Research Article

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Influence of pharmaceutical services organization on the availability of essential medicines in a public health system

Wenderson Henrique Rocha*[,1], Juliana Álvares Teodoro[1,2], Francisco de Assis Acurcio[1,2], Augusto Afonso Guerra Jr[1,2], Isabel Cristina Gomes Moura[3], Brian Godman[4,5,6], Amanj Kurdi[4,7], Renata Cristina Rezende Macedo do Nascimento[8] & Alessandra Maciel Almeida[1,3]

[1]Faculty of Pharmacy, Postgraduate Program in Medicines & Pharmaceutical Services, Federal University of Minas Gerais (UFMG), Belo Horizonte, MG, Brazil

[2]School of Pharmacy, SUS Collaborating Centre for Technology Assessment & Excellence in Health, UFMG, Belo Horizonte, MG, Brazil

[3]Faculty of Medical Sciences of Minas Gerais, Postgraduate Program in Health Sciences, Belo Horizonte, MoG, Brazil

[4]Strathclyde Institute of Pharmacy & Biomedical Sciences, University of Strathclyde, 161 Cathedral St. G4 0RE. Glasgow, UK

[5]Division of Clinical Pharmacology, Karolinska Institutet. Karolinska University Hospital Huddinge. SE-141 86, Stockholm, Sweden

[6]Division of Public Health Pharmacy & Management, School of Pharmacy, Sefako Makgatho Health Sciences University, Ga-Rankuwa, Pretoria, 0208, South Africa

[7]Department of Pharmacology & Toxicology, College of Pharmacy, Hawler Medical University, Erbil, Iraq

[8]Departament of Pharmacy, School of Pharmacy, Federal University of Ouro Preto (UFOP), Ouro Preto, MG, Brazil

*Author for correspondence: whenriquerocha@pbh.gov.br

Objective: To evaluate the influence of organizational structure and technical-management activities on the availability of essential medicines in the primary healthcare. **Materials & methods:** Cross-sectional, exploratory and evaluative study. The availability was evaluated according to parameters established by the WHO. **Results:** The average availability of standardized essential medicines was 83.3 and 73.3% for medicines purchased centrally by the Brazilian government. Among the therapeutic groups evaluated, the lowest average availability were for the tuberculostatics (24.1%) and psychotropic/special control medicines (30.3%). **Conclusion:** The availability of essential medicines was positively influenced by the presence of the pharmacist and by the computerized system deployed, and negatively associated with essential medicines purchased centrally by the federal government, especially in the smaller municipalities.

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Keywords: availability • drugs, essential • pharmaceutical services • primary health care • unified health system

Ensuring access to medicines and promoting rational use of medicines (RUM) are fundamental requirements to improving public health in resource constrained environments [1]. Access to medicines is a particular issue in low- and middle-income countries exacerbated by issues of affordability and availability [2–10].

Availability of medicines in public health services is an important and challenging factor especially in universal health systems supported by public funds. Analysis of medicine availability is often measured as a proxy to evaluate the access to essential medicines [11]. In 2015, among the nine global targets to reduce the load of nontransmissible chronic diseases, the WHO emphasized the importance and the need to make available at least 80% of basic technologies and essential medicines that are necessary to treat key nontransmissible chronic diseases [12].

In Brazil, the constitutional right to health is guaranteed and the implementation of the SUS – *Sistema Único de Saúde* (National Health System), a universal coverage health system, has enabled greater access to healthcare [11]. However, studies undertaken among Brazilian primary healthcare (PHC) facilities have pointed out concerns with the low availability of essential medicines and deficiencies in logistics and supply chain management [13,14], although the impact of pharmaceutical services (PS) organization and technical-managerial activities on medicines'

availability have not been evaluated in these previous studies. This is despite the legal framework of PS and growing investments made by SUS [11,15].

One of the key challenges linked to an effective PS in PHC is ensuring managers' awareness of the importance of structuring municipal PS by investing in infrastructure, process organization and in continuing educational programs for workers in this field. Improving management and supply chains can result in a more feasible, rational and efficient supply of medicines building on evidence from other countries including South Africa [16].

We have previously published on the development of a single indicator of access to medicines for Brazil as well as concerns with inequality regarding the availability of essential medicines at PHC [11,17,18] and statins in Brazil [19]. These studies demonstrate the importance given to access to medicines from either public and/or private pharmacies considering that most health interventions especially in ambulatory care involve the use of medicines and the lack of access will have a detrimental effect on patients' outcomes [20–22]. Besides, addressing inequalities in access to medicines is an important step in achieving improved health. In view of this, the aim of this present study was to assess the municipal PS organization and technical-managerial activities within SUS pharmacies. Subsequently, to verify if these factors have influenced the availability of medicines contained within the Municipal List of Essential Medicines (*Relação Municipal de Medicamentos Essenciais – Remume*), which takes into account key parameters set by WHO in medicine availability and strategy including disease prevalence; treatment facilities; training and experience of available personnel; financial resources; as well as genetic, demographic and environmental factors [23]. The WHO Essential Medicines List (EML) is recognized as a guide to the development of national EMLs based on public health relevance within a country as well as evidence of the efficacy, safety, comparative costs and cost–effectiveness of the medicines selected within a country [24–26]. Not aware if that such studies have been performed before in Brazil, especially involving the Municipal List of Essential Medicines. The findings will provide a current situation analysis aiding the development of future policies to improve access and availability of medicines within the PHC system in Brazil with universal access a key parameter.

