prescription medications are in Table 3. For this category, no significant associations were found between the MRCI at first hospital discharge and time to first readmission. Similarly, the average MRCI for other prescription medications was unrelated to time to each readmission or readmission frequency.

MRCI Score: OTC Medications

The MRCI scores for OTC medications are in Table 3. No significant association was found between the MRCI at first hospital discharge for OTC medications and time to first readmission. However, a significant association was found between the average MRCI for OTC medications and readmission frequency ($P=.029$) but no significant association with the time between each readmission.

MRCI Score: Total

The total MRCI scores are in Table 3. For this category, no significant associations were found between the total MRCI at first hospital discharge and time to first

TABLE 1: Baseline characteristics of patient population

Patient Characteristic	No. (%)
Sex	
Male	74 (44)
Female	94 (56)
Race	
White	109 (65)
African American	42 (25)
Asian	4 (2)
Other	13 (8)
Age, y	
<25	30 (18)
25-44	71 (42)
45-64	57 (34)
>65	10 (6)
Employment	
Employed	25 (15)
Unemployed	86 (51)
Unknown	55 (33)
Insurance	
Medicaid/Medicare	17 (11)
Private	14 (9)
Unknown	132 (80)
Primary and comorbid diagnoses	
Bipolar	31 (19)
Depressive disorder	52 (31)
Unspecified depressive disorder or unspecified bipolar disorder	29 (17)
Schizophrenia	23 (14)
Schizoaffective disorders	24 (14)
Substance-related disorders	25 (15)
Other	55 (33)
High-utilizer criteria	
Psychiatric readmission within 30 d	152 (90)
≥5 Psychiatric readmissions only	3 (2)
≥5 Psychiatric readmissions and psychiatric readmissions within 30 d	13 (8)
Length of stay, d	
0-4	125 (25)
5-9	206 (41)
10-14	79 (16)
15-19	29 (6)
20 or more	57 (11)
Time between readmissions, d	
0-5	68 (20)
6-10	50 (15)
11-15	41 (12)
16-20	23 (7)
21-25	29 (9)
26-30	9 (3)

TABLE 1: Baseline characteristics of patient population (continued)

Patient Characteristic	No. (%)
31-60	29 (9)
61-90	26 (8)
91-120	17 (5)
>120	45 (13)
No. of psychiatric readmissions	
2	86 (51)
3	45 (27)
4	21 (13)
5	12 (7)
6	5 (3)
7	1 (1)
8	0 (0)
9	1 (1)

readmission. Similarly, the average total MRCI was unrelated to time to each readmission or readmission frequency. However, a significant association was found when the average total MRCI scores were split into percentiles. The mean MRCI ranged from 6.21 for the 25th percentile to 20.06 for the 99th percentile. An MRCI in the highest (99th) percentile (range 19.8 to 55.2) was associated with shorter times to readmission compared to the 25th, 50th, and 75th percentiles (14 days vs 59, 33, and 33 days, respectively, $P=.026$).

Medication Count

The medication counts for all MRCI categories are in Table 4. The average total medication count at first discharge was 5.76, and the average medication count for all readmissions was 5.83. Of all the MRCI medication categories, there was a significant association between the average psychotropic medication count (2.66) for all readmissions and the average time to readmission ($r=.18$, $P=.019$). The top 3 psychotropic medication classes prescribed at discharge were sedative hypnotics ($n=80$, 25%), antipsychotics ($n=324$, 24%), and antidepressants ($n=283$, 22%). No other significant associations to readmission were found for medication counts for other categories.

