Studies published in indexed journals on lawsuits for medicines in Brazil: a systematic review

Estudos publicados em periódicos indexados sobre decisões judiciais para acesso a medicamentos no Brasil: uma revisão sistemática

Estudios publicados en revistas indexadas acerca de decisiones judiciales para el acceso a los medicamentos en Brasil: una revisión sistemática

Vanessa Santana Gomes [1]
Tânia Alves Amador [1]

[1] *Programa de Pós-graduação em Assistência Farmacêutica, Universidade Federal do Rio Grande do Sul, Porto Alegre, Brasil.*

Correspondence
T. A. Amador
Programa de Pós-graduação em Assistência Farmacêutica, Universidade Federal do Rio Grande do Sul.
Av. Ipiranga 2752, sala 602A, Porto Alegre, RS
90610-000, Brasil.
tania.alves@ufrgs.br

Abstract

The aim of this systematic review was to identify and characterize articles in indexed scientific journals with quantitative data surveys on administrative or legal proceedings for access to medicines. The SciELO, LILACS, MEDLINE via PubMed, Embase, and Scopus databases were used. We identified 45 articles, of which 17 were selected. The larger studies, each covering between 2,000 and 2,927 lawsuits, were done in the states of São Paulo, Rio de Janeiro, and Santa Catarina, Brazil. Eleven studies specified the type of legal representation, of which six examined cases with public attorneys and five with private attorneys. Only two studies reported whether the lawsuit was individual or class action, and in both the claims were individual. Since the majority of the medicines requested in the lawsuits were medium to high-cost, the review indicates that lawsuits contributed to the incorporation of these drugs into current pharmaceutical care in Brazil.

Judicial Decisions; Pharmaceutical Services; Right to Health

Resumo

O objetivo desta revisão sistemática foi identificar e caracterizar artigos disponíveis em periódicos científicos indexados em bases eletrônicas, que realizaram levantamento de dados quantitativo, em processos administrativos ou judiciais, sobre a questão do acesso a medicamentos por meio de ações judiciais. Foram usadas as bases de dados SciELO, LILACS, MEDLINE via PubMed, Embase e Scopus. Identificamos 45 artigos, dos quais foram selecionados 17 artigos. Os estudos com faixa de 2.000 a 2.927 processos foram conduzidos em São Paulo, Rio de Janeiro e Santa Catarina, Brasil. Em 11 estudos foram pesquisadas qual a representação jurídica da ação. Em seis estudos predominaram a representação de advogados públicos e em cinco particulares. Somente dois estudos observaram se a ação era coletiva ou individual, sendo que nas duas pesquisas a prevalência era de ações individuais. Como a maioria dos medicamentos envolvidos nas ações é de médio e alto custo, acredita-se que as demandas judiciais tenham contribuído para incorporação de medicamentos nas ações de assistência farmacêutica atuais.

Decisões Judiciais; Assistência Farmacêutica; Direito à Saúde

Introduction

Various segments of Brazilian society have increasingly discussed health-related lawsuits, or the "judicialization" of health care. Health-related lawsuits have drawn extensive media coverage, with frequent newspaper and magazine stories reporting on right-to-health legal claims. The discussion is also high on the agendas of the health sector and the judiciary. Based on Article 196 of the 1988 *Federal Constitution*, that "*Health is the right of all persons and the duty of the State*", the number of Brazilians that sue to ensure this right has grown exponentially.

Data from the Brazilian Ministry of Health show that health-related lawsuits have increased year by year. There were 10,486 new lawsuits filed against the federal government in 2009, followed by 11,203 in 2010, 12,811 in 2011, and 13,051 in 2012 [1]. According to government data, most of these lawsuits are for access to medicines [2].

Due to this growing demand, studies in different states of Brazil have attempted to explain the judicialization phenomenon, identifying the general profile of lawsuits, drawing inferences on the claims, describing the various issues involved, and proposing alternatives to solve the problems.

The current study thus aimed to conduct a systematic review to identify and characterize articles published in indexed scientific journals with quantitative data surveys on administrative or legal proceedings for access to medicines in Brazil.

The government is aware that the majority of the claims are for access to medicines [2].

Studies on the phenomenon of judicialization have thus been done in various states of Brazil, drawing a profile of the lawsuits, identifying the underlying causes, describing the issues involved, and seeking alternatives to solve problems.

The growing number of lawsuits related to medicines and the number of publications on this issue motivated this systematic review, which aims to identify and characterize studies with surveys on lawsuits related to medicines in Brazil.

Methods

This descriptive study used the criteria defined by *Preferred Reporting Items for Systematic Reviews and Meta-Analyses* (PRISMA) [3].

Eligibility criteria for articles

The following criteria were adopted for the inclusion of articles: (1) surveys of data on administrative claims involving health administrators or lawsuits; (2) claims that involved medicines; (3) studies available in the form of scientific articles; (4) publication in journals that were indexed in the selected databases; and (5) quantitative data surveys. The review excluded studies that were theoretical analyses of the health judicialization phenomenon in general or of access to medicines in particular, as well as proceedings of meetings, monographs, theses, and bulletins and newsletters by health administrators.

Search strategy for the identification of articles

The articles were identified by searches in the SciELO, LILACS, MEDLINE via PubMed, Embase, and Scopus databases. In addition to use of the single databases, we also used the search interface in the Virtual Health Library (BIREME). Identification of studies began with a broad review in order to identify descriptors that were sufficiently sensitive to locate articles the met the study's objectives. The search strategy was prepared by identifying Health Sciences Descriptors (DeCS) in BIREME in English and Portuguese.

