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Clinical outcomes of the comprehensive medication management services offered to patients with rheumatoid arthritis

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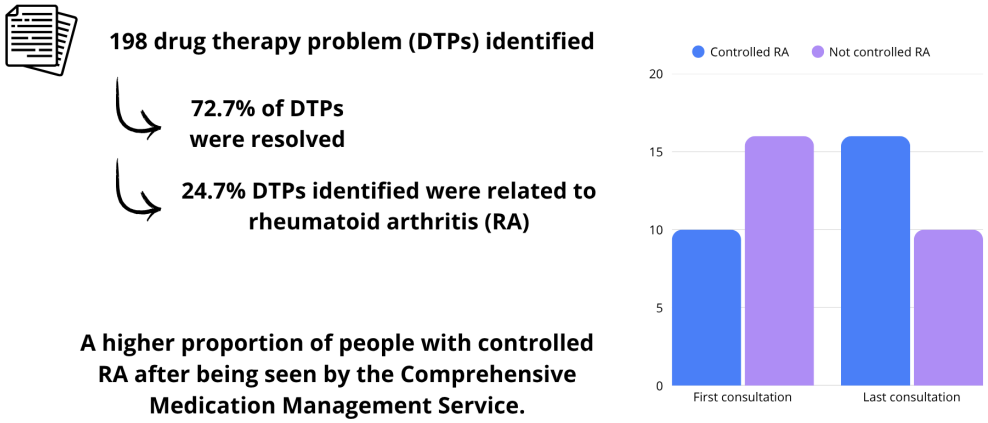
Graphical Abstract



Highlights

- *Assessment of pharmacotherapeutic needs for all diseases.*
- *Drug therapy problem identified and resolved.*
- *Impact of the comprehensive medication management service on rheumatoid arthritis control.*

Abstract

The treatment of rheumatoid arthritis (RA) requires a complex and high-cost pharmacotherapy, to which patients exhibit low persistence rates. In this context, offering the comprehensive medication management (CMM) service to individuals with RA is an important initiative to address their pharmacotherapeutic needs and, thereby, optimize their health outcomes. Therefore, the present study aimed to evaluate the clinical outcomes of the CMM service provided to RA patients in a rheumatology outpatient clinic. To this end, a quasi-experimental study was conducted with a single group of RA patients enrolled in an CMM service. Drug therapy problem (DTPs) identified and resolved were described. McNemar's test was employed to compare the proportions of patients within and outside the therapeutic target for RA control before and after the intervention. A total of 50 patients with RA were evaluated. There was a significant increase in the proportion of individuals presenting controlled RA at the last visit compared to the first visit (p = 0.0143). Thus, the present study indicates that the offered CMM service was effective, demonstrating the potential to contribute to achieving RA control.

Keywords: Rheumatoid Arthritis. Medication Therapy Management. Pharmaceutical Services. Patient Outcome Assessment.

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INTRODUCTION

Rheumatoid arthritis (RA) is an autoimmune, inflammatory, chronic, and progressive disease that primarily affects the joints[1,2,3]. It is estimated that this disease affects approximately 17.6 million people worldwide[4], leading to a decline in quality of life, varying degrees of disability, and reduced life expectancy[1,5].

Pharmacological management of RA is essential for its control and generally begins with the introduction of synthetic disease-modifying antirheumatic drugs (DMARDs), with methotrexate (MTX) being the first-line treatment. If there is an inadequate response, biologic DMARDs should be included, followed by targeted synthetic DMARDs, such as tofacitinib, usually associated with MTX[1,5]. Consequently, RA inherently requires a complex and costly pharmacotherapy, which can vary considerably throughout the disease course, and to which patients show low persistence rates[6].

In a national cohort study including 76,351 patients with RA, it was observed that Brazilian patients with RA demonstrate low persistence to both synthetic DMARDs and anti-tumor necrosis factor (anti-TNF) therapies, particularly during the first two years of treatment. Discontinuation was more frequent among female patients, those with lower income, non-residents of regions with the highest Human Development Indices (HDI), and those with higher comorbidity scores. Such findings suggest that socioeconomic and clinical factors play an important role in treatment persistence[6].

Furthermore, individuals with RA have a higher likelihood of developing alterations in multiple organs and, consequently, developing other diseases, which generates a demand for the use of medications beyond those intended for RA treatment[7]. In this regard, it is important to highlight the need to optimize not only the RA treatment itself but also the overall pharmacotherapy for the effective management of coexisting comorbidities.

