



Research Article

Profile of Drugs Used by the Population of a Municipality in the Southern Brazil Region: Strategies for Pharmaceutical Service and Assistance

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Abstract

Introduction: Pharmaceuticals remained a top priority for the government bodies in both national and international levels, contributing to a significant rise in the overall healthcare cost. **Objective:** To describe medication waste and its cost to a public health system that provides medicine free of charge. **Methods:** We analyzed permanent drug donation box collections located in Basic Health Units in Santa Maria, Brazil, for a total of 12 months, starting September 2017. We outlined medication quantity, chemical substance, drug classification and whether the medication was expired, unused, a leftover or a sample. The cost of the wastage was estimated. **Results:** We collected 80.16 kilograms of medication, which included 390 chemical substances. On average, 69.6% of the medications were expired, and therefore wasted. More than a half of the medications (53.3%) were unused. Medication prescribed for chronic diseases accounted for 60.4% of the waste. Most medicines were related to the nervous system, alimentary tract and metabolism, and cardiovascular system. Total cost of the wasted medication was R\$3,286.94 (US\$878,86). **Conclusion:** In order to reduce therapeutic non-adherence and the amount of wasted medication, besides policies that provide free essential medication, it is imperative to enhance the rational use of medication through better medical and pharmaceutical assistance.

Keywords: Medication; Medication waste; Public health system

Introduction

Non-adherence to long-term pharmacological therapies in developed countries exceeds 50% when compared to developing countries [1]. Adherence to treatment is a socio-cultural phenomenon that manifests itself in different population groups, according to geographic location, habits, economic conditions and organization of care services [2]. Impediments to adherence to prescription drugs imply a challenge to the comprehensiveness and efficiency of health systems and services by deterring effective disease control, increasing the risk of hospitalizations, and mortality rates [3,4].

Through Brazilian constitutional universal right to health, pharmaceutical services in the Brazilian Unified National Health System (SUS) comprise administrative activities that ensure the adequate availability of medicines that satisfy critical health care needs, besides providing assistance services, focusing on therapeutic effectiveness and safety [5]. In Brazil, the government institutionalized a Brazilian Essential Medicines List (RENAME), in which all comprised medication are freely dispensed to the population when prescribed by a health professionals (physician or dentist) from all levels of care of the SUS [6].

In Brazil, the SUS allowed great progress towards Universal Health Coverage (UHC). However, the economic, structural and

political crises have limited public expenditure in the field of health, threatening sustainability and its results [7,8].

Between 2008 and 2015, there was a 74% increase in Federal Government spending on essential medicines. Since then, the federal budget for medicines has continued to grow, even in 2015, when the Health Budget fell 20% compared to the average of the last five years [9].

Even though ensuring the access of free medication to the underserved population is an important part of health care, integrating pharmaceutical and physician assistance to the primary care is a key strategy to guarantee the rational use of medication and the reduction of pharmaceutical waste.

In this context, simply improving the population access to medication does not guarantee treatment adherence and may yield economic and medication waste. In that matter, we sought to estimate the cost, extent and characteristics of donated medications obtained in unwanted-medication return programs and promote discussions around medication waste to the SUS.

Methods

This was an exploratory cross-sectional study conducted among users of Basic Health Units (UBS) in the municipality of Santa Maria, Rio Grande do Sul, Brazil, from September 2017 to September 2018.

The city of Santa Maria had approximately 280,505 inhabitants and 33 UBSs in 201810, and is divided into 8 administrative regions besides rural districts. Seven points of drug collection were established for this study. Of these, five UBSs belonged to two distinct administrative regions and two UBSs were from rural districts, with an estimated population of 45,000. The UBSs that took part on the study were participating in a permanent drug take-back program run by the Federal University of Santa Maria and constituted in points of collection of unwanted drugs.

Through weekly extension activities carried out by medical and pharmacy academics, users of these health centers were instructed to drop-off their unwanted medications to the accessible donation boxes available at each participating UBS.