Materials & methods

The present study was part of National Survey on Access, Use and Promotion of Rational Use of Medicines (PNAUM – Services), a cross-sectional, exploratory and evaluative survey. Data were collected from a representative sample of municipalities, PHC services, users, physicians and medicine dispensers in all five Brazilian regions. Sample planning took into consideration several study populations and estimated different sample sizes for each one of these populations [27]. Health services were randomly chosen in a sample comprising 300 municipalities, which were stratified into capitals (26 and the Federal District), and municipalities with the bigger (0.5% of the bigger municipalities per country region – total = 27 municipalities) and smaller number of inhabitants (246 were randomly chosen among municipalities accounting for up to 290 thousand inhabitants) [28]. Medicine dispensing unities that are integrated into PHC health services (Basic health units – UBS, health centers, mixed units, among others) were considered "UBS pharmacies"; and dispensing units that did not share space and structure with other health services were considered "independent pharmacies" [28].

For the PNAUM study, a structured questionnaire was developed and contained questions related to the service's organizational structure and to technical-managerial activities (selection, planning, acquisition, storage and dispensing activities). An observation guide was also developed to assess pharmaceutic service facilities and medicine availability in order to investigate the conditions where the dispensing of medicines was undertaken in addition to storage conditions, registration of activities and the availability of selected medicines. Availability has been determined through stock checking, with single data collection at each location. A photographic record was used to evaluate medication dispensing units. The observer photographed storage areas, medication shelves and dispensing areas. Places of storage and delivery of medicines were observed in order to investigate the conditions in which the dispensing or delivery of medicines was undertaken in addition to accessing and observing storage conditions and the availability of the selected medicines. For this study, questions were selected from the structured questionnaire regarding services' organizational structure, in other words, dispensing unit type: independent pharmacies, UBS pharmacies; presence of professionals in charge of dispensing units, whether the person in charge had a qualification in Pharmacy; the presence of Information Technology (IT) systems as well as technical-managerial activities, in other words, Municipal List of Essential Medicines – Remume selection/presence, storage, supply; and stock/inventory control. Interviews were undertaken face to face by trained interviewers using the standardized questionnaire in the dispensing units, with data collected from July 2014 to May 2015.

Table 1. Tracer medicines grouped based on therapeutic class.

Therapeutic class (ATC† classification - 2nd level)	Tracer medicines (ATC† classification - 5th level)
Antianemics (B03)	Ferrous sulfate (B03AD03) Folic acid (B03BB01)
Anti-asthmatics (H02/R03)	Prednisolone (H02AB07)/prednisone (H02AB06) Salbutamol sulfate (R03AC02) Ipratropium bromide (R03BB01)
Antidiabetics (A10) Oral hypoglycemic agents (A10B) Insulins (A10A)	 Metformin (A10BA02) Glyburide (A10BB01)/gliclazide (A10BB09) Regular human insulin (A10AB) Neutral Protamine Hagedorn (NPH) human insulin (A10AC)
Antihypertensives (C03/C07/C09)	Hydrochlorothiazide (C03AA03) Propranolol (C07AA05)/metoprolol (C07AB02) Atenolol (C07AB03)/carvedilol (C07AG02) Captopril (C09AA01)/enalapril (C09AA02)
Anti-infectives (D01/G01/J01/J02)	Miconazole cream/ointment (D01AC02) Nystatin cream (G01AA01) Benzathine benzylpenicillin (J01CE08) Ciprofloxacin (J01MA02) Fluconazole (J02AC01)/itraconazole (J02AC02)
Nonsteroidal anti-inflammatory drugs (NSAIDs) or analgesics/antipyretics/ anti-inflammatory agents (N02B/M01)	Dipyrone solution (NO02BB02) Acetaminophen (N02BE01) Ibuprofen (M01AE01)
Antiparasitic (P01/P02/P03)	Metronidazole (P01AB01)/keyboardozan (P01AC04) Albendazole (P02CA03) Permethrin (P03AC04)
Antisecretory/antacids (A02)	Aluminum hydroxide (A02AB01) Ranitidine (A02BA02) Omeprazole (A02BC01)
Contraceptives/hormones (G03)	Norethisterone + estradiol (G03AA05) Ethinyl estradiol + levonorgestrel (G03AA07) Norethisterone (G03AC01) Levonorgestrel (G03AD01) Estriol vaginal cream (G03CA04) Conjugated estrogen vaginal cream (G03CA57) Medroxyprogesterone tablet (G03DA02)
Psychotropic/special control (N03/N06)	Clonazepam (N03AE01) Carbamazepine (N03AF01) Amitriptyline (N06AA09) Fluoxetine (N06AB03)
Tuberculostatics/antimicobacterial (J04)	Rifampicin 300 mg (J04AB02) Rifampicin + isoniazid + pyrazinamide + ethambutol (J04AM06)

Source: PNAUM (National Survey on Access, Use and Promotion of Rational Use of Medicines) 2015.
†WHO, 2018; WHO, 2019.
ATC: Anatomical Therapeutic Chemical; NPH: Neutral protamine Hagedorn.

Brazil has a National List of Essential Medicines that is common based on the WHO list. However, the municipicalities have autonomy to adjust the list, according to local health demands. In order to carry out a research on the availability of essential medicines in health services, the WHO advises selecting a maximum of 50 items from a list of essential medicines. This list of key medicines, called tracer medicines, should contain items intended for the treatment of the main health conditions of the population, including a standard list of 14 medicines, to allow international comparisons, a basic regional list of up to 16 medicines and a supplementary list of at least 20 medicines of national relevance [29].

