RESEARCH

Access to high-cost medications for psoriatic arthritis in the National Health System in Brazil: the long path up to dispensation

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Abstract

Background: Pharmaceutical Assistance (PA) is a dynamic and multidisciplinary process that aims to supply health systems, programs or services with quality medicines, enabling access and health care, in an efficient and timely manner. The objective of the study was to evaluate the profile of administrative processes for the treatment of PsA, identify the time elapsed in the flow of processes and its associated factors.

Methods: A cross-sectional study of medication requests for the treatment of PsA was carried out between November 2014 and December 2016. Linear regression was used to verify the factors associated with time to delivery.

Results: A total of 218 cases containing 250 drugs were analyzed. The median time between the medical appointment and the first dispensation was 66 days (interquartile range, 44–90). The State proceedings, which includes requesting the drug until the authorization of treatment, was the stage that most contributed to the total time spent. The factors associated with the longer time to delivery of medications were prescriptions coming from clinics and specialty centers, from dermatologists, non-authorized processes and non-persistent patients in the treatment in 12 months.

Conclusion: The median time to receive medicines for the PsA treatment in Belo Horizonte health region after a medical prescription was higher than 2 months. The time between the solicitation of the medicines and the authorization of the treatment in the SUS (State administrative procedure) was the main component of the total time spent.

Keywords: Psoriatic arthritis, Antirheumatic agents, Health policy, Pharmaceutical services

Background

Pharmaceutical Assistance is a dynamic and multidisciplinary process, which aims to supply health systems, programs, or services with medications of quality, enabling patients to access their required medications and the healthcare services they need. Its purpose is to support the health actions required by the community, which should be developed by means of the efficient and opportune provision of medications to inpatient and outpatient care [1]. It is defined as part of the right to health and has been implemented by a set of social and economic policies along the last years in Brazil [2].

In this sense, we could mention the creation of the National Policy of Medications (1998), of the Generic Medications Policy (1998), of the National Agency of Health Surveillance (1999), of the National Policy of Pharmaceutical Assistance (2004) and, more recently, in 2011, the creation of the National Commission of Incorporation of Health Technologies (NCIHT) as

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important measures in the building and consolidation of pharmaceutical assistance in Brazil [3]. Besides the creation of NCIHT, the Law 12,401 of 2011 has instituted also the 'Clinical Protocols and Therapeutic Guidelines' (CPTG) as a strategy to orientate and regulate the access to medications and health procedures in the ambit of the Specialized Component of Pharmaceutical Assistance (SCPA), responsible for the supply of high-cost medications [4].

In practical terms, the access to medications takes place by means of opening of an administrative process by the patient or his/her responsible, which takes place in the health unit designated by the state manager. This process contains the patient's cadastral information, medical reports, laboratory and images results, and a standardize form (appraisal for request, evaluation, and authorization of drugs). An independent evaluator with formation in health sciences analyzes this documentation and the process could be accepted, dismissed or returned, according to criteria established by the CPTG. In case of acceptance, the standardize form originates an authorization of outpatient procedures of high cost/complexity, which corresponds to three billings /dispensations of medication by SCPA [5].

In the last years, there was a large focus on the incorporation of new technologies to the National Health System (Sistema Único de Saúde - SUS) [6]. However, despite the large advances in PA implementation, few studies have addressed the management processes involved in the access to such technologies, to the practical implementation of services, and to healthcare. This is particularly important given the cost of these new therapies. The amount spent with anti-TNF agents for the treatment of patients with PsA in the SUS between 2010 and 2015 was approximately US\$ 300 million (dollar adjusted by purchasing power parity), corresponding to 90% of the total costs with PsA [7].

The present study was conducted to describe the profile of administrative processes for the treatment of PsA and to identify the time elapsed in the flow of processes in the Minas Gerais State, understood as the time elapsed between the prescription and the first dispensation of the medication and the factors associated to this.

Methods
Type of study
This is a cross-sectional study about the medication requests for treatment of PsA to the Minas Gerais Secretary of State for Health during the period between November 4th, 2014, date of publication of the first CPTG of PsA, and December 31st, 2016, with an ancillary analysis of medication persistence in 12 months.

