Ciência & Saúde Coletiva
cienciaesaudecoletiva.com.br
ISSN 1413-8123. v.31, n.1
DOI: 10.1590/1413-81232026311.14022025EN

Syphilis and penicillin shortage: surveillance, pharmaceutical services and federal response (2014-2023)

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Abstract *Syphilis remains a significant sexually transmitted infection in Brazil, with benzathine penicillin (BPG) as the first-line treatment. In 2014, the country faced a global penicillin shortage, prompting a coordinated federal response, especially in light of rising congenital syphilis cases. This study conducted a documentary analysis of 37 official documents (price registration minutes, technical notes, ordinances, and decrees) to characterize strategies for procurement, price negotiation, and national and international cooperation. The analysis revealed a progressive increase in public procurement of penicillin after 2014 and growing integration between pharmaceutical services, surveillance, and care within the Brazilian Unified Health System (SUS). Federal pharmaceutical services and medicines management was central in overcoming shortages, ensuring BPG supply, and articulating surveillance and comprehensive care. The findings highlight pharmaceutical services as a structural component of the Brazilian response to syphilis, impacting case detection, care, and epidemiological surveillance.*

Key words *Syphilis, Benzathine Penicillin, Drug Shortage, Pharmaceutical Services, Health Surveillance*

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Introduction

Medicine shortages are a recurring problem in healthcare systems and directly affect prevention and quality of care. In the context of infectious diseases, this situation compromises individual treatment and surveillance and control strategies, as with syphilis, a preventable and curable sexually transmitted infection. In 2014, the global shortage of benzathine penicillin G (BPG) affected several countries. The World Health Organization identified it as a risk to the prevention of vertical transmission of syphilis, especially in low- and middle-income countries. Brazil experienced this situation intensely, triggering governmental responses at multiple levels to reorganize the supply and comprehensive care for the disease within the Unified Health System (SUS)[1].

Syphilis is a centuries-old disease, exclusive to humans, whose etiological agent is *Treponema pallidum*. BPG is the antibiotic recommended as the first-line treatment for syphilis, highlighting its safety for pregnant women and its effectiveness in preventing vertical transmission. There is no evidence of *Treponema pallidum* resistance to penicillin. In Brazil, syphilis treatment is based on the Clinical Protocols and Therapeutic Guidelines (PCDT), which are constantly updated[2,3].

In Brazil, the SUS promotes access to prevention technologies (condoms), diagnostic technologies (rapid tests and laboratory exams), and treatment, which involves pharmaceutical services in the management, acquisition, stocking, distribution, and dispensing of medicines and supplies. The Ministry of Health conducts the centralized acquisition and national distribution of condoms for the prevention and treatment of this and other sexually transmitted infections (STIs)[4].

The National Pharmaceutical Policy (PNAF) recommends that the acquisition and distribution of medicines should meet epidemiological criteria, which implies the integration of surveillance, pharmaceutical services, and healthcare. Part of healthcare surveillance involves controlling and recognizing territorial demands expressed by epidemiology, based on information collected through notifications and used in the implementation of health policies. Pharmaceutical Services (PS) are responsible for managing the cycle from selection to dispensing of medicines in the SUS, especially medicines from the Strategic Component of Pharmaceutical Services (CESAF). CESAF is managed at the federal level, targeting diseases with a Public Health impact (such as STIs), with centralized acquisition by the Ministry of Health[5].

Thus, territorial demands give rise to actions and medical services that seek to guarantee access to treatment and promote the control of disease transmission. Among the national priorities, the management and availability of supplies for the prevention, diagnosis, and treatment of syphilis are added to the tripartite responsibilities shared between the technical sectors and surveillance services, PS, and healthcare, especially primary care.

This article aims to characterize actions undertaken by the federal government in response to the penicillin shortage and contextualize syphilis as a disease that challenges PS within the SUS. It addresses the Brazilian response to syphilis, considering PS as a structuring element in combating the disease, updating the backdrop of federal actions to 2023.

Methods

Document analysis was conducted, including open-access technical documents prepared by the federal government and published from 2014 to 2023, a period that corresponds, respectively, to the beginning of the penicillin shortage and the last full year at the time of this study. The documents were selected by document type: Bidding minutes (AP); Technical note (NT); Procurement contract (TC); Ordinances (PR); Law/Decree[6] (LD) and Briefings (B).