The terms located with this strategy were applied one by one to test their sensitivity, which produced the following combination: "drugs and judicial decisions", "right to health" and "judicial power", "Unified National Health System (SUS)", and "pharmaceutical services", "health policy" and "judicialization". These three intersections were applied one by one, since we found that grouping them decreased their search sensitivity. Another finding related to the term "judicialization", which is not a DeCS descriptor or Medical Subject Headings (MeSH) keyword, but has been used in the titles of articles in some Brazilian journals, accepted as a keyword, and has been accepted as a term to locate articles, which led to its inclusion in our search strategy. The search was limited to English and Portuguese. The references of the selected articles were checked manually to identify other articles that met the inclusion criteria but had not been located in the databases. The search was conducted in April and May 2012, and in June 2014 an updated search was done in MEDLINE via PubMed and SciELO.

Literature review methods

Two researchers independently performed the search and initial screening of article titles, and

their findings were compared to identify similar results. In case of disagreement, the method was reviewed and the search was repeated. The articles were first selected independently by the two researchers based on the titles, and in case of doubt, by reading the abstracts. The selected articles were transferred to EndNote (Thomson Reuters. http://www.endnote.com/) for storage and management of the references, and duplicates were excluded. In case of disagreement on inclusion or exclusion, a third researcher was consulted. The full texts of articles were retrieved and read by the principal investigator, and in case of doubt on the inclusion or exclusion of a given article, the decision was discussed between the review's authors.

Data extraction

After selection and complete reading of the articles, a database was created in Excel (Microsoft Corp., USA) to manage the information. The data's reliability and validity were evaluated according to the description of each study's method and generalization in the study's context. No scale was found to evaluate the quality of articles that reported studies on health-related lawsuits, so information from the articles was extracted and analyzed using the checklist from *Strengthening the Reporting of Observational Studies in Epidemiology* (STROBE) [4]. Although the latter is not a quality evaluator, it served as a parameter for finding relevant information in the articles in comparison to the checklist's criteria. The following information was collected and recorded: title, authors, periodical, year, country and language of publication, objectives, methods (design, study subjects, variables, data sources, study size), results, conclusions, and limitations.

Results

The search in the electronic databases identified 1,023 studies, of which 45 were selected for reading the full text. After a more detailed analysis and applying the exclusion criteria, the number was reduced to 15 articles. When the data were updated in June 2014, five more articles were identified, of which three were excluded because they failed to meet the selection criteria. Thus, 17 articles were finally selected and included (Figure 1). As for adequacy of the information in the articles according to the STROBE criterion of specifying limitations, seven articles did not refer to limitations, and those which did so reported the following principal limitations: small number of lawsuits analyzed (preventing external validation), access to data on patients, and the diseases involved in the claims for medicines.

Of the studies that were analyzed, 43.7% were published in the years 2010 and 2011 in Brazil (93.7%). The Brazilian states with the most publications on the issue of lawsuits for medicines were São Paulo (31.2%) and Rio de Janeiro (25%). A total of 17,783 lawsuits for medicines were analyzed from 2005 to 2013. The journal with the most articles on health-related lawsuits was *Revista de Saúde Pública* (Table 1).

Description of publications, document sources, and legal aspects

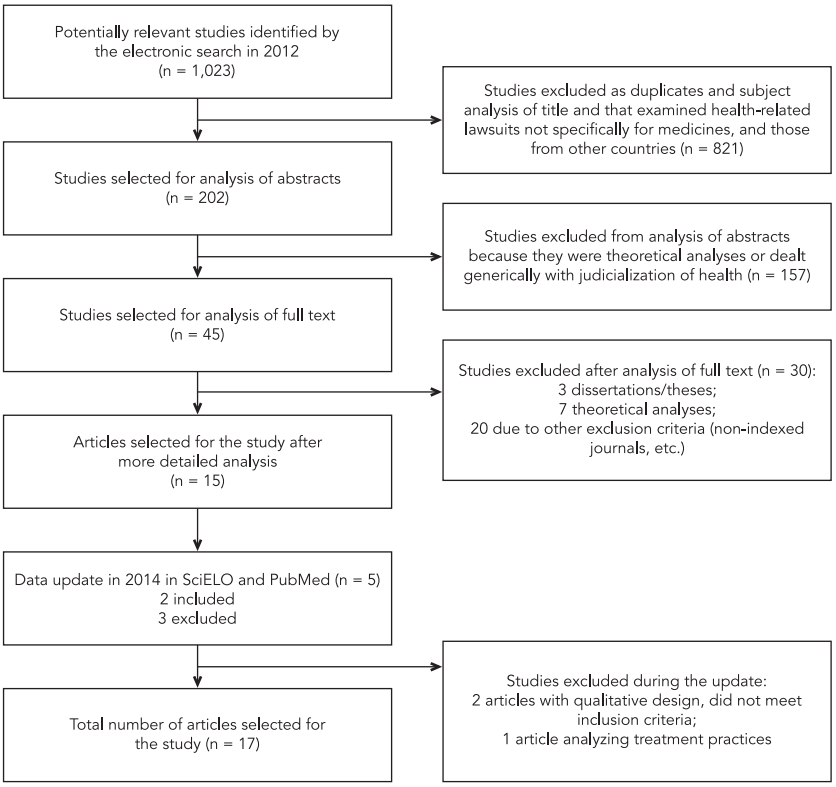
Tables 1 and 2 summarize the overall data in the publications, study characteristics, and sources used in the data collection. The first year of the publications included in the review was 2005, and there was a peak in the years 2010 and 2011. The data refer to studies done in the states of Pernambuco [5], Rio Grande do Sul [2,6], Minas Gerais [7,8], Rio de Janeiro [9,10,11,12], and São Paulo [13,14,15,16,17], besides one article that collected data directly from the Ministry of Health in Brasilia [18]. The studies that examined the most lawsuits (between 2,000 and 2,927 cases) were done in the states of São Paulo, Rio de Janeiro, and Santa Catarina [7,12,14,16,19].

