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Profile of requests for non-standard drugs in a Brazilian' public hospital

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Abstract

Objective: This is a cross-sectional retrospective study with the objective of evaluating the profile of requests for non-standard drugs requested (NSDR) at the Complexo Hospital de Clínicas of the Federal University of Paraná (CHC-UFPR) in 2021. Methods: For data collection, NSDR forms were used, which were requested by the CHC-UFPR prescriber and sent to the dispensing sector from January to December 2021. Data were collected in the Microsoft Excel program and expressed in graphs and tables. Results: 482 forms were included for analysis. Of these, 261 (54.15%) were female, with a mean age of 43.46 years, standard deviation 22.95. 139 forms were requested for the elderly and 69 for pediatrics. The month with the most requests was October (60 forms). The most requested medication was dexmedetomidine 200 mcg f/a (197 forms), followed by sugammadex 200mg f/a 2mL (88 forms). The unit that most requested NSDR was the Surgical Center (176 forms), followed by the General intensive care unit (36 forms). During the study period 35 NSDR were denied (7.26%). Results showed that 84.85% of the medications were dispensed on the same day of the request. The cost of CHC-UFPR in the year 2021 with non-standard drugs was R$ 512,033.82 (US$ 104,306). Most drugs (71.43%) are not incorporated into the SUS. Conclusion: The study showed that the drug dexmedetomidine was the most requested in the year 2021, so it is a strong candidate for standardization. Therefore, it is concluded that the list of standardized drugs must be constantly reviewed and updated to include new drugs. Thus, the analysis of requests for non-standardized drugs is an important tool for consulting potential candidates for standardization.

Keywords: access to essential medicines and health technologies, hospital care, pharmacy and therapeutics committee.

Perfil de solicitações de medicamentos não padronizados em um hospital público brasileiro

Resumo

Objetivo: Avaliar o perfil de solicitações de medicamentos não padronizados solicitados no Complexo Hospital de Clínicas da Universidade Federal do Paraná (CHC-UFPR) no ano de 2021. **Métodos:**Foi conduzido um estudo transversal retrospectivo.Para a coleta de dados foram utilizados os formulários de Solicitações de Medicamentos Não Padronizados (SMNP) que foram solicitadas pelo prescritor do CHC-UFPR e encaminhadas ao setor de dispensação em janeiro a dezembro de 2021.Os dados foram coletados no programa Microsoft Excel e foi conduzida uma análise descritiva, expressa em gráficos e tabelas. **Resultados:** 482 formulários foram incluídos para análise. Destes, 261 (54,15%) eram do sexo feminino, com média de idade de 43,46 anos (desvio padrão 22,95). Foram solicitados 139 formulários para idosos e 69 para pediatria. O mês com mais solicitações foi outubro (60 formulários). O medicamento mais solicitado foi a dexmedetomidina 200 mcg f/a (197 formulários), seguido do sugamadex sodico 200mg f/a 2mL (88 formulários). A unidade que mais solicitou SMNP foi o Centro cirúrgico (176 formulários), seguido da unidade de terapia intensiva Geral (36 formulários). Foi verificado que 35 SMNP foram negadas (7,26%). E foi constatado que 84,85% dos medicamentos foram dispensados no mesmo dia da solicitação. O custo do CHC-UFPR no ano de 2021 com os medicamentos não padronizados foi de R$ 512.033,82 (104,306). E foi verificado que a maioria dos medicamentos (71,43%) não está incorporado no SUS. **Conclusão:** O estudo demonstrou que o medicamento dexmedetomidina foi o mais requisitado no ano de 2021, portanto sugere-se avaliar a sua padronização. Portanto, conclui-se que a lista de medicamentos padronizados deve ser constantemente revista e atualizada para a inclusão de novos medicamentos. Deste modo, a análise das solicitações de medicamentos não padronizados é uma importante ferramenta para consulta de possíveis candidatos a padronização.

Palavras-chave: acesso a medicamentos, assistência hospitalar, comitê de farmácia e terapêutica.

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Introduction

According to Ordinance No. 3,916 of October 30th, 1998, "The list of essential medications includes those products considered basic and indispensable to meet most of the health problems of the population"[1]. Therefore, medications are part of health control and belong to one of the most important stages in the treatment of many pathologies. However, when these medications are used irrationally, they become a high-risk problem that can compromise the patients' conditions and consequently lead to harmful and irreversible risks to their patient[2].