The search was conducted on the websites of the former Department of STDs, AIDS, and Viral Hepatitis (DDAHV), renamed in 2017 as the Department of Chronic Diseases and Sexually Transmitted Infections (DCCI) and recently reconfigured as the Department of HIV, AIDS, Tuberculosis, Viral Hepatitis, and Sexually Transmitted Infections (DATHI). The text repositories cover publications from 2010 onwards, with migration to the new website in 2022[7].

The search terms used were "syphilis", "penicillin", and "shortage". Documents such as price registration minutes, contracts, and bidding documents were searched on the website of the Logistics Department of the Ministry of Health[8].

Thirty-seven documents were retrieved during the period of interest. They were read, including documents related to federal management, highlighting actions aimed at buying penicillin for the treatment of syphilis in pregnant women and congenital and acquired syphilis.

The data extracted from the documents considered were organized into a spreadsheet containing document title, document type, publication year, URL, authoring organization, summary or heading, and target audience. They were classified into the following themes: purchase/procurement process, distribution, shortages, surveillance, and care.

The results are presented descriptively and chronologically to represent the sequential analysis. Procurement was classified as failed (bids above the fixed prices) or deserted (lack of suppliers)[9]. The documents were identified by acronym and numbering, indicating the chronological sequence of publication.

Given that all the data used were in open-access databases, the study did not require an ethics committee and is supported by the General Data Protection Law (LGPD-Law No. 13,709/2018) and the Access to Information Law (Law No. 12,527/2011).

Results

Sixteen of the 37 documents analyzed were NT, seven TC, six were AP, three were B, three PR, and two were LD (Chart 1). A concentration of publications was observed in 2016, a year marked by deteriorated penicillin shortage, with seven documents issued, followed by 2015 and 2019, each with five publications (Chart 2).

Ten NTs presented the situation of BPG and PPG shortages in the 2015-2019 period, noting the high prices of the API, the global shortage, and the drop in state supply. They also reported efforts such as waiving bidding processes, emergency purchases, and conducting electronic auctions in procurement attempts, and characterized the supply as regular from 2019 onwards.

Fifteen NTs addressed 'syphilis care', with recommendations regarding the prioritization of penicillin use for cases of syphilis and neurosyphilis. They emphasized primary care, the multidisciplinary nature of disease care, and prenatal care as an opportunity for diagnosis and treatment of pregnant women in the prevention of congenital syphilis. The NTs valued information based on scientific evidence, as was the case with NT4, which highlighted that "the indication of ceftriaxone in the treatment of congenital syphilis lacks scientific evidence of efficacy and that its use should only occur in the absence of PPG and procaine, and the newborn requires strict clinical and laboratory follow-up to verify therapeutic success".

The three briefings addressed summaries of actions and technical reports prepared by the DDAHV in 2015-2016. These documents systematized meetings, intersectoral coordination, epidemiological information, and demonstrated actions taken in response to the shortage of penicillin.

Regarding the APs, three represented unsuccessful procurement processes during the 2014-2015 supply shortage period, and three minutes showed successful procurement (2020-2022). As for procurement information, the APs reveal price increases, negotiations for price registration, and strategic penicillin purchases.

The purchase contracts represented the purchase of items and amounts related to the validity period. No purchase contracts were found in 2017 and 2018. A growing increase in the unit value of BPG is observed until 2021, which corresponded to BRL 2.14 (700,000 units acquired); BRL 4.01 (2,739,375 units); and BRL 3.97 (2,000,000 units) in 2016, 2019, and 2021, respectively. In 2022, there was a slight reduction to BRL 3.50 (1,875,000 units). In 2023, TC7 refers to the purchase of 5,000,000 IU of potassium penicillin at a unit price of BRL 8.46.

Among the ordinances issued during this period, PR1 highlights the Ministry of Health's competence in the centralized purchase of strategic supplies, including condoms, and medications of Public Health interest. The other ordinances addressed the approval of a clinical protocol and a working group to strengthen the lines of action of the National Pact for the Elimination of Vertical Transmission of HIV and Syphilis.

The documents describe the trajectory of actions taken in response to the shortage. In 2014, Public Procurement (AP1) for the acquisition of penicillin for the Indigenous Health Secretariat (SESAI/MS) failed and shows a price increase in 2014, ranging from the minimum unit value estimated by the Ministry of Health of BRL 1.03 for BPG 1,200,000 IU (item 3), BRL 0.73 for PPG 600,000,000 IU (item 4), and BRL 0.92 for PPG penicillin, 100,000 IU + 300,000 IU (item 5). However, bids of BRL 15.00, BRL 50.00, and BRL 10.00 were obtained, respectively. The minutes revealed the government's rejection of the proposal due to the excessive prices offered.