In a cohort of individuals with RA, 81% presented comorbidities after a 15-year follow-up; the presence of comorbidities increased the risk of cardiovascular and all-cause mortality, as well as functional decline[8]. In a rheumatology outpatient clinic, 97.5% of RA patients presented at least one comorbidity, and 94.5% used five or more medications[9]. These findings highlight the challenge of maintaining long-term therapy in RA patients in real-world settings and reinforce the need for strategies to improve medication adherence. Accordingly, RA treatment guidelines recommend adopting a treat-to-target strategy, which is based on the rigorous monitoring of disease activity and treatment adjustment[1,5]. In this context, offering a clinical pharmaceutical service to patients with RA is a critical initiative to address their pharmacotherapeutic needs and, thereby, significantly contribute to therapeutic success in controlling RA and other health problems the patients may present.

Clinical services based on the pharmaceutical care framework are known as comprehensive medication management (CMM) and are premised on providing holistic, patient-centered care. In this service, the pharmacist establishes a therapeutic relationship with the patient and assumes responsibility for assessing all medications used by the patient and all reported health problems[10,11]. Thus, this service is provided by a clinical pharmacist in collaboration with the patient and other healthcare professionals to optimize medication use and improve health outcomes. It involves the evaluation of all medications – prescription, non-prescription, and complementary – to ensure that each medication is indicated, effective, safe, and convenient for the patient[10,12].

The provision of the CMM service has demonstrated improvements in clinical, economic, and humanistic outcomes among assisted patients[13,14,15,16,17,18,19,20,21,22,23,24]. Previous studies indicate that the CMM service contributed to the optimization of pharmacotherapy in older adult patients with hypertension and diabetes[13,17] and with cardiovascular diseases[22], as well as in the control of heart failure[20] and psychiatric disorders[24]. However, findings from an integrative review indicate a lack of studies evaluating the clinical outcomes of the CMM service when offered to individuals with RA[25]. Given this, the objective of this study was to evaluate the impact of the comprehensive medication management service offered to people with rheumatoid arthritis on drug-related problems and the clinical control of rheumatoid arthritis.

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METHODS

Study design

This is a quasi-experimental study with a single group of RA patients enrolled in an CMM service, using a pre-test/post-test design and without a control group to describe the clinical outcomes of the service and evaluate its clinical impact. The quasi-experimental study design is recommended by the World Health Organization (WHO) for the evaluation of real-world interventions in the healthcare system[26], as is the case for the CMM service offered at a rheumatology outpatient clinic of a public university hospital in Belo Horizonte.

Population and study setting

The CMM service was offered to individuals with a previous diagnosis of RA receiving care at a rheumatology outpatient clinic, without the adoption of specific inclusion criteria, according to appointment scheduling and the availability of the professionals associated with the service. Thus, patients were assisted without demographic or disease duration restrictions, according to the local profile of the outpatient clinic. That is, people of both sexes, of any age, and at different stages of RA could be assisted by the CMM service. In the present study, the population of patients attended by the CMM service at the rheumatology outpatient clinic was evaluated. The CMM consultations were conducted from June 2018 to March 2020 by three pharmacists with over two years of experience in CMM. Furthermore, they received specialized tutoring during the initial implementation phases of the service.

The present study was conducted at a rheumatology outpatient clinic of a public university hospital integrated into the Brazilian Unified Health System (SUS), located in Belo Horizonte. Consultations with the rheumatologist for RA patients in this outpatient clinic were held on Wednesday mornings. Visit frequency varied according to the complexity of each patient's clinical condition; those with a stable overall clinical condition had follow-ups scheduled at longer intervals than patients with uncontrolled disease. Thus, some patients returned every three months, six months, or only once a year.

It is important to point out that outpatient care is intended for managing non-acute chronic conditions that justify the provision of specialized services at the secondary care level. Therefore, specialized outpatient care constitutes an important healthcare point within the SUS healthcare networks, where patients with more complex chronic conditions are attended by medical specialists in the management of health conditions uncommon in primary healthcare[27].

Patient care process in the CMM service

The patient care process followed the theoretical and methodological framework of pharmaceutical care[10,11]. Therefore, in each consultation, the pharmacist collected pertinent information to assess all medications used and all health problems of the patient in order to ensure that all medications in use were the most indicated, effective, safe, and convenient for them[10,11,12].