Within a hospital, drug standardization is responsibility of the Pharmacy and Therapy Commission (*Comissão de Farmácia e Terapêutica*, CFT), a collegiate body of an advisory and deliberative nature whose objective is to select medications to be used in the health system at the three care levels[3]. Its responsibility is to develop actions to ensure safe and rational use of medications and health products in a participatory, multiprofessional and multidisciplinary process aimed at improving the quality of the care provided to patients[4]. However, the list of standardized drugs is not always enough to meet exceptional needs; for example, in the case of hospitals that provide quaternary-level health services and welcome patients with countless pathologies, many of them rare and with different severity levels. Such situations can hinder comprehensive and timely care; therefore, it is important to have a method that ensures the use of non-standardized drugs. Therefore, when used judiciously, requests for these medications significantly contribute to improving health care services and provide an improvement in the quality of life of the patients assisted[5].

The objective of this study was to evaluate the profile of Non-Standardized Drug Requests (NSDRs) at the Clinical Hospital Complex belonging to the Federal University of Paraná (*Complexo Hospital de Clínicas-Universidade Federal do Paraná*, CHC-UFPR) to verify which are the most requested medications, collect data on costs, hospital units that requested the most medications, and the number of request authorizations. In addition to that, assessing the time elapsed from drug request to dispensing, and if these requested drugs are incorporated into the Unified Health System (*Sistema Único de Saúde*, SUS).

Methods

Study design

This is a descriptive, retrospective and cross-sectional study. Its description was conducted according to the *Strengthening the Reporting of Observational Studies in Epidemiology* tool (STROBE Statement)[6]. This research was approved by the CHC-UFPR Research Ethics Committee (*Comitê de Ética em Pesquisa*, CEP) on April 26th, 2022, under CAEE No. 56838022.8.0000.0096.

Context

The study was carried out in a university hospital from the state of Paraná, city of Curitiba, namely: CHC-UFPR. The Clinical Hospital Complex belonging to UFPR/Ebserh, comprised the Clinical Hospital (*Hospital de Clínicas*, HC) and the Victor do Amaral Hospital (*Hospital Victor do Amaral*, HVA), is a supplementary body of the Federal University of Paraná (*Universidade Federal do Paraná*, UFPR) and part of the Ebserh Network of Federal University Hospitals (*Hospitais Universitários Federais*, HUFs). CHC-UFPR has a capacity of 440 active beds.

Study participants and sample size

Inclusion criteria: All NSDR forms correctly filled-in (all required fields/information) by prescribers to patients admitted to the hospital during the data collection period were included in the study.

Variables and data sources

For data collection, the NSDR forms that were requested by the CHC-UFPR prescriber and sent to the dispensing sector in the 2021 were used. When filling out the non-standardized drug form, the prescriber indicates the patient's treatment time and the medication amount per day. Each form is valid for up to 30 days. Therefore, if the treatment is longer, a new NSDR must be completed.

When the inpatient dispensing sector receives the NSDR, it records the data in a Microsoft SharePoint spreadsheet; therefore, all the information necessary for the current study was extracted from this database. In addition to that, data were taken from the Management App for University Hospitals (*Aplicativo de Gestão para Hospitais Universitários*, AGHU), which is a patient-focused hospital management system adopted as a standard for all Federal University Hospitals from of the Ebserh network and the Hospital Information System (*Sistema de Informação Hospitalar*, SIH), a hospital management system developed by the CHC/UFPR IT Service used before incorporating AGHU.

For each request, the patient's gender and age were collected. In addition, other variables collected were as follows: the most requested medications; data on costs; the hospital units that most requested medications; the number of request authorizations; the time since drug request to dispensing; and if these requested medications are incorporated into the SUS. The data were collected between May and September 2022.

Data analysis

The data collected were added to Microsoft Office Excel (Microsoft, USA), expressed in graphs and tables and reported using descriptive statistics such as absolute frequencies and mean values. To analyze the patients' age, they were considered older adults when ≥60 years old[8] and children when ≤12 years old[7].