As for the data sources, the majority of the studies analyzed the legal proceedings (83.3%), and one study only examined the initial lower court rulings [13], while another examined both initial rulings and the results of appeals [9]. The main data sources were: State Health Departments (41.2%) and the São Paulo State Online System for Monitoring Legal Proceedings (17.6%) (Table 2).

Table 3 lists the relevant legal variables presented in the studies. Of all the studies, 64.7% (n = 11) specified the form of legal representation for plaintiffs. Six studies [2,9,10,11,14,17] reported a predominance of public legal representation (Office of the Public Defender, Office of the Public Prosecutor, Offices of Municipal, State, and Federal Attorneys). In five studies [6,7,8,16,20], most plaintiffs were represented by private attorneys. In one study, free legal aid was provided to all the plaintiffs [6]. According to two studies, a small number of attorneys and physicians were involved in a large number of lawsuits [7,17]. For example, one study found that in one of the law firms representing plaintiffs (165 suits), 43.6% involved the same physician prescribing adalimumab (for treatment of rheumatoid arthritis), suggesting a possible association between the manufacturing laboratory, prescribers, and attorneys [7].

Figure 1

Flowchart for article selection in the literature review.



A study in the state of Pernambuco found that in the first half of 2009, the cost of purchasing the medicines in the lawsuits was approximately BRL 4.5 million, and for 70.9% of the drugs claimed by plaintiffs, the pharmaceutical companies had filed for patents on through the Brazilian National Patent Office (INPI), thus characterizing market control. In addition, 80% of these drugs were manufactured by eight pharmaceutical companies, and 90.95% of the funds from the Pernambuco State Health Department (SES-PE) for purchasing these drugs went to just seven laboratories [5].

Four studies [2,5,6,12] (23,5%) analyzed the plaintiffs' allegations in the lawsuits, or the grounds for the suit. The main claims involved urgency in the patient's health condition, imminent risk of death, and prescriptions and/or medical and laboratory reports proving the need for the product. In a study in the state of Rio Grande do Sul, 29% of the lawsuits claimed delay or denial of the drug when requested through normal administrative channels [2]. The fundamental right to health ensured by the *Federal Constitution* was cited as a justification for claims in at least articles [2,6,12].

Only two studies [6,10] (11.8%) specified whether the lawsuits were individual or class action, and in two studies the suits were predominantly individual. Three articles [2,6,10] (17.6%) examined petitions for advance relief or other types of court injunctions, and the results were the following: two studies showed 100% of such petitions [6,10] and one 98% [2]. The majority of the studies (76.5%; n = 13) collected specific data to determine whether there was more than one defendant in the suits, four conducted this analysis [2,6,9,10], in two of them the defendants were states and municipalities [9,13] and in the others the defendants were states, municipalities, and the Federal Government [2,6].

Table 1

Characterization of studies on lawsuits for medicines in Brazil published from 2005 to 2013.

Information on publications	n	%
Year of publication		
2013-2012	5	29.4
2011-2010	8	47.0
2009-2008	2	11.8
2007-2006	1	5.9
2005	1	5.9
Scope		
Federal Government	1	5.9
São Paulo State	5	29.4
Rio de Janeiro State	4	23.5
Minas Gerais State	2	11.8
Rio Grande do Sul State	2	11.8
Santa Catarina State	2	11.8
Pernambuco State	1	5.9
Language of publication		
Portuguese	16	94.1
English	1	5.9
Country of publication		
Brazil	16	94.1
United States	1	5.9
Journal		
Ciência & Saúde Coletiva	2	11.8
Revista de Saúde Pública	8	47.0
Cadernos de Saúde Pública	5	29.4
Health and Human Rights	1	5.9
Revista do Direito Sanitário	1	5.9
Study design		
Quantitative/descriptive	14	82.3
Mixed descriptive (theoretical/ quantitative)	3	17.7
Number of lawsuits (sample size)		
≤ 500	8	47.0
500-1,000	2	11.8
1,000-1,500	2	11.8
1,500-2,000	0	0.0
2,000-2,500	3	17.6
2,500-3,000	2	11.8

Characteristics of the claims examined in the articles

Table 4 shows the characteristics of the type of drug involved in the claim, type of health care service (public versus private), supply of the drug to the patient, presence of the drug on standard government lists, and registration of the drug in Brazil. Two articles dealt specifically with lawsuits for rare diseases [6,18], and one focused on claims filed by cancer patients [17]. Of the five studies that examined more than 2,000 lawsuits, only one verified whether the origin of the supply was from the public or private sector, and whether the drugs were registered with the Brazilian National Health Surveillance Agency (ANVISA) [14], and three studies analyzed whether the drugs claimed through lawsuits were part of official government lists [12,14,19]. In these same studies with the most lawsuits, one studied a period of more than ten years [7] and the others covered from one to three years [12,14,16,19]. Two of these studies were by the same research group and published analyses from the same sample in different time periods and with different analyses [14,16].

In two studies, the authors used the available data to attempt to classify the plaintiffs based on socioeconomic criteria. In one study, 53% of the patient-plaintiffs claimed income less than one minimum wage [2] and in another study socioeconomic status was assessed using place of residence as a proxy. In this case, 63% of the plaintiffs whose addresses were located actually lived in less impoverished areas [18].

In eight studies, the authors avalyzed the most frequent therapeutic indications. Diabetes mellitus and hypertension led the list (n = 5 and 4, respectively), followed by chronic obstructive pulmonary disease (COPD), chronic hepatitis C, cancer (n = 3), rheumatoid arthritis and kidney disease (n = 2). Eleven articles also examined the most frequent drugs in the claims. Insulin glargine was among the most frequent drugs (n = 5), followed by adalimumab, etanercept, and infliximab (n = 4).