Administrative processes
All of the administrative processes involving medications request for the treatment of PsA have been selected in the Belo Horizonte health region, which meets a population over five million inhabitants, distributed throughout 39 municipalities. The data collection was developed from the Information System of Management of Pharmaceutical Assistance (ISMPA), where the listing of registered patients and administrative processes digitalized between the years of 2014 and 2016 has been obtained. For processes not digitally available, a consultation to physically filed processes has been done close to the Superintendence of Pharmaceutical Assistance of the Minas Gerais Secretary of State for Health.

The variables that were analyzed at baseline were the information contained in the administrative processes, according to the checklist for the request of medicines for the PsA treatment,[1] being: i. sociodemographic profile (city, age, and sex), ii. clinical profile of patients [body mass index (BMI)], iii. Process characteristics (procedure of steps necessary to request approval and current situation - accepted, dismissed or under evaluation), iv. requested medications, v. profile of units responsible for the request (health establishment and prescriber). The information about the facility was complemented with data coming from the National Registration of Health Establishment.

Time of administrative procedure
To evaluate the time elapsed between the date of medication prescription by the physician and its first dispensation by the Pharmacy of Belo Horizonte health region, the following dates have been registered: T_0 = date of medical prescription; T_1 = date of administrative claim (registered at ISMPA); T_8 = date of process sending to its original unit, after appraisal from the analyst (registered at ISMPA); T_9 = date of the first dispensation (registered in the Information System of Hospital Management [ISHM]).

For the calculation of the total time between the medication prescription by the physician (T_0) and the first dispensation of medication (T_9), it was executed the subtraction of T_9 date from T_0 date. For the time between the medical prescription (T_0) and the administrative claim / process opening (T_1), it was executed the subtraction of T_1 date from T_0 date. To evaluate the time of administrative procedure in the State, which embraces the period from the administrative procedure opening (T_1) up to sending to its original Regional Unit (T_8), it was executed the subtraction of T_8 date from T_1 date. Finally, to calculate the time between the date of process output from the State (T_8) and the first dispensation of the medication (T_9), it was executed the subtraction of T_9 date from T_8 date. The processes flow has been built utilizing the *Bizagi Modeler* software version 3.2.6.094 (Fig. 1).

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[1]Available in: http://www.saude.mg.gov.br/formularioceaf. (last updated version in February of 2019).
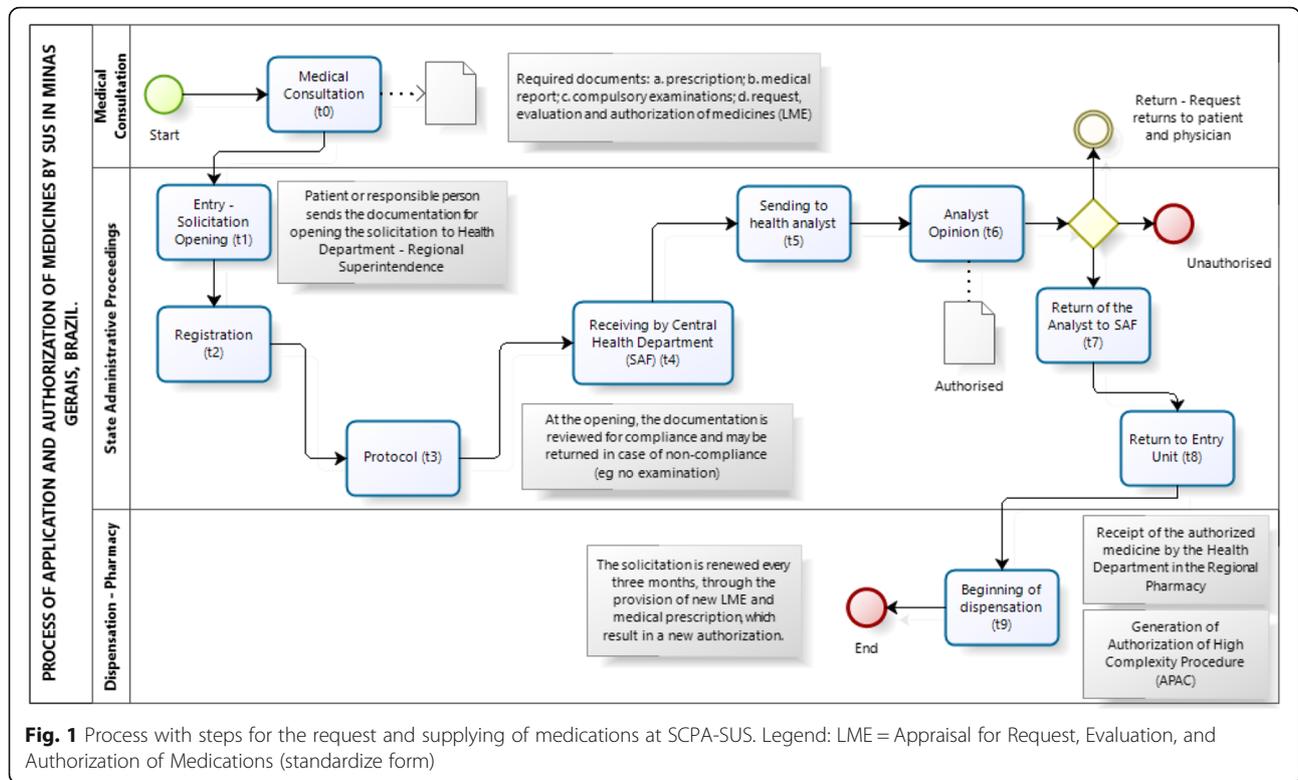
Fig. 1 Process with steps for the request and supplying of medications at SCPA-SUS. Legend: LME = Appraisal for Request, Evaluation, and Authorization of Medications (standardize form)