For this study, a group of experts selected 58 medicines from 2012 Rename (National Relation of Essential Medicines), which were grouped into 50 assessment items. The selection was based on parameters set by WHO to undertake research concerning the availability of essential medicines [11,23]. The availability of a medicine was defined as the presence of at least one pharmaceutic unit of standardized tracer medicines in the municipality (Remune) at data collection. For groups of tracers presenting more than one medicine, the availability was defined as the existence of at least one unit among the pharmacologic options into the group.

Of the total number of tracers, 39, were grouped into therapeutic classes, as shown in Table 1 [30,31]. The other tracers – including herbal medicines (guaco, soy isoflavone, *unha-de-gato*, *espinheira-santa*, mastic, *cáscara-*

Table 2. Description of the medicine dispensing units and the professionals in charge of medicine dispensing.

Features	n	%	95% CI
Unit type			
– Independent pharmacies	116	13.4	(9.6–18.3)
– UBS pharmacies	1.059	86.6	(81.7–90.4)
Presence of pharmacists in the DU			
– Complete shift of primary healthcare services	396	44.5	(38.7–50.3)
– Half shift	170	13.0	(10.0–16.6)
– Eventually, once in a while or nondaily/lack of him	609	42.6	(37.7–47.7)
Pharmacist in charge for the DU?			
– Yes	506	43.0	(37.8–48.4)
– No (other professionals such as nurse and pharmacy technician)	669	57.0	(51.6–62.2)
Does the DU have an IT system to record the PS activities?			
– Yes	449	39.4	(34.0–45.0)
– No	721	60.6	(55.0–66.0)
Is there a Municipal List of Essential Medicines?			
– Yes	995	89.5	(82.3–94.0)
– No	56	10.5	(6.0–17.7)
Does it have a locker to store medicines under special control?			
– Yes	502	43.4	(38.0–49.0)
– No	673	56.6	(51.0–62.0)
How are the thermolabile medicines (e.g., insulin) stored?			
– Exclusive fridge to store medicines	650	47.2	(42.0–52.5)
– Fridge to store medicines and other products	101	7.8	(5.9–10.1)
How often is the medicines stock inventory carried out?			
– At least once a month	853	71.7	(64.5–78.0)
– Every two months or at longer time intervals	219	28.3	(22.0–35.5)

Source: PNAUM (National Survey on Access, Use and Promotion of Rational Use of Medicines) 2015.
DU: Dispensing unit; IT: Information Technology; PS: Pharmaceutical Service; UBS: Basic Health Unit.

sagrada, *garra-do-diabo* and artichoke), dexamethasone cream/ointment, nicotine and rehydration salts – were only considered in general availability evaluations that consider all tracers including herbal medicines.

Categorical variables (unit type, presence of pharmacist in the dispensing unit, pharmacist in charge, Municipal List of Essential Medicines, IT system, Inventory frequency and storage) were presented as absolute and relative frequencies; and availability indices were presented as means and 95% CI. To compare groups, it was used the linear model for complex samples. Data analysis was carried out in SPSS software, version 22, using the complex samples package. It was considered significative p-value <0.05.

Ethical approval was obtained from the National Research Ethics Committee under CONEP Opinion n. 398.131/2013. All interviews were preceded by research-objective clarification to interviewees and informed written consent form were sought on the same day.

Results

Overall, 1139 personnel in charge of medication dispensing within the various PHC facilities were interviewed and 1175 observation guides were completed. Of the PHC facilities and dispensing units included, 86.6% (n = 1059/1175) were UBS pharmacies and 13.4% (n = 116/1175) were independent pharmacies. Almost half of the dispensing units (44.5%, n = 396/1175) had a pharmacist present throughout the whole shift; however, 42.6% (n = 609/1175) of dispensing units did not have such a professional on a daily basis or did not have one at all. Nurses, nurse technician, pharmacy technician or another professional were in charge of the pharmacy in 57% (n = 669/1175) of these dispensing units (Table 2). Overall, 74.2% of professionals in charge of the dispensing units were women and 61% of them were between18 and 39 years old.

Approximately 60% (n = 721/1170) of dispensing units did not have an IT system to record PS activities. However, 89.5% (n = 995/1051) of the municipalities have a local EML, and 71.7% (n = 853/1072) of them

Table 3. Average availability of essential medicines based on therapeutic class and acquisition form in Brazil and on group of municipalities.