Seven studies examined whether the medicines were registered with the ANVISA, and none of the studies showed more than 5% of unregistered products. One study examined only two drugs, one of which was registered with ANVISA and the other was not. A study in São Paulo (2010) compared the therapeutic indications claimed in the lawsuits with those in the product registrations. Unapproved indications accounted for 14% of the claims in 2006 and 10% in 2007, based on data from ANVISA, EMEA (European Agency for the Evaluation of Medicinal Products), and the FDA (U.S. Food and Drug Administration). Ten studies specified whether the medicines were on the official lists for pharmaceutical care and the RENAME (the Brazilian National List of Essential Drugs).

Table 2

Characterization of types of documents and agencies used as data sources.

Data source (type of document and location)	n	%
Documents		
Preliminary rulings on lawsuits and reports on drug costs	1	5.9
Files on lawsuits for medicines, Ministry of Health	1	5.9
Court proceedings	14	82.3
File on financial authorizations for purchase of drugs	1	5.9
Data collection site		
Municipal Health Secretariats *	2	11.8
State Health Secretariats	7	41.2
Ministry of Health, print and electronic files	1	5.9
Website, Court of Justice	2	11.8
Office of the State Attorney (PGE)	2	11.8
System for Registration of Court Proceedings (SCJ)	3	17.6

* One study also collected data from the Secretariat for Children, Adolescents, Elderly, Family, and Social Development of the Florianopolis Association of Volunteers.

Table 3

Legal variables analyzed by studies on lawsuits for medicines in Brazil.

Legal variables	n	%
Plaintiffs' legal representation (public, private, free legal aid)	11	64.7
Plaintiffs' allegations, and judges' reasons for ruling in favor of claims	4	23.5
Nature of lawsuit (individual or class-action)	2	11.8
Petition for advance relief or other injunctions	3	17.6
Defendants (Federal, state, or municipal government or a combination thereof)	4	23.5

Discussion

The publication of articles on lawsuits for access to medicines has increased significantly in Brazil since 2005, as shown in the data presented in this review. Brazil has four institutions that act to safeguard citizens' rights and compliance with the laws: (1) private attorneys hired by individuals; (2) public advocacy, represented by the Federal, State, and Municipal attorneys, responsible; (3) the Office of the Public Prosecutor, the institution responsible for defending the legal order and overseeing laws; and (4) the Office of the Public Defender, a relatively new institution whose objective is to ensure access to justice for persons with insufficient means [21].

The lawsuits analyzed in the studies were often filed individually, which raises the issue of distribution of funds in the Brazilian Unified National Health System (SUS), whose principles include universal access and questions concerning whether expenditure of funds to meet an individual claim might lead to lack of funds to supply collective needs [21]. There is no consensus among the parties involved in the judicialization of health, since it involves analyses with different concepts, leading to rulings by judges that generally favor the patient-plaintiff.

One approach used in the studies to identify whether the plaintiffs belong to higher income strata was to analyze their legal representation (public versus private), which in some cases could mean a loss of equity in the health system. Ten studies analyzed the plaintiffs' legal representation [2,6,7,8,9,10,14,16,17,20], of which three [7,14,16] examined more than two thousand lawsuits, whose plaintiffs were represented predominantly by private attorneys. These studies were done in São Paulo, Rio de Janeiro, and Minas Gerais, states with large populations, and two of the three

Table 4

Analysis of articles: most frequent therapeutic indications, drugs most frequently requested, origin of health services, registration with ANVISA, and inclusion on government distribution lists.

Authors	Therapeutic indications	Most frequently requested drugs	Health services	% without ANVISA registration	Inclusion on government distribution lists	Year of publication
Stamford et al. [5] (n = 105)	NA	Antineoplastic drugs and immune modulators	NA	NA	NA	2012
Campos Neto et al. [7] (n = 2,412)	Rheumatoid arthritis, type I diabetes mellitus, chronic obstructive pulmonary disease, and ankylosing spondylitis	Adalimumab, etanercept, ursodeoxycholic acid, infliximab, and insulin glargine	NA	NA	NA	2012
Sartoni Junior et al. [6] (n = 13)	Fabry's disease *	Alpha-galactosidase **	Private	0%	NA	2012
Diniz et al. [19] (n = 196)	Type IV mucopoly-saccharidosis ***	Galsulphase **	NA	NA	NA	2012
Biehl et al. [2] (n = 1,080)	Essential hypertension, diabetes mellitus, chronic viral hepatitis, ischemic heart disease, and chronic obstructive pulmonary disease	Teriparatide, clopidogrel, insulin glargine, rituximab, infliximab	Public	NA	Essential drugs 28%; exceptional drugs 27%; special drugs 11%; one strategic action; 56% not on list	2012
Macedo et al. [13] (n = 81)	NA	NA	NA	NA	14.3% primary care and 19.5% exceptional	2011
Machado et al. [8] (n = 827)	NA	Adalimumab, etanercept, insulin glargine, omeprazole, aripiprazole	Private	5%	19.6% on RENAME list; 11.1% WHO essential drugs; 24.3% high-cost; 10.9% primary care, 3.5% strategic. 56.7% not on list	2011
Sant' Ana et al. [9] (n = 27)	NA	Furosemide; digoxin; clonazepam; acetyl-salicylic acid; enalapril and bromazepam	50% private, 50% public	0.9%	45.2% RENAME; 13.9% exceptional	2011
Borges & Ugá [12] (n = 2,062)	NA	NA	NA	NA	52% on Ministry of Health lists	2010
Chieffi & Barata [16] (n = 2,927)	NA	Insulin glargine and lispro, adalimumab, etanercept, infliximab	NA	NA	NA	2010
Lopes et al [17] (n = 1,220)	Cancer #	Bevacizumab, capecitabine, cetuximab, erlotinibe, imatinibe, rituximab, temozolomide	Private	2006: 14% 2007: 10% ##	NA	2010
Pepe et al. [10] (n = 185)	Hypertension, diabetes mellitus, degenerative diseases of the nervous system, chronic lower airway diseases, and end-stage renal disease	NA	NA	NA	35.8% of drugs on RENAME list and 48.1% on government distribution lists	2010

