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Research Article

One-Year Evolution of Multi-Morbidity, Polypharmacy, And Medication Regimen Complexity Among Adults with Chronic Conditions Attending Outpatient Care: A Prospective Longitudinal Cohort Study

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Abstract

Background: Multi morbidity is increasingly common in adult outpatient practice and frequently results in the use of multiple medications and increasingly demanding treatment schedules. Although medication count is commonly used to describe polypharmacy, it does not fully capture the complexity of a patient's treatment regimen. Dosage forms, dosing frequency, and additional administration instructions may substantially influence the practical burden of medication use.

Objective: To assess the one-year evolution of multi morbidity, polypharmacy, and medication regimen complexity among adults receiving longitudinal outpatient care.

Methods: A prospective longitudinal cohort study was conducted among adults aged 18 years or older receiving ongoing outpatient care for chronic medical conditions. Participants were assessed at baseline, 6 months, and 12 months. Multi morbidity was defined as the presence of two or more chronic conditions. Polypharmacy was defined as the concurrent use of five or more long-term medications, while hyper-polypharmacy was defined as the use of ten or more medications. Medication regimen complexity was assessed using the Medication Regimen Complexity Index (MRCI).

Results: A total of 1,250 adults were enrolled, and 1,128 (90.2%) completed the 12-month follow-up. The reported prevalence of multi morbidity increased from 54.2% at baseline to 61.8% at 12 months. Polypharmacy increased from 38.4% to 45.6%, while hyper-polypharmacy increased from 11.2% to 15.1%. Mean MRCI increased from 14.2 ± 6.1 at baseline to 18.9 ± 7.4 at 12 months. Longitudinal analysis in the original study summary showed a significant increase in MRCI over follow-up. The relationship between increasing chronic disease burden and regimen complexity was also assessed.

Conclusion: Multi morbidity, polypharmacy, and medication regimen complexity increased over the one-year observation period. The findings support the use of medication regimen complexity measures alongside medication counts when assessing patients with multiple chronic conditions. Regular medication review may help identify opportunities for appropriate treatment simplification and better coordination of outpatient care.

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KEYWORDS: multi morbidity; polypharmacy; hyper-polypharmacy; medication regimen complexity; Medication Regimen Complexity Index; chronic disease; outpatient care; longitudinal

1. INTRODUCTION

The number of adults living with multiple chronic conditions has increased as populations age and survival from chronic diseases improves. Multi morbidity, generally defined as the coexistence of two or more chronic conditions, has become an important challenge for outpatient healthcare because patients often require continuing treatment, monitoring, and coordination across several areas of care [1].

As chronic conditions accumulate, medication use commonly increases. Polypharmacy has no single universally accepted definition, but the use of five or more medications is the most frequently reported numerical threshold in the literature [2]. Importantly, the presence of polypharmacy does not by itself indicate inappropriate prescribing. Several medications may be clinically justified in patients with multiple chronic diseases.

The number of medications, however, does not fully describe the demands placed on patients. A regimen involving several different dosing times, multiple dosage forms, or specific administration instructions may be substantially more difficult to follow than a regimen containing the same number of medicines taken once daily. Treatment burden in multi morbidity extends beyond medication use and may include monitoring, appointments, self-care requirements, financial costs, and the effects of these tasks on daily life [3,4].

The Medication Regimen Complexity Index (MRCI) was developed to provide a standardized measure of medication regimen complexity. It incorporates three major components: dosage form, dosing frequency, and additional administration instructions. The original 65-item instrument demonstrated high reliability and validity in its development study [5]. Subsequent work has supported its use for assessing regimen complexity at the patient level [6].

Medication regimen complexity has been associated with several clinical and treatment-related outcomes, although the strength and direction of these relationships vary between populations [7,8]. A systematic review of MRCI-based studies found associations with a range of clinical, humanistic, and economic outcomes, supporting the relevance of regimen complexity as a distinct aspect of medication management [8].

Despite extensive research on multi morbidity and polypharmacy, fewer studies have followed the same outpatient population longitudinally while examining disease burden, medication burden, and regimen complexity together. Understanding how these factors change during routine care may help clinicians identify patients whose treatment requirements are becoming increasingly difficult to manage.

The present study therefore evaluated the one-year evolution of multi morbidity, polypharmacy, and medication regimen complexity among adults receiving longitudinal outpatient care.

