Knowledge, Perceptions, and Utilization of Generics and Biosimilars in Latin America and the Caribbean: A Scoping Review

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Abstract: We conducted a scoping review to map and critically examine the knowledge, perceptions and utilization of generics and biosimilars, among physicians, pharmacists, patients, the general population, and other stakeholders from LAC.

1. Introduction

Health care and pharmaceutical expenditure has been rising in most countries due to many factors including aging populations, increasing patient expectations, and the introduction of new and more expensive drugs.[1] Pharmaceutical spending accounts for 16.4% of overall health care expenditures across OECD countries.[2] In Latin America and the Caribbean (LAC) the picture is varied, but on average 16% of health care spending goes to pharmaceuticals and in many countries, out-of-pocket payments on drugs account for a substantial portion of household expenditure.[3] To deal with these challenges, LAC governments have implemented a number of initiatives to promote rational use of drugs and reduce their cost. In this context, generic drugs and biosimilars play an important role as an alternative to more costly branded innovator medicines in the treatment of diseases.

Generic drugs (hereafter, just 'generics') are drug products comparable with an innovator/reference drug product (hereafter, just 'reference product') and are usually manufactured without a license from the innovator company. They are marketed after the expiry of the patent or other exclusivity rights with a nonproprietary name ('pure generic') or under a brand ('similar'). Their price is commonly cheaper than their reference products (up to 66% less) and in most cases continues to decline as time passes.[4] As for biosimilars, they are biological products that are highly similar in terms of quality, safety, and efficacy to an already licensed reference biotherapeutic product and have no clinically meaningful differences with them. In comparison with generics, biosimilars are expensive due to their higher investment costs, more complex production process, and greater marketing entry restrictions. However, they still constitute less costly alternatives with up to 50% price reduction.[5]

According to the literature, one barrier that may be preventing widespread usage of generics and biosimilars relates to a lack of knowledge and negative perceptions regarding these products among consumers, physicians, and other stakeholders.[6] A number of systematic reviews have examined perceptions of generics and biosimilars among these different actors.[7] Noteworthy, these reviews have included only a handful of studies from LAC countries, either due

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to language restrictions or narrow timeframes for the search. To our knowledge, no review has focused on the LAC region nor included literature in Spanish and Portuguese.

In this scoping review, we aim to map and critically examine the existing empirical literature on the knowledge, perceptions, and utilization of generics and biosimilars in LAC. We include physicians, pharmacists, patients, the general population, and other stakeholders involved in the provision and purchasing of these products. We used a systematic review methodology to obtain a rigorous picture of the available literature on this topic.

2. Policies Concerning Generics and Biosimilars in LAC

Several LAC countries have introduced policies to regulate and encourage the utilization of generics and biosimilars. Part of this effort includes strengthening National Medicine Agencies (hereafter, 'national agencies'), which are tasked with defining the pathway and regulations for the approval of generics and biosimilars—an essential step towards generating a favorable environment for drug interchangeability policies. Many countries have also implemented policies to develop health technology assessment, that is, the systematic evaluation of properties, effects, and/or impacts of health care technology. Health technology assessment policy reports or suggestions are important to increase the level of confidence in the quality, safety, and efficacy of generics and biosimilars, as well as for the successful implementation of access to medicines programmes (which often involve generics and biosimilars). Additional policies concerning generics and biosimilars include educational and promotional campaigns to improve utilization of these products among all healthcare stakeholders, and efforts for regulatory harmonization.

Despite policy improvements across the region, the regulatory landscape in LAC is varied. There are also important differences among LAC countries with respect to size of gross domestic product (GDP), public spending, health spending in relation to GDP, as well as the existence of high-level regulatory agencies, drug-producing capacities, and government norms/strategies related to drugs and procurement. However, the World Health Organization (WHO) has estimated that six countries in LAC have legal norms and adequate organizational frameworks for drug regulation: Argentina, Brazil, Chile, Colombia, Cuba, and Mexico.[8] Below, we present some notable efforts in policies concerning generics and biosimilars in the LAC region focusing on these six countries, but also considering progress made by additional countries such as Ecuador and Peru. We conclude by briefly discussing the stance of other countries in the region that are less developed in this respect.

Most national agencies in the region are inspired by the Food and Drug Administration of United States (FDA), the European Medicines Agency (EMA), and the World Health Organization (WHO) regulatory frameworks, and while it is possible to identify nuances in the adoption of these organizations' guidelines, there are sustained efforts over time to converge. Brazil has also implemented measures to increase domestic production of medicines, with the aim of reducing reliance on imports and improving access to affordable treatments. This includes tax incentives and investment in research and development. Colombia is in the process of strengthening its National Institute for Food and Drug Surveillance (INVIMA) and the health technology evaluation agency to establish new roles for approval, value-based pricing and funding. Mexico is trying to centralize purchases under the United Nations Office for Project Services (UNOPS), update a National drug formulary, and optimize their Federal Commission for the Protection against Sanitary Risks (Cofrepris) and equivalence agreements with other national agencies.[9] Mexico has also implemented price control mechanisms for medicines in the private sector, including reference pricing and negotiation of prices with pharmaceutical companies.

In this scoping review, we aim to map and critically examine the existing empirical literature on the knowledge, perceptions, and utilization of generics and biosimilars in LAC. We include physicians, pharmacists, patients, the general population, and other stakeholders involved in the provision and purchasing of these products. We used a systematic review methodology to obtain a rigorous picture of the available literature on this topic.