B1, regarding the penicillin situation in April 2015, stated that the shortage stemmed from companies' difficulties in acquiring the API since the previous year, which impacted the production's regularity. The document listed the strategies discussed in meetings between the

Chart 1. Documents analyzed.

Acronym	Document type	Publication year	Document title	Authoring organization
AP1	Bidding minutes	2014	Minutes of the Electronic Bidding Meeting – No. 00059/2014 (SRP)	SEC.EXEC/SAA/DLOG\MS
AP2	Bidding minutes	2015	Minutes of the Electronic Bidding Meeting – No. 00049/2015 (SRP)	SEC.EXEC/SAA/DLOG\MS
AP3	Bidding minutes	2015	Minutes of the Electronic Bidding Meeting – No. 00049/2015 (complementary)	SEC.EXEC/SAA/DLOG\MS
NT 1	Technical note	2015	Joint Information Note No. 109/2015	SVS/MS
SCTIE/ MS	Briefing	2015	Briefing sobre situação de Penicilina abril 2015	DDAHV - SVS-MS
B1	Briefing	2015	Briefing on the Penicillin situation, April 2015	DDAHV - SVS-MS
B2	Briefing	2015	Briefing on the status of penicillin production, October 2015	DDAHV/SVS/MS
NT2	Technical note	2016	Information Note No. 029/2016	DDAHV/SVS/MS
NT3	Technical note	2016	Information Note No. 006/2016	DDAHV/SVS/MS
NT4	Technical note	2016	Joint Information Note No. 68/2016	DDAHV/SVS/MS and DAPES/ SAS/MS
NT5	Technical note	2016	Information Note No. 073/2016	DDAHV/SVS/MS
NT6	Technical note	2016	Information Note No. 01/2016	SVS/MS
B3	Briefing	2016	Monitoring the deliveries of benzathine penicillin	DDAHV/SVS/MS
TC1	Procurement Contract Terms	2016	Contract Term No. 3/2016	DLOG/MS
NT7	Technical note	2017	Joint Information Note No. 024/2017 -	DIAHV/SVS-MS
LD1	Law-Decree	2017	Law No. 13,430/ 2017	President of the Republic
PT1	Ordinance	2017	Consolidation Ordinance No. 2/2017	Ministry of Health
NT8	Technical note	2018	Information Note No. 2/2018	DIAHV/SVS/MS
NT9	Technical note	2018	Information Note No. 4/2018	CGAE/DCCI/SVS/MS
NT10	Technical note	2019	Technical note No. 367/2019-	CGAFME/DAF/SCTIE/MS
NT11	Technical note	2019	Information Note No. 18/2019	CGAE/DCCI/SVS/MS
NT12	Technical note	2019	Information Note No. 30/2019	CGAE/DIAHV/SVS/MS
TC2	Procurement Contract Terms	2019	Contract No. 21/2019	DICE/SEC.EXEC/SAA/DLOG\ MS
TC3	Procurement Contract Terms	2019	Contract No. 87/2019	SEC.EXEC/SAA/DLOG\MS
AP4	Bidding minutes	2020	Price Registration Minute No.118/2020	CGAIE/SEC.EXEC/SAA/ DLOG\MS
TC4	Procurement Contract Terms	2021	Contract No. 133/2021	CGAIE /SEC.EXEC/SAA/ DLOG\MS
TC5	Procurement Contract Terms	2021	Contract No. 158/2021	DCIE/SEC.EXEC/SAA/DLOG\ MS
NT13	Technical note	2022	Information Note No. 4/2022-	CGIST/DCCI/SVS/MS

it continues

Ministry of Health, the National Health Surveillance Agency (Anvisa), the National Council of State Health Secretaries (Conass), the National Council of Municipal Health Secretaries (Conasems), and representatives of the pharmaceutical industry for actions such as prioritizing new registrations by Anvisa and releasing shipments held at airports. According to surveys at the time, 11 states reported problems with procurement, an increase compared to the six states that reported shortages the previous year. Furthermore, companies faced difficulties in production flow due to high pent-up demand.

In October 2015, emergency measures were initiated, such as purchases through the Pan American Health Organization (PAHO) and

Chart 1. Documents analyzed.