2. METHODS

Study Design and Setting

This was a prospective longitudinal cohort study involving adults receiving continuing outpatient care for chronic medical conditions. Participants were followed for 12 months and assessed at baseline, 6 months, and 12 months. The study period extended from July 2025 to June 2026.

Study Population

Adults aged 18 years or older receiving ongoing outpatient treatment for at least one chronic medical condition were eligible for inclusion. Patients were excluded if they had terminal illness with an expected life expectancy of less than six months, were receiving hospice or end-of-life care, or had cognitive impairment that prevented reliable participation without an appropriate proxy. Participants were followed during routine outpatient care.

Assessment of Multi morbidity

Chronic conditions were identified from documented clinical diagnoses and medical records. For this study, multi morbidity was defined as the presence of two or more chronic conditions. This definition is widely used in multi morbidity research [1]. The number of chronic conditions was recorded at baseline and at subsequent follow-up assessments.

Medication Assessment

Medication information was recorded at each assessment. Long-term medications used for chronic disease management were included in the medication count. Short-term medications prescribed for acute conditions were excluded where applicable. Polypharmacy was operationally defined as the concurrent use of five or more long-term medications. Hyper-polypharmacy was defined as the concurrent use of ten or more medications. The choice of five medications as the polypharmacy threshold was based on its widespread use in the literature, while recognizing that numerical definitions vary substantially between studies [2]. Medication count was used to describe treatment burden and was not interpreted as evidence of inappropriate prescribing.

Medication Regimen Complexity

Medication regimen complexity was assessed using the Medication Regimen Complexity Index. The MRCI is a 65-item instrument consisting of three components:

- **Section A :** dosage form ;
- **Section B :** dosing frequency ; and
- **Section C:** additional administration instructions.

The individual components are combined to produce a total MRCI score, with higher scores representing greater regimen complexity [5]. The MRCI was selected because it captures characteristics of medication regimens that are not reflected by medication count alone [5,6].

Other Clinical Variables

Clinical and demographic variables recorded during the study included age, sex, educational level, and socioeconomic characteristics. Clinical variables included the total number of chronic medical conditions, number of long-term medications, presence of polypharmacy, presence of hyper-polypharmacy, and Medication Regimen Complexity Index (MRCI) score.

Functional status was also assessed, along with the number of treating specialists involved in the patient's ongoing care. These variables were recorded to characterize the study population and to evaluate their potential association with changes in medication regimen complexity during the follow-up period.

Follow-Up

Participants were assessed at three predefined time points:

- **T0:** baseline;
- **T1:** 6 months; and
- **T2:** 12 months.

At each assessment, chronic disease burden and medication regimen were reviewed.

Statistical Analysis

Continuous variables were summarized using mean ±standard deviation or median with interquartile range, depending on distribution. Categorical variables were expressed as frequencies and percentages. Changes in continuous outcomes across follow-up were assessed using repeated-measures statistical methods appropriate to the distribution of the data. Changes in categorical variables were assessed using appropriate paired methods. Longitudinal mixed-effects models were used to evaluate changes in MRCI while accounting for repeated observations within individuals. Potential demographic and clinical predictors of increasing MRCI were evaluated using multivariable modeling. A two-sided p-value <0.05 was considered statistically significant. Statistical analyses were performed using R statistical software.

