# **Medication Regimen Complexity in Patients with Comorbid Conditions**

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## Abstract

The Medication Regimen Complexity Index (MRCI) is a tool developed and used in both clinical and research settings to determine the difficulty of an individual's medication process. Each route, dose and frequency is taken into account to determine a score and then it can be used for comparison to see how additional prescriptions may affect the medication dispensing process. An example of complexity might be that a medication taken orally once a day is less complex and less difficult than an inhaler that must be used every 3.5 hours. The second requires more attention to the prescription and is therefore more difficult thus receiving a higher complexity ranking. The purpose of this research study was to determine factors that would be more likely to result in a higher MRCI score. Characteristics taken into account were demographics and comorbidities. The individual comorbidities were also taken and placed into categories dealing with particular body systems (i.e., cardiovascular), which were later compared to the MRCI scores. Each variable was taken into consideration and compared to the MRCI scores using various statistical tests such as Mann-Whitney U and bivariate correlations. The data for this study were collected from a sample size of 310 participants who were enrolled in a parent study observing effects of establishing routines on medication adherence and assess how various personality traits and cognitive function abilities affected the complex medication process. The participants were adults, diagnosed with Type 2 Diabetes Mellitus in addition to hypertension and/or hyperlipidemia, who completed questionnaires for demographics, medication regimen, and their self-reported diagnosed comorbidities. MRCI scores were calculated from participants' medication regimen data. Data to fit the intended research question were available for 146 participants. The sample was mostly white (68%) and female (58%). The average age was 62 years old with a range of 40 to 94 years old. MRCI total scores ranged from 4.0-68.5 with an average of 18.12 (SD=8.75). Age and gender were not associated with MRCI score. However, individual comorbidities yielded significant results using a Mann-Whitney U test, including neuropathy (p=0.001), blood and circulatory disorders (p=0.008), and heart conditions (p=0.016). In a combined comparison, the systems that resulted in significant relationships were neurological conditions (p=0.004), gastrointestinal conditions (p=0.019) and respiratory conditions (p=0.031). Overall, the results showed that there was a strong positive correlation (Spearman's Rho=0.848; p=.000) between the number of medications and MRCI score, which is consistent with the original MRCI findings. As one might expect, certain comorbidities showed increased medication regimen complexity. Additional research is needed to determine the effects of these relationships on the patients.

#### Keywords: Regimen, Comorbidities, Medication

# **1. Introduction**

According to the Centers for Disease Control and Prevention (CDC), approximately 117 million US adults have at least one chronic condition. Of those, an estimated 60 million reported more than one chronic coexisting (comorbid) condition. <sup>6</sup> Many of these conditions exacerbate one another and/or occur in tandem, and some share similar or the same underlying causes. The more comorbid conditions with which an individual is diagnosed, the greater the

likelihood of additional prescribed medications to treat them. An increase in the number of medications may lead to a more complex treatment regimen for patients to follow and maintain. As regimen complexity increases, the potential for poor medication adherence, such as missed doses or incorrect timing, increases.<sup>2</sup>A first step in minimizing complex medication regimens is to identify and quantify them. The Medication Regimen Complexity Index (MRCI) is a promising tool for this purpose.<sup>6</sup> This is critical to realize because as the incidences of medication complexity increase the leaders of healthcare will need to be prepared in determining ways to minimize complications and ensure patients are able to follow difficult instructions surrounding polypharmacy and its possible effects.

According to the CDC, there are increasing numbers of individuals diagnosed with diseases and furthermore comorbid conditions. In the event of conditions building on one another and occurring simultaneously, it becomes quite difficult for the individual to continue following instructions and medications properly. The more conditions with which an individual is diagnosed, the greater the likelihood of an increase in the number of prescribed medications. This could potentially lead to a more complex structure or regimen that these individuals need to maintain and follow, and ultimately may result in poor medical adherence and further complications, such as missed doses or incorrect timing.

Keeping these problems to a minimum could further be reduced if there were an easier way to identify the potential patients who may have this problem. This is where the Medication Regimen Complexity Index (MRCI) can take effect.

#### 1.1 Medication Regimen Complexity Index

The Medication Regimen Complexity Index was a tool designed to view how certain conditions and disease processes can affect medication complexity, which can be further connected with medication adherence. According to George<sup>1</sup> et al the different measurements of the MRCI can be a predictor of patient outcomes, which is vital in preserving health and wellness. These measurements include dosing route, dosing frequency, number of medications, and special instructions given from the prescribing physician. All of these play a key role in the development of outcomes of patient health.

The work of George<sup>1</sup> and colleagues was done to validate the MRCI as a clinical tool to be used in practice. In their study, the researchers used information from patients and their medical regimen to test the effects of the complexity. The authors concluded that the MRCI was both a reliable and valid tool for determining medication complexity.