(continues)

Table 4 (continued)

Authors	Therapeutic indications	Most frequently requested drugs	Health services	% without ANVISA registration	Inclusion on government distribution lists	Year of publication
Pereira et al. [20] (n = 622)	Rheumatoid arthritis, ankylosing spondylitis, psoriatic arthritis, hepatitis C, ischemic heart disease, hypertension, cancer, and diabetes	Infliximab, leflunomide, etanercept, adalimumab, propatyl nitrate, clopidogrel, enalapril,carvedilol, simvastatin, insulin glargine	Private	1,4%	Exceptional/high-cost drugs 26.4%; primary pharmaceutical care 2.4%; mental health 1.5%; strategic 1.4%; cystic fibrosis 1%	2010
Chieffi & Barata [14] (n = 2,927)	NA	NA	Public	3%	23% supplied by SUS,;13% belonged to Program for Dispensing Exceptional Drugs;	2009
Leite et al. [18] (n = 2,426)	NA	NA	NA	NA	32% of requested drugs were part of standard distribution in the SUS	2009
Vieira & Zucchi [15] (n = 170)	Diabetes mellitus, cancer, comorbidities related to hypertension and diabetes	NA	Public	2 without registration	62% part of REMUME – São Paulo, or the list of the Program for Dispensing Exceptional Drugs (High-Cost)	2007
Messeder et al. [11] (n = 389)	Until 1998: HIV. 2000: Crohn's disease, chronic hepatitis C, and kidney disease 2001 and 2002: essential hypertension and chronic ischemic heart disease	2000: botulin toxin type A, riluzole and olanzapine. 2001: cyproterone acetate and goserelin acetate. 2002: sevelamer hydrochloride and mesalazine	Public	NA	31.4 % exceptional, 18.2% strategic, 14/08% primary care, 19% mental health, 3.7% state, 30.8% with no definition of funding	2005

ANVISA: Brazilian National Health Surveillance Agency; n: number of cases and lawsuits analyzed; NA: not analyzed; RENAME: National List of Essential Drugs;
REMUME: Municipal List of Essential Drugs;
* Study limited to patients with Fabry's disease;
** Most frequent;
*** Study limited to briefs from lawsuits on drugs for mucopolysaccharidosis;
# Study in São Paulo on the seven antineoplastic drugs with the greatest financial impact on the Brazilian Unified National Health System (SUS);
Analysis based on the therapeutic indications approved by EMEA, FDA, and ANVISA.

studies were by the same authors. An important characteristic of the study in São Paulo is that most of the lawsuits were filed by individuals that were less economically deprived; meanwhile, the drugs claimed in the study in Minas Gerais are among the most costly and most recently available on the Brazilian market. The study identifies an association between the claims and the small number of attorneys and physicians involved in the lawsuits. Despite the high number of lawsuits and the characteristics of the claims, it is difficult to establish a relationship between public versus private legal representation and a conflict with health equity as a common practice in the entire country.

In some states, such as Rio Grande do Sul and São Paulo, in order to receive legal aid from the Office of the Public Defender, there is a limit on the plaintiff's income (three times the minimum wage) [2], while in other states such as Rio de Janeiro and the Federal District it is necessary to prove insufficient economic means with documents and an affidavit signed by the plaintiff[10]. In this case, one might infer that, in principle, individuals filing claims through the Office of the Public Defender have the lowest socioeconomic status. However, it is not possible to affirm the opposite, since private legal defense is not a good indicator of economic class. The legal costs may often be covered by institutions that have an in-

terest in judicialization, such as pharmaceutical laboratories and distributors [22]. In addition, such costs would be unaffordable for individuals with very low income, but they would not be an impediment for the majority of the population. An important issue that is discussed among patient-plaintiffs is that in states of Brazil that do not have an Office of the Public Defender (or where such an office exists, but with an insufficient number of attorneys), it is possible to hire a private law firm and petition the court for free legal defense. This was reported in at least one study, in which all the patient-plaintiffs received free legal aid [6]. Thus, it cannot be proven that access to medicines via lawsuits in Brazil is mainly for individuals with higher purchasing power.

Four studies analyzed the allegations by patient-plaintiffs, private attorneys or public defenders, and judges to justify the claim for the medicine. The researchers found that the main argument by judges was the fundamental right to health, guaranteed by Article 196 of the 1988 *Federal Constitution* and *Law n. 8,080/1990*. According to Stamford & Cavalcanti [5], the Constitution has the power to ensure enforcement of public policies. Meanwhile, the allegations by patient-plaintiffs and their attorneys and defenders are based on urgent or emergency need, risk of death, and/or need for the medicine as attested by the physician, and the judges do not generally request any additional information.

Most of the diseases reported in the studies are chronic, such as diabetes mellitus, hypertension, COPD, chronic hepatitis C, ischemic heart disease, and cancer. According to data for 2012 from the International Diabetes Federation, diabetes mellitus affected some 13.4 million adults in Brazil, which represents 6.5% of the population from 20 to 79 years of age [23]. Another factor to consider in relation to the prevalence of chronic diseases is the change in the population's epidemiological profile related to aging and socioeconomic conditions [14]. Data on the therapeutic indications for the medicines were analyzed by nine of the 17 articles included in the review [2,6,7,10,11,15,17,18,20] and show that in most cases the prescribed drugs can be classified as medium to high cost, while four studies were designed to clarify points on rare diseases. Thus, it is not possible to infer that the high cost of lawsuits is due to the lack of organization in primary care. The data in the studies are specific, and are not able to answer this question.