The clinical pharmacists conducted their consultations prior to the medical consultations, allowing for the discussion of each patient's case with the rheumatologists and the patient themselves, thereby enabling shared decision-making. During the pharmaceutical consultations, the clinical pharmacist evaluated the patient's pharmacotherapy based on the clinical and laboratory parameters available in their medical records and the results of the exams and tests that the patient brought to the consultation. In cases where an exam was necessary to evaluate the pharmacotherapy and the patient did not have it, the pharmacist referred the patient to the physician, suggesting that the exam be requested. These data were used by the clinical pharmacist to evaluate whether each medication was effective and safe for the patient.

In cases where drug therapy problem (DTPs) were identified, they were categorized as follows: DTP1, when the medication was unnecessary; DTP2, in cases where additional medication was needed; DTP3, in cases of medication ineffectiveness; DTP4, when the dosage was too low; DTP5, in the event of an adverse reaction; DTP6, when the dosage was too high; and finally, DTP7 regarding non-adherence, when the pharmacotherapy was inconvenient for the patient[10,11].

Upon identifying a DTP, the pharmacist, together with other healthcare professionals, presented the available alternatives to the patient to resolve it. After providing sufficient information to the patient, the healthcare team assisted them in exploring the available alternatives, and together, they decided on the best care plan for the patient. Subsequently, the care plan was implemented, and the outcomes were evaluated later. That is, it was verified whether the identified DTPs were resolved with the interventions proposed in the care plan. If the therapeutic goal was not achieved, a new care plan was designed[10,11,12].

The entire pharmaceutical care process aimed to resolve possible identified DTPs, thereby ensuring that the pharmacotherapeutic needs of the person with RA were met. This entire care process, as well as patient outcomes, were documented in the service's own medical records built in the Microsoft Office Excel® program. An integral assessment of the patients' pharmacotherapy and their outcomes was performed in all CMM consultations. As this service is based on an individualized, patient-centered practice, the frequency and number of consultations for each patient are expected to vary according to their clinical profile.

Data Collection

All data were collected directly from the CMM service medical records by a pharmacist with experience in CMM but who did not participate in providing the service at the outpatient clinic. Data were collected and entered into a database in the Microsoft Office Excel® program. Subsequently, they were transferred to, stored, and analyzed using Stata® software. The entire data collection was coordinated by a principal investigator who validated the collected data through double-checking the summations of the variables.

The following data referring to the first consultation were collected: sex; age (full years at the first consultation); number of years since the patient received the RA diagnosis; number of health problems; number of medications used (prescribed and non-prescribed). Furthermore, the total number of CMM consultations per patient, number and type of DTPs identified and resolved for all diseases, and specifically, the number of DTPs identified and resolved related to RA across all consultations were collected.

The values of the composite Disease Activity Score 28 (DAS28) were measured by the rheumatologist during the medical consultation and recorded in the patient's medical record. According to DAS28, a patient is in disease remission when scores are below 2.6; scores between 2.6 and 3.2 indicate low disease activity; between 3.2 and 5.1, moderate activity; and above 5.1 indicate high activity[1].

It is noteworthy that this study was conducted in a real-world setting, and it was observed that the DAS28 score was not systematically evaluated in all consultations. In these cases, the patient's overall clinical condition was assessed using the Visual Analog Scale for Pain (VAS-Pain). Although RA control should not be defined solely by pain, pain reduction is an important indicator of treatment effectiveness in RA management, as demonstrated by Mota *et al.*[28].

In cases where the pain intensity reported by the patient at the time of the consultation was used, scores less than or equal to 34 were considered indicative of "mild pain," scores between 35 and 67 "moderate pain," and greater than 67 "severe pain"[29]. The VAS-Pain is a unidimensional scale that assesses pain from 0 to 100 mm, with the extremes indicating "no pain" and "the worst pain possible"[29]. The evaluation of RA treatment effectiveness was based on these records, as well as on the discussion of each clinical case with the rheumatologist and the patient following the medical consultation. Therefore, what was recorded in the CMM service medical record was used as a parameter for analyzing RA control, collecting the values recorded at the first and last CMM consultations[1,5,29].

Study variables and data analysis

Descriptive data analysis was performed by determining the absolute and relative frequencies of qualitative variables and the mean, standard deviation, and minimum and maximum values of quantitative variables.