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Ecuador is moving towards the consolidation of the National Public Procurement Service (SERCOP) process for purchases in the public sector and the actualization of its national formulary.

Some of the most notable progress in the region has been in the introduction of access to medicines programmes, which are often accompanied by health technology assessment systems. In Argentina, the Comprehensive Medical Care Program (PAMI) is a public agency that provides health and medical insurance services targeting elderly people. Its decisions are informed by health technology assessment and participation of the public.[10] Colombia has implemented several policies aimed at improving access to medicines, especially for vulnerable populations. One of the most significant policies is the Comprehensive National Health Plan, which includes strategies to increase access to medicines, improve the supply chain, and promote the use of generic drugs. Colombia has also established a High-Cost Drug Fund, which provides financial support for patients who require expensive medications for chronic and rare diseases.[11] In Mexico, one of the main initiatives is the Popular Insurance program, which provides health insurance coverage to individuals without social security and includes a basic package of health services.[12] Peru has implemented an Essential Medicines Program which seeks to ensure the availability of essential medicines at all levels of the health system. The program includes a list of essential medicines that are procured and distributed by the government to public health facilities. Another key policy is the Unified Health System which provides a comprehensive package of health services, including access to medicines, through public health facilities.[13]

Some countries have introduced coverage development policies for high-cost medicines. In Brazil, the National Commission for Incorporation of Technologies (CONITEC) evaluates the clinical effectiveness and cost-effectiveness of new health technologies, including drugs and medical devices. CONITEC's evaluations are used to determine whether new technologies should be incorporated into the Brazilian public health system, and at what price. Another key policy is the creation of the Strategic Medicine Program (PME), which provides free access to high-cost medicines for certain chronic diseases, including cancer, multiple sclerosis, and rheumatoid arthritis. Chile has implemented several access-to-medicines programs, including Plan of Explicit Health Guarantees for health care, Ricarte Soto Plan for high-cost diseases, and High-Cost Drugs Committee for cancer medicines.

Brazil has emerged as a leader in promoting the use of generic drugs and biosimilars in Latin America. The country has implemented various policies to incentivize the use of these drugs, including price controls, tax exemptions, and educational campaigns. The Brazilian government has also established a robust regulatory framework for biosimilars, which has facilitated their entry into the market and ensured their safety and efficacy. As a result of these efforts, Brazil has seen a significant increase in the use of generics and biosimilars.[14] According to a report by the Brazilian Ministry of Health, generics accounted for over 35% of the total drug market in 2020, while biosimilars represented around 8%.[15] This trend has led to substantial cost savings for both patients and the public health system, while improving access to essential medicines.[16] Chile has implemented several policies to promote the use of generic medicines, such as allowing pharmacists to substitute branded medicines with generic equivalents, and promoting the use of international non-proprietary names (INN) for medicines.[17] In Peru, the Good Practices in Prescription and Dispensation of Medicines is another policy aimed at improving the quality of care and rational use of medicines. This policy includes guidelines for prescribing and dispensing medicines to ensure appropriate use and avoid overuse or misuse.[18]

Another sign of improvement in the LAC region is that many countries have adopted common definitions for generic and biosimilar medicines. Regarding generics, differences between countries are mainly based on the mechanisms to consider interchangeability, marketing authorizations, and the role of bioequivalence studies as a mandatory requirement for this purpose. With respect to biosimilar products, although the WHO provides a definition that has been widely adopted, countries differ in their regulatory pathways for approval, which is relevant with respect to the specific types of studies for preclinical/clinical data, the possible extrapolation of indications, pharmacovigilance, and risk management plans.[19]

Besides the LAC countries already mentioned, there are a number of countries with smaller economies and different levels of development. They have less developed markets and their main health challenge is to achieve socially and financially sustainable health systems. In those countries, mostly in the Caribbean basin, their drug access policies mainly adhere to PAHO/WHO guidelines.

Overall, variations in the regulatory frameworks regarding generics and biosimilars in the LAC region can be understood as local adaptations of the WHO and EMA guidelines based on local realities and

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underlying pressures as a result of the configurations of their health sectors and the differences in the access to medicines.[20] These regulatory differences, can constitute potential elements that could influence or be used as drivers for policy developments that promote generic and biosimilar drugs in Latin America.

3. Methods

Study Design

The study is a scoping review. We report the study in accordance with the Preferred Reporting Items of Systematic Reviews and Meta-Analyses (PRISMA).[21]

Search Strategy and Selection Criteria

We searched the literature indexed in PubMed and Epistemonikos. All databases were searched from inception to October 14, 2022. We employed a search strategy based on medical subject headings and text words combined using Boolean operators. We used the terms 'generic drug' and 'biosimilar' and included the names of all countries in Latin America and the Caribbean plus the term 'Latin America'. The full search strategy can be found in the Supplementary Appendix (Table S1). To obtain additional records, we handsearched the reference lists of the included research studies. There were no language or other restrictions.

We included research records if they met the following criteria: (1) the target population was from countries in the LAC region, including health professionals, pharmacists and other stakeholders, patients in all levels of care and the general population; (2) the outcomes of the study were knowledge, perceptions, and/or utilization of any generic drug or biosimilar. We included all types of observational or experimental studies, regardless of study design. We excluded research records that did not involve data collection, such as editorials or commentaries. We distinguished patients and the general population based on the study sampling strategy. Participants in studies conducted in health centers, hospitals, and pharmacies were considered patients, while participants from population-based sampling strategies were considered as the general population.