Statistical analysis

The categorical variables were described by means of the distribution of frequencies and the continuous variables by means of mean and standard deviation at baseline. The time spent in the request of medications was described by median and interquartile interval and, additionally, by mean and standard deviation.

The linear regression model was utilized to identify the independently associated variables with the time spent in the request of medications. A significance level of 20% has been adopted for the simple linear regression and another of 5% for the multiple linear regression. The explanatory variables were subdivided into two different groups; a) the *proximal* ones (cross-sectional variables): variables contained in the administrative processes (per requested process); and b) the *distal* ones (longitudinal variables): variable of persistence in the 12 months treatment, identified by means of medication dispensations registered on the ISHM (per requested medication; a patient could request for more than one medication). The therapy discontinuation has been defined as the absence of any medication dispensation after 90 days. The statistical analyzes were developed using the software STATA, version 15.1.

Results

As a total, 218 administrative processes containing requests for 250 medications have been analyzed. Among the biological disease modifying anti-rheumatic drugs

(bDMARD), tumor necrosis factor alpha inhibitors (anti-TNF α) were the most requested ones, corresponding to 68% of the requests. Adalimumab was the most requested anti-TNF, followed by etanercept and infliximab. Between the conventional synthetic disease modifying anti-rheumatic drugs (csDMARD) (28.4%), the medications methotrexate and leflunomide were the most requested ones (Fig. 2).

Out of total processes, 89% were accepted and contained all documents and exams necessary for the evaluation. The mean age of patients was 52.3 years (12.4) and 56.9% were female patients (Table 1).

The larger part of requests came from rheumatologists (74.2%). In relation to the health unit originating the request, 43.4% of requests came from private practices and 32.6% from hospitals. The majority of requesting units were private (62.2%) and 63.7% of them were not accredited to public health service. Between the patients who started the treatment, 54.5% remained in the treatment up to 12 months (Table 1).