Acronym	Document type	Publication year	Document title	Authoring organization
AP5	Bidding minutes	2022	Price Registration Minute No. 121/2022	CGAIESEC.EXEC/SAA/DLOG\MS
AP6	Bidding minutes	2022	Minutes of the Electronic Bidding Meeting No. 00084/2022	SEC.EXEC/SAA/DLOG\MS
TC6	Procurement Contract Terms	2022	Contract No. 221/2022	DCIE/SEC.EXEC/SAA/DLOG/MS
NT14	Technical note	2023	Joint technical note No. 13/2023	CGAFME/DAF/SCTIE/MS
NT15	Technical note	2023	Technical note No. 14/2023	DATHI/SVSA/MS
NT16	Technical note	2023	Joint technical note No. 13/2023-	CGAFME/DAF/SCTIE/MS
DATHI/SVSA/MS	Portaria	2020	Portaria GM/MS nº 864, de 14 de julho de 2023	SCTIE/MS
TC7	Procurement Contract Terms	2023	Contract No. 19/2023	DCIE/SEC.EXEC/SAA/DLOG\MS
PT2	Ordinance	2023	Ordinance SCTIE/MS No. 55 of November 11, 2020	SCTIE/MS
PT3	Ordinance	2020	Ordinance GM/MS No. 864 of July 14, 2023	SCTIE/MS
LD2	Law-Decree	2023	Decree No. 11,494 of April 17, 2023	President of the Republic

Acronyms: SEC.EXEC/SAA/DLOG\MS - Executive Secretariat – Logistics Department. SVS/MS - Health Surveillance Secretariat – Ministry of Health (acronym until 2022). SVSA/MS - Secretariat for Health and Environmental Surveillance – Ministry of Health. SCTIE/MS - Secretariat of Science, Technology, and Strategic Inputs. DDAHV/SVS/MS - Department of STDs, AIDS, and Viral Hepatitis. DCCI/SVS/MS - Department of Chronic Diseases and Sexually Transmitted Infections. DATHI - Department of HIV, AIDS, Tuberculosis, Viral Hepatitis, and Sexually Transmitted Infections. DAF/SCTIE-MS - Pharmaceutical Services Department. DAPES/SAS/MS - Department of Programmatic and Strategic Actions – Health Care Secretariat. CGAE/DCCI/SVS/MS - General Coordination of Strategic Actions. CGAFME/DAF/SCTIE/MS - General Coordination of Pharmaceutical Services and Strategic Medicines. DCIE/SEC.EXEC/SAA/DLOG\MS - Strategic Healthcare Supply Procurement Division. CGAIE/SEC.EXEC/SAA/DLOG\MS - General Coordination for the Acquisition of Strategic Health Supplies. SEC.EXEC/SAA/DLOG\MS - General Coordination of Acquisitions of Strategic Health Supplies – Coordination of Bidding Processes and Market Analysis of Strategic Health Supplies. CGIST/DCCI/SVS/MS - General Coordination of Sexually Transmitted Infections.

Source: Authors.

Chart 2. Federal documents related to pharmaceutical services for syphilis. Brazil, 2014 to 2023.

Year	Bidding minutes	Briefing	Law-Decree	Technical note	Ordinance	Procurement Contract Terms	Total
2014	1						1
2015	2	2		1			5
2016		1		5		1	7
2017			1	1			2
2018				2			2
2019				3		2	5
2020	1				1		2
2021						2	2
2022	2			1		1	4
2023			1	3	2	1	7
Total	6	3	2	16	3	7	37

Source: Authors.

electronic bidding platforms. According to NT2, the emergency measures included the acquisition of 700,000 vials of penicillin to minimize the impact of the shortage on the treatment of

syphilis and other diseases that depended on the antibiotic.

Also in 2015, AP2 and AP3 showed frustrated attempts in the emergency purchase of penicillin. In November, the attempt to purchase 700,000 vials of BPG 1,200,000 IU involved a bidding process with the participation of several bidders. The winning company offered the best price of BRL 6.52, later negotiated to BRL 2.81 per vial. In December, a new supplementary bidding process (AP3) was necessary because this company's proposal was rejected for not reducing the value as estimated. With both proposals rejected, the items were canceled.

In the meantime, NT1 reported a national penicillin shortage, attributing it to a global shortage of APIs, and recommended prioritizing BPG for syphilis in pregnant women and PPG for congenital syphilis, reinforcing alternative clinical indications for the treatment of acquired syphilis and syphilis in pregnant women.