Data Screening and Extraction

We downloaded research records, eliminated duplicates and exported them to a spreadsheet. Each title and abstract was screened by one reviewer (divided between SP and BA). Whenever in doubt, we coded the record as 'may be' and moved it to full-text review. We used Google Translate to screen articles in Portuguese.

One reviewer (divided by SP and BA) extracted the data using a standardized extraction sheet. We extracted data on: year, country, setting, population, design, findings, and funder. We included the funder given the strong body of evidence showing that studies funded by interested parties could lead to biased results, which is also in accordance with current critical appraisal tools for systematic reviews.[22]

Data Synthesis

We developed a narrative synthesis along three domains: knowledge, perceptions, and utilization of generics and biosimilars. Meta-analysis was not possible due to the paucity of studies and heterogeneity of populations.

Results

We identified 680 research records. After removing duplicates, we screened 661 research records, resulting in the inclusion of 15 studies. Manual cross-reference search of the bibliographies of included papers then led to the inclusion of 7 further studies. Finally, a total of 22 studies met the inclusion criteria (Figure 1).

Seventeen studies (77%) were related to generic drugs and five studies (33%) were related to biosimilars. Seventeen studies (77%) were conducted with populations in Brazil, followed by one in Argentina, Mexico, Colombia, and Brazil, one in Guatemala, one in Jamaica, one in Peru, one in Colombia, and one study with participants from 18 Latin American countries. The study populations were health professionals (i.e., medical doctors and pharmacists, 7 studies), patients (9 studies), the general population (7 studies), and stakeholders from regulatory agencies, policy experts, and industry (one study). Note that in two studies more than one population group was included (e.g., physicians and pharmacists), which is why a total of 24 populations were targeted in the 22 studies.

Regarding the sources of funding, ten studies did not report them; four studies reported none, however in one of them the authors had extensive conflicts of interest (it was a study on biosimilars). Two studies were funded by pharmaceutical companies and one by an organization that has pharmaceutical companies as member partners, all three on biosimilars. Six studies reported funding from a governmental institution, all of them from Brazil focusing on generics.

Knowledge, Perceptions, and Utilization of Generics

Physicians

Two studies examined physicians' perceptions of generics (Table 1).[23] A Jamaican study with 60 physicians showed that 48% of participants agreed that there are no therapeutic differences between generics and their

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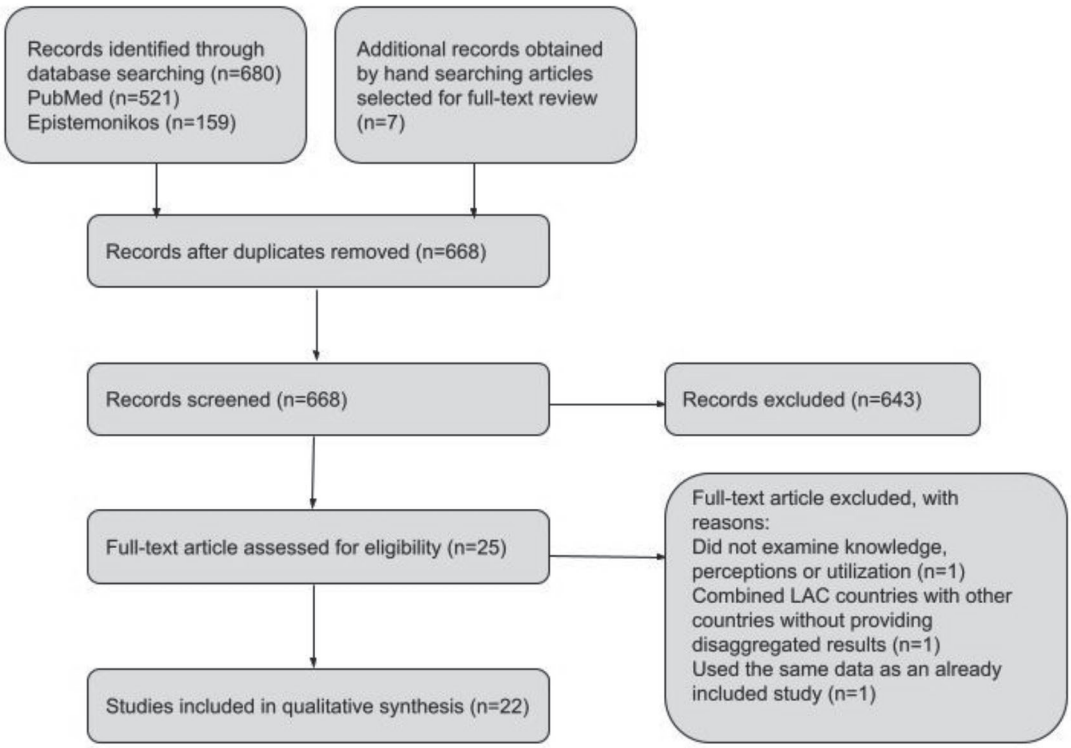
Figure 1
Flowchart of Study Selection and Data Extraction



reference products and 60% agreed that "therapeutic failure" is a serious problem with some generics. Regarding perceptions about prescription of generics, 87% of physicians were supportive of generic substitution for reference products and 70% of responding physicians agreed that they must offer generics to their patients given the lower cost of these medications.[24] In a mixed-methods study involving 12 physicians in Guatemala, 55% of respondents held that low-cost generics are less safe and effective than branded drugs, with some also believing that the low cost of generic drugs was itself indicative of inadequate quality.[25]

The same two studies mentioned above asked about utilization of generics. In the Jamaican study 55% disagreed with the claim that they generally prescribe the reference products and leave it to the pharmacist to discuss generic alternatives.[26] Meanwhile, physicians in Guatemala expressed that concerns regarding the effectiveness and safety of generics influenced their prescribing practices.[27] No studies explicitly asked physicians about their knowledge of generics.