The median time between the medication prescription by the physician (T_0) and its first dispensation (T_9) was of 66 days; Interquartile Range [IQR 44–90] (mean of 75.2 days [standard deviation of 47.4]). Between the medication prescription by the physician (T_0) and the process opening (T_1), the median time was of 6 days, IQR 0–24 (mean of 13 days [SD 24.6]). The median time for the administrative procedure within the 'Secretary of
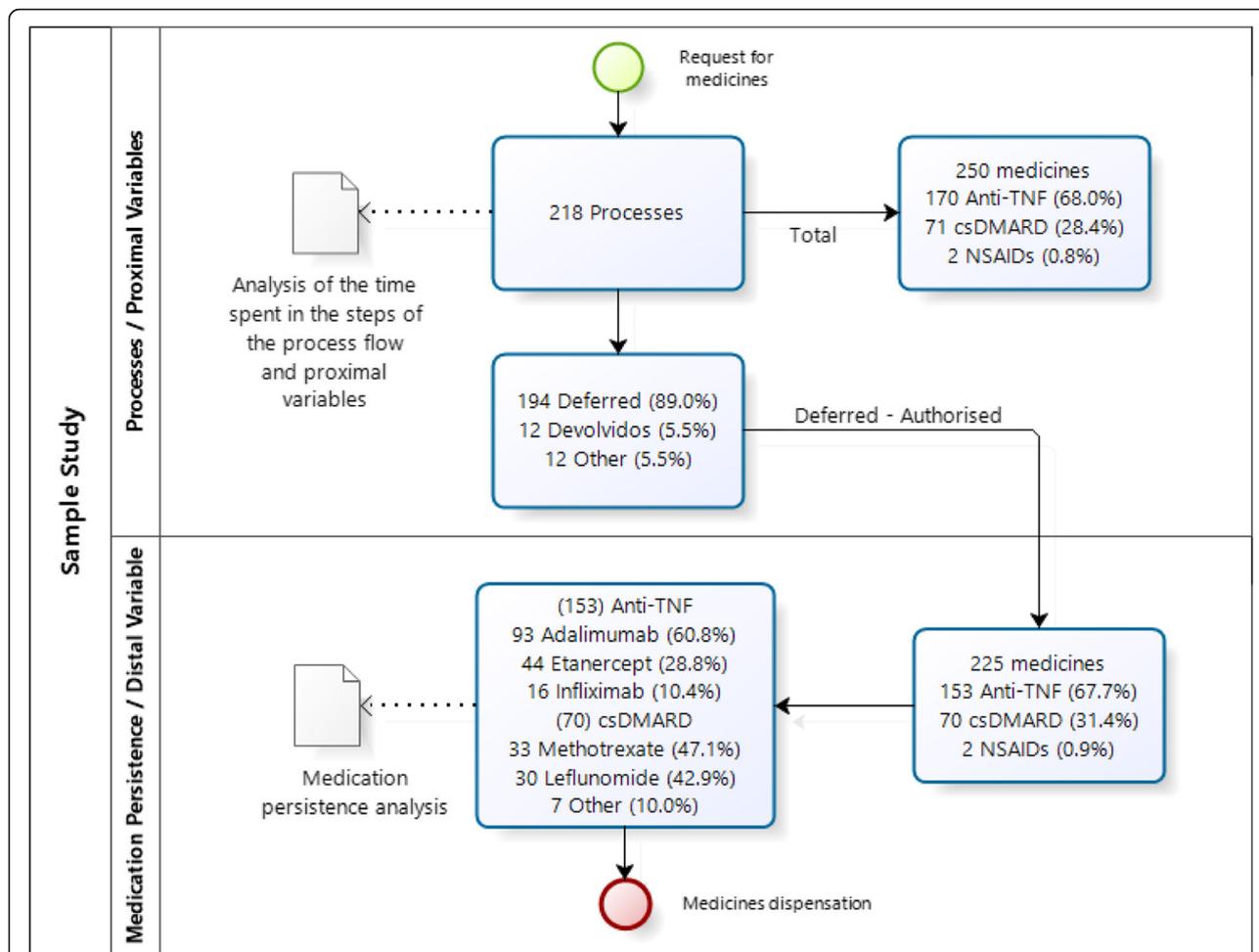
Fig. 2 Quantitative of processes requested and accepted at Belo Horizonte. Legend: csDMARD = conventional synthetic disease-modifying antirheumatic drugs; NSAID = Nonsteroidal anti-inflammatory drug. Proximal variables = cross-sectional variables, collected in the administrative processes. Distal variable = longitudinal variable, collected after 12 months in the information systems

State for Health', considered from the process opening (T_1) in the regional unit up to process output, with its sending to the original regional unit (T_8) was of 33 days; IQR 25–45 (mean of 40.1 days [SD 26.0]). Finally, the median time spent between the end of the administrative procedure (T_8) and the first medication dispensation (T_9) was of 19 days; IQR 14–27 (mean of 23.8 days [SD 34.6]) (Table 2). There was no difference between the total median time ($T_9 - T_0$) for the anti-TNF and csDMARD medication processes.