Over the course of one year, the research team traveled every week to each collection sites to register data (151 total visits). Data collected included total donation weight (kilograms), date of collection; chemical substance; dosage form; expiration date; if medicine was: (i) free sample, (ii) unused or leftover, and (iii) inside their original packaging.

The medication was classified according to the Anatomical Therapeutic Chemical (ATC), classification adopted by the World Health Organization (WHO) [11]. Among the donated unused drugs, which were not free samples, the chemical substances that belonged to the RENAME were identified. The cost of the donated drugs was estimated through the Health Price Bank, a system available on the website of the Brazilian Ministry of Health that provides information on governmental purchases of medicines and health product [12-14]. It was used current US Dollar/Brazilian Real quotation rate (US\$1/R\$3.74).

The data was gathered and encoded into the database through the Microsoft for Excel® Program. Subsequently, they were analyzed by the statistical program IBM SPSS Statistics, version 23.0.0 and expressed through absolute, relative, average

frequencies. Associations were tested by chi-square ($p < 0.05$).

Results

During the study period, a total of 4254 units (controlled, noncontrolled and over-the-counter medication) were donated by the users of the UBSs to drug take-back points and cataloged for analysis. In total, it was collected 80.16 kilograms of medication, which included 390 chemical substances. Approximately 60.4% of the medication were for chronic conditions. This rate is four and seven times higher than in North America (17.0%) and Europe (8.5%) respectively [1].

Most donated medication was passed expiration date (69.6%), more than a half (57.3%) were completely unused drugs, less than a quarter (23%) were in the original package and only 16.7% were free samples. The ratio of unused to in-use medication was 1.34.

Tablets, capsules and liquids accounted for the most common dosage forms (88.8%) and approximately one quarter (24.4%) of them were donated in their original package. Most of the medications assessed by SUS pharmaceutical health system are not dispensed in their original packages. This might explain why there is such a significant disproportion between donated drugs in the original package and unused drugs. Patients that returned medicines discussed in our study were all clients of UBSs.

Approximately 3.5% of the donated drugs were opioids and benzodiazepines. These medications are usually prescribed for treatment of pain, insomnia or anxiety and have the potential of being abused (used in excessive and non-therapeutic quantities by patients), causing dependence and withdrawal symptoms [15,16]. By providing further sites in which patients can accessibly dispose unwanted medication, the extent of donated medication with abuse potential could improve even more, potentially leading to greater prevention of medication abuse [17].

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Drug Name (ATC – Anatomical Group)	Number	(%)	Ratio of unused to used medication
Levonorgestrel and Ethinylestradiol (G)	227	5.3	44:1
Acetylsalicylic Acid (B)	137	3.2	5:2
Ferrous Sulfate (B)	105	2.5	1.4:1
Clonazepam (N)	78	1.8	2:1
Metformin (A)	76	1.8	3.6:1
Fluoxetine (N)	75	1.8	3:1
Simvastatin (C)	72	1.7	3:1
Paracetamol (N)	67	1.6	1:2
Omeprazole (A)	64	1.5	2:1
Metamizole Sodium (N)	56	1.3	1:2

Table 1: Ten most common chemical substances collected from permanent drug donation boxes

Table 2 lists the ATC main group distribution of the drugs. Medication related to the nervous system consistently accounted for the largest proportion of results (23.1%), followed by alimentary tract and metabolism (17.3%) and cardiovascular medication (14.3%), 3.0% could not be classified according to the ATC classification system.