Classifications	Availability % (IC 95%)			
	Capitals	Bigger municipalities[†]	Smaller municipalities[‡]	Brazil
General	84.0 (82.8–85.2)	85.0 (82.4–87.7)	80.9 (78.9–83.0)	83.3 (82.1–84.5)
Therapeutic class (ATC 2nd level)				
Antianemics (B03)	86.0 (83.7–88.3)	90.4 (85.8–95.0)	83.6 (80.5–86.6)	84.0 (81.4–86.7)
Anti-asthmatics (H02/R03)[§]	86.5 (84.1–88.9)	82.9 (77.2–88.5)	81.2 (78.1–84.4)	81.7 (78.9–84.6)
Antidiabetics (A10)[§]	85.3 (83.1–87.4)	86.8 (82.1–91.5)	79.7 (76.8–82.5)	80.4 (77.9–82.9)
Insulin (A10A)[§]	86.5 (83.5–89.5)	81.3 (72.7–89.9)	72.2 (67.6–76.9)	73.8 (69.8–77.8)
Oral hypoglycemic agents (A10B)	86.5 (84.2–88,8)	91.6 (87.3–95.8)	88.6 (85.7–91.5)	88.5 (86.0–91.1)
Antihypertensives (C03/C07/C09)	88.8 (86.8–90.9)	91.2 (86.8–95,7)	86.0 (83.6–88.5)	86.4 (84.3–88.6)
Anti-infectives (D01/G01/J01/J02)[§]	79.5 (77.2–81.9)	80.5 (75.4–85.6)	74.0 (71.1–76.9)	74.7 (72.2–77.2)
NSAIDs (NO02B/M01)	88.5 (86.2–90.8)	91.3 (86.9–95.7)	85.6 (82.8–88.5)	86.1 (83.6–88.6)
Antiparasitic (P01/P02/P03)	86.4 (84.1–88.7)	90.2 (85.9–94.4)	85.1 (81.7–88.5)	85.4 (82.4–88.4)
Antisecretory/antacids (A02)[§]	66.1 (62.6–69.5)	70.6 (62.5–78.7)	73.4 (69.3–77.5)	72.7 (69.1–76.3)
Contraceptives/hormones (G03)[¶]	84.6 (82.5–86.8)	85.5 (81.0–89.9)	76.2 (72.4–80.0)	77.3 (74.0–80.5)
Psychotropic/special control (N03/N06)[#]	44.3 (40.8–47.8)	25.7 (14.5–36.9)	29.1 (23.1–35.1)	30.3 (25.0–35.5)
Tuberculostatics (J04)[#]	57.3 (53.1–61.5)	26.6 (17.0–36.1)	20.9 (15.0– 26.7)	24.1 (19.0–29.2)
About acquisition				
Centralized purchase[¶]	82.2 (80.5– 84.0)	80.4 (76.2–84.7)	72.1 (68.7–75.6)	73.3 (70.3–76.3)
Others	84.8 (83.6– 86.0)	86.9 (84.2–89.7)	83.9 (82.0–85.7)	84.1 (82.4–85.7)

Source: PNAUM (National Survey on Access, Use and Promotion of Rational Use of Medicines) 2015.
[†]Bigger municipalities = more than 290 thousand inhabitants.
[‡]Smaller municipalities = less than 290 thousand inhabitants.
Association was assessed through linear model for complex samples.
[§]Significant difference between capital groups and the smaller municipalities.
[¶]Significant difference between the group of the smaller municipalities and the other two groups.
[#]Significant difference between the groups of capitals and the other two groups.

had conducted a medicines stock inventory at least once a month. Regarding medicines shortages, in the 3 months prior to the interview, 35.3% of the dispensing units faced stock shortage all the time or very often; 38.1% of them faced shortages sometimes and 26.6% rarely or never had a shortage problem. Most dispensing units (56.6%, n = 673/1175) did not have a locked cabinet to store medicines subjected to special control. The presence of an exclusive fridge to store medicines was observed in 47.2% (n = 650/1175) of the dispensing units and 71.7% (n = 853/1072) of personnel within dispensing units undertook a medicine stock inventory at least once a month (Table 2).

Considering the average availability lower than 80%, the lower average availability was observed in the following therapeutic groups: tuberculostatics (J04) and psychotropic drugs/special control medicines (N03/N06) in Brazil as a whole, the capital cities of Brazilian states and the municipalities (smaller and bigger). The average availability was also lower than 80% among the assessed therapeutic groups: antidiabetics (A10), insulins (A10A), anti-infectives (D01/G01/J01/J02), antisecretory/antacids (A02) and contraceptives/hormones (G03). In capitals availability lower than 80% was observed among anti-infectives (D01/G01/J01/J02) and antisecretory/antacids (A02). In smaller municipalities, shortages were seen with antidiabetics (A10) including insulins (A10A), anti-infectives (D01/G01/J01/J02), antisecretory/antacids (A02) and contraceptives/hormones (G03) and in bigger municipalities with antisecretory/antacids (A02). In Brazil, generally shortages happened with insulins (A10A), anti-infectives (D01/G01/J01/J02), antisecretory/antacids (A02) and contraceptives/hormones (G03). The average availability of essential medicines overall reached 83.3% in Brazil, which means a number of facilities had availability higher than 80% in both the capitals of Brazilian states as well as smaller and bigger municipalities.

Regarding the purchasing strategy, the national availability of centralized purchased medicines by Federal government was 73.3%; however, a mean up to 80% was observed in the capital cities and the largest municipalities indicating problems in the logistics to the smaller cities (Table 3).

Table 4. Average availability of essential medicines based on therapeutic class and features.