# 2. Methodology

In this current study, data were extracted from a parent study, which aimed to observe how establishing routines on medication adherence and how certain personality traits and abilities of the individuals affected the complex medication process. The parent study focused on patients diagnosed with Type 2 Diabetes in conjunction with hypertension and/or hyperlipidemia. After extracting the data, it was compared with various comorbid conditions to determine their individual and combined effects on medication regimen complexity.

The purpose of this study was to determine factors that may contribute to medication regimen complexity, specifically, participant characteristics of race, gender, and age. A further aim was to determine if participants with certain comorbid conditions or groups of conditions had significantly higher MRCI scores than those without the conditions. The group of conditions refers to an entire body system specifically within that one participant and if that individual had multiple conditions within that one category (i.e. multiple respiratory conditions).

After individual conditions were evaluated, each was assigned into a set of closely associated conditions. Condition sets were compared with MRCI scores to determine if overall body system conditions would result in a higher and more complex medication regimen. Significance for all statistical testing was set at 0.05.

#### 2.1 Sample

The sample for the original study consisted of 310 adults diagnosed with Type 2 Diabetes in conjunction with hypertension and/or hyperlipidemia. This study used 146 of those participants who had complete data records. The

majority of participants were white (68%) and female (52%). The average age was 62 years old with a broad range of 40-94 years old.

## 2.2 Data Collection

The subjects for the original study were interviewed and asked to complete paper and pencil questionnaires. One questionnaire aimed to determine the demographics of the population whereas another was aimed at health conditions, including self-reported comorbidities. The participants also reported their medication regimen.

The secondary study used the same collected information and used it in a new set of statistical sets to determine the intended research objective. The main demographics that were extracted were gender, age, and race. Also extracted were the full medication regimens and the reporting of the health conditions for each participant.

Using information that was gathered from questionnaires, the secondary study took the chosen information and used it in a new set of statistical sets to investigate the stated research objectives. Extracted information included the full medication regiment and the self-reported health conditions.

### 2.3 Statistical Tests

Using each of the conditions associated with a participant, different statistical tests were used to determine the significance of each against the individualized MRCI score. Each condition was statistically tested individually, such as neuropathy and thyroid conditions.

After all the separate individual conditions were evaluated, each was then assigned into a set to which they were closely associated. For example, all the singular cardiovascular conditions included heart conditions, peripheral vascular disease, hypertension, hyperlipidemia and blood/circulatory disorder were grouped into a set. Statistical tests determined if any overall body system conditions would result in a higher and more complex medication regimen. The tests used to evaluate these variables to the MRCI scores were the Mann-Whitney U and bivariate correlations. Other tests were used to compare the MRCI scores to the demographics including gender, race and age.

## 3. Data

This sample consisted of 146 adults with complete information on medication regimen and comorbid conditions. Descriptive statistics were used to summarize demographic information (Table 1) and MRCI scores (Table 2). The majority were white (68%) and female (52%). The average age was 62 years old, with a broad range of 40-94 years old. The MRCI scores ranged from 4.0-68.5 (average 18.120 $\pm$ 8.753). Within the additional categories the range of scores for the total number of medications 2-22 (7.38 $\pm$ 3.215), category "A", a subscale quantifying difficulty of various drug administration routes, ranged from 1-11 (2.32 $\pm$ 2.110), category "B", a subscale quantifying dosing frequencies, ranged from 3.0-26.5 (9.668 $\pm$ 4.297) and finally category "C", a quantification of difficulty of special instructions, ranged from 0-32 (6.26 $\pm$ 4.452).

Table 1. Ranges And Averages Among Medication Regimen Complexity Index Scores

Measure	Range of Scores	Average Scores
Total Number of Medications	2-22	7.38±3.215
Total of "A" in MRCI Scoring	1-11	2.32±2.110
(Dosage Forms of Medications)		
Total of "B" in MRCI Scoring	3.0-26.5	9.668±4.297
(Dosing Frequency of Medications)		
Total of "C" in MRCI Scoring	0-32	6.26±4.452
(Special Instructions or		
Considerations)		
Total for MRCI Scores (A+B+C)	4.0-68.5	18.120±8.753

# 4. Results

# 4.1 Demographics

Using the major demographics of gender, race, and age the information was compared with the total MRCI score to determine if any relationship existed. After running the statistical analysis there was no relationship between any of the demographics and the total MRCI score.

# 4.2 Comorbid Conditions

Individual comorbidities were significant using the Mann-Whitney U test with the significance set at 0.05. The conditions that were significant included neuropathy, blood and circulatory disorders and heart conditions.