During the provision of the CMM service, the pharmacist must evaluate whether the patient is responding to treatment, that is, they must verify whether the desired therapeutic goals have been achieved. In this regard, to assess the clinical impact of the CMM service, McNemar's test was used to compare the proportions of patients with controlled RA at the first and last CMM consultations. This analysis was chosen because it is consistent with the quality indicator used in the CMM service, which aims to monitor the percentage of patients with controlled RA. For this purpose, the CMM service medical records were consulted, and individuals with RA who had a record of sustained remission or low disease activity according to DAS28 were considered controlled. Or, alternatively, those who had a medical record of having mild pain at the time of consultation on the VAS-Pain scale[1,5,28,29].

The time between the first and last consultation varied for each patient, since the number of consultations and follow-up periods are individualized according to their pharmacotherapeutic needs.

Ethical aspects

This study was approved by the Research Ethics Committee of the Universidade Federal de Minas Gerais (UFMG), under approval number CAAE-25780314.4.0000.5149. Participant anonymity and information confidentiality were ensured.

RESULTS

In total, 50 individuals with RA were evaluated, with a mean age of 62.8 ± 10.8 years (min = 36; max = 85), the majority being female (n = 46; 92.0%). When analyzing the number of years patients had the RA diagnosis, a mean of 17.1 ± 10.0 years (min = 2; max = 41) was observed. The mean number of health problems identified at the baseline evaluation was 5.2 ± 1.6 (minimum = 3; maximum = 10). At the first consultation, 56.0% of the patients (n = 28) were using ten or more medications. The total number of consultations performed was 97 (mean = 1.9 ± 1.0 consultations; min = 1; max = 5) (Table 1).

Across all CMM consultations, a total of 198 DTPs were identified, the majority of which (n = 144; 72.7%) were resolved. Approximately one in four identified DTPs were related to RA; the remainder involved other diseases, as observed in Table 2. Furthermore, 60% (n = 30) of the patients attended by the CMM service presented some DTP related to RA, whereas almost all assisted patients presented some DTP related to other diseases (n = 44; 88.0%).

The majority of identified DTPs regarding RA involved an ineffective medication (n = 11; 22.4%) or an adverse drug reaction (n = 10; 20.4%). For other diseases, the most frequent DTPs were ineffective medication (n = 41; 27.5%) and non-adherence (n = 31; 20.8%) (Table 2). Among patients followed up in two or more consultations, it was observed that those with controlled RA at the last consultation had a higher mean for both DTPs identified for RA (mean of 1.19 among controlled patients versus 0.80 among uncontrolled patients) and DTPs resolved for this disease (mean of 1.00 among controlled patients versus 0.50 among uncontrolled patients).

Table 1 - Demographic, health, and medication use profile of individuals with rheumatoid arthritis enrolled in the comprehensive medication management (CMM) service offered at a rheumatology outpatient clinic of a public university hospital in Belo Horizonte, Minas Gerais. 2018-2020.

Characteristics	n (%)
Sex	
Female	46 (92.0)
Male	4 (8.0)
Age (completed years)	
≤ 49	6 (12.0)
50-59	11 (22.0)
60-69	19 (38.0)
≥ 70	14 (28.0)
Number of medications at the initial assessment	
≤ 9	10 (20.0)
10-19	22 (44.0)
≥ 20	15 (30.0)
Not reported	3 (6.0)
Number of consultations	
1	21 (42.0)
2	16 (32.0)
≥ 3	13 (26.0)
Number of years with rheumatoid arthritis	
≤ 9	22 (44.0)
≥ 10	28 (56.0)
Number of health problems at the initial assessment	
≤ 4	21 (42.0)
≥ 5	29 (58.0)
Hypertension	
Yes	40 (80.0)
No	10 (20.0)
Diabetes *mellitus*	
Yes	14 (28.0)
No	36 (72.0)
Dyslipidemia	
Yes	32 (64.0)
No	18 (36.0)
Central nervous system diseases	
Yes	21 (42.0)
No	29 (58.0)
Osteoporosis	
Yes	24 (48.0)
No	26 (52.0)

*Initial assessment = first CMM consultation.

Table 2 - Frequency of types of drug therapy problem (DTPs) related or not to rheumatoid arthritis identified and resolved in the consultations of the comprehensive medication management (CMM) service offered at a rheumatology outpatient clinic of a public university hospital in Belo Horizonte, Minas Gerais. 2018-2020.