Discussion

To our knowledge, this is the first study to assess MRCI scores and their association to readmissions in a sample of adult, high-utilizer psychiatric patients. A previous study¹³ in psychiatric patients defined high utilizers based on service utilization, such as 6 visits in 1 year or 4 visits within 1 quarter. To date, there are limited studies that

TABLE 2: Medication regimen complexity index (MRCI) and associations to readmission by demographic data

Patient Characteristic	MRCI Average	Time to Readmission, d	Readmission Frequency, N
Age, y			
<25	12.59	28.28	2.79
25-44	13.61	41.56	3.00
45-64	20.01	34.07	2.93
>65	23.75	22.22	2.78
<i>P</i> value	.0001	NS	NS
Sex			
Female	17.81	35.77	2.94
Male	13.88	35.97	2.92
<i>P</i> value	.0032	NS	NS
Race			
White	16.98	33.67	2.97
African American	15.26	52.02	3.05
Asian	8.98	27.25	2.50
Other	13.26	6.44	2.44
<i>P</i> value	NS	NS	NS
Length of stay, d			
0-4	13.34	39.43	2.84
5-9	17.91	34.68	3.01
10-14	18.81	28.66	3.03
15-19	10.96	8.75	2.38
20 or more	16.31	55.83	2.66
<i>P</i> value	NS	NS	NS
Employment			
Employed	15.55	26.08	2.92
Unemployed	14.07	29.26	2.91
Unknown	19.36	50.92	2.96
<i>P</i> value	NS	NS	NS
Insurance			
Medicare/Medicaid	16.95	28.88	3.12
Private	14.12	46.43	3.07
Uninsured	15.26	35.95	2.87
<i>P</i> value	NS	NS	NS
Diagnosis			
Bipolar disorder	20.11	48.58	3
Depressive disorder	14.92	18.78	2.76
Unspecified depressive or bipolar	16.22	67.24	3.21
Schizophrenia	12.75	31.13	2.95
Schizoaffective disorders	13.88	44.41	3.29
Substance-related disorders	13.90	52.11	3.11
Other	13.26
<i>P</i> value	.046	.0185	NS
Percentiles (range)			
25	6.21 (0-8.8)	59.51	3.16
50	11.81 (8.9-14.3)	33.15	3.02
75	16.73 (14.4-19.7)	33.21	3.00
99	20.06 (19.8-55.2)	14.62	2.45
<i>P</i> value	.001	.026	NS

NS = not significant.

TABLE 3: Correlation data for medication regimen complexity index (MRCI)^a

Variable	MRCI (range)	Days Between First Discharge and First Readmission	Average Days Between Each Readmission	Readmission Frequency
MRCI at first discharge				
Psychotropic	6.86 (0-19)	$r = .065$ $P = .40$
Other prescription	6.01 (0-46)	$r = -.00028$ $P = 1.00$
Over the counter	2.53 (0-19.5)	$r = -.047$ $P = .54$
Total	15.36 (0-62.5)	$r = .0054$ $P = .94$
Average MRCI (all readmissions)				
Psychotropic	7.09 (0-17.5)	...	$r = .16$ $P = .044$	$r = .11$ $P = .16$
Other prescription	5.90 (0-38.25)	...	$r = -.03$ $P = .70$	$r = .049$ $P = .53$
Over the counter	2.98 (0-18.9)	...	$r = .059$ $P = .44$	$r = .17$ $P = .029$
Total	16.00 (0-57.75)	...	$r = .064$ $P = .41$	$r = .14$ $P = .07$

^aBoldface indicates statistical significance $P < .05$.

have investigated the MRCI in psychiatric patient populations outside of those greater than 65 years of age and with depression.⁴ The findings of our study can inform future research on this topic in psychiatric adult patients age 18 years or older with a variety of psychiatric diagnoses and frequent psychiatric readmissions.