Therapeutic classes (ATC 2nd level)	Availability % (IC 95%)							
	Features							
	Unit type		Pharmacist in charge		Does the DU have an IT system?		Inventory frequency	
	Independent pharmacy	UBS pharmacy	Yes	No	Yes	No	At least once a month	Every two months or at longer time intervals
Anti-infectives (G01/J01)	83.0 (76.7–89.2)†	73.4 (70.7–76.1)	83.7 (80.3–87.1)†	67.9 (64.4–71.4)	82.5 (78.9–86.2)†	69.8 (66.4–73.2)	74.0 (71.1–76.9)	76.5 (70.8–82.3)
Contraceptives/hormones (G03)	83.6 (74.9–92.2)	76.3 (72.7–79.9)	83.0 (77.6–88.4)†	73.0 (68.8–77.0)	84.1 (78.3–89.9)†	72.8 (68.8–76.8)	74.6 (70.8–78.3)†	83.9 (77.1–90.6)
NSAIDs (NO02B/M01)	92.4 (87.0–97.9)†	85.1 (82.3–87.8)	91.8 (88.4–95.1)†	81.7 (78.2–85.3)	93.7 (90.2–97.2)†	81.1 (77.7–84.6)	85.5 (82.8–88.2)	87.5 (81.4–93.7)
Antianemics (B03)	87.7 (80.8–94.6)	83.4 (80.6–86.3)	87.3 (83.4–91.2)†	81.5 (78.0–85.1)	89.6 (85.9–93.2)†	80.4 (76.8–84.0)	83.3 (80.3–86.2)	87.8 (82.3–93.4)
Anti-asthmatics (R03/H02)	84.0 (73.6–94.4)	81.4 (78.5–84.3)	87.8 (83.6–92.0)†	77.1 (73.4–80.9)	88.1 (83.7–92.6)†	77.6 (74.0–78.2)	80.9 (78,1–83,8)	83.6 (76.2–90.9)
Antidiabetics (A10)	86.2 (80.7–91.6)†	79.5 (76.7–82.3)	88.1 (84.7–91.4)†	74.6 (71.1–78.1)	85.9 (82.2–89.6)†	76.8 (73.4–80.1)	78.7 (76.0–81.4)†	85.6 (80.1–91.1)
Antisecretory/antacid (A02)	70.6 (57.4–83.9)	73.0 (69.3–76.7)	77.5 (71.1–84.0)†	69.0 (64.9–73.2)	82.6 (76.5–88.7)†	66.3 (61.8–70.8)	72.6 (69.1–76.0)	76.7 (64.4–85.1)
Antihypertensives (C03/C07/C09)	91.0 (86.4–95.7)†	85.7 (83.4–88.1)	91.2 (88.6–93.8)†	82.8 (79.7–85.9)	90.6 (87.7–93.5)†	83.7 (80.7–86.6)	84.3 (81.7–86.8)†	91.7 (87.9–95.4)
Antiparasitic (P01/P02/P03)	81.3 (66.7–96.0)	86.1 (83.5–88.6)	87.8 (82.2–93.3)	83.7 (80.5–86.8)	89.2 (83.2–95.2)	83.1 (80.0–86.3)	84.2 (81.4–87.0)	88.1 (79.6–96.7)
Psychotropic/special counter (N03/N05/N06)	59.5 (44.1–75.0)†	25.7 (20.5–30.9)	54.7 (45.2–64.2)†	11.8 (4.4–19.2)	54.8 (44.8–64.9)†	14.4 (7.2–21.5)	23.7 (19.8–27.6)†	50.1 (34.2–66.1)
Tuberculostatics (J04)	30.5 (16.1–44.9)	23.1 (17.6–28.6)	29.7 (21.8–37.7)	19.9 (12.7–27.0)	28.8 (20.5–37.1)	21.2 (14.5–28.0)	20.8 (17.2–24.5)	35.4 (19.2–51.6)
General (11 classes)	84.6 (79.4–89.9)	80.8 (78.9–82.8)	87.2 (84.5–89.8)†	76.9 (74.5–79.3)	87.6 (84.7–90.4)†	77.3 (75.0–79.6)	79.9 (78.1–81.6)†	85.5 (81.1–89.8)

Source: PNAUM (National Survey on Access, Use and Promotion of Rational Use of Medicines) 2015. Association was assessed through linear model for complex samples.
†$p < 0.05$.
DU: Dispensing unit; IT: Information Technology; UBS: Basic Health Unit.

Average availability lower than 80% was observed for psychotropic drugs/special control medicines ($p < 0.05$) and tuberculostatic drugs ($p > 0.05$) in all assessed situations based on dispensing units' features (unit type, pharmaceutical in charge, IT system and inventory frequency; Table 4). The same was observed for antisecretory/antacids, except for dispensing units lacking IT systems (82.6%). Antidiabetic drugs recorded the worst mean availability in units without a pharmacist in charge (74.6%), which were followed by dispensing units without IT systems (76.8%), units making stock inventory at least once a month (78.9%) and UBS pharmacies (79.5%). The same was observed for contraceptives/hormones, which recorded a mean availability lower than 80% in locations without IT systems (72.8%), which were followed by dispensing units lacking pharmaceutical professionals (73.0%), places that make stock inventory at least once a month (73.4%) and UBS pharmacies (76.3%). With regard to anti-infective medicines, the worst mean availability was observed in dispensing units without pharmaceutical professionals (67.9%), followed by those lacking IT system (69.8%) and UBS pharmacies (73.4%) regardless of inventory frequency. The other classes of drugs recorded mean medication availability higher than 80% under all assessed conditions (Table 4).

The presence of the pharmacist in charge of the dispensing unit and having an IT system to record PS activities were factors associated with a higher mean availability of all groups of medicines when all 50 tracers were taken into consideration. With respect to the dispensing units, the mean availability of essential medicines in independent pharmacies was higher than in UBS pharmacies; however, such differences were not statistically significant. Curiously, the mean availability was higher in the units that made stock inventories bimonthly or less (Table 5).

Most dispensing units did not have a locked cabinet to store medicines subjected to special control and the mean availability of these medicines was positively influenced by the presence of specific places to store them. However, it was observed that this parameter was higher in dispensing units that had unlocked cabinets. The packaging analysis

Table 5. General mean availability of essential medicines based on infrastructure and techno-managerial features.