Type of DTP	Total DTPs identified n (%)	DTPs identified RA n (%)	DTPs identified other diseases n (%)	Total DTPs resolved n (%)	DTPs resolved RA n (%)	DTPs resolved other diseases n (%)
1 Unnecessary medication	26 (13.1%)	5 (10.2%)	21 (14.1%)	22 (15.3%)	5 (11.9%)	17 (16.7%)
2 Need for additional medication	33 (16.7%)	9 (18.4%)	24 (16.1%)	23 (16.0%)	7 (16.7%)	16 (15.7%)
3 Ineffective medication	17 (8.6%)	4 (8.2%)	13 (8.7%)	8 (5.6%)	2 (4.8%)	6 (5.9%)
4 Low dose	52 (26.3%)	11 (22.4%)	41 (27.5%)	41 (28.5%)	10 (23.8%)	31 (30.4%)
5 Adverse reaction	25 (12.6%)	10 (20.4%)	15 (10.1%)	18 (12.5%)	10 (23.8%)	8 (7.8%)
6 High dose	9 (4.5%)	5 (10.2%)	4 (2.7%)	7 (4.9%)	4 (9.5%)	3 (2.9%)
7 Non-adherence	36 (18.2%)	5 (10.2%)	31 (20.8%)	25 (17.4%)	4 (9.5%)	21 (20.6%)
Total	**198 (100.0%)**	**49 (100.0%)**	**149 (100.0%)**	**144 (100.0%)**	**42 (100.0%)**	**102 (100.0%)**

Legend: RA: rheumatoid arthritis; drug therapy problem (DTP).

When evaluating the clinical impact of the CMM service, an increase was observed in the proportion of individuals presenting controlled RA at the last consultation (61.5%) compared to the first consultation (38.5%), which was statistically significant (p = 0.0143) (Table 3).

Table 3 - Proportion of individuals with rheumatoid arthritis (RA) enrolled in the comprehensive medication management (CMM) service offered at a rheumatology outpatient clinic of a public university hospital in Belo Horizonte, Minas Gerais. 2018-2020.

		RA control assessment at the last consultation		Total n (%)
		Uncontrolled n (%)	Controlled* n (%)	
RA control assessment at the first consultation	Uncontrolled n (%)	10 (38.5)	6 (23.0)	16 (61.5)
	Controlled* n (%)	0 (0.0)	10 (38.5)	10 (38.5)
	Total	**10 (38.5)**	**16 (61.5)**	**26 (100.0)**

*Controlled rheumatoid arthritis (RA): Disease Activity Score 28 (DAS28) values lower than 3.2 and/or Visual Analog Scale for Pain (VAS-Pain) score lower than 34[1,5,28,29].

DISCUSSION

In recent years, in Brazil, an expansion of clinical services offered by pharmacists has been observed, but few studies have evaluated the clinical outcomes of the CMM service offered in an outpatient setting[30,31]. Thus, to our knowledge, this is the first quasi-experimental study that evaluated an CMM service aimed at patients with RA attended at an outpatient clinic in Brazil.

The findings of the present study indicate that offering the CMM service to people with RA contributes to achieving the therapeutic target for this disease. These results are in line with previous research that found an improvement in clinical outcomes among patients attended by the CMM service[13,14,15,20,21,22,23,24,30,31].

The majority of patients attended by the service were older adults and female. This patient profile was already expected, considering that about 55% of people living with RA are over 55 years old, and women are two to three times more likely to manifest this disease[4].

Most of the assisted patients had been diagnosed with RA for over 10 years, and 58% of them had five or more health problems, which consequently led them to use multiple medications (56% of patients used 10 or more medications). This health profile points to the need for these patients to be assisted by a holistic clinical service that evaluates the patient as a whole, without fragmenting them, as is the case with pharmaceutical care practice[10,11].

According to the theoretical-methodological framework of pharmaceutical care, the pharmacist must evaluate all health problems and all medications in use by the patient, making it inappropriate for the pharmacist to select one medication and/or health problem and ignore the others[10,11]. This is because patients with comorbidities and taking multiple medications present higher risks of harm, since polypharmacy is associated with an increased occurrence of adverse events, adverse drug reactions, drug-drug interactions, drug-disease interactions, and mortality[32,33]. In this context, it is imperative to perform a careful assessment of pharmacotherapy, also considering that the use of multiple medications may be clinically indicated, effective, and safe for the patient's clinical situation[32,34].