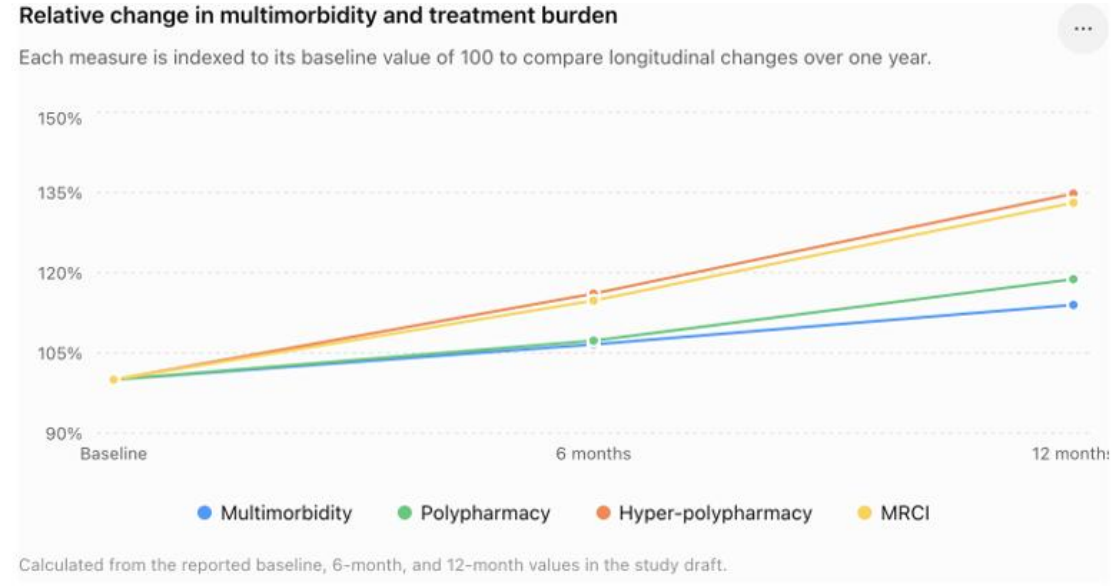

Figure 1. Relative Longitudinal Change in Multi morbidity, Polypharmacy, Hyper-Polypharmacy, and Medication Regimen Complexity Over One Year

3. RESULTS

Participant Characteristics

A total of 1,250 participants were enrolled. Of these, 1,128 participants (90.2%) completed the 12-month follow-up. The mean age of participants was 66.4 ±11.2 years, and 54.8% were female. The mean number of chronic conditions at baseline was 2.8 ±1.4. At baseline, 54.2% of participants met the study definition of multi morbidity, while 38.4% were receiving five or more long-term medications.

Evolution of Multi morbidity and Medication Burden

The study demonstrated a progressive increase in multi-morbidity and medication burden during the observation period. The reported prevalence of multi morbidity increased by 7.6 percentage points between baseline and 12 months. Polypharmacy increased by 7.2 percentage points, while hyper-polypharmacy increased by 3.9 percentage points during the same period. The mean number of chronic conditions increased from 2.8 at baseline to 3.5 at 12 months.

Table 1. Longitudinal changes in multimorbidity, polypharmacy, hyper-polypharmacy, and MRCI

Variable	Baseline	6 months	12 months	P value
Multimorbidity ≥2 conditions	54.2%	57.8%	61.8%	<0.001
Mean chronic condition count	2.8 ± 1.4	3.1 ± 1.5	3.5 ± 1.6	<0.001
Polypharmacy ≥5 medications	38.4%	41.2%	45.6%	<0.001
Hyper-polypharmacy ≥10 medications	11.2%	13.0%	15.1%	<0.001
Mean MRCI	14.2 ± 6.1	16.3 ± 6.8	18.9 ± 7.4	<0.001

Medication Regimen Complexity

Mean MRCI increased progressively during follow-up, from 14.2 ±6.1 at baseline to 16.3 ±6.8 at six months and 18.9 ±7.4 at 12 months. The reported increase in total MRCI was greater than the change in medication count alone, suggesting that changes in dosing frequency and administration requirements contributed to the overall increase in regimen complexity.

Table 2. Changes in MRCI components during one-year follow-up

MRCI component	Reported change over 12 months
Section A – Dosage form	0.8
Section B – Dosing frequency	1.9
Section C – Additional instructions	2.0
Total MRCI	4.7

Predictors of Increasing Regimen Complexity

The longitudinal analysis reported a significant association between time and MRCI. The original analysis reported an estimated increase of 2.35 MRCI points per six-month interval ($p<0.001$). An additional chronic condition was reported to be associated with an estimated 3.21-point increase in MRCI ($p<0.001$). Lower baseline functional independence, female sex, and management by three or more outpatient specialists were reported as additional factors associated with faster increases in regimen complexity.

Table 3. Reported factors associated with increasing MRCI

Factor	Reported association with MRCI	P value
Time, per 6-month interval	+2.35 points	<0.001
Additional chronic condition	+3.21 points	<0.001
Lower baseline functional independence	Positive association	<0.001
Female sex	Positive association	<0.001
≥3 outpatient specialists	Positive association	<0.001

4. DISCUSSION

This prospective longitudinal study examined changes in multi morbidity, medication burden, and medication regimen complexity among adults receiving outpatient care. The available findings show a progressive increase in the number of chronic conditions, polypharmacy, hyper-polypharmacy, and MRCI over the one-year observation period. The increase in multi morbidity was accompanied by an increase in medication use. This relationship is clinically plausible because patients who develop additional chronic conditions may require additional pharmacological treatment. However, the relationship between disease count and medication burden is not necessarily straightforward. Treatment decisions are influenced by disease severity, therapeutic goals, patient preferences, contraindications, and the expected benefit of individual treatments.