Features	Availability % (IC 95%)
Unit type	
– Independent pharmacies	85.5 (80.7–90.4)
– UBS pharmacies	81.7 (79.8–83.7)
Pharmacist in charge	
– Yes	87.6 (85.0–90.3)†
– No	78.2 (75.8–80.6)
Does the DU have an IT system to record PS activities?	
– Yes	88.4 (85.6–91.2)†
– No	78.3 (76.0–80.6)
How often is the inventory carries out?	
– At least once a month	81.0 (79.2–82.8)†
– Every two months or at longer time intervals	85.8 (81.6–90.0)
Is there a specific and adequate place to store special-control medicines?‡	
– Yes, there is a specific location (locked cabinets)	86.7 (82.1–91.3)
– Yes, however, it is not a specific locked cabinet	98.1 (95.4–100)
– There is no specific location	70.6 (47.1–94.1)
How are the thermolabile medicines stored?§	
– Fridge with a thermometer to control and register the temperature	90.1 (87.3–93.0)
– In fridge, but without temperature control and register	82.3 (64.1–100)

Source: PNAUM (National Survey on Access, Use and Promotion of Rational Use of Medicines) 2015. The association was assessed through linear model for complex samples.
†$p < 0.05$.
‡Availability of controlled medications, significant difference between the first and the second responses, and the second and third responses.
§Availability of thermolabile medicines.
DU: Dispensing unit; IT: Information Technology; PS: Pharmaceutical Service; UBS: Basic Health Unit.

of thermolabile medicines (insulins) showed that only 55% of dispensing units had a fridge for their storage and only 47.2% of these were exclusive for medication storage. Mean insulin availability was higher in pharmacies that had a fridge with a thermometer to control and register the temperature.

Discussion

To best of our knowledge, this is the first study in Brazil to use Remume (local EML) to assess the availability of essential medicines by taking into consideration the particular features of each municipality.

Encouragingly, the average availability of essential medicines (83.3%, 95% CI: 82.1–84.5) was higher than that recommended by Pan American Health Organization (PAHO)/WHO [12] and higher than previously observed in two studies undertaken on a national scale which also used tracer medicines [11,17]. These differences can be attributed to the use of the local EML as a parameter to analyze the availability of tracer medicines in this study because not all assessed municipalities in previous studies had the availability of medicines quantified based on the total number of assessment items. While the selection of tracers was based on the Brazilian EML (Rename), according to Mendes *et al.* [17] municipal managers are responsible for ensuring the availability of medicines that most meets the needs of the local epidemiological profile. Consequently, one cannot discard the possibility that the low availability of some items was compensated by the availability of alternative medicines for the same indication. On the other hand, the possibility of municipalities having the standardization of medicines other than tracers cannot be discarded, which could result in a mismatch of local health demands with the EML. It is important to highlight that The Brazilian National List (Rename) has a list of medicines carefully selected based on the best available scientific evidence.

While there is a national policy to encourage the use of herbal medicines [32], such practices remain variable with the availability of such medicines reaching 0.8% in the dispensing services of PHC, according to Mendes *et al.* [17], and 8.8% according to Nascimento *et al.* [11]. In this present study, the number of tracer medicines could be reduced from 58% to a maximum 50% in most municipalities where Remume did not encompass herbal medicines. It is another factor that might have affected the overall availability of medicines (83.3%) in comparison with the 58.5% recorded by Mendes *et al.* [17], and to the 62.5% found by Nascimento *et al.* [11].

Significant difference between the availability of essential medicines in municipal extracts were not found, except when this was associated with centralized purchasing. This contrasted with other studies in Brazil which did find a correlation between availability and the number of inhabitants in the locality [17,33]. However, a negative influence of a centralized acquisition system were found on medicine availability in the smaller municipalities.

Out of the five therapeutic classes with mean availability lower than 80%, two of them referred to medicines subjected to centralized acquisition, in other words, contraceptives/hormones and tuberculostatics. The highest availability of tuberculostatics was in the state capitals, which can be explained by the high incidence of tuberculosis cases in such cities. Sixteen capitals recorded coefficient of incidences higher than the national mean (9.3% new cases/100,000 inhabit.) in 2014 [34]. In order to rationalize medicines use and availability, municipalities can apply logistic strategies to centralize the dispensing of tuberculostatics and establish their distribution based on local demands. This strategy can be estimated through PS management in those municipalities with a lower incidence of tuberculosis cases. However, it is not possible to determine whether this logistics management impairs access to appropriate treatment, as stated by the Ministry of Health [35]. Another hypothesis for low availability could lie on the inclusion of rifampicin 300 mg in the list of tracer medicines rather than a combination since monotherapy with rifampicin is typically not recommended in favor of combination therapy including rifampicin + isoniazid + pyrazinamide + ethambutol [36]. These factors may have influenced the low general availability found in the current study for this therapeutic class (24.1%). Brazil is currently ranked 20th among countries with the highest incidence of tuberculosis [35]; consequently, it is important to investigate whether such low mean availability of medicines to treat tuberculosis would have any negative impact on the ability to control this disease. More investigation will be necessary further in future research projects.

With respect to other anti-infective medicines, it is worth pointing out that the tracer medicines used in our study may not fully meet the demands of different municipalities. Because these medicines are used to treat acute conditions, their availability may have been influenced by seasonal and epidemiological effects. The incorporation of ceftriaxone 500 mg (injectable) to the list of medicines recommended to treat gonorrhea resistant to ciprofloxacin hydrochloride [37] in April 2015 may have impacted the low availability of ciprofloxacin hydrochloride (65.3%) due the exchange for another anti-infectious agent. Another consideration relates to the mean availability of benzylpenicillin benzathine used to treat syphilis. It is the only safe and effective medication to treat syphilis at pregnancy and the recommended option to treat congenital syphilis [37,38]. Back in 2014, there were problems concerning the acquisition of raw-materials with the shortage lasting until 2017 [38] coinciding with the data collection period. Consequently, this might have influenced the low mean national availability of this antimicrobial (49.5%) in our study; the lowest availability among anti-infective medicines according to Nascimento *et al.* [11], and highlighted generally as a shortage across South America increasing rates of syphilis in Brazil [39].