However, in the present study, an average of four DTPs were identified per attended patient, with the identification of DTPs for other diseases being more frequent than DTPs for RA. These results indicate that the attended patients presented other health problems that were not being effectively monitored. This fact may stem from multifactorial causes, associated with both the user and the management of the health system[35,36].

This is because communication failures between primary healthcare (PHC) professionals and those in secondary care, combined with inefficient control of referrals, the reference system, and counter-reference, can compromise the comprehensiveness of care and contribute to a set of negative outcomes in the care process[37]. In addition, users often may prefer to be followed up only by the secondary care service, whether due to disbelief in the quality of PHC services, lack of knowledge about the organization and functioning of the health system, or failures in guidance regarding the importance of their care being coordinated and ordered by the PHC team[36].

In this context, the implementation of CMM services stands out as an important strategy to optimize the patient's global pharmacotherapy. Indeed, in the present study, it was found that approximately three-quarters of the DTPs identified by the pharmacists were related to other health conditions, demonstrating that when clinical pharmacists evaluate the patient holistically, considering all medications used and all their health problems, they can contribute to improving the patient's overall condition. However, future research addressing the context of managing other health conditions in patients attended in secondary healthcare would be interesting to deepen the knowledge on the subject.

Regarding the frequency of DTPs, it was observed that almost all DTPs related to RA were resolved (85.7%), whereas those related to other diseases had a lower resolution rate (68.4%). These findings may be due to the fact that DTPs related to RA were discussed and resolved with the outpatient clinic team themselves and/or with the patients, while the resolution of DTPs related to other diseases often required referrals, either to PHC or to other outpatient clinics, such as the cardiology clinic. These results reinforce how essential the presence of the clinical pharmacist in the same place as the health team is for the CMM service to be more effective, since this context allows for better professional interaction, which in turn facilitates the acceptance and understanding of the proposed interventions[38].

Furthermore, it should be noted that patients considered to have controlled RA at the last consultation had a higher average of identified and resolved DTPs when compared to individuals with uncontrolled disease at the last consultation. These findings corroborate results from other studies indicating that the CMM service has the potential to optimize the pharmacotherapy of patients with high pharmacotherapeutic complexity, who are not achieving disease control and who consequently require a more careful assessment of their pharmacotherapeutic needs[13,14,18,20,21,22,23,24].

The most frequent types of identified DTPs were low dose (26.3%), non-adherence (18.2%), and need for additional medication (16.7%). This profile of identified DTPs was also found in a study that evaluated the clinical outcomes of the CMM service in a diabetes *mellitus* (DM) outpatient clinic[31] and in other Brazilian studies that followed patients within the scope of PHC[13,15]. In addition, the same types of DTPs were found to be the most frequent in a study that evaluated the clinical outcomes of the CMM service offered in a US health system for ten years[18].

Regarding RA, the most prevalent DTPs were low dose (22.4%), adverse reaction (20.4%), and need for additional medication (18.4%). The low dose DTP was also the most prevalent in the study that evaluated the clinical outcomes of patients with DM followed by the CMM service in an outpatient clinic[31]. Such findings may arise both from the prescription of a drug dose that is insufficient to achieve treatment effectiveness and from the underutilization of medications by the patients.

In the present study, it was identified that low dose DTPs generally arose from the need to increase the dose of prednisone or methotrexate to improve the therapeutic response or from the patients' preference to take folic acid or leflunomide at a dosing interval longer than necessary to achieve therapeutic goals (results not described). Both situations reinforce the need for periodic follow-up of the attended patients, either to adjust

the medication dose according to the patients' current clinical state or for healthcare professionals to ensure that patients are using the medications as prescribed (RA protocol). These findings indicate the importance of periodically monitoring the clinical response of these patients, since the lack of RA control can lead to complications, deformities, and functional disability[1,2,3,5].

The second most frequent DTP related to RA was adverse drug reaction. In the present study, this DTP was mainly linked to the use of nonsteroidal anti-inflammatory drugs (NSAIDs), prednisone, and methotrexate. Patients frequently used NSAIDs through self-medication to control RA pain (results not described). However, they were exposed to the manifestation of adverse reactions, such as gastritis and dyspepsia. Furthermore, the chronic use of these medications, besides increasing the risk of gastrointestinal bleeding, indicates that RA activity may not be adequately controlled[1]. Therefore, periodic follow-up is necessary to evaluate not only their safety and effectiveness but also as an indicator of the ineffectiveness of the established RA treatment protocol for the patient.