In comparison to the 1 published study⁴ in psychiatry patients that reported average MRCI scores of 17.62 and 19.36 for geriatric patients, our study found a lower total average MRCI score of 16.00. This could be explained by our patient sample not being limited to geriatric patients, who tend to have a higher number of chronic medica-

TABLE 4: Correlation data for medication count^a

Variable	Average Medication Count (range)	Days Between First Discharge and First Readmission	Average Days Between Each Readmission	Readmission Frequency
Medication count at first discharge				
Psychotropic	2.63 (0-8)	$r = .096$ $P = .22$
Other prescription	2.14 (0-15)	$r = -.0092$ $P = .91$
Over the counter	0.99 (0-8)	$r = -.041$ $P = .60$
Total	5.76 (0-22)	$r = .063$ $P = .42$
Average medication count (all readmissions)				
Psychotropic	2.66 (0-6)	...	$r = .18$ $P = .019$	$r = .11$ $P = .17$
Other prescription	2.07 (0-12.67)	...	$r = -.04$ $P = .61$	$r = .05$ $P = .52$
Over the counter	1.09 (0-6.67)	...	$r = .036$ $P = .64$	$r = .14$ $P = .063$
Total	5.83 (0-18)	...	$r = .052$ $P = .50$	$r = .13$ $P = .091$

^aBoldface indicates statistical significance $P < .05$.

tions. To our knowledge, this is the first study to report on MRCI percentiles and impact on readmission in psychiatric patients, indicating MRCI scores greater than 19.7 may result in a shorter time to readmission. Additional studies should be conducted in psychiatric patients to expand on our findings to better define high- or low-complexity scores and relation to readmissions for this unique population.

Other findings also suggest that patient characteristics, specifically age and sex, significantly impact MRCI and readmissions and that specific MRCI categories impact readmissions. Although one may suspect that the complexity of a patient's entire medication regimen and the total medication count would contribute to a shorter time to readmission, this study found that it was only the complexity of the psychotropic medication regimen and psychotropic medication count that impacted the time to readmission, specifically in those who had more than 1 readmission. Therefore, findings suggest that, in addition to MRCI scores greater than 19.7, using average psychotropic medication count, average psychotropic MRCI, and depression diagnosis in the risk stratification for readmissions may be warranted. Although these findings should not undervalue the importance of reviewing the entire medication regimen as a whole, for psychiatric patients with frequent readmissions, a more targeted focus on these factors at discharge may have more influence on time to subsequent readmission. Last, ensuring a thorough medication review on OTC medications as an additional factor is important in the holistic care of patients, considering OTC regimen complexity was associated with higher readmission frequency.

It should be noted that there may be barriers to implementing the MRCI tool in practice. In this study, the MRCI score for each patient was hand-coded by 1 investigator using the Microsoft Access database. This process can be time-consuming and prone to human error. Automated coding in a patient's electronic medical record is more clinically relevant and practical in the inpatient practice setting as incorporating an automated algorithm into the electronic medical record reduces individual coding error and would allow for quick and efficient identification of high-risk patients.^{4,13-15} By implementing a tool such as the MRCI in the electronic medical record, members of the care team may be able to use it as an additional factor to more easily identify patients who would benefit from increased attention and targeted services throughout transitions of care. It is important to note, additional services can address complex medication regimens and also improve overall transitions of care and include obtaining medication histories, performing medication reconciliation, discharge medication reconciliation review and medication education, postdischarge calls, and hospital follow-up visits. The impact of these interven-

tions, including proposed benefits of MRCI implementation, warrants further study.

There are several limitations to this study. First, the MRCI tool was created on the basis that multiple and unique dosage formulations, dosing frequencies, and additional instructions likely complicate a patient's ability to maintain appropriate and consistent medication administration practices. However, for psychiatric patients, the demands of maintaining medication adherence may be further complicated by other factors, such as unstable mental capacity and social stigma surrounding psychiatric diagnoses.³ Future studies should evaluate the impact of multiple factors on adherence. Additionally, the definition of a high-utilizer cohort for this study may have skewed the interpretation of the results. Although only a small percentage had 5 or more admissions, 78% of the patients did have 2 to 3 psychiatric admissions. Results may not be generalizable to broader psychiatric populations based on the nonrandomized patient sample from a single institution.