ATC Class	Events Number	(%)
N. Nervous System	938	23.2
A. Alimentary Tract and Metabolism	738	17.3
C. Cardiovascular system	608	14.3
G. Genito-Urinary System and Sex Hormones	382	9.0
R. Respiratory System	319	7.5
B. Blood and Blood Forming Organs	252	5.9
J. Antiinfectives for Systemic use	230	5.4
M. Muculo-Skeletal System	229	5.4
D. Dermatologicals	159	3.7
H. Systemic Hormonal Preparations, Excluding Sex Hormones and Insulins	96	2.3
Others	258	6.1
Total	4254	100.0

Table 2: Donated drugs (number and percentage) according to the ATC classification system

Discussion

These findings are not unexpected. For instance, medication related to the nervous system usually is related to unpleasant side-effects, nonattendance to medical appointments and patients' active resistance to taking medication [18]. Furthermore, the vast amount of the medication for the nervous system is used in the treatment of mental disorders, which in addition of being linked with poor prognosis, are related to poor patient adherence. It is suggested that psychiatric patients might experience intense guilt towards their need of pharmacological treatment and do not accept their need to be treated [19]. In such way, patients might engage in false beliefs that depressive or anxious symptoms are not real.

Drugs for metabolic and cardiovascular diseases are prescribed in conditions that are hardly related with acute symptoms of greater discomfort or pain; this represents a challenge to adherence. Patients with chronic diseases usually interrupt their drug treatment or do not even start it, as they believe they do not really need medication since they do not feel sick [20,21]. These reasons might contribute to the abundant quantity of donated expired medications for chronic diseases.

Omeprazole, vitamins and metformin comprise almost one third of the donated medication related to the alimentary tract and metabolism. Omeprazole is mostly prescribed for dyspeptic conditions and is well known for its rapid treatment response, which beings on day 1 for many patients [22]. This may explain why omeprazole is one of the most donated drugs (Table 1). After experiencing the therapeutic effect of the medication, patients possibly believe they do not need to take it any longer, and remaining medication is thus wasted.

Levonorgestrel and ethinyl estradiol are the most donated drugs (Table 1). Possible reasons are the experienced side effects, fear of use and misinformation about this oral contraceptives. The use of injectable contraceptives has increased in Brazil, especially among adolescents. This increase may explain reasons for giving up using oral contraceptives [23]. The increase in the use of injectable hormonal contraceptives may be due to the greater availability, acceptability and access to this contraceptive. Almost all units (98%) of this oral contraceptives were donated completely unused. The data highlight the importance of medication return programs that create awareness for proper pharmaceuticals disposal. A recent study with the Brazilian population indicate that 57% to 80.4% of the general public practice improper disposal in household garbage [16]. Hormonal contraceptives when improperly disposed cause a considerable environmental impact, particularly in aquatic life, causing a reproductive disruption in wild fish populations [24,25].

Acetylsalicylic acid is the second most predominant donated medication and despite being from the Blood and blood forming organs group (ATC code B), it is used as a drug for the prevention of cardiovascular disease [26,27]. Thus, it is believed that its prevalence among the donated drugs is associated with the same reasons presented for the drugs for cardiovascular diseases. Fluoxetine and clonazepam also constitute some of the study's most unconsumed disposed drugs. As the onset of fluoxetine therapeutic actions are usually not immediate and often is delayed for 2–4 week [28], patients may discontinue treatment by not believing this medication could ever improve their condition [18]. Fear of dependence on antidepressant medication and anxiety about side effects are also common variables associated with non-adherence to fluoxetine [29].

Clonazepam is commonly prescribed for anxiety disorders

and insomnia. Although optimal treatment of these conditions is non-pharmacological, entailing psychological and behavioral therapies, clonazepam is still overprescribed as a long-term treatment in primary care. The results of chronic use of benzodiazepines include tolerance, withdrawal syndrome, long-term brain changes, symptom remission inefficacy and cognitive decline in older patient [30]. Because of tolerance and withdrawal symptoms, clonazepam can lead to dose escalation and worsening of the underlying condition. This along with clinician errors in selecting and delivering an appropriate and effective treatment are reasons for high prevalence of clonazepam disposal.