Pharmacists

In a Brazilian study with 72 pharmacists, 97.2% of them believed that generics are of good quality. Using qualitative methods, the same study showed that (lower) price, (warrantee of) quality, and credibility (of the product) were core concepts in the pharmacist's perception of generics. Peripheral concepts were pharmaceutical assistance, social impact, novelty, accessibility, options and interchangeability.[28]

The study in Guatemala based on interviews with staff at community pharmacies found that 41% of the interviewees believed that generics were not as safe as drugs with commercial brand names, whereas 33% believed that they were not as effective. Additionally, a significant portion of this staff reported customer's experiences of different therapeutic responses when switching between branded drugs and generics as evidence of generics' inferiority.[29]

Regarding utilization, the Guatemalan study many participants emphasized that the decision to use a generic was ultimately up to the patient, however their general view was that they were less likely to dispense generics to wealthier and sicker patients.[30] No studies explicitly asked pharmacists about their knowledge of generics.

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Table 1

Summary of Findings of Studies Assessing Knowledge, Perceptions, and/or Utilization of Generics
To simplify the text, percentages were approximated to the nearest entire value.

Reference, country	Subjects	N	Data collection/ Study design	Knowledge	Perceptions	Utilization
Gossell-Williams, 2007 Jamaica	Physicians	60	Questionnaire		48% agreed that there are no therapeutic differences between generics and their reference products and 60% agreed that "therapeutic failure" is a serious problem with some generics. 87% willing to prescribe generics and 70% agree they must offer generics given their lower cost.	55% disagreed with the claim that they generally prescribe the reference products and leave it to the pharmacist to discuss generic alternatives.
Flood et al. 2017 Guatemala	Physicians	12	Semi-structured interviews		55% believed that low-cost generics are less safe and effective than branded drugs.	Several expressed that concerns regarding effectiveness and safety of generics influenced their prescribing practices.
Monteiro et al. 2016 Brazil	Patients	603	Questionnaire		66% of those with hypertension and 59% of those with diabetes mentioned that generic drugs are not as good as the reference drug. 71% mentioned lower cost as one advantage of generic drugs.	33% of people with hypertension and 26% of people with diabetes used generic drugs.
da Rocha, Barros, and Silva 2007 Brazil	Patients	498	Questionnaire	68% knew how to identify and differentiate generics from the reference drug. 65% knew how to define generics. knew how to define generics.		
Vosgerau, de Souza, and Soares, 2011 Brazil	Patients	374	Questionnaire		64% believed that generics have the same quality when compared to their reference drug. 61% manifested preference for generics and 89% reported that they are cheaper compared to their reference drug.	Out of 251 participants who used any medication during the last week, 15% used generics.
Nardi and Ferraz, 2016 Brazil	Patients	100	Questionnaire	44% of pharmacy customers and 28% of patients knew that generics have different regulatory demands than reference drugs, while 64% and 76% respectively knew that generics must be priced at least 35% cheaper than reference drugs.	64% of pharmacy customers and 62% of patients considered generics as effective as reference drugs, 66% and 46% respectively considered them to have the same side effects; 64% and 66% respectively considered they had the same quality.	

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Table 1 (Continued)

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Reference, country	Subjects	N	Data collection/ Study design	Knowledge	Perceptions	Utilization
Mendoza-Chuctaya et al., 2019 Peru	Patients	4914	Questionnaire		47% agreed that generics have lower efficacy than reference drugs, 39% agreed that they have larger side effects, 40% agreed that they are more appropriate for mild or less severe conditions. 60% agreed with a stament that without a price difference they would use the reference drug.	
Goldszmidt et al., 2019 Brazil	Patients	101	Randomized controlled trial		93% indicated that generics were of equivalent quality than the reference drugs and 78% considered them less expensive.	54% under the generic arm discontinued treatment versus 33% in the branded arm. 26% in the generic arm used non-prescribed analgesics, versus none in the branded arm.
Carvalho, Accioly, and Raffin, 2016 Brazil	General population	400	Word Association Test	93% had some knowledge of generics.	The central concepts evoked were (lower) price, (good or dubious) quality and equivalence (to the reference drug).	
Bertoldi, Barros, and Halla, 2005, Brazil	General population	3182	Questionnaire	57% could identify some of the packaging characteristics of generics. 50% mistakenly identify a similar medicine as a generic.	70% believed that generics have equivalent quality as their ref drugs; 86% believed that generic drugs were cheaper than their reference drugs.	4% of participants used generic drugs in the last 15 days
Tierling et al., 2014 Brazil	Patients	124	Interviews	11% demonstrated good knowledge of generics, 49% some knowledge, and 40% no knowledge.		
Faria and Tavares-Neto 2006 Brazil	General population	140	Mixed-method	85% were able to properly recognize a generic drug.	67% considered generics to be of good quality. Those with higher knowledge were more likely to report a better perception on generics. 87% agreed that generics have lower price. 79% would accept generic substitution when purchasing drugs.	
Blatt et al., 2012 Brazil	General population	234	Interviews	91% correctly identified two generic medications.	77%. believed generics have the same effect as their reference products. 74% would agree to switch to generic drug if suggested by the pharmacist. 97% considered generics to be cheaper.	