Despite the limitations noted, the study findings provide insight into patient-specific and medication complexity factors of psychiatric patients who utilize services frequently and highlight factors that are most associated with lengthening time to subsequent readmissions. This study reflects a preliminary step in the investigation of this topic, necessitating future studies in a broader psychiatric population to expand on these findings and gain a more comprehensive understanding of the significance of MRCI. Assessing the relationship of severity of illness and medication complexity on adherence and readmissions should also be explored. In addition, evaluation of the use of an automated MRCI tool to help identify patients for targeted transitions of care services to decrease medication complexity in high utilizers could be helpful.

Conclusion

In a sample of psychiatric patients with a history of frequent readmissions, age and sex were associated with higher MRCI scores. Psychotropic regimen complexity, psychotropic medication count, total MRCI greater than 19.7, and having depression contributed to a shorter time to readmission. More research is needed to confirm our findings and determine the clinical significance of the MRCI score and the impact of targeted services on MRCI at discharge.

Acknowledgments

The authors acknowledge Ina Liu and Alyson Aldridge for their assistance and support with data collection for this research.

References

1. Readmissions Reduction Program (HRRP). Centers for Medicare and Medicaid Services [cited 2017 Mar 2]. Available from: <https://www.cms.gov/Medicare/Medicare-Fee-for-Service-Payment/AcuteInpatientPPS/Readmissions-Reduction-Program.html>
2. Abou-Karam N, Bradford C, Lor KB, Barnett M, Ha M, Rizos A. Medication regimen complexity and readmissions after hospitalization for heart failure, acute myocardial infarction, pneumonia, and chronic obstructive pulmonary disease. *Sage Open Med*. 2016;4:2050312116632426. DOI: [10.1177/2050312116632426](https://doi.org/10.1177/2050312116632426). PubMed PMID: [26985392](https://pubmed.ncbi.nlm.nih.gov/26985392/).
3. Tomko JR, Ahmed N, Mukherjee K, Roma RS, Dilucente D, Orchowski K. Evaluation of a discharge medication service on an acute psychiatric unit. *Hosp Pharm*. 2013;48(4):314-20. DOI: [10.1310/hpj4804-314.test](https://doi.org/10.1310/hpj4804-314.test). PubMed PMID: [24421481](https://pubmed.ncbi.nlm.nih.gov/24421481/).
4. Linnebur SA, Vande Griend JP, Metz KR, Hosokawa PW, Hirsch JD, Libby AM. Patient-level medication regimen complexity in older adults with depression. *Clin Ther*. 2014;36(11):1538-46.e1. DOI: [10.1016/j.clinthera.2014.10.004](https://doi.org/10.1016/j.clinthera.2014.10.004). PubMed PMID: [25456562](https://pubmed.ncbi.nlm.nih.gov/25456562/).
5. Barnett BS, Kusunzi V, Magola L, Borba CPC, Udedi M, Kulisewa K, et al. Risk factors for readmission among a cohort of psychiatric inpatients in Lilongwe, Malawi. *Int J Psychiatry Clin Pract*. 2020;24(1):25-30. DOI: [10.1080/13651501.2019.1699116](https://doi.org/10.1080/13651501.2019.1699116). PubMed PMID: [31799886](https://pubmed.ncbi.nlm.nih.gov/31799886/).
6. Rylander M, Colon-Sanchez D, Keniston A, Hamalian G, Lozano A, Nussbaum AM. Risk factors for readmission on an adult inpatient psychiatric unit. *Qual Manag Health Care*. 2016;25(1):22-31. DOI: [10.1097/QMH.000000000000077](https://doi.org/10.1097/QMH.000000000000077). PubMed PMID: [26783864](https://pubmed.ncbi.nlm.nih.gov/26783864/).