Regarding prednisone, the reported adverse reactions were associated with the occurrence of insomnia (results not described). To solve this problem, the medication administration time was adjusted to the morning period[39]. In cases where prednisone was used twice a day, it was recommended to take the second dose at 4:00 PM, aiming to minimize the impacts of this medication on the patients' sleep pattern.

Concerning the use of methotrexate, the reported adverse reactions involved nausea, vomiting, loss of appetite, malaise, and hair loss (results not described). To manage gastrointestinal problems, ondansetron was prescribed. In cases where the patient did not tolerate the medication, it was necessary to change the pharmacotherapy[40].

In the present study, it was found that the CMM service offered to RA patients in the rheumatology outpatient clinic positively impacted the achievement of RA control. This finding was also observed in other studies that evaluated the impact of the CMM service on the control of patients with DM[31] or HIV[30] attended within the scope of secondary care. The results of this study reinforce the need to implement and qualify the CMM service as a continuous monitoring strategy for complex patients, such as RA patients.

The absence of clinical and laboratory parameters in the medical records of patients attended by the CMM service was a limiting factor in the present study, which may have led to an underestimation of the frequency and resolution of DTPs in the studied population. Another study limitation was the reduced time availability of the consultation room for the pharmacy team to perform consultations, given the high multiprofessional demand in the outpatient clinic, which may have limited the total number of patients attended, as well as the number of consultations performed per patient. Consequently, the small number of patients followed by the service and the absence of data recorded in the medical records precluded the performance of other statistical analyses, since the number of observations in each analysis category could be substantially smaller, which would fragment the data and compromise the analysis. This fact also raised the need to evaluate RA control using the parameters recorded in the medical record; that is, DAS28 values or VAS-Pain scores recorded at the first and last CMM consultations were collected. This important limitation indicates the need to optimize the documentation of interventions analyzed in a real-world setting so that the evaluation of these services is not hindered and their clinical impact underestimated.

In addition, the present study has inherent limitations of the quasi-experimental study type, such as the lack of randomization and a control group. On the other hand, although studies evaluating clinical services in real-life settings present some intrinsic limitations to their design, they generate scientific evidence of high practical relevance, providing subsidies closer to the reality of care settings. Furthermore, this type of study allows for the evaluation of intervention contexts where conducting randomized clinical trials would be unfeasible for ethical, operational, and/or financial reasons. Moreover, this design is recommended by the WHO for evaluating real-world interventions[26], as is the case of the service evaluated in the present study. Finally, it should be noted that the findings of this study refer to the particular setting of the outpatient clinic in which the study was developed, and external validity cannot be asserted.

Despite these limitations, it should be highlighted that the obtained results refer to a population with high pharmacotherapeutic complexity, which presented a considerable number of DTPs related both to RA and to other diseases, emphasizing the pertinence of offering this CMM service to people with RA. In addition, the findings demonstrate the effectiveness of the CMM service offered in the study setting, showing its potential to contribute to achieving RA control in the outpatient setting.

CONCLUSION

The results of the present study indicate that the CMM service offered at the outpatient level has the potential to improve the clinical control of rheumatoid arthritis. The frequency of identified DTPs was high, but a large part of them was resolved by the pharmacists, especially those related to RA.

CRediT author statement

Conceptualization: Rezende CP; Nascimento, MMG. Methodology: Rezende CP; Oliveira, IV; César, ALM; Silva, PVR; Silva, HM; Ramalho-de-Oliveira, D; Nascimento, MMG. Validation: Rezende CP; Nascimento, MMG. Statistical analysis: Rezende CP; Nascimento, MMG. Formal analysis: Rezende CP; Oliveira, IV; César, ALM; Silva, PVR; Nascimento, MMG. Investigation: Rezende CP; Oliveira, IV; César, ALM; Silva, PVR; Silva, HM; Nascimento, MMG. Resources: Nascimento, MMG. Writing-original draft preparation: Rezende CP. Writing-review and editing: Rezende CP; Oliveira, IV; César, ALM; Silva, PVR; Silva, HM; Ramalho-de-Oliveira, D; Nascimento, MMG. Visualization: Rezende CP; Oliveira, IV; César, ALM; Silva, PVR; Silva, HM; Ramalho-de-Oliveira, D; Nascimento, MMG. Supervision: Nascimento, MMG. Project administration: Nascimento, MMG.

All authors have read and agreed to the published version of the manuscript.

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Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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