The monetary values are expressed in reais (R$), the currency in force in Brazil at the time of the analysis. The values are also expressed in American dollars, using the exchange rate valid on June 8th, 2023 (1 US$ = 4.92 R$).

Results

Participants

A total of 530 NSDR forms received by the inpatient dispensing pharmacy were analyzed. Of these, 48 did not meet the inclusion criteria (for example: incomplete filling-in of the dispensing record, patient record and drug use authorization record fields), totaling 482 for analysis. In relation to the profile of patients to whom the NSDRs were directed, the majority [54.15% (n=261)] were women. The patients' mean age was 43.5 years old (Standard Deviation = 22.9), with 139 (28.8%) considered as older adults and 69 (14.3%), as children.

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Main results

It was observed that October was the period with the most requests, with 60 (Figure 1). The results showed that 35 different types of medications were requested. Among these, the most requested were dexmedetomidine 200 mcg a/v (197 forms), sugammadex sodium 200 mg a/v 2 mL (88 forms) and ceftazidime + avibactam 2 g + 500 mg a/v (37 forms). In addition to that, it can be noticed that some belong to the same therapeutic class (Table 1).

The unit that most requested non-standardized drugs (Table 2) was the Surgical Center (176 forms), followed by the General Intensive Care Unit (ICU) (36 forms) and by the Cardiac ICU (35 forms). In addition, it was verified that 35 of the 482 NSDRs were denied (7.26%). Finally, the medication that had the most non-authorizations was ceftazidime + avibactam 2 g+500mg a/v (9 forms), followed by dexmedetomidine 200 mcg a/v (6 forms). Other medications were denied once at the most.

Figure 1. Number of non-standardized drug requests by month in the Clinical Hospital Complex belonging to the Federal University of Paraná (Curitiba, 2021)

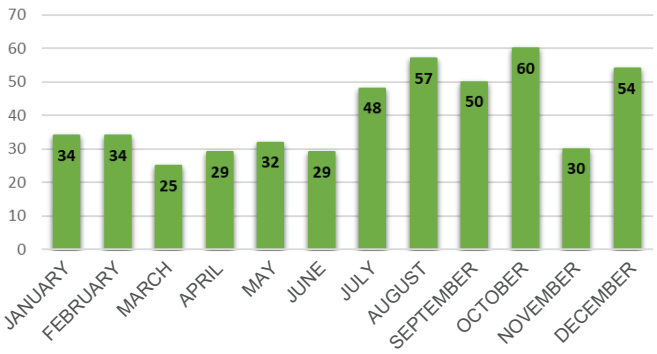

Table 1. Number of requests by medication and therapeutic class in the Clinical Hospital Complex belonging to the Federal University of Paraná (Curitiba, 2021).

Medication	Therapeutic class (ATC classification)	Number and frequency of requests (Total = 482) N (%)
Dexmedetomidine 200mcg a/b	Antipsychotic, anxiolytic	197 (40.9)
Sugammadex 200mg a/b 2mL	Antidotes	88 (18.3)
Ceftazidime + Avibactam 2g+500mg a/b	Antiinfective	37 (7.7)
Doxycycline 100mg tablet	Antiinfective	29 (6.1)
Isavuconazole 100mg capsule	Antiinfective	20 (4.2)
Dexmedetomidine 400mcg/100mL a/b	Antipsychotic, Anxiolytic	18 (3.8)
Sertraline 50mg tablet	Psychoanaleptic, Antidepressants	15 (3.1)
Topiramate 100mg tablet	Antiepileptic	14 (2.9)
Lamotrigine 100mg tablet	Antiepileptic	9 (1.9)
Permethrin 50mg/mL lotion - 60mL	Ectoparasiticide	7 (1.5)
Indometacin 25mg cap	Antiinflammatory and antirheumatic products	5 (1.0)
Remifentanil 2mg a/b	Opioid anesthetics	4 (0.8)
Terlipressin 1mg a/b	Posterior pituitary lobe hormones	4 (0.8)
Potassium Alumen 1% - 500mL	Ophthalmologicals	3 (0.6)
Cimetidine 300mg amp	Drugs for peptic ulcer and gastro-oesophageal reflux disease	3(0.6)
Ciprofloxacin + Dexamethasone ophthalmic ointment	Antiinflammatory agents and antiinfectives in combination	3(0.6)
Erythromycin 50mg/mL - 60mL	Antiinfectives	3(0.6)
Metoprolol 100mg tablet	Cardiovascular system, beta blocking agents	3(0.6)
Hydroxyzine 2mg/mL	Allergens	2(0.4)
Sucralfate 2g oral suspension - 10mL	Drugs for peptic ulcer and gastro-oesophageal reflux disease	2(0.4)
Trihexyphenidyl 5mg tablet	Anti-Parkinson drugs, anticholinergic agents	2(0.4)
Amoxicillin + Clavulanic acid 500/125mg	Antiinfectives	1(0.2)
Sodium bicarbonate 5g sachet	Drugs for acid related disorders, antacids	1 (0.2)
Caffeine 20mg ampoule 1mL	Psychoanaleptics	1 (0.2)
Clobazam 10mg tablet	Psycholeptics	1 (0.2)
Sotalol 120mg tablet	Cardiovascular system, beta blocking agents	1 (0.2)
Fentanyl 2,5mg transdermal patch	Opioid anesthetics	1 (0.2)
Linezolid 600mg tablet	Antiinfectives for systemic use	1 (0.2)
Orlistat	Antiobesity preparations	1 (0.2)
Piperazine 10% syrup	Antiparasitic, anthelmintics	1 (0.2)
Quetiapine 25mg coated tablet	Psycholeptics, antipsychotics	1 (0.2)
Quetiapine 200 mg tablet	Psycholeptics, antipsychotics	1 (0.2)
Retinol	Vitamins	1 (0.2)