7. Manzano-García M, Pérez-Guerrero C, Álvarez de Sotomayor Paz M, de Las Aguas Robustillo-Cortés M, Almeida-González CV, Morillo-Verdugo R. Identification of the medication regimen complexity index as an associated factor of nonadherence to antiretroviral treatment in HIV positive patients. *Ann Pharmacother*. 2018;52(9):862-7. DOI: [10.1177/1060028018766908](https://doi.org/10.1177/1060028018766908). PubMed PMID: [29592537](https://pubmed.ncbi.nlm.nih.gov/29592537/).
8. Libby AM, Fish DN, Hosokawa PW, Linnebur SA, Metz KR, Nair KV, et al. Patient-level medication regimen complexity across populations with chronic disease. *Clin Ther*. 2013;35(4):385-98.e1. DOI: [10.1016/j.clinthera.2013.02.019](https://doi.org/10.1016/j.clinthera.2013.02.019). PubMed PMID: [23541707](https://pubmed.ncbi.nlm.nih.gov/23541707/).
9. Hirsch JD, Metz KR, Hosokawa PW, Libby AM. Validation of a patient-level medication regimen complexity index as a possible tool to identify patients for medication therapy management intervention. *Pharmacotherapy*. 2014;34(8):826-35. DOI: [10.1002/phar.1452](https://doi.org/10.1002/phar.1452). PubMed PMID: [24947636](https://pubmed.ncbi.nlm.nih.gov/24947636/).
10. Rettig SM, Wood Y, Hirsch JD. Medication regimen complexity in patients with uncontrolled hypertension and/or diabetes. *J Am Pharm Assoc* (2003). 2013;53(4):427-31. DOI: [10.1331/JAPhA.2013.13003](https://doi.org/10.1331/JAPhA.2013.13003). PubMed PMID: [23892818](https://pubmed.ncbi.nlm.nih.gov/23892818/).
11. Ferreira JM, Galato D, Melo AC. Medication regimen complexity in adults and the elderly in a primary healthcare setting: determination of high and low complexities. *Pharm Pract (Granada)*. 2015;13(4):659. DOI: [10.18549/PharmPract.2015.04.659](https://doi.org/10.18549/PharmPract.2015.04.659). PubMed PMID: [26759621](https://pubmed.ncbi.nlm.nih.gov/26759621/).
12. Alves-Conceição V, Rocha KSS, Silva FVN, Silva ROS, Cerqueira-Santos S, Nunes MAP, et al. Are clinical outcomes associated with medication regimen complexity? A systematic review and meta-analysis. *Ann Pharmacother*. 2020;54(4):301-313. DOI: [10.1177/1060028019886846](https://doi.org/10.1177/1060028019886846). PubMed PMID: [31718244](https://pubmed.ncbi.nlm.nih.gov/31718244/).
13. Pasic J, Russo J, Roy-Byrne P. High utilizers of psychiatric emergency services. *Psychiatr Serv*. 2005;56(6):678-84. DOI: [10.1176/appi.ps.56.6.678](https://doi.org/10.1176/appi.ps.56.6.678). PubMed PMID: [15939943](https://pubmed.ncbi.nlm.nih.gov/15939943/).
14. McDonald MV, Peng TR, Sridharan S, Foust JB, Kogan P, Pezzin LE, et al. Automating the medication regimen complexity index. *J Am Med Informatics Assoc*. 2012;20(3):499-505. DOI: [10.1136/amiajnl-2012-001272](https://doi.org/10.1136/amiajnl-2012-001272). PubMed PMID: [23268486](https://pubmed.ncbi.nlm.nih.gov/23268486/); PubMed Central PMCID: [PMC3628060](https://pubmed.ncbi.nlm.nih.gov/PMC3628060/).
15. McDonald MV, Feldman PH, Barrón-Vayá Y, Peng TR, Sridharan S, Pezzin LE. Outcomes of clinical decision support (CDS) and correlates of CDS use for home care patients with high medication regimen complexity: a randomized trial. *J Eval Clin Pract*. 2016;22(1):10-9. DOI: [10.1111/jep.12383](https://doi.org/10.1111/jep.12383). PubMed PMID: [26009977](https://pubmed.ncbi.nlm.nih.gov/26009977/).