The factors associated to the time spent in the request of medications were: original unit, process status, medical specialty, and persistence in the treatment up to 12 months. Requests coming from clinics and medical specialty centers took 22.35 additional days as compared to requests from private practices. Dismissed processes (returned/dismissed/inactive) took 181.08 additional days as compared to accepted processes. Requests coming from dermatologists took 28.29 additional days as

compared to requests from rheumatologists. Finally, requests of patients who did not persist in the treatment up to 12 months took 15.73 additional days as compared to patients who effectively persisted in the treatment (Table 3).

Discussion

In our study, the median time between the medical consultation and the first medication dispensation was of, approximately, 2 months (66 days). Such a time interval could be essential in the treatment of rheumatic diseases, mainly when the patient is without any current treatment or will begin his/her first drug treatment for the disease.

A total of 218 administrative processes have been analyzed, which contained requests for 250 medications. Adalimumab was the more requested anti-TNF, followed by etanercept. This profile of anti-TNF utilization is consistent with the literature, finding Adalimumab the most

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Table 1 Profile of requests of medication for psoriatic arthritis at Belo Horizonte health region

Variables	Number	Percent
Proximal variables		
Sex – Female	124	56.9
Race – White	95	54.0
Age in years	*52.31 (12.37)*	
BMI in Kg/m²	*27.20 (4.84)*	
Appraisal – Accepted	194	89.0
Correct/complete Documentation	194	89.0
Correct/complete examinations	194	89.0
Requested medications per class		
Biological	144	68.2
Synthetic	40	19.0
Both	27	12.8
Medical Specialty		
Rheumatology	161	74.2
Dermatology	42	19.4
General Practice	14	5.4
Type of Requesting Unit		
General Practice	92	43.4
Hospital	69	32.6
Clinic/Center of Specialties	33	15.6
Other	18	8.5
Attends the SUS		
Yes	77	36.3
No	135	63.7
Organization		
Private	132	62.2
Public	61	28.8
Philanthropic	19	9.0
Distal variable		
Persistent along 12 months	110	54.5
Mean Time of Persistence along 12 months	*265.25 (128.18)*	

Italic: continuous variables, described by mean and standard deviation
Proximal variable = cross-sectional variables, collected in the administrative processes
Distal variables = longitudinal variable, collected after 12 months in the information systems

commonly utilized medication to treat PsA and other rheumatic diseases in Brazil [8–10].

The higher frequency of requests comes from rheumatologist physicians, and it is in concert with the CPTG of PsA. Such CPTG recommends that individuals with PsA are attended by a team in a specialized service, which counts on a rheumatologist, for his/her adequate diagnosis, treatment inclusion, and follow-up [11]. According to the European League Against Rheumatism (EULAR), rheumatologists are the specialists who should primarily treat the musculoskeletal manifestations of patients with PsA; and in the presence of clinically significant cutaneous involvement, a rheumatologist and a dermatologist should collaborate in the diagnosis and treatment management [12].

However, the literature describes the existence of difficulties in the early forwarding of patients to specialized physicians by the primary care physicians, mainly for patients of countryside small cities, as well as in the maintenance of treatment follow-up and management of patients after forwarding. This difficulty could impact the time up to correct diagnosis of the disease, in association with the time spent on medication supplying by SUS [13].

Clinical recommendations and guidelines mark the diagnosis delay as a great challenge that needs to be approached, as it negatively impacts the treatment result; so, strategies to promote the early forwarding and decrease the delay in diagnoses and inflammatory arthritis treatment have been proposed [14]. This is a problem that has been confronted in Brazil and one of the challenges found is represented by the concentration of rheumatologist physicians in the larger cities and the low availability of rheumatologists at SUS [15].