In the evaluation of the combined comparisons of the body systems significant results included neurological conditions, gastrointestinal conditions and respiratory conditions. Similarly to the individual comparisons, the combined resulted in both significant and insignificant relationships to the MRCI scores.

Comorbidity	Significance Level (p value)
Neuropathy	0.001
Blood and Circulatory Disorders	0.008
Heart Condition	0.010
Neurological (Combined)	0.004
Gastrointestinal (Combined)	0.019
Respiratory (Combined)	0.031

Table 2. Significant Results Among Individual And Combined Conditions

The overall results also proved there was a strong, positive correlation (Spearman's Rho=0.848) between the number of medications and the MRCI score, which is consistent with the original MRCI findings. This is also consistent with prediction of the more medications an individual is prescribed the more complex the regimen becomes.

# 5. Conclusions and Discussion

The findings for participant characteristics indicate that there is no significant relationship between age and medication regimen complexity. Similarly, there is no significant difference in complexity in men and women as well as between whites and nonwhites.

This study found that certain conditions and condition sets are significantly associated with higher medication complexity scores. The MRCI tool could easily be used in the clinical setting to alert providers of highly complex regimens and help identify patients at risk of medication regimens too complex to follow with the normal instructions. Identifying those at risk will assist healthcare providers to spend more preparation time with these patients or perhaps simplifying the regimen, both of which may result in better health outcomes.

One limitation of the study was that the analyses were individually conducted on conditions and condition sets. There may be other variables that may influence medication complexity. For example, a patient with a heart condition may have a cholesterol condition, with complexity influencing both. Further analyses of these data will be helpful. Another limitation is that the data were extracted from existing self-reported data.

As a clinical and research tool the MRCI has been progressively used recently and still continues to be developed and validated. However, more research could be done to not only better establish its indication status but also the outcomes of individuals who have difficult medication regimens and see how this correlates with medication adherence. More research may further help to shed light on the topic to improve the healthcare system as more diseases are being diagnosed in concurrence with others.

The MRCI could potentially be used to facilitate reducing complexity or improving medication adherence. In a study by Corsonello and colleagues<sup>2</sup> it was observed that more complex medication regimens may contribute more

to nonadherence than the actual number of medications that a person is taking. The Corsonello study researched the elderly, who typically struggle with polypharmacy. Subscale C, the special instructions portion of the MRCI, may be helpful in identifying these patients. If there are too many specific and difficult directions to take a medication then the patient may become confused and have a poorer health outcome. Therefore, this subscale C is vital in determining what patients are at a higher risk of not adhering to the medications. With this portion of the MRCI, the healthcare providers can visualize how many instructions have been given for all medications and then make corrective adjustments in the teaching portion. This idea of polypharmacy, or patients on multiple medications, has been identified as a major concern and stumbling block for patients. Muir and associates<sup>3</sup> implemented a visual aid to assist physicians' insight into how patients took their medications. The form they developed was a medication grid containing the drugs and the times they were to be taken. The aim was to see if physicians could understand nonadherence better when serious complexity was involved. The study resulted in providers significantly decreasing the total number of medications and doses when a medication grid was used. An encouraging aspect of this study was that physicians were receptive to focusing on the patients with major medication complexity. Authors determined that the grid was helpful for identifying medication regimen complexity. Therefore, this study supports that identifying complex regimens may effectively lead to a lessening the medication load to further decrease complications.

Coupling with the work of Muir<sup>3</sup>, a study by Witticke and partners<sup>4</sup> showed that certain characteristics of a patient's medication regimen may further complicate it and thus weaken patient outcomes. The main characteristics reported were multiple medications, multiple doses, tablet splitting and dosing intervals, all of which are assessed in the MRCI. Authors concluded that simple modifications could help with this and further stressed more targeted interventions to assist the patient with tackling this medication barrier. Therefore, it may have been useful if physicians would have had a method to see what the patient was already on and then this individual could have had a greater focus to help avoid any negative outcomes. There are many opportunities to decrease complexity but there needs to be a simpler way to determine and actually quantify regimen complexity.

Therefore, the MRCI can be used as a clinical tool to help identify patients at risk of medication regimens that are too complex to follow with the normal instructions. The MRCI is an effective visual tool that can easily be used in clinical settings. According to the work by McDonald and associates<sup>5</sup> who researched automation of the MRCI found that it effectively identifies patients at high risk of adverse events for both research and clinical decision support to improve patient outcomes. Further research is necessary to explore the relationships of comorbidities and combinations of comorbidities on regimen complexity and adherence. Complexity, comorbidities and the patient are pieces of the complex puzzle of medication adherence. Having the provider address complexity with the MRCI may help to shed light on patient challenges and improve care for the millions diagnosed with comorbid conditions.

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