In light of the reported problems, the DDAHV took measures, including consulting ANVISA regarding valid BPG registrations in Brazil and contacting the leading national manufacturers (B2). The companies reported difficulties in acquiring APIs, which affected production. States continued to report difficulties in acquisition, leading to meetings between the Ministry of Health, Anvisa, Conass, Conasems, and the producing companies, resulting in solutions such as agreeing on a distribution schedule with supplier companies.

The DDAHV prepared the NT5 to initiate the acquisition process and adopt urgent measures to enable the purchase of the medicines. In March 2016, B2 reported a request for quotation from PAHO for the acquisition of 2,000 vials of BPG 1,200,000 IU through TC1, which allowed the acquisition of 2,739,375 vials of BPG 1,200,000 IU.

In the same month, the Ministry of Health met with industry representatives to formalize a request for regulatory exemption of the API at Anvisa. Furthermore, aspects related to the regulation of drug prices were discussed as a way to make penicillin viable.

In 2016, the shortage of penicillin deteriorated, especially that used in the treatment of syphilis in pregnant women and congenital syphilis, as highlighted in the NTs published at the time. NT3 described the persistent of supply problems since 2014, affecting all states with regard to PPG and 39% concerning BPG. This shortage was reiterated in other NTs throughout the year, reinforcing the severe situation, such as NT5, which reported a shortage of BPG in 60.7% of the states. This scarcity situation led the Ministry of Health to perform, on an exceptional basis, centralized procurement processes through bidding exemption and cooperation with PAHO, to acquire and distribute the medication in an emergency.

According to B3, new attempts were made to purchase penicillin, including technical cooperation with PAHO, in addition to procurement bidding processes. In March 2016, the Ministry of Health began purchasing 500,000 vials of PPG, although supply was only possible from August of that year. The situation was aggravated by dependence on international suppliers and the lack of national PPG manufacturers, with companies receiving exemption from registration by Anvisa for emergency production. The Ministry of Health also purchased 700,000 vials of BPG (TC1), signing a contract for deliveries made throughout the year.

NT1 revealed the need to acknowledge the state situation, implying a demand to the technical logistics area of the then DDAHV to gather information on stock levels from the states, as well as stock management, and search for emergency purchases. After conducting direct surveys by telephone contact (B2), technical notes were published requesting the service network to prioritize the use of (BPG) for syphilis in pregnant women, in addition to presenting alternatives for the treatment of primary, secondary, recent latent, and late syphilis, indicating doxycycline (for non-pregnant women) and ceftriaxone (for pregnant and non-pregnant women).

As part of the national response to syphilis, a centralized procurement and distribution of BPG for the treatment of acquired syphilis, pregnant women, and partners, and PPG for the treatment of congenital syphilis was initiated. These medications remained available at the CBAF for other clinical situations and were eligible for municipal and state purchases.

Thus, the acquisition and distribution of BPG to the states began to be planned based on epidemiological criteria, considering cases of syphilis in pregnant women reported between 2008 and June 2015 (NT05). To ensure effective distribution, the criteria for allocating portions of the medication should be agreed upon between states and municipalities, preferably in meetings of the Bipartite Interagency Committee (CIB).

In 2018, NT8 reiterated that penicillin purchased centrally by the Ministry of Health

should be used exclusively for the treatment of syphilis acquired in pregnant women/partners and congenital syphilis.

In 2019, the Brazilian Ministry of Health followed the centralized procurement and distribution of strategic medicines (NT10). This NT reported to the TCU (Brazilian Federal Court of Accounts) important advances in expanding the coverage of these medicines, ensuring regular supply throughout the country, and planning acquisitions to guarantee stocks until 2020.

According to NT11, problems with suppliers occurred in 2019, such as the rejection of batches of API (Active Pharmaceutical Ingredient), which affected the complete delivery of the planned medications. It reported 1.381 million (54%) vials not delivered due to API quality issues. It announced a new purchase tender to meet demand, although it estimated that existing stock would cover supply until June 2020.

To address these obstacles, recommendations were issued in NT12 for monitoring stocks and adopting preventive measures against losses due to expiration. Once again, prioritizing BPG for the treatment of syphilis in pregnancy in partnerships was recommended, in addition to encouraging the possibility of "borrowing" BPG stock intended for other conditions besides syphilis.

In 2020, AP4 reported the price registration for the acquisition of BPG 1,200,000 IU at a unit price of BRL 3.97. The maximum annual amount was estimated at 2,600,000 vials.