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Table 2. Units requesting non-standardized drugs in the Clinical Hospital Complex belonging to the Federal University of Paraná (Curitiba, 2021).

Name of the unit	Number of requests (Total = 482) N (%)
Surgical Center	176 (36,5)
General ICU	36 (7,5)
Cardiology ICU	35 (7,3)
Pediatric ICC	31 (6,5)
ICC for Adults III	26 (5,4)
Bone Marrow Transplantation	26 (5,4)
Rooming-In II	19 (4,0)
Respiratory ICC	19(4.0)
ICC for Adults IV	17 (3,6)
Medical Clinic I	13 (2,7)
Surgical ICC	10 (2,1)
Pediatric Surgical Clinic	9 (1,9)
Adult Referenced Unit	9 (1,9)
Day Hospital - TMO	7 (1,4)
Neurology	7 (1,4)
Surgical Clinic I	6 (1,2)
Rooming-In I	5 (1,0)
Pediatrics	5 (1,0)
Cardiology Clinic	4 (0,8)
Infectology	4 (0,8)
High-Risk Chemotherapy	4 (0,8)
Obstetric Center	3 (0,6)
Intermediate-Risk Neonates	3 (0,6)
Neonatal ICU	2 (0,4)
Outpatient Surgical Center	1 (0,2)
Respiratory ICC VII	1 (0,2)
Surgical Clinic II	1 (0,2)
Medical Clinic II	1 (0,2)
Respiratory Ward II	1 (0,2)
Hematopediatrics	1 (0,2)

The time elapsed from drug the request to dispensing was also evaluated; as a result, it was found that 84.85% (409 forms) of the medications were dispensed on the same day of the request (Table 3).

Table 3. Time elapsed from drug request to dispensing (in days) at the Clinical Hospital Complex belonging to the Federal University of Paraná (Curitiba, 2021).

Time elapsed from drug request to dispensing (in days)	Requests	%
0	409	84,9
1	24	5,0
2	3	0,6
3	3	0,6
4	3	0,6
5	2	0,4
16	1	0,2
No dispensing	37	7.7
Total	482	100

Key: 0: Dispensed on the same day of the request; 1: Dispensed the day after the request; 2: Dispensed two days after the request; 3: Dispensed three days after the request; 4: Dispensed four days after the request; 5: Dispensed five days after the request; 16: Dispensed sixteen days after the request.

This study also analyzed the cost for CHC-UFPR in 2021 in terms of non-standardized drugs. Such being the case, the hospital's total expenses were R$ 512,033.82 (US$ 104,306.57). It was found that the medication with the highest cost was ceftazidime + avibactam 2 g+500 mg a/v (R$ 270,279.03 = US$ 54,887.14); the mean cost for each bottle of this drug is R$ 665.71. It was followed by isavuconazol 100 mg cap (R$ 165,501.64 = US$ 33,607.60), with a unit of R$ 249.49 (Table 4).