One of the important findings of this study is the increase in MRCI. Medication count alone does not describe how a regimen is administered. The MRCI was specifically developed to incorporate dosage form, dosing frequency, and additional instructions, providing a broader assessment of regimen complexity [5]. This distinction may be particularly relevant in patients with multi morbidity. A patient taking five medicines once daily may have a considerably different treatment experience from a patient taking five medicines at several different times of the day, using multiple dosage forms, or following medication-specific instructions.

Previous research has demonstrated that medication regimen complexity can be associated with medication adherence and other clinical outcomes [7,8]. A systematic review of MRCI-based studies identified associations between regimen complexity and a range of health outcomes, although the evidence was heterogeneous [8]. Therefore, a higher MRCI should be regarded as a marker of treatment complexity rather than automatically interpreted as inappropriate prescribing. Treatment burden in multi morbidity is broader than medication complexity alone. It can include medication taking, attending appointments, monitoring health parameters, making lifestyle changes, and dealing with the financial and emotional consequences of chronic disease management. Recent reviews have emphasized that these demands can affect adherence, quality of life, and other health outcomes [3,4].

The longitudinal design of the present study is clinically relevant because treatment burden can change over time. A patient with a relatively simple regimen at the beginning of follow-up may accumulate additional diagnoses and treatments as chronic disease progresses. Repeated assessment may therefore identify changes that would not be apparent in a single cross-sectional evaluation. The reported association between increasing chronic disease burden and MRCI is also clinically meaningful. It suggests that adding a new chronic condition may be accompanied not only by another medication but by additional complexity in how the overall regimen is administered. This reinforces the importance of reviewing the complete medication regimen whenever a new chronic condition is diagnosed.

Patients managed by multiple specialists may require particular attention to medication coordination. Multiple prescribers may be necessary for complex disease, but fragmented treatment can make it more difficult to maintain a coherent overall medication plan. Regular medication reconciliation and communication between treating clinicians may help reduce

unnecessary duplication and simplify treatment where appropriate. Importantly, simplification should not be pursued solely because a regimen has a high MRCI score. A complex regimen may be entirely appropriate for a patient with several serious chronic conditions. Medication review should instead consider indication, treatment goals, disease control, adverse effects, interactions, expected benefit, patient preferences, and the feasibility of the regimen. The findings therefore support the use of medication regimen complexity as an additional clinical measure rather than as a replacement for clinical judgement.

Strengths and Limitations

The principal strength of this study is its prospective longitudinal design. Following the same outpatient population over one year allows changes in disease burden and medication burden to be assessed over time. A further strength is the use of the MRCI, which captures several dimensions of medication complexity rather than relying exclusively on medication count. The study also reflects routine outpatient care rather than a narrowly selected disease-specific population, potentially increasing its clinical relevance to general outpatient practice.

Several limitations should be considered. First, the study population was drawn from outpatient care and may not represent adults who have limited access to healthcare or those receiving care in other settings. Second, medication information was based on documented medication regimens and may not reflect actual medication-taking behavior. Third, the observational design permits identification of associations but does not establish causality. Fourth, the follow-up period was limited to one year. Longer observation would be useful to determine whether the increase in medication and regimen complexity continues over several years. Finally, the available study summary contains a discrepancy between the reported 12-month completion number and the denominators used for some of the 12-month percentages. This should be resolved from the original patient-level dataset before submission. The final analysis should also report confidence intervals and complete regression output.

5. CONCLUSION

Multimorbidity, polypharmacy, hyper-polypharmacy, and medication regimen complexity increased over one year among adults receiving longitudinal outpatient care. The findings highlight an important distinction between the number of medications prescribed and the complexity of the overall treatment regimen. MRCI provides additional information regarding dosing frequency, dosage forms, and administration instructions and may therefore be useful when evaluating patients with multiple chronic conditions.

Routine medication review should consider not only whether individual medications remain appropriate but also whether the overall regimen remains manageable for the patient. Identifying increasing regimen complexity may provide an opportunity for medication reconciliation, appropriate treatment simplification, and better coordination of chronic disease care.

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