At any rate, the most recent data collected in the studies are from 2011, and some changes may have occurred in the management of pharmaceutical care. Today, drugs that were formally claimed through lawsuits are now covered by the Ministry of Health's budget. Drugs for rheumatoid arthritis (adalimumab, etanercept, and infliximab) [7] are an example of inclusion on the standard drug list of the SUS in 2012. Since 2006 these drugs had already been part of the treatment alternatives listed in clinical protocols and therapeutic guidelines for the disease, which provide for the use of cytokine antagonists as alternative treatment in patients that have failed on other therapies. This time lag is due to the fact that most of the published data are from lawsuits that were tried between 2002 and 2006. No more recently published data on lawsuits were found, while public policies have advanced in Brazil, due largely to the increase in legal claims for medicines.

One limitation to this review is the lack of homogeneity among the studies, since each one focused on a specific aspect of health-related lawsuits, thus hindering a comparative analysis of the articles. The methods adopted in the current review, such as application of descriptors and the criterion of including articles published in indexed journals, may have led to a loss of relevant studies done in different states of Brazil. Another limitation involved quality analysis of the articles with the characteristics of studies on judicialization, requiring the use of STROBE, which is not recommended for backing the analysis for this purpose.

The main limitation to the articles was external validity. The states of Brazil covered in the studies, especially Rio de Janeiro and São Paulo, have populations that are better informed and showed more health-related lawsuits (their populations are presumably more able to identify and claim their rights). Since most of the drugs involved in the claims are medium to high-cost, we believe that the lawsuits contributed to the inclusion of drugs on the current official list for pharmaceutical care, even though the volume of information analyzed and the different research models did not allow a joint analysis of the data. Some characteristics of the lawsuits, such as the fact that the majority of the patient-plaintiffs had chronic diseases and turned to the Office of the Public Defender or private attorneys to access medium to high-cost medicines, do not allow inferences on the management of primary care or a possible breach in health equity. There is a need for further analyses and follow-up on the phenomenon in the health system's management, given that drugs that were not on the Ministry of Health's standard list in 2011 have now been incorporated into the public health system. Evaluation of therapies, elaboration of protocols, and specific proposals for the treatment of rare diseases may prevent the need for

lawsuits, thereby decreasing the cost of purchasing these drugs.

Of the selected articles, 25% reported that at some point in the proceedings there was a petition for advance relief or some other type of injunction, and that in the majority of cases the judges did not request further clarification before granting such requests, but relied only on the medical prescription and the documents presented at the initial hearing. According to the studies, before granting advance relief or injunctions, the courts do not conduct any detailed analysis of the patient's health status, backed by such evidence as laboratory tests, physician's reports, or the urgency of need.

There are first-line therapies for all the most frequent diseases, described in Brazilian and international clinical protocols. The incorporation of new technologies and patient care practices should be based on clinical trials that prove the new drug's safety and efficacy, in addition to cost-benefit analysis in relation to existing treatments. Thus, when decisions are made to purchase a given drug without a prior analysis of the treatment alternatives that are already included in the SUS budget, health policy is being overlooked, with potential harm to both the user and the system as a whole. In addition, existing flaws in the organization of the country's pharmaceutical care can lead to shortages in the government pharmacies.

Of the four drugs with the highest demand through lawsuits (insulin glargine, adalimumab, etanercept, and infliximab), the only one not on RENAME for 2013 was insulin glargine, although its use has been standardized in some states, like Minas Gerais [10]. Insulin glargine is a long-acting insulin analogue. The Brazilian Bulletin on Health Technology Assessment was published in 2010, comparing insulin determir and glargine for the treatment of type I diabetes mellitus, using a literature review of clinical trials on the efficacy and safety outcomes of insulin glargine and detemir, with NPH insulin (neutral protamine Hagedorn).

The clinical evidence and methodological biases identified in the studies do not allow stating whether there is a difference between detemir, glargine, and NPH insulin in terms of glycemic control, and insulin glargine only proved superior in preventing episodes of nocturnal hypoglicemia. A cost-effectiveness study in Canada concluded that replacing NPH insulin with detemir and glargine for the treatment of type I diabetes mellitus would be costly for the national health system [24].

Ten studies dealt with the issue of funding the drugs and their inclusion on the government lists for free distribution, but it was not possible to group the results, since the studies used different classifications from those of the Ministry of Health. In all the studies that conducted this type of analysis, medicines with free distribution in the public system were requested by lawsuits, especially medicines from the specialized component. The presence of such medicines can be justified since their supply is tied to the Clinical Protocols and Therapeutic Guidelines, and many patients may be using them for off-label treatment. The presence of the medicines on the RENAME list, when analyzed, varied from 19.6% to 52%.

Finally, the researchers found that the data were insufficient to establish a socioeconomic profile of the patient-plaintiffs. The lawsuits did not generally contain data on place of birth, schooling, profession, employment, or income, or in some cases even the name of the drug requested or the plaintiff's disease. Many of the researchers identified such lack of information as a major limitation to the studies.

Resumen

El objetivo de esta revisión sistemática fue identificar y caracterizar los artículos disponibles en revistas científicas indexadas en bases de datos electrónicas, que llevaron a cabo un estudio cuantitativo de datos, procedimientos administrativos o judiciales sobre la cuestión del acceso a los medicamentos a través de demandas judiciales. Los estudios fueron localizados en las bases de datos SciELO, LILACS, MEDLINE vía PubMed, Embase, Scopus. Se identificaron 45 artículos, de los cuales se seleccionaron 17. Los estudios que se llevaron a cabo engloban de 2.000 a 2.927 procesos judiciales en São Paulo, Río de Janeiro y Santa Catarina, Brasil. En once estudios se realizaron encuestas a los representantes legales de la acción judicial. En seis estudios predominó la representación pública legal y en cinco abogados privados. Sólo dos estudios examinaron si la acción era individual o colectiva y en los dos hubo prevalencia de acciones individuales. Como la mayoría de los medicamentos estaba involucrada en acciones legales de medio y alto coste, se cree que las demandas han contribuido a la incorporación de fármacos en la política pública actual.