The results of this study show that more than half (57.3%) of donated medicines were not consumed. This rate is higher than those reported in other countries such as Saudi Arabia (25.8%) [31]. Of the 2437 unconsumed medications, the ten chemical substances most disposed belonged to the RENAME. These top ten drugs represent 27% (656 drugs) of all unconsumed medication.

Previous extensive data has suggested that medication non-adherence is greatly related to out-of-pocket medication cost [32]. Yet, universal access to essential medication was standardized by SUS in 1998 and there has been an increase in the supply of medication for health care since this date [33]. Therefore, it is unclear the reasons underlying the fact that patients retrieve free medicines from public pharmacies and still lack commitment to their treatment by not taking them.

The prevalence of unused medications, along with the prevalence of expired medications in this study, were associated with chronic diseases ($p < 0.0001$). The rate of disposal of unused medication for acute conditions was clearly lower (37.7%) compared medication for chronic diseases (70.6%). Patients who are treated for chronic diseases are four times as likely (OR=3.98, 95% CI: 3.48; 4.54) to have donated completely unused medication. This risk is underestimated because the drugs have been classified according to their on-label indication, in which clonazepam is for acute illnesses.

There is significant concern regarding the economical and health impact of chronic medication non-adherence. Non-adherence to medication is said to contribute to nearly 200,000 premature deaths annually in Europe, 125,000 avoidable hospitalizations in the United States, 2–3% of all hospital admissions in Australia and 23% of nursing home admissions [34,35]. Furthermore, chronic conditions as hypertension, diabetes, and hyperlipidemia are known to contribute directly and indirectly to 68% of all deaths worldwide. Therefore, tackling medication non-adherence has the prospective to increase life expectancy and prevent deaths [36,37].

Regarding expired medication, the majority of collected drugs (56.3%) was for chronic conditions, while 43.7% were for acute conditions (OR= 0.554, 95% CI: 0.481; 0.639). These results

point to the possibility that patients with chronic conditions do not even begin their treatment and dispose completely untouched medication. In contrast, those who suffer from acute conditions might interrupt treatment and the medication expires at home, or might have completed treatment and dispose leftover drugs.

To address Brazil's growing medication waste problem, there are tracking and monitoring systems for prescribed medications that are listed in RENAME. Through these systems, pharmacies are able to manage repeat prescriptions, avoiding multiple dispensations.

A major concern with this waste that is being generated is that, although access to medicines has improved in Brazil due to the SUS pharmaceutical system, therapeutic loss is occurring due to lack of information and commitment of patients to follow the treatment correctly. As a rule, patients have very little insight into the actual cost of providing them with health services. This is particularly the case of SUS in which the patient is rarely confronted with the costs associated with health assistance received [2].

Medication is seen as a free commodity, and if it is free, patients easily may engage to stock piling and order every line on a repeat prescription regardless of commitment to their treatment.

On average, Brazilian families commit 30% of their household income to medication and this average expenditure is even higher among low-income populations [30]. Henceforth, the fear of not being able to access free medication might trigger a social culture of stock piling that is more prominent in the low-income population.

The practice of domiciliary stock piling of medicines associated with non-use and non-adherence of treatments are factors that contribute to the inefficacy of the drug management and use systems, and consequently to the advancement of social policies and universal access to health.

In this sense, assuming that the unused donated drugs belong to RENAME, a comparison was made with the same drugs dispensed by the SUS in the period of the study to estimate the economic waste (Table 3).