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Reference, country	Subjects	N	Data collection/ Study design	Knowledge	Perceptions	Utilization
Guttier et al., 2017 Brazil	General population	2925	Questionnaire	76% could identify some of the packaging characteristics of generics. 33% of participants mistakenly identify a similar medicine as a generic.	69% believed that generics have equivalent quality as their ref drugs; 87% believed that generic drugs were cheaper than their reference drugs.	24% of participants used generic drugs in the last 15 days.
Lira et al., 2014 Brazil	General population	278	Questionnaire	99% had already heard about generic drugs, but 49% correctly defined them.	79% were confident about their efficacy, 75% believed they had the same effect than the reference drug and 75% believed they had the same safety than reference drugs. If cheaper, 66% would agree to switch to the generic drug, while just 26% would agree to switch if the drugs had same price. 88% generic drugs are less expensive.	
Nardi et al., 2015 Brazil	General population	5000	Questionnaire		30% considered generics to be less effective and 28% to have more side effects than their reference drug. 41% agreed that generics are more suitable for mild, banal or less serious conditions. If there was no price difference, 59% would always prefer taking the reference drug.	45% of participants were taking or have taken generics in the past three months.
Flood et al., 2017 Guatemala	Pharmacists	30	Semi-structured interviews		41% believed that generics were not as safe as drugs with commercial brand names, whereas 33% believed that they were not as effective.	Many emphasized that the decision to use a generic was ultimately up to the patient, however the general view was that they were less likely to dispense generics to wealthier and sicker patients.
Carvalho et al., 2005 Brazil	Pharmacists	72	Word Association Test		97% believe that generics are of good quality. The central concepts evoked in the word association test were (lower) price, (warrantee of) quality, and credibility (of the product). Peripheral concepts were pharmaceutical assistance, social impact, novelty, accessibility, options and interchangeability.	

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Table 1 (Continued)

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Reference, country	Subjects	N	Data collection/ Study design	Knowledge	Perceptions	Utilization
Nardi and Ferraz, 2016 Brazil	Other Stakeholders	48	Questionnaire	More informed of the regulatory requirements for marketing generics, but less informed about the price difference between generics and their reference drugs, than the general population.	73% believed generics are equally effective as their reference products and 90% belleived that generic drugs cause as many side effects as brand name drugs.	

Patients

Three studies in Brazil[31] examined knowledge of generic drugs among patients. Among patients at a general medicine clinic, 68.1% of respondents could identify and 65,3% managed to define a generic drug; 40% did so by appealing to its lower price and 72% pointed out the generic drug labeling required by Brazilian law (a "G" letter and a yellow stripe).[32] In another study, 92.7% of pharmacy customers had knowledge of generics.[33] The third study focused on regulatory knowledge and included patients from secondary care and customers surveyed at pharmacies. Among patients, 28% knew that generics have different regulatory requirements than reference drugs and 76% knew that by law they might be priced at least 35% cheaper than reference drugs.[34] Pharmacy customers had greater knowledge on the regulatory requirements but slightly lower knowledge on pricing requirements.[35]

Five studies in Brazil and one in Peru examined perceptions of generics among patients. In Brazil, a qualitative study showed that price, quality and equivalence were the core concepts of perceptions of generics.[36] Overall, a clear majority of patients considered generics to have lower prices than reference drugs.[37] In one study, 65.9% of patients with hypertension and 59.4% of patients with diabetes considered generics not as good as the reference drugs.[38] In a Peruvian study, 46.7% of participants agreed with a statement that generic drugs have lower efficacy than reference drugs.[39] Similarly, 62% of patients and 64% of pharmacy customers considered generics as effective as reference drugs in a Brazilian study.[40] Regarding side effects, 38.8% of participants in the Peruvian study agreed with the statement that generic drugs have larger side effects,[41] while in a Brazilian study 46% of patients and 66% of pharmacy customers considered that generics have the same side effects as reference drugs.[42]

A randomized controlled trial conducted in a Brazilian dental clinic assessed perceptions and utilization of generics. Before dental surgery, 93.1% of patients stated that generics were of equivalent quality to the reference drugs. After surgery, all patients received the same analgesic (a reference product) for 7 days, but either with a reference product label or a generic label. 54% of patients in the generic-label arm discontinued treatment versus 33% in the reference-product-label arm, and 26% of participants in the generic-label arm used non-prescribed analgesics, versus none in the reference-product-label arm.[43]

Two further studies examined utilization. In a Brazilian study, only 33% of patients with hypertension and 26.3% of patients with diabetes used generic drugs.[44] Similarly, low utilization was reported in another study in Brazil: only 14.7% of patients who had used any medication over the past week had used generics.[45]

General Population

We found six studies exploring knowledge of generics, all of them from Brazil. Two studies showed that more than three-quarters of participants were able to correctly identify a generic drug.[46] This appears to have increased over time, as shown by two studies conducted in the same Brazilian city, using the same methodology and separated by 10 years, in which participants' ability to identify some of the packaging characteristics of generics increased from 57% in 2002[47] to 76,6% in 2012.[48] Studies looking at more specific knowledge of generics yielded more modest results. In one study, 48.6% of participants could correctly defined them[49] and, in another, 11% had good knowledge of generics (were able to identify the substance, the therapeutic class and the use of all specialties presented), while 49% had some knowledge.[50]