Decisiones Judiciales; Servicios Farmacéuticos; Derecho a la Salud

Contributors

V. S. Gomes and T. A. Amador collaborated in the study planning, data collection, analysis, and interpretation, writing and critical revision of the article, and approval of the final version for publication.

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Gomes VS, Amador TA. Studies published in indexed journals on lawsuits for medicines in Brazil: a systematic review. Cad Saúde Pública 2015; 31(3):1-12.
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The journal has been informed about some errors in the paper. The corrections are follows:
A revista foi informada sobre alguns erros no artigo. As correções seguem abaixo:
La revista fue informada sobre algunos errores en el artículo. Siguen las correcciones:

- On page 5, second column, first paragraph, line 10, where the text reads:
...and three studies analyzed whether the drugs claimed through lawsuits were part of official government lists [12,14,19]*...*
it should read:
...three studies [12,14,18] *analyzed whether the drugs claimed through lawsuits were part of official government lists...*

- On page 5, second column, third paragraph, line 29, where the text reads:
...In eight studies, the authors avalyzed the most frequent therapeutic indications. Diabetes mellitus and hypertension led the list (n = 5 and 4, respectively), followed by chronic obstructive pulmonary disease (COPD), chronic hepatitis C, cancer (n = 3), rheumatoid arthritis and kidney disease (n = 2)...
it should read:
...In eleven studies [2,6,7,8,9,10,11,15,17,19,20]*, the authors avalyzed the most frequent therapeutic indications. Diabetes mellitus and hypertension led the list (n = 6 and 4, respectively), followed by chronic obstructive pulmonary disease (COPD), chronic hepatitis C, cancer (n = 3), rheumatoid arthritis and kidney disease (n = 2)...*

- On page 5, second column, third paragraph, line 35, where the text reads:
...Eleven articles also examined the most frequent drugs in the claims. Insulin glargine was among the most frequent drugs (n = 5), followed by adalimumab, etanercept, and infliximab (n = 4)...
it should read:
...Twelve articles [2,6,7,8,9,10,11,13,16,17,18,19] *also examined the most frequent drugs in the claims. Insulin glargine was among the most frequent drugs (n = 4), followed by adalimumab, etanercept, and infliximab (n = 3)...*

- On page 5, second column, fourth paragraph, line 40, where the text reads:
...Seven studies examined whether the medicines were registered with the ANVISA, and none of the studies showed more than 5% of unregistered products...
it should read:
...Eight studies [6,8,9,10,14,15,17,20] *examined whether the medicines were registered with the ANVISA, and none of the studies showed more than 5% of unregistered products...*

- On page 5, second column, fourth paragraph, line 53, where the text reads:
...Ten studies specified whether the medicines were on the official lists for pharmaceutical care and the RENAME (the Brazilian National List of Essential Drugs)...
it should read:
...Eleven studies [2,8,9,10,11,12,13,14,15,18,20] *specified whether the medicines were on the official lists for pharmaceutical care and the RENAME (the Brazilian National List of Essential Drugs)...*

- On page 9, first column, second paragraph, line 43, where the text reads:
...Data on the therapeutic indications for the medicines were analyzed by nine of the 17 articles included in the review [2,6,7,10,11,15,17,18,20]*...*
it should read:
...Data on the therapeutic indications for the medicines were analyzed by 12 of the 17 articles included in the review [2,6,7,8,9,10,11,14,15,17,19,20]*...*

- On page 10, first column, third paragraph, line 31, where the text reads:
...Of the four drugs with the highest demand through lawsuits (insulin glargine, adalimumab, etanercept, and infliximab), the only one not on RENAME for 2013 was insulin glargine, although its use has been standardized in some states, like Minas Gerais...
it should read:
...Of the five drugs with the highest demand through lawsuits (insulin glargine, adalimumab, etanercept, infliximab and acetyl-salicylic acid), the only one not on RENAME for 2013 was insulin glargine, although its use has been standardized in some states, like Minas Gerais...

- Table 4 in its correct form is:

Table 4

Analysis of articles: most frequent therapeutic indications, drugs most frequently requested, origin of health services, registration with ANVISA, and inclusion on government distribution lists.