Table 4. Cost by non-standardized drug in the Clinical Hospital Complex belonging to the Federal University of Paraná (Curitiba, 2021).

Medicine	Quantity dispensed (UP)	Average unit price (in R$)	Average unit price (in US$)	Total price (in R$)	Total price (in US$)
Ceftazidime + Avibactam 2g+500mg f/a	406	665,71	135.19	270.279,03	54,887.14
Isavuconazole 100mg cap	562	294,49	59.80	165.501,64	33,607.60
Sugammadex Sodico 200mg f/a 2mL	88	267,07	54.24	23.501,86	4,773.12
Terlipressin 1mg f/a	61	293,45	59.59	17.900,17	3,634.99
Dexmedetomidine 200mcg f/a	1177	14,74	2.99	17.347,80	3,519.23
Dexmedetomidine 400mcg/100mL f/a	66	128,48	26.09	8.479,68	1,721.94
Remifentanil Hydrochloride 2mg f/a	215	34,47	7.00	7.411,42	1,505.00
Caffeine Citrate 20mg amp 1mL	7	119,22	24.21	834,53	169.47
Permethrin 50mg/mL lotion 60mL	9	22,59	4.58	203,31	371.61
Topiramate 100mg comp	293	0,47	0.10	137,39	29.30
Cimetidine 300mg amp	39	2,85	0.58	111,32	22.62
Lamotrigine 100mg comp	104	0,73	0.15	76,07	15.60
Doxycycline 100mg comp	251	0,27	0.05	67,49	12.55
Ciprofloxacin + Dexamethasone pom oft	2	29,57	6.01	59,14	12.02
Erythromycin 50mg/mL fr 60mL	6	4,79	0.97	28,74	5.82
Sucralfate 2g oral suspension 10mL	5	5,35	1.09	26,74	5.45
Hydroxyzine Hydrochloride 2mg/mL fr	4	5,77	1.17	23,08	4.68
Indomethacin 25mg cap	23	0,61	0.12	14,02	2.76
Sertraline Hydrochloride 50mg comp	99	0,12	0.02	11,96	1.98
Metoprolol 100mg comp	17	0,70	0.14	11,92	2.38
Trihexyphenidyl 5mg comp	17	0,21	0.04	3,57	0.68
Clobazam 10mg comp	7	0,42	0.09	2,94	0.63
Total				512.033,82	104,306.57

Legend: UP: dosage unit; amp: ampoule; comp: tablet; cap: capsule; f/a: ampoule bottle; fr= bottle; pom oft: ophthalmic ointment.

Finally, it was evaluated if the non-standardized drugs are incorporated into the Unified Health System. It was verified that most of them (71.43%) are not.

Discussion

The medication with the highest number of requests was dexmedetomidine (197 forms), a selective alpha-2 agonist with sedative, anxiolytic and analgesic effects that can be used in mechanically ventilated patients in ICUs. In addition to that, it can be used as an adjuvant agent in surgeries, which may reduce the need for sedative-hypnotics and opioids in general anesthesia. Administration begins with an infusion dose of 1 mcg/kg over 10 minutes, and the maintenance dose can range from 0.2 to 1.5 mcg/kg/hour, titrated to the desired sedation level[9].

During the COVID-19 pandemic, there was a need to use sedation and analgesia alternatives for the patients, as there was an increase in the consumption of this class of medications and difficulty replenishing stocks in most Brazilian health institutions. Such being the case, it is necessary to seek alternatives to reduce the drug administration frequency and dose. Dexmedetomidine, for example, can be used to reduce the dose and frequency of opioid administration[10].

Within this context, it can be considered that the increase in the number of dexmedetomidine requests in 2021, the second year of the pandemic, was to save the use of higher doses of sedation and analgesia medications in the hospital environment. Therefore, the request profile for non-standardized drugs could be different in previous years. Dexmedetomidine is not incorporated into the SUS.