Despite the large increase in the public formation of rheumatologists by means of medical residences in the last years, the provision of such specialists at SUS is lower than that of private practices and well below than the level recommended in other countries. Internationally, the ideal proportions are pointed out as something between 52,000 and 85,000 inhabitants per rheumatologist. In 2013, Brazil had an approximate ratio of 118,000 inhabitants per rheumatologist, being that, at SUS, such ratio overcomes 400,000 users per rheumatologist. Therefore, SUS has proven to be inefficient to retain a sufficient number of these specialists, who, once finished the medical residence, migrate to private care [15].

Prolonged duration of symptoms in rheumatic diseases is associated with radiographic progression and a lower chance of sustained remission without the use of DMARD [16]. Then, it is observed that as early the treatment in rheumatic diseases as better the clinical results obtained [16, 17]. This is coherent with the observation, in this study, that patients who had larger time between the medication request and its supplying presented lower persistence to treatment in 12 months.

It was identified that the larger part of requests came from private practices, followed by hospitals. Most units requesting medication was private and were not accredited to the SUS. Such data reflect the profile of prescriptions of high-cost medications offered by SUS. It is valid to emphasize that the Belo Horizonte health region is the largest one all over the State, and it is placed in a

Table 2 Mean and median time between the request and the treatment starts

Main Dates	Step Description	Mean (SD)	Median (IQR)
$T_9 - T_0$	Prescription to dispensation	75.2 (47.4)	66 (49–90)
$T_1 - T_0$	Prescription to opening	13.0 (24.6)	6 (0–24)
$T_8 - T_1$	State Procedure	40.1 (26.0)	33 (25–45)
$T_9 - T_8$	Acceptance to Dispensation	23.8 (34.6)	19 (14–27)
State Proceedings	Step Description	Mean	Median
$T_2 - T_1$	Opening to registration	4.3 (8.3)	0 (0–6)
$T_3 - T_2$	Registration to protocol	1.2 (7.3)	2 (1–3)
$T_4 - T_3$	Protocol to SAF	12.0 (23.0)	5 (3–7)
$T_5 - T_4$	SAF to analyst	8.1 (7.1)	6 (3–13)
$T_6 - T_5$	Analyst to appraisal	7.6 (6.3)	6 (5–8)
$T_7 - T_6$	Appraisal to SAF	5.3 (3.2)	5 (3–7)
$T_8 - T_7$	SAF to Regional	1.6 (1.2)	1 (1–3)

SD standard deviation, *IQR* interquartile range

central and metropolitan area. In this sense, the large number of requests coming from private practices and clinics, specialized units, and hospitals could be expected, and it demonstrates that the follow up of the patients in this setting is appropriate and regular, and allow the prescription of drugs that demand constant vigilance in terms of effectiveness and safety.

A recent study conducted in patients with PsA using biological medications, who were attended at Belo Horizonte health region, has demonstrated that the larger part of patients using such medications possesses, at least, complete high school (77.5%). No illiterate patient has been evaluated (0%) and, about 11% of them had incomplete elementary school. This indicates a possible access difficulty for patients with lower education, who that corroborates the large frequency of prescriptions coming from private units, mainly medical offices, as patients with higher education often use private health services more than the public ones [9]. In this sense, it is observed the existence of gaps and challenges that

Table 3 Factors associated with time spent in the medications request for PsA at Belo Horizonte health region

Linear Regression	Simple		Multiple	
Explanatory Variables	β (CI 95%)	*P*-value	β (CI 95%)	*P*-value
Proximal variables				
Establishment		**0,0387**		–
Private Practice	Reference		Reference	
Hospital	10.72 (− 4.88; 26.33)	0.177	6.91 (− 6.13; 19.95)	0.297
Clinics/Centers	32.44 (10.11; 54.78)	0.005	22.35 (3.74; 40.97)	**0.019**
Other	12.11 (− 14.00; 38.23)	0.361	17.38 (− 4.39; 39.15)	0.117
Process Status		**< 0.001**		**< 0.001**
Accepted	Reference		Reference	
Dismissed	197.00 (150.59; 243.41)		181.08 (135.79; 226.38)	
Medical Specialty		**< 0.001**		–
Rheumatology	Reference		Reference	
Dermatology	38.12 (21.01; 55.23)	**< 0.001**	28.29 (13.17; 43.41)	**< 0.001**
Clinical Medicine	16.13 (− 10.76; 43.03)	0.238	13.87 (− 9.51; 37.25)	0.243
Distal variable				
Persistence along 12 months				
Persistent	Reference		–	–
Non persistent	15.73 (29.14; 2.33)	**0.022**	–	–