Authors	Therapeutic indications/diagnosis *	Most frequently requested drugs/pharmacological classes	Health services	% without ANVISA registration	Inclusion on government distribution lists	Year of publication
Stamford et al. [5] (n = 105)	NA	Antineoplastic drugs and immune modulators	NA	NA	NA	2012
Campos Neto et al. [7] (n = 2,412)	Rheumatoid arthritis, type I diabetes mellitus, chronic obstructive pulmonary disease, and ankylosing spondylitis.	Adalimumab, etanercept, ursodeoxycholic acid, infliximab, and insulin glargine	87.5% private; 12.5% public	NA	NA	2012
Sartoni Junior D et al. [6] (n = 13)	Fabry's disease **	Alpha-galactosidase ***	UH	0	NA	2012
Diniz et al. [19] (n = 196)	Type IV mucopolysaccharidosis #	Galsulphase, idursulphase, laronidase ***	NA	NA	NA	2012
Biehl et al. [2] (n = 1,080)	Essential hypertension, diabetes mellitus, chronic viral hepatitis, ischemic heart disease, and chronic obstructive pulmonary disease	Budesonide, acetyl-salicylic acid, formoterol, simvastatin and hydrochlorothiazide	45.1% public; 36.8% private; 14.7% university health services; 3.4% WI	NA	Essential drugs 28%; exceptional drugs 27%; special drugs 11% ##	2012
Macedo et al. [13] (n = 81)	PI	Teriparatide, clopidogrel, insulin glargine, rituximab, infliximab	NA	NA	14.3% primary care and 19.5% exceptional	2011
Machado et al. [8] (n = 827)	Rheumatoid arthritis, diabetes mellitus type I, hypertension, Schizophrenia and Alzheimer disease	Adalimumab, etanercept, insulin glargine, omeprazole, aripiprazole	70.5% private; 25.8% public; 3.7% public + private	4.8	19.6% on RENAME list; 11.1% WHO essential drugs; 24.3% high-cost; 10.9% primary care, 3.5% strategic. 56.7% not on SHS list	2011
Sant' Ana et al. [9] (n = 27)	Diseases of the circulatory system, diseases of the osteomuscular system and conjunctive tissue and mental and behavioral disorders	Furosemide, digoxin; clonazepam, acetyl-salicylic acid, enalapril and bromazepam	50% private (± 86.7% private doctors and 13.3% health mutualistic associations); 50% public (40% UH and 60% other units of SUS)	0.9	57.4% belonged to any official list (45.2% RENAME; 32.2% other lists)	2011
Borges & Ugá [12] (n = 2,062)	NA	NA	NA	NA	52% on Brazilian Ministry of Health lists; 48% out of the official lists	2010
Chieffi & Barata [16] (n = 2,927)	NA	Insulin glargine and lispro, adalimumab, etanercept, infliximab	NA	PI ###	NA	2010
Lopes et al. [17] (n = 1,220)	Cancer §	Bevacizumab, capecitabine, cetuximab, erlotinibe, imatinibe, rituximab, temozolomide	Most private §§	2006: 14 2007: 10 §§	NA	2010

(continues)

Table 4 (continued)

Authors	Therapeutic indications/diagnosis *	Most frequently requested drugs/pharmacological classes	Health services	% without ANVISA registration	Inclusion on government distribution lists	Year of publication
Pepe et al. [10] (n = 185)	Hypertension, diabetes mellitus, degenerative diseases of the nervous system, chronic lower airway diseases, and end-stage renal disease	Furosemide, acetyl-salicylic acid, digoxin, enalapril, propatilnitrate clonazepam and captropil	NA	NA	35.8% of drugs on RENAME list and 48.1% on government distribution lists	2010
Pereira et al. [20] (n = 622)	Rheumatoid arthritis, ankylosing spondylitis, psoriatic arthritis, hepatitis C, ischemic heart disease, hypertension, cancer, and diabetes	PI ###	55.8% private; 33% public and 11.3% could not identify	1.4	62.2% nonstandard; 37.8% at any program	2010
Chieffi & Barata [14] (n = 2,927)	PI ###	Therapeutical classes: alimentary tract and metabolism; cardiovascular system; nervous system	48% SUS; 47% complementary system and 4% could not identify	3% (n = 954)	77.46% out of SUS official lists; 22.54% at SUS official list	2009
Leite et al. [18] (n = 2,426)	PI ###	Carbamazepine, pimecrolimus, "insulines"	IP ###	NA	32% of requested drugs were part of standard distribution in the SUS	2009
Vieira & Zucchi [15] (n = 170)	Diabetes mellitus, cancer, comorbidities related to hypertension and diabetes	PI ###	59.2% public (25.8% municipal; 33.3% other) and 40.8% private (13.3% outsourced by the SUS, 27.5% no outsourced)	2 without registration	62% at SUS official lists	2007
Messeder et al. [11] (n = 389)	Until 1998: HIV. 2000: Crohn's disease, chronic hepatitis C, and kidney disease. 2001 and 2002: essential hypertension and chronic ischemic heart disease	2000: botulin toxin type A, riluzole and olanzapine. 2001: cyproterone acetate and goserelin acetate. 2002: sevelamer hydrochloride and mesalazine	36.8% UH, 19.5% clinics/outsourced by SUS; 11.1% FH; 10.5% MHS posts; 10.5% private doctors; 5.5% clinics/ not outsourced by SUS; 3.5% MH; 1.3% PH and 1.3% WI	NA	31.4% exceptional, 18.2% strategic, 14.0% primary care, 19% mental health, 3.7% state, 30.8% with no definition of funding	2005

ANVISA: Brazilian National Health Surveillance Agency; FH: Federal Hospital; MH: Municipal Hospital; MHS: Municipal Health Secretariat; n: number of cases and lawsuits analyzed; NA: not analyzed; PH: Provincial Hospital; PI: partial information; REMUME: Municipal List of Essential Drugs; RENAME: National List of Essential Drugs; SHS: State Health Secretariat; SUS: Brazilian Unified National Health System; UH: University Hospital; WHO: World Health Organization; WI: without infromation.

* In some studies were presented as "therapeutic indication" and others only "diagnosis" was chosen for the table include the diagnosis as well;

** Study limited to patients with Fabry's disease;

*** Most frequent;

Study limited to briefs from lawsuits on drugs for mucopolysaccharidosis;

Percentage relative to the total of "drugs" on official lists (n = 1,956), and 455 have different "drugs" and 56 % of these drugs were outside the official lists;

In these cases the data could not be separated for a quantitative analysis, or being presented as "majority" (if the health service, that "most of the SUS prescriptions") or not has been made for % of the variable in question alone;

§ Study in São Paulo on the seven antineoplastic drugs with the greatest financial impact on the SUS;

§§ Analysis based on the therapeutic indications approved by EMA, FDA, and ANVISA.