The medication with the second highest number of requests was sugammadex (88 forms), which is used to reverse the neuromuscular blockade induced by rocuronium or vecuronium. Its dose varies according to the type of blockade, deep or moderate, 4 mg/kg and 2 mg/kg, respectively, in a single dose[11]. This is a high-cost medication, with a mean of R$ 267.07 each bottle, and is not included in the SUS. Therefore, non-standardization by the hospital can be due to the fact of its price. In addition to that, the hospital has standardized neostigmine, which can be used to reverse neuromuscular blockade and has a lower cost when compared to sugammadex.

Standardization of all CHC-UFPR medications goes through the CFT, which selects and standardizes drugs and pharmaceutical supplies according to the reality of the hospital. In addition to that, it considers costs and patient safety. That said, in this study it was observed that some non-standardized drugs are incorporated into the SUS, such as the following: amoxicillin + clavulonate (500+125 mg), clobazam 10 mg tablet, doxycycline 100 mg tablet, erythromycin 50 mg/ml, lamotrigine 100 mg tablet, linezolid 600 mg tablet, metoprolol 100 mg tablet, quetiapine 25 and 200 mg tablet, and topiramate 100 mg tablet. Therefore, non-inclusion of the aforementioned medications can be associated with the fact that the institution has other drugs with the same purpose or with the low demand for consumption of each drug.

However, if the demand for such medications continues, the CFT may evaluate their incorporation into the hospital. Therefore, a non-standardized drug request should be used, judiciously and as an exception, only when the hospital does not have therapeutic options for a given patient, as it demands time from professionals to assess the need to use the medication, in addition to the cost for the institution.

We observed that only one NSDR took 16 days to dispense the medication. This period can be explained by the possibility that the prescriber waited to initiate the patient's treatment or that the hospital lacked stock, thus requiring a non-standardized drug purchase process. In addition to that, we verified that only 35 NSDRs (7.26%) were denied, although we did not have access to the reasons for non-authorizations.

A retrospective descriptive and exploratory study evaluated "Non-Standardized Sporadic Use Drug Requests" forms, authorized by the Clinical Director of the Clinical Hospital at the Ribeirão Preto Medical School, from April to September 2010. In all, 222 requests were analyzed. As a result, the cost for the hospital during the period was R$ 69,514.36[5].

In our study, the expenses on medications were higher (R$ 512,033.82 = US$ 104,306.57), although the period analyzed was also longer. In addition to that, the value found in our paper may have been influenced by requests for high-cost medications, as is the case of the ceftazidime + avibactam antimicrobial (37 requests generated a cost of R$ 270,279.03 = US$ 54,887.14).

An exploratory study analyzed 232 requests for non-standardized drugs during 6 months in 2014. It was observed that the ICC for adults was the unit that requested the most medications (9.91% of the requests) and that the most requested drug was methadone (19.39%)[12]. In another retrospective descriptive study characterized as exploratory, 153 forms were analyzed from August to December 2018, the Medical Clinic made the most requests (37.25%) and the most requested drug was alprazolam 1 mg tablet (7.19%)[13].

That said, our study differs from those cited, with the Surgical Center (176 forms) and the General ICU (36 forms) as the units that requested the most medications. And the most requested drug was dexmedetomidine 200 mcg. Therefore, each hospital will have its profile of non-standardized drugs based on the epidemiological profile of its hospitalized patients, as each institution has its particularities, whether it is public or private, or general or specialized.

Development of this research contributes data that prove the need to standardize non-standardized drugs constantly requested at CHC-UFPR. The data found may be used by the CFT of this institution in the possible review of the current list of standardized drugs.

Limitations

This study has limitations, as the year analyzed was 2021, the second year of the COVID-19 pandemic; therefore, the hospital's request profile for non-standardized drugs may be different in previous or later years.

Conclusion

The study showed that dexmedetomidine was the most requested medication in 2021. In the same year, the drug was standardized for COVID-19 and Pediatrics units at CHC-UFPR. In the following year (2022), the medication was undergoing the standardization process for the other Intensive Care units in the hospital. Therefore, it is concluded that the list of standardized drugs should be constantly reviewed and updated to include new medications. Consequently, analyzing the requests for non-standardized drugs emerges as an important query tool for possible standardization candidates.

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Collaborators

AW, LR and MLDV took part in conception, design and data analysis and interpretation, as well as in writing of the article and of the final version to be published.

Declaration of conflict of interests

The authors declare no conflicts of interest.

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