Proximal variable = cross-sectional variables, collected in the administrative processes
Distal variables = longitudinal variable, collected after 12 months in the information systems
Bold: *p*-value < 0.05

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hamper the access of patient to an adequate follow-up among the different levels of health care [18].

The majority of processes obtained acceptance opinion, which corresponds to processes presenting the entire necessary documentation, with the mandatory exams for their evaluation and acceptance. In this sense, it is emphasized the importance of correct filling and accomplishment of all legal requisites to obtain the respective process acceptance. The proportion of processes acceptance for PsA was larger than that observed for Alzheimer disease and similar to that observed for renal transplantation [19, 20].

The awareness from the physician respecting to the CPTGs accomplishment and the correct filling of all documents approximate the assistant physician and the State, responsible for the medications supplying. An alternative allowing such integration would be the application of the academic detailing tool, which proposes the dissemination and communication to prescribers of the norms and operating conditions of health systems. Besides, it is possible to hear the unmet needs, doubts, and questionings from the physician directly attending the patient, respecting to difficulties found for the medication request [21].

As another challenge, it is observed that populations' access to medicines is addressed mainly through fragmented, often vertical approaches usually focusing on supply, unrelated to the wider issue of access to health services and interventions [22]. In this case, alternatives to improve the articulation in the health service are needed. One proposal is the approximation of the pharmacist to the patient and physician with the purpose of assist to the pharmacotherapy and improve the information about access to medicines, with impact on quality and efficiency of health services [23].

Proposals of indicators to evaluate the SCPA management capacity have been elaborated to improve results in health [24]. In this sense, measures could be taken to improve the efficiency of medications requesting processes at SCPA. As a proposal, we could indicate in the first process step, between the medical consultation and the process opening (t_0 to t_1), the suggestion of computerizing the request for medicines with integration to ISMPA from the part of Secretary of State for Health. This way, the physician could forward the requests directly to the Regional Health Unit responsible for the process opening.

In the administrative procedure step (T_1 to T_8), a similar proposal could be indicated. If the process is digitally and electronically started by the physician, the processes sequence could follow in the same way, without requiring the use of a process on paper. So, this flow could result in higher efficiency for the service, for the physician, and for the patient. A temporary alternative to this proposal would be the computerization of physical processes in the Regional Superintendencies of Health with lower technological capacity, until the implementation of the initial proposal of computerization.

At last, the launch of the applicative "MG App" in 2018, available for Android and iOS, created to facilitate the access to State services can be used to to facilitate the access to information and state services, simplifying the problems resolution and the search for information in mobile phones and other mobile devices. In this applicative is possible: a) to consult medications standardized by the SUS in the state level; b) to follow-up the situation of medication request to SCPA, c) to consult the availability medications in the pharmacy stock; and d) to make scheduling of attendance in the regional pharmacies [25]. So, the time spent in the last step of the process could be reduced and the access to information could be improved for patients.

As a study limitation, it is indicated the occurrence of ignored information in the processes, which could be useful for analysis, besides the supposition that all information available was reliable. Another limitation is that the study was conducted only in the Belo Horizonte health region, responsible for a half of the processes in the State of Minas Gerais. So, the mean time up to dispensation could vary according to the analyzed health region. Despite such limitations, the study has identified relevant aspects that influence the access to medications for the treatment of PsA at SUS, and where interventions could be developed to improve the System efficiency. Besides, the results could be utilized as a comparator for other health regions or to verify the access to treatment of other health conditions in the ambit of SCPA.

Conclusion

The median time to receive medicines for the PsA treatment in Belo Horizonte health region after a medical prescription was higher than 2 months. The time between the solicitation of the medicines and the authorization of the treatment in the SUS (State administrative procedure) was the main component of the total time spent.

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