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Five studies in Brazil found that a clear majority of participants perceived generics as having lower costs than reference drugs.[51] Perceptions were also positive regarding the efficacy of generics. In two studies, around three-thirds of participants considered that generics had the same effect as reference drugs,[52] while in another study 58.8% of participants disagreed with the claim that generic drugs are less effective than brand name drugs.[53] Similarly, in one study 69.1% of participants considered that generics were of equivalent quality as reference drugs.[54]

Some studies also examined perceptions related to the substitution of reference products with generics. In two studies, around three-thirds of participants were willing to accept generic substitution when purchasing drugs.[55] However, some studies suggest that this could depend on the price of generics. One study showed that even though 65.8% of respondents would accept substituting reference products with generics, only 26% would accept substitution if the drugs had the same price.[56] Similarly, in another study 59,2% of participants would always prefer taking the reference drug if there was no price difference with the generic alternatives.[57]

Regarding utilization, the two aforementioned studies conducted in the same Brazilian city with a 10-year difference asked about the use of generics in the past 15 days; they showed that reports of generic use increased from 3.6% to 23,6% over the 2002-2012 period.[58] Another Brazilian study from 2015 showed that 45% of patients were taking or had taken generics in the past three months.[59]

Other Stakeholders

We found no study explicitly asking other stakeholders about their utilization of generics.

One Brazilian study included "50 healthcare opinion-leaders from government, hospitals, health plans, academia, and pharmaceutical companies."[60] Regarding their knowledge of generics, they were generally more informed of the regulatory requirements for marketing generics, but less informed about the price difference between generics and their reference drugs, than other populations also included in the study (customers visiting commercial pharmacies, patients and their companions).

The same study found that 73% of healthcare opinion-leaders believed generics are equally effective as their reference products and that 90% of them believed that generics cause as many side effects as the reference products.

Knowledge, Perceptions, and Utilization of Biosimilars

Physicians

Three studies surveyed physicians' knowledge of biosimilars (Table 2). In a Brazilian study with rheumatologists attending a National Congress of Rheumatology, 67% of respondents asserted that they knew what biosimilars are, however, they had wrong beliefs regarding the regulation and availability of biosimilars in Brazil.[61] In another study with rheumatologists, this time from multiple (18 in total) LAC countries, 67% of respondents were aware of biosimilars being approved for use in their respective countries, however, many ignored or had mistaken beliefs regarding certain issues such as the availability and interchangeability of biosimilars.[62]

A web questionnaire completed by 399 physicians from multiple specialities and from Argentina, Brazil, Colombia and Mexico, showed that 65% of respondents considered themselves familiar with biosimilars; this was higher in Brazilians and lower in Argentinians.[63] Many physicians, however, had limited awareness of certain key issues; for example, 51% respondents were unaware of the difference between biologicals, biosimilars and non-comparable biologicals.

Two of the above-mentioned studies looked at perceptions of physicians regarding biosimilars. In the Brazilian study most rheumatologists identified safety and bioefficacy as major problems related to the approval of biosimilars in Brazil, while more than one-third pointed to efficacy and therapeutic failure as major problems after the commercialization of these products.[64] In the same study 67% of respondents claimed that an advantage of biosimilars was their lower price. The study with physicians from Argentina, Brazil, Colombia, and Mexico showed that 44% believed that patients could safely switch between biologicals sharing the same non-proprietary name during a course of treatment, with respondents from Colombia being comparatively less akin to switching between biologicals, than respondents from other countries.[65] The same study showed that 85% of respondents considered it either critical or very important that physicians have sole prescribing authority when selecting biological products.

Regarding utilization, the study with rheumatologists from multiple LAC countries showed that less than 30% of respondents indicated that they had prescribed a biosimilar from a list provided.[66]

Patients

None of the studies found in this review examined knowledge or utilization of biosimilars by patients, but

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Table 2

Summary of Findings of Studies Assessing Knowledge, Perceptions, and/or Utilization of Biosimilars To simplify the text, percentages were approximated to the nearest entire value.

Reference, country	Subjects	N	Data collection/Study design	Knowledge	Perceptions	Utilization
Azevedo, Felippe, and Machado, 2011 Brazil	Physicians	189	Questionnaire	67% stated that they know what biosimilars are, however they had wrong beliefs regarding the regulation and availability of biosimilars in Brazil.	67% claimed that an advantage of biosimilars is their lower price. 62% physicians identified safety and 57% bioefficacy as major problems related to the approval of biosimilars in Brazil. More than one third pointed to efficacy and therapeutic failure as major problems after the commercialization of these products.	
Reilly and Gewanter, 2015 Argentina, Brazil, Colombia, Mexico	Physicians	399	Questionnaire	65% considered themselves familiar with biosimilars. However, many had limited awareness of key issues, such as the difference between biologicals, biosimilars and non-comparable biologicals.	44% believed that patients could safely switch between biologicals sharing the same non-proprietary name during a course of treatment. 85% considered it either critical or very important that physicians have sole prescribing authority when selecting biological products.	
Castañeda-Hernández et al., 2019 Multiple (18) LAC countries	Physicians	104	Questionnaire	67% were aware of biosimilars being approved for use in their respective countries, however many ignored or had mistaken beliefs regarding certain issues such as the availability and interchangeability of biosimilars.		Less than 30% of the rheumatologists indicated that they had prescribed a biosimilar from a list provided.
Graham-Clarke et al., 2020 Colombia	Patients	200	Discrete choice experiment		Respondents prefered an original biologic medicine to a biosimilar.	
Garcia et al., 2021 Brazil	Patients	102	Questionnaire	63% had heard about biosimillars.	63% expressed concerns regarding the efficacy of biosimilars and 53% expressed concerns about the molecular differences between them and their reference products. 27% would agree with biosimilar substitution (offered by the pharmacist), if their physician gives his approval and none would agree without that approval.	