ATC 5	Units Dispensed	Cost of Dispensing (R\$)	Collected Units	Waste (%)	Waste (R\$)
Levonorgestrel and ethinylestradiol	1390	239.75	4662	335.4	804.11
Calcium Carbonate	16325	889.10	1620	9.9	88.23
Levothyroxine sodium	24260	1586.84	1500	6.2	98.11
Clonazepam	51690	2119.29	1150	2.2	47.15
Lithium	61820	12951.28	1075	1.7	225.21
Acetylsalicylic acid	116006	1602.20	940	0.8	12.98
Ferrous sulfate	26010	792.32	800	3.1	24.37
Simvastatin	1130	64.41	765	67.7	43.61
Captopril	51840	829.92	760	1.5	12.17
Fluoxetine	201330	7176.53	742	0.4	26.45
Nortriptyline	8040	1419.60	720	9.0	127.13
Warfarin	6980	989.05	680	9.7	96.35
Enalapril	5293	185.25	640	12.1	22.40
Metformin	5360	1310.50	550	10.3	134.47
Valproic acid	73110	16126.44	500	0.7	110.29
Promethazine	2473	148.57	480	19.4	28.84

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Furosemide	43740	890.60	460	1.1	9.37
Omeprazole	278522	13544.10	434	0.2	21.10
Glibenclamide	13140	2801.34	420	3.2	89.54
Atenolol	5808	255.96	420	7.2	18.51
Propranolol	12350	152.62	400	3.2	4.94
Hydrochlorothiazide	10074	943.17	400	4.0	37.45
Carbamazepine	78630	4288.83	390	0.5	21.27
Chlorpromazine	22550	5981.20	360	1.6	95.49
Allopurinol	19880	795.20	340	1.7	13.60
Amoxicillin-clavulanate	5133	3437.09	336	6.5	224.99
Amitriptyline	88360	2746.40	320	0.4	9.95
Norethisterone	33	27.30	245	742.4	202.68
Phenobarbital	21140	1479.80	240	1.1	16.80
Spirolactone	28600	3965.40	240	0.8	33.36
Haloperidol	940	109.70	220	23.4	25.67
Paracetamol	57058	3218.63	210	0.4	11.85
Diazepam	41582	1957.77	210	0.5	9.89
Metamizole sodium	2424	156.83	180	7.4	11.65
Isosorbide	42670	2745.52	160	0.4	10.29
Methyldopa	5480	1072.00	150	2.7	29.34
Amiodarone	8970	2097.60	150	1.7	35.08
Carvedilol	62460	6616.35	120	0.2	12.71
Calcium and vitamin D	4680	614.22	120	2.6	15.75
Amlodipine	56880	797.58	120	0.2	1.68
Diclofenac	9090	184.84	100	1.1	2.03
Cefalexin	8350	3160.47	100	1.2	37.85
Finasteride	8376	2474.10	90	1.1	26.58
Ciprofloxacin	6444	855.16	90	1.4	11.94
Losartan	5164	2022.26	80	1.5	31.33
Prednisone	6964	1352.18	60	0.9	11.65
Dexchlorpheniramine	278	242.06	60	21.6	52.24
Aciclovir	577	164.44	60	10.4	17.10
Nitrofurantoin	4014	877.58	56	1.4	12.24

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Risperidone	1110	199.80	40	3.6	7.20
Metronidazole	3209	896.70	40	1.2	11.18
Metoprolol	29496	7716.39	40	0.1	10.46
Ibuprofen	17815	1236.08	40	0.2	2.78
Norethisterone and ethinylestradiol	62	46.50	31	50.0	23.25
Glimepiride	22450	1616.40	30	0.1	2.16
Digoxin	6160	203.28	30	0.5	0.99
Biperiden	27105	4537.56	30	0.1	5.02
Folic acid	13560	497.77	30	0.2	1.10
Folic acid	13560	497.77	30	0.2	1.10
Oral rehydration salt formulation	602	283.53	26	4.3	12.25
Fenoterol	5	7.8	25	500.0	39.00
Sulfamethoxazole and trimethoprim	53	45.25	20	37.7	17.08
Lidocaine	38	44.97	16	42.1	18.93
Azithromycin	2643	1321.55	15	0.6	7.50
Metoclopramide	112	42.40	14	12.5	5.30
Dexamethasone	328	206.48	10	3.0	6.30
Betamethasone	25	8.16	10	40.0	3.26
Albendazole	906	466.65	10	1.1	5.15
Glucose	5	15.60	4	80.0	12.48
Timolol	30	29.16	3	10.0	2.92
Insulin	154	224	3	1.9	4.36
Atropine	8	1.4	3	37.5	0.53
Prednisolone	193	491.06	2	1.0	5.09
Permethrin	142	140.58	2	1.4	1.98
Medroxyprogesterone	361	1463.81	2	0.6	8.11
Hydrocortisone	50	57.59	2	4.0	2.30
Fluconazole	2048	418.28	2	0.1	0.41
Nystatin	75	153.64	1	1.3	2.05
Total	RS 142841.84		RS 3286.94		