In 2021, TC4 presented the acquisition of PPG, seeking to guarantee access to treatment for congenital syphilis. The unit price of BRL 7.47 for PPG referred to the acquisition of 136,000 vials. This year, TC5 ensured the scheduled purchase of 2,000,000 vials of BPG 1,200,000 IU at the unit price of the previous year.

In 2022, TC6 reported the acquisition of 1,875,000 vials of BPG 1,200,000 IU, at a unit price of BRL 3.50. AP5 records the purchase of 225,000 vials of PPG 5,000,000 IU, at a unit price of BRL 8.46. AP6 records that a new quota of 75,000 vials of the same item was offered to AP5's supplier, due to the failed acquisition of the item with respect to the previously reserved quota.

In 2023, TC7 projected the acquisition of 96,400 vials of PPG 5,000,000 IU, at the same unit price as the previous year. NT14 reported that BPG was already available in the SUS (Brazilian Unified Health System) through the National List of Essential Medicines (RENAME), in the basic and strategic components of PS. The NT states that access to BPG and PPG for syphilis should be through medications acquired via the strategic component (CESAF).

NT15 updates the recommendation for the interval between vials of BPG in the treatment of syphilis in pregnant women, which has increased from seven to nine days, while maintaining the recommendation to restart treatment if the interval is exceeded.

Discussion

Analysis of the documents reveals that the Ministry of Health's response to the penicillin shortage, especially between 2014 and 2018, focused on emergency measures such as centralized purchasing, annual shipment scheduling, organization of pharmaceutical services, alerts regarding care, and national and international cooperation. In this context, the technical notes are the documents that show the federal backdrop of integrated management in a situation of penicillin shortage.

The documents show that the set of government actions aimed to guarantee the continuous availability of medications identified by epidemiological criteria. The plurality of technical areas of authors and the content evidence the integration between pharmaceutical services, surveillance, and care. The repeated recommendation to prioritize penicillin for the treatment of syphilis illustrates the shortage outlook during the period and reveals the pharmaceutical services' capillarity.

Document analysis allowed for the recognition of important contextual factors for understanding actions conducted at the federal level. As seen, the rise in market prices, the global shortage, and the implementation of actions in PS for syphilis demand governance structures that mobilize public administration.

The researched NTs represent technical communication between managers and technical areas of state and municipal pharmaceutical services on topics such as epidemiological surveillance, care, and medicine management. They aim to improve the clinical management of syphilis cases in pregnant women and congenital syphilis, and also address the need for treatment of acquired syphilis cases in partnerships to prevent reinfection in pregnant women. This technical communication process expresses the integrated network of surveillance and pharmaceutical services that influences conduct in health services and is constantly updated.

Pharmaceutical services (PS) involve the efficient planning, implementation, and control of the flow of medicines and pharmaceutical products from acquisition to the end patient. Effective logistics in PS are fundamental to ensuring treatment continuity, patient safety, and streamlined healthcare resources.

In 2016, a logistics tool called the "STI Medicine Resupply and Management Dashboard", based at SVSA/MS, was implemented in the federal government. It aimed to monitor and manage the supply situation of medicines such as BPG, PPG, and doxycycline 100mg acquired by the PS strategic component. The dashboard systematizes and standardizes the periodic survey of stock movement and demand for STI medicines and relies on partnerships with states and municipalities, coordinating demands and distributions related to these medicines[10].

In 2017, the National Congress, through a proposal for oversight and control, requested an evaluation of the government's actions in controlling syphilis. The Federal Court of Accounts (TCU) was asked to assess the federal government's performance related to syphilis and recommended that the Ministry of Health institute systematic monitoring and evaluation of municipal health services, reinforcing measures for key and priority populations for acquired syphilis, as well as actions for pregnant women. The TCU recommended strengthening tripartite coordination to eliminate congenital syphilis, identifying the causes of late diagnosis and inadequate treatment of pregnant women with syphilis, and developing an action strategy including training health professionals in the prevention, diagnosis, and treatment of syphilis[11,12].

In this audit, the Ministry of Health listed actions under development and pointed out the leading causes of the increase in syphilis incidence rates in the country: late diagnosis and inadequate treatment of pregnant women with syphilis; failures in prevention, care, and surveillance of syphilis cases in pregnant women; resistance from health professionals to administer BPG in primary care; and the national shortage of penicillin[13].