While the antidiabetic class presented a mean availability higher than 80%, insulins – which are also funded and purchased by the federal government – recorded lower mean availabilities. Overall, the mean availability of antidiabetic drugs associated with UBS pharmacies reached 79.5%. It is important that these medicines are routinely available as diabetes currently affects 8–9% of the population [40], and high blood glucose is currently estimated to be the third most important cause of early mortality in Brazil with only high blood pressure and tobacco use causing higher mortality [41]. However, the distribution logistics of insulins, as well as of contraceptives/hormones, could have contributed to their lower mean availability among the dispensing units of the smaller municipalities. This is because the distribution of these medicines by the federal government focuses on direct shipment to warehouses only in capital cities and in municipalities with more than 500,000 inhabitants [42]. To the other municipalities, the health departments of the Brazilian States receive the medicines and are responsible for ongoing distribution from the regional facilities. Despite the necessity of making routinely available thermolabile substances such as insulin, their mean availability in pharmacies that actually have fridges was 73.8% at a national level. However, the national rate of dispensing units that have such fridges was low in our study mirroring the findings of Costa *et al.* [43] who pointed out that only 47.2% of pharmacies in Brazil have fridges to store medicines. The authors also documented the unequal frequency of fridges among all five Brazilian regions, ranging from 21.3% in the Northeastern region to 76.0% in the Southeastern region. This is a considerable concern and again needs further investigation.

The availability of psychotropic/special control medicines is conditioned by the regulatory requirements such as the mandatory presence of a restricted access location for medicine storage and the requirement of having a pharmacist in charge in the dispensing units [17,44]. The fact that the availability of these medicines is higher in independent pharmacies suggests that their dispensing can be centralized in these dispensing units and in part of UBS pharmacies which could be selected based on criteria established by local public managers. Overall in this

study, less than half of dispensing units surveyed had a pharmacist in charge as well as a restricted access location. Mendes *et al.* [17] found that only a few UBS pharmacies provided psychotropic drugs (5.7%); moreover, only 3.3% of pharmacies that dispensed these medicines had availability equal to, or higher than, 80%. This confirms a need to restrict these medicines to principally independent pharmacies.

It is not possible to infer from the present study that pharmaceutical professionals are concentrated in units that dispense medicines subjected to special control; however, such a trend was observed. Dispensing centralization may be attributed to regulatory requirements; however, this could have been influenced by costs since 42.6% of the dispensing units surveyed functioned without the daily assistance of pharmacists. Despite the regulatory aspects, it is important to highlight the relevance of having such professionals in units that dispense medicines subjected to special control, which contribute to a proper delivery of these medicines coupled with guidance on their use and patients' safety (pharmacovigilance). In addition, proper assessment of the need for health education strategies to promote RUM.

In Brazil, nervous system medication such as antipsychotics, anxiolytics, antidepressants, hypnotics and sedatives are subject to special control, according to the Federal Ordinance 344/98 [44]. It was not possible in this study to correlate the proximity of pharmacies that dispense special control medicines and the mental health clinic support network (generalists, psychiatrists and psychologists). Similarly, it was not possible to assess the standardization of other medicines in this therapeutic class. Tracer medicines such as amitriptyline and fluoxetine are constant in WHO list of essential medicines [45] to treat depression disorders. They can have their availability reduced or compensated by other antidepressants that have the same effectiveness or are seen as safer mainly for the elderly population; however, acknowledging safety concerns with some of the selective serotonin re-uptake inhibitors [46,47].

Overall, less than half of the dispensing units in our study had a pharmacist available throughout the day. This is a concern as the presence of such professionals allows for the supervision of technical-managerial activities and influences the availability of medicines. In addition, such professionals can provide advice and guidance to patients about the use of their medicines [48–51] including enhancing adherence to medicines to improve patient outcomes. Mendes *et al.* [17] also observed a greater chance of medicine availability in dispensing units that had these professionals as well as a medicine storage room and a fridge for medicine storage. In addition, Melo *et al.* [52] showed that adding PS as part of UBS teams significantly reduced the lack of medicine availability as well as contributing to the promotion of RUM. Overall, the greater presence of pharmacy professionals in dispensing units could lead to greater monitoring of medicines dispensed, their greater availability based on local epidemiological profiles with a potential reduction in the number of avoidable shortages, as well as improved patient care generally. With regards to the presence of pharmacists in PHCs, they could potentially have part of their workload distributed among general and assistant activities. In addition, they could potentially work in more than one dispensing unit depending on the municipal PS organization. Even working part-time, pharmacists could contribute to the greater availability of medicines in the dispensing units they are responsible for. Despite Brazilian legislation indicate that pharmacists are responsible for pharmacies, there are dispensing units in the public sector that operate without the supervision of these professionals. Thus, it is necessary to strengthen the role of the pharmacist in PHC in Brazil, ensuring that all dispensing units have full-time supervision of pharmacists at some stage during the day, ideally all day. We will be following this up in the future to improve pharmaceutical care in Brazil building on positive comments in other countries including other lower- and middle-income countries [49,53–55].

No recommendations were found in the researched literature for the ideal frequency of carrying out inventories in public pharmacies, which can be daily or even annual. Interestingly, conducting medicines inventories at shorter time-intervals did not lead to a higher availability of medicines. However, the existence of IT systems in PS management did lead to a higher availability of essential medicines in PHCs. Vieira [56] observed that municipalities lacking medicines suffered from a lack of medicine control activities, adding to our findings. Efficient stock control can help stabilize medicine availability to the benefit of patients [57].