Table 3: Estimated waste of unused medication

The cost was calculated based on the Health Price Bank, available on the website of the Brazilian Ministry of Health. Approximately 2.3% of SUS expenditures could have been saved in the period. This sum represents approximately that R\$1 (US\$0.27) in every R\$43 (US\$11.47) spent on pharmaceutical primary care was wasted. Based on the financing and implementation rules of the Basic Component of Pharmaceutical Assistance of SUS, it is possible to estimate that the total wasted investment would have been able to finance the medical treatment for 273 people in one year.

The exploratory analysis of these data allows refinements of causal hypotheses that can be corroborated by analytical studies and endorse management actions within the public health system. For instance, adolescents frequently do not comply with methods that require daily adherence. In order to decrease teenage pregnancy, intrauterine devices and contraceptive implants are considered first-line contraceptives for adolescents [38]. Hence, the purchase of medicines should consider the epidemiological profile of the population in order to guarantee better social policies and the rational use of medicines. If such considerations had been taken into perspective, it is possible that Levonorgestrel and Ethinylestradiol would have not been the most collected unused drug and accounted for almost one quarter (24.4%) of the unused medication as seen in our study.

Amoxicillin-clavulanate accounts for 6.8% of the wastage. This antibiotic should have never been donated unused, besides being a high-cost medication, there are severe SUS protocols that ensure that its use is only indicated for a few specific clinical conditions.

This waste could have been avoided if there had been a rational use of medicines, as directed by the health professionals involved in the care. In Brazil, the population has less difficulty accessing medication than medical care. In this sense, the doctor-patient interaction should be better worked on with the objective of better monitoring of patients with chronic diseases, on long drug regimens, in addition to the commitment and accountability of both parties in health care. Pharmaceutical assistance is crucial, as it also helps to avoid waste by reinforcing the guidelines on the relevance of care and education on the use of medicines with patients, in addition to managing the correct dispensing of medicines.

Although this study has presented relevant data on access to medicines by patients in Primary Health Care of the SUS, the profile of donated medicines and their costs to the system, it still has important limitations. The study estimated waste based on data from donated unwanted drugs but did not estimate the cost of impact on the environment and health outcomes.

Our study intended to highlight issues related to the waste of medication and the data are underestimated for different reasons, such as: i. the drugs delivered (N=4254) were used as a sample by the population of an area of almost 45 thousand inhabitants, if there was a collection in households, the number would have increased; ii. it was considered for the wastage estimation only the 100% unused drugs (2437 units), not reflecting the waste of the total drugs donated unused from the study (4254 units).

Final Considerations

The analysis of the medication waste from different perspectives helps healthcare systems and the society diminish the extent of medication wastage.

Our findings show that the cost of medicine wastage in Santa Maria is equivalent to the cost of medical treatment for 273 people in a year. Additionally, the results obtained in this study provide important data regarding the amount of chronic medication being disposed completely unused and expired medication indicated for acute conditions, suggesting that strategies for drug use management could be implemented to promote waste reduction.

With the help of prescribers and pharmacists, strategies for medication management may alleviate the culture of stockpiling that exists in the population investigated, reduce excessive and irrational prescriptions, and promote an increase in patient adherence, thus reducing costs and improving health outcomes of the SUS.

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