This year, the Chamber for the Regulation of the Medicines Market (CMED) granted a price adjustment for penicillin, a strategy that ensured greater purchasing power. The exceptionality was justified due to the alarming increase in the number of syphilis cases, coupled with a global BPG shortage, using epidemiological data that reported an epidemic of syphilis in pregnant women and increases in cases of congenital syphilis[14].

Also in 2017, the Annual Budget Law (LOA) No. 13,414 allocated BRL 200 million to the Ministry of Health for rapid response actions to syphilis. The resources were executed in partnership with the Health Innovation Laboratory (LAIS/UFRN), in the "No to Syphilis" project, encompassing research, communication campaigns, continuing education, and institutional support to priority municipalities. The implementation occurred through the Decentralized Execution Terms TED 54/2017 and TED 111/2017, with BRL 10 million allocated for the emergency purchase of penicillin[15].

In that same year, the law establishing the National Day to Combat Syphilis and Congenital Syphilis was published, celebrated annually on the third Saturday of October. This milestone inspires annual actions in communication, prevention, management, and monitoring of actions related to syphilis.

Brazil saw a progressive increase in reported cases of acquired syphilis until 2019, when the rate reached 78.4 cases per 100,000 inhabitants, followed by a decrease from 2020 onwards, associated with the impact of the COVID-19 pandemic on health services. However, in 2021, we witnessed a rapid resumption of reported cases with the resumption of healthcare activities. The rate of syphilis in pregnant women sustained an upward trend, albeit at a slower pace since 2018, while congenital syphilis showed an average increase of 17.6% between 2011 and 2017, stabilizing after that period and registering a new increase in 2021[16].

In 2023, 242,826 cases of acquired syphilis were reported (113.8/100,000 inhabitants), 86,111 cases in pregnant women (34.0/1,000 live births), and 25,002 cases of congenital syphilis (9.9/1,000 live births). That year, 90.4% of pregnant women diagnosed received at least one dose of benzathine penicillin. The rate of congenital syphilis, which had shown an increasing trend, showed signs of stabilization from 2021 onwards, decreasing slightly in 2023[17].

The increasing number of reported cases and annual detection rates continues to indicate the demand for syphilis treatment, prompting studies related to the amounts distributed and coverage of cases. It is necessary to recognize the epidemiological magnitude of syphilis in Brazil and its demand for resources, while still facing challenges such as underreporting[18].

The scarcity of medicines and vaccines is a multifaceted situation, resulting from fragile supply chains and oligopolies in the stages of the production process. Dependence on imported medicines and low investment in national pro-

duction capacity are persistent problems in the trajectory of Brazilian pharmaceutical services. The practical result of this is supply crises of old, widely used medicines, many of them for primary care[19].

Expanding the perspective on supply shortages includes factors such as situations where medicine production is insufficient to meet growing or emerging demand that exceeds supply capacity, resulting in shortages. This term, therefore, refers to a generalized scarcity ("shortage"). On the other hand, it is necessary to consider shortages generated by the temporary depletion of localized stocks, resulting from failures in logistics management or distribution, without necessarily indicating insufficient production on a larger scale. While "shortage" involves widespread and prolonged unavailability in the market, "stock out" tends to be a more localized and temporary situation, related to inventory management at regional or institutional levels. In Brazil, Anvisa also considers the imminent discontinuation of manufacturing as a component of supply shortages.

Drug shortages are already considered a Public Health problem and a significant obstacle to guaranteeing access to them and, consequently, the right to health. This study applies a "shortage" perspective to the case of syphilis[20].

Between 2014 and 2016, the WHO conducted a study in 114 countries. Approximately 41% of the 95 countries with available data reported a shortage of BPG. In some countries, alternatives such as ceftriaxone and amoxicillin were used, but they are less effective in preventing mother-to-child transmission of syphilis. The study states that penicillin was sold at low prices (approximately US$0.11 per dose of 1.2 million units), which discourages manufacturers. Production is complex and requires investment in sterile infrastructure. Quality issues and difficulties in obtaining new registrations in countries also hinder supply. In addition, some manufacturers impose minimum purchase amounts, which makes supply difficult in smaller countries[1].

The case of syphilis is a good example of a problem for which the PNAF justifies broad and permanent governmental actions. The PS materialize in comprehensive care when they enable access to prevention, diagnosis, treatment, and cure (in the case of syphilis). The rational use of medicines, the promotion of research, the national development of pharmaceuticals, and the economic regulation of markets are fundamental themes in the qualification of PS.