The present study has some limitations. Some results, by therapeutic class, may be overestimated because the item that had at least one pharmaceutical unit in stock at the time of observation by the interviewer was considered 'available'. In these cases, this minimum amount observed may not represent what is necessary to meet the demand for treatment/control of the health condition in question, that is, for practical purposes, this item would partially meet the patient's need. This limitation was also highlighted by Mendes *et al.* [17] and Nascimento *et al.* [11] in previous studies. Another limitation concerns the cross-sectional design of the study, which allows determining the availability of medicines considering only the momentary stock levels. Thus, it was not possible to evaluate the processes that can influence availability, such as the frequency of deliveries and the storage capacity of medicines

for each dispensing unit. The tracer medicines were selected in order to contemplate the most prevalent health conditions in Brazil, however, it was not possible to assess, in this study, if the probable variability between the Municipal List of Essential Medicines would cause clinical impact for the population. Thus, the availability measure may be underestimated in some municipalities, and it is not possible to assess the existence of an association between availability and the local arrangements adopted for the supply of medicines. However, despite the limitations, our results are robust, pointing to a direction for the future studies.

Conclusion

Availability of essential medicines in Brazil was positively influenced by the presence of the pharmacist responsible for the dispensing units and by the availability of computerized system systems in the pharmacy. Availability was negatively associated with essential medicines purchased centrally by the federal government and by the logistics of distribution to smaller municipalities.

Integral PS are a challenge within universal healthcare systems especially in a country with a large geographical spread and important social-economic differences as seen in Brazil. Strategies focusing on ensuring and amplifying funds for medicine purchase, on raising the number of pharmaceutical professionals in PHCs, on updating EMLs, on improving the infrastructure with dispensing medicines units, on operationalizing pharmaceutic activities through IT systems and on enhancing distribution logistics systems applied to centralized-acquisition medicines are all important to ensure universal access to essential medicines that meet the epidemiological demands of the population.

Considering Brazil does not yet have a national database on PS, further studies are needed to monitor and evaluate the performance of public PS. Although data from this study were collected some years ago, no improvements in the infrastructure and organization of public PS have been observed so far. This is a concern that will continue to be communicated based on the findings from ongoing studies in Brazil and wider. Studies that allow a longitudinal evaluation could also help to understand the dynamics of the availability of medicines in PHC. Studies with a qualitative approach, involving managers and workers, can also be useful to improve and recognize other factors that influence the availability of medicines in each type of dispensing unit. These are projects for the future.

From the perspective of Universal Health Systems, especially in countries of greater territorial extension, such as Brazil, this study reinforces the importance of establishing an EML appropriated to the different local epidemiological realities. Additionally, it highlights the relevance of a careful selection of tracers for future research, in order to reflect the real availability of essential medicines. Further investigations are needed to assess the impact of the structure, organization of PS and logistical strategies in the availability of medicines in PHC, verifying the influence of the pharmacist's role in public health services.

Future perspective

Access to medicines provided by universal health systems, especially in countries of great territorial extension such as Brazil, is still a challenge. According to the results of the present study, the distribution logistics of medicines throughout the territory, combined with the infrastructure and human resources of the local health services are important points to be worked on, as there has been no progress in the last 5 years. As there is no forecast for an increase in the provision of resources, the prospect of improvement in this field may be compromised, even though the study points to greater availability of medicines in services that have the presence of a pharmacist responsible for the medicine dispensing unit and a computerized systems for recording PS. There is a prospect of incorporating medicines into the National List of Essential Medicines, but it is unlikely to adequately address the different epidemiological profiles of the entire territory. However, the use of appropriate tracer medicines in the next studies is a useful tool that can serve to verify the quality of PS to the population in the coming years.

Summary points

- Availability of standardized essential medicines was in line with WHO recommendation.
- Among the therapeutic groups evaluated, the lowest average availability were for the tuberculostatics (24.1%) and psychotropic/special control medicines (30.3%).
- The packaging analysis of thermolabile medicines (insulins) showed that only 55% of dispensing units had a fridge for their storage and only 47.2% of these were exclusive for medication storage.
- Almost half of the dispensing units had a pharmacist present throughout the whole shift; however, 42.6% of dispensing units did not have such a professional on a daily basis or did not have one at all.
- Approximately 60% of dispensing units did not have an Information Technology system to record pharmaceutical services (PS) activities.
- The availability of essential medicines was positively influenced by the presence of the pharmacist responsible for the medicine dispensing unit and a computerized systems for recording PS.
- The centralized purchasing system negatively influenced the medicines availability, especially in the smaller municipalities.
- Integral PS are a challenge within universal healthcare systems especially in a country with a large geographical spread and important social-economic differences as seen in Brazil.

Author contributions

WH Rocha contributed toward conceptualization, data curation, writing (original draft), writing (review and editing), visualization and supervision. JA Teodoro contributed toward methodology, resources and project administration. FA Acurcio contributed toward methodology and resources. AA Guerra Jr contributed toward methodology and resources. ICG Moura contributed toward methodology, formal analysis and data curation. B Godman contributed toward writing (review and editing) and visualization. A Kurdi contributed toward writing (review and editing) and visualization. RCRM Nascimento contributed toward conceptualization, data curation, writing (original draft), writing (review and editing), visualization and supervision. AM Almeida contributed toward conceptualization, methodology, formal analysis, data curation, writing (original draft), writing (review and editing), visualization and supervision.

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Ethical conduct of research

Ethical approval was obtained from the National Research Ethics Committee under CONEP Opinion n. 398.131/2013. All interviews were preceded by research-objective clarification to interviewees and informed written consent form were sought on the same day.

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