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two studies explored perceptions of biosimilars. One study in patients with inflammatory bowel disease compared Brazilian and non-Brazilian patients. Brazilian patients expressed concerns about the efficacy of biosimilars (65%) and the molecular differences with the reference biological medication (53.1%). These proportions were higher than non-Brazilian patients.[67] In an discrete choice experiment in patients with osteoporosis, patients showed a preference for reference biological medications over biosimilars as well as specific administration characteristics (shorter needle, needle angle from 45 to 90 degrees and automatic dosing).[68]

Other Stakeholders

We found no studies addressing knowledge, perceptions, or utilization of biosimilars in this population group.

Discussion

We conducted a scoping review to map and critically examine the existing empirical literature on the knowledge, perceptions and utilization of generics and biosimilars in LAC. To our knowledge, this is the first review of this kind focusing on studies conducted in LAC. Surprisingly, a vast majority of the studies identified were conducted in Brazil. This could be explained, as discussed above, by Brazil being a leader in generics policy in the 1990s and early 2000s, sparking interest in both the scientific community and funding agencies to carry out research on these policies. Another explanation, however, could relate to selection bias as many Brazilian journals are indexed in PubMed and might be more interested in national studies.

We found that physicians, patients, and the general population generally hold negative perceptions regarding the efficacy, quality, and safety of generics, which were likely to influence their prescribing or purchasing behavior. Perceptions were relatively more positive in pharmacists and other stakeholders. Patients and the general population (all from Brazil in this case) expressed relatively good knowledge of generics. Regarding biosimilars, we identified relatively low knowledge, negative perceptions, and low utilization of biosimilars among physicians. Patients also had strong concerns about their efficacy and molecular differences with biologicals. Overall, our findings are relatively consistent across generics and biosimilars, despite there being important differences among these drug categories.

Our study found that physicians tended to have negative perceptions regarding the efficacy, quality and safety of generics. This is consistent with earlier results from a systematic review showing that close to one-third of physicians considered generics to be less safe, effective and of lower quality.[69] Toverud et al. argue that physicians from less developed countries were highly concerned about manufacturing sources and trustworthiness of generic producers, which could explain why in Jamaica and Guatemala these negative perceptions appear to be close to 50%.[70] Another reason could be higher exposure to marketing from pharmaceutical companies, in settings where physician-industry interactions are less regulated.[71]

In our study, pharmacists from Brazil and Guatemala had contrasting views. In Brazil, pharmacists reported a highly positive perception of generics' efficacy, safety, and quality, while pharmacists in Guatemala had a less positive perception of generics. One interpretation of these findings could be that Brazil's longstanding developments in generics policies have greatly improved perceptions of generics among pharmacists. This is in line with a systematic review reporting a higher level of confidence in generics' efficacy and safety among pharmacists in Northern Europe than in other countries, another region with sustained efforts in generics' policies.[72]

Our findings in patients and the general population suggest good levels of knowledge of generics combined with lower perceptions of their efficacy, quality, safety, and low utilization. These findings are generally consistent with previous systematic reviews[73] and, overall, suggest that increasing knowledge might not readily translate into improved perceptions and utilization. Noteworthy, we were able to distinguish between patients and the general population, and our findings suggest that results in the general population were somewhat more positive than those in patient samples. While this might be a reflection of selection bias, i.e., patients with negative perceptions might be more likely to participate in the study, it could also be explained by the transmission of negative perceptions from physicians and health care professionals, as well as personal experiences in the use of generics.

Our findings regarding biosimilars suggest low knowledge and a negative perception and utilization among physicians. This is in line with two recent systematic reviews showing overall negative perceptions and utilization of biosimilars by physicians.[74] We found that patients expressed concerns about the efficacy of biosimilars and showed a preference for reference biological products over biosimilars. These results are generally consistent with studies with patients from the U.S. and the European Union who expressed concerns (though less pronounced) about the safety and efficacy of biosimilars.[75]

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An important difference between studies on generics and biosimilars lies in the funding source. All studies on generics were either self-funded or publicly funded, while studies on biosimilars were mostly industry-funded. This likely reflects the interest of transnational pharmaceuticals in the biologics market, given that they require advanced production mechanisms that are potentially beyond the capabilities of generics producers in low and middle-income countries. This should also raise awareness of the potential influence of commercial interests in the use of biosimilars. It has been reported that among the barriers preventing more widespread use of these products are tactics by the manufacturers of reference biologicals to delay market entry of approved biosimilars and impede patients' access to them.[76]

Major strengths in our study include the use of a scoping review methodology with a structured search of the literature and data screening, extraction and synthesis protocols. This allowed us to identify a large number of studies in the region and synthesize the evidence comprehensively. However, some limitations are noted. First, the study was not pre-registered. Second, we only included two databases (PubMed and Epistemonikos), which means we might have missed studies indexed in different databases or published as gray literature, potentially resulting in selection bias of research studies. Third, record screening was not conducted in duplicate, and as a result, we might have excluded relevant studies from full-text review. For transparency, we report a list of excluded studies, allowing researchers to identify which studies were excluded during screening and data extraction. (See Supplementary Appendix online, Table S2.)