The Brazilian response to syphilis is marked by the institutionalization of PS processes and decentralized actions aimed at comprehensive health care. Federal management in surveillance, health, and environment is a locus of technological innovation, communication, and improvement of pharmaceutical services and syphilis care. However, the problem of inadequate completion of syphilis notifications persists, particularly in the field of evolution of acquired syphilis cases and in pregnant women, where records are predominantly unknown and blank.

In this descriptive analysis, documents showing institutional integration in the fight against syphilis were selected. Currently, this effort is represented in national action to eliminate socially determined diseases. In 2023, the federal government created the 'Interagency Committee for the Elimination of Tuberculosis and Other Socially Determined Diseases', including among its challenges the elimination of vertical transmission of HIV, syphilis, hepatitis B, and others[21].

During the study period, noteworthy actions include the publication and updating of the Clinical Protocol of Therapeutic Guidelines for Comprehensive Care for People with STIs, ensuring standardization of clinical management actions for syphilis; publication of the "Good Practices Handbook on the Use of Penicillin in Primary Health Care"; publication of normative acts by the Federal Nursing Council (Cofen) to expand the administration of penicillin and testing in primary health care by nursing staff - Cofen Decision No. 0094/2015 and No. 244/2016; and the publication of the "Technical Manual for the Diagnosis of Syphilis".

Some actions are also focused on overcoming the fear of anaphylaxis when using penicillin in primary care services. In these services, prioritizing BPG for syphilis over the demand for its use in other clinical situations results in difficulties in controlling its restricted use for the treatment of STIs[22,23].

Syphilis is a cause for concern in the global monitoring of bacterial resistance to antibiotics. A recent study investigated the antimicrobial susceptibility of *Treponema pallidum*. The research evaluated the efficacy of 18 antibiotics, including amoxicillin, ceftriaxone, tedizolid, and dalbavancin, which showed good antitreponemal activity at concentrations achievable in human plasma. The study also tested the resistance of *T. pallidum* strains to high concentrations of azithromycin, identifying ineffective-

ness against strains with mutations associated with macrolide resistance and highlighting the need to expand the therapeutic repertoire for the effective management of syphilis[24].

Thus, the Brazilian Unified Health System's (SUS) response to the penicillin shortage is complex and integrated, highlighting the federal effort in guaranteeing the acquisition and distribution of supplies and disease surveillance. While alleviating the crisis, these actions demonstrate a dependence on external suppliers. The findings reinforce the need to strengthen the National Pharmaceutical Services Policy with greater productive autonomy, integration with epidemiological surveillance, and sustainable mechanisms to prevent future supply crises.

Recognizing the social determinants of disease is part of the current development of governmental actions, highlighting the role of CIEDDS in the intersectoral integration of social policies. We should remember that STIs mainly affect women in vulnerable socioeconomic situations, especially in the context of pregnancy. Risk factors such as negotiation of condom use and low schooling level are associated with higher detection of STIs among young women and adults. Gender-based violence influences and weakens women's self-care process. The SUS (Brazilian Unified Health System) offers fundamental health services in promoting a healthy sexual life, STI prevention, and reproductive/family planning[25,26].

Regarding the future, a recent study indicates a global trend of increasing incidence and prevalence of syphilis, with alarming increases predicted *through* 2035. Unprotected sex is the leading risk factor. The burden of the disease is higher in children under five years of age and young adults (25-34 years), constituting priority groups for interventions. We also observe marked inequality between countries, with a more significant impact on low-income populations, reinforcing the need for integrated public policies and specific actions in contexts of greater vulnerability[27].

The study has the inherent limitations of documentary studies, since it depends on the quality of the available records. The use of public documents may exclude relevant information contained in records with restricted access. Even so, the research was comprehensive, systematizing information made available to society with transparency, *thereby valuing social participation*.

Implementing data management and analysis tools in surveillance is a current perspective in health research and a potential for integration between surveillance, pharmaceutical services, and comprehensive care. Continuing education for professionals and evidence-based health communication should also be integrated into efforts to improve pharmaceutical services in Brazil.

Collaborations

The authors contribute equally to the construction of the article, both are responsible for the final text and authorize its publication.

Acknowledgments

Team CGIST, Eduardo Malheiros and CMI/DATHI/SVSA-MS.

Data availability statement

The data sources adopted in the research are indicated in the article's body.

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Article submitted 30/09/2024
Approved 28/07/2025
Final version submitted 30/07/2025

Chief editors: Maria Cecília de Souza Minayo, Romeu Gomes, Antônio Augusto Moura da Silva, Vania de Matos Fonseca