Our study reveals important gaps in the literature regarding the knowledge, perceptions, and utilization of generics and biosimilars in LAC. More research is needed to better inform and evaluate policies aiming to promote the use of these products in the region — especially beyond Brazil — and particularly in the emerging field of biosimilars. Public health implications of our study are twofold. First, our study clearly demonstrates that there is room for improvement in the knowledge, perception, and utilization of generics and biosimilars in LAC, via national policies and recommendations. Education directed at health care providers and the general population will likely help to alleviate existing misunderstandings and close the knowledge gaps, especially with respect to biosimilars. Second, the observed secular changes in Brazil shed light on the potential substantial improvements derived from sustained and comprehensive policies regarding generics and biosimilars.

Public health implications of our study are twofold. First, our study clearly demonstrates that there is room for improvement in the knowledge, perception, and utilization of generics and biosimilars in LAC, via national policies and recommendations. Education directed at health care providers and the general population will likely help to alleviate existing misunderstandings and close the knowledge gaps, especially with respect to biosimilars. Second, the observed secular changes in Brazil shed light on the potential substantial improvements derived from sustained and comprehensive policies regarding generics and biosimilars.

Conclusions

Generics and biosimilar products can provide cost-effective alternatives to their reference products and contribute to reducing pharmaceutical expenditure in LAC. A significant portion of physicians, patients, and the general population hold negative perceptions and have concerns regarding the use of generics and biosimilars. Governments and regulatory authorities in LAC countries should strengthen their policies to improve information, availability, and affordability of generics and biosimilars. They should also implement initiatives to improve confidence in generics and biosimilars and increase prescribing of these products. Future studies should assess the knowledge, perceptions, and utilizations of generics and biosimilars in LAC and examine the impact of policy interventions on these domains.

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Note

The authors do not have any financial conflicts of interest to disclose. They are members of the Chilean non-profit organization Medicos Sin Marca (Doctors Without Brands).

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Table S1

Search Strategy in PubMed and Epistemonikos

PubMed
Search date: Oct 14, 2022 Search query: (generic drug[MeSH Terms] OR biosimilar) AND (Antigua & Barbuda OR Aruba OR Bahamas OR Barbados OR Cayman Islands OR Cuba OR Dominica OR Dominican Republic OR Grenada OR Guadeloupe OR Haiti OR Jamaica OR Martinique OR Puerto Rico OR Saint Barthélemy OR St. Kitts & Nevis OR St. Lucia OR St. Vincent and the Grenadines OR Trinidad & Tobago OR Turks & Caicos Islands OR Virgin Islands OR Belize OR Costa Rica OR El Salvador OR Guatemala OR Honduras OR Mexico OR Nicaragua OR Panama OR Argentina OR Bolivia OR Brazil OR Chile OR Colombia OR Ecuador French Guiana OR Guyana OR Paraguay OR Peru OR Suriname OR Uruguay OR Venezuela OR "Latin America") **Hits: 521**
Epistemonikos
Search date: Oct 14, 2022 Search query: (title:((title:(generic drug OR biosimilar) OR abstract:(generic drug OR biosimilar)) AND (title:(Belize OR Costa Rica OR El Salvador OR Guatemala OR Honduras OR Mexico OR Nicaragua OR Panama OR Argentina OR Bolivia OR Brazil OR Colombia OR Ecuador OR French Guiana OR Guyana OR Paraguay OR Peru OR Suriname OR Uruguay OR Venezuela OR "Latin America")) OR abstract:(Belize OR Costa Rica OR El Salvador OR Guatemala OR Honduras OR Mexico OR Nicaragua OR Panama OR Argentina OR Bolivia OR Brazil OR Colombia OR Ecuador OR French Guiana OR Guyana OR Paraguay OR Peru OR Suriname OR Uruguay OR Venezuela OR "Latin America"))) OR abstract:((title:(generic drug OR biosimilar) OR abstract:(generic drug OR biosimilar)) AND (title:(Belize OR Costa Rica OR El Salvador OR Guatemala OR Honduras OR Mexico OR Nicaragua OR Panama OR Argentina OR Bolivia OR Brazil OR Colombia OR Ecuador OR French Guiana OR Guyana OR Paraguay OR Peru OR Suriname OR Uruguay OR Venezuela OR "Latin America") OR abstract:(Belize OR Costa Rica OR El Salvador OR Guatemala OR Honduras OR Mexico OR Nicaragua OR Panama OR Argentina OR Bolivia OR Brazil OR Colombia OR Ecuador OR French Guiana OR Guyana OR Paraguay OR Peru OR Suriname OR Uruguay OR Venezuela OR "Latin America")))) **Hits: 159**
Inclusion criteria: Primary studies in Latin America and the Caribbean that have examined the perceptions, attitudes and utilisation of generic drugs or biosimilars (coded 1). Secondary studies examining similar ideas will be included with code 9 for completeness and reference search.
Total hits: 680 **Duplicates: 8** **Total hits to review: 672**

Appendix Table S2 can be found online.

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