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Types and Costs of Medications Returned by Outpatients at a Malaysian Teaching Hospital: A One-Year Cross-Sectional Study.

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ABSTRACT

Introduction: Medication wastage is attributable to various factors, including therapeutic failure, over-prescription, and poor compliance. Data regarding the cost and types of returned medications are essential to estimate the financial burden that can be reduced locally through targeted intervention. This study aimed to investigate the types and cost of medications returned by outpatients at a teaching hospital in Kuantan, Pahang.

Materials and methods: This cross-sectional study collected data from the electronic medical record based on the list of returned medications at the outpatient pharmacy department at Sultan Ahmad Shah medical Centre (SASMEC) @IIUM between January and December 2021. All medications with SASMEC patients' label were included. The medications were classified according to the classification index based on the British National Formulary. The data were analysed using Microsoft Excel version 16.52. The cost associated with returned medications was calculated, referring to the latest cost price of the respective medications.

Results: A total of 134 patients returned their medications in 2021 (mean \pm SD age: 63 \pm 13 years), with 52% females. The total quantities of returned medications were 11,054 units. These included pills, devices (inhalers, insulin pens), bottles, and plastic containers. The overall cost of these medications was Ringgit Malaysia (RM) 13,594.90 (mean per patient: RM 101.45). The highest number of returned medications was from the cardiovascular group (32.5%), followed by the endocrine group (26%) and musculoskeletal group (11.9%). The highest cost for returned medications was the endocrine group (49%), followed by the cardiovascular group (20%) and the musculoskeletal group (10%).

Conclusion: Medications used for cardiovascular diseases were the most frequently returned at outpatient pharmacy, whereas those for endocrine diseases contributed to the highest cost. Future research could focus on identifying modifiable factors that can contribute to the sustainability of health resources by reducing the cost of returned medications.

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Introduction

Medication wastage occurs when medications are expired and unused throughout the supply chain of the medications. It adversely affects the economy and the patients themselves, thus requiring appropriate education to minimise pharmaceutical waste (West et al., 2015; Smale et al., 2021). In addition, it has been reported that expired or unused medications could threaten both the healthcare system and the environment (Ebrahim et al., 2019). For example, multiple strains of antibiotic-resistant bacteria have also been identified in unused medications disposal sites (Watkinson & Costanzo, 2017).

Medication wastage could also lead to loss of resources (Ali & Ibrahim, 2009; Alnahas et al., 2020). For example, in Sultan Qaboos University Hospital, approximately three million Omani Rial of the hospital budget was spent on purchasing the medications, where 40% and 60% of the hospital pharmacy itself had spent on its medications budget for inpatients and outpatients, respectively (Al-siyabi & Al-riyami, 2007). In the United States, the average annual cost of wasted medications was USD30.47 per person, resulting in a total annual cost of over USD1 billion for adults over the age of 65 (Morgan, 2001). In the United Kingdom, about £300 million was spent on unused prescription medication by the National Health Services annually in 2009 (Trueman et al., 2011). In addition, around €10,000 was spent in Malta on 80 different types of medications handed in to government pharmacies by the public over three months (Times of Malta, 2012; West et al., 2015). In Japan, the annual medical expenses were increased to more than JPY43 trillion (Matsuda, 2019), and the prescription medication cost was estimated at JPY10 trillion (Ueki et al., 2022).

Generally, the medication cost contributes to a large percentage of overall medical costs. It may be due to the rising price of new medications (Ghinea, Lipworth & Kerridge, 2016). It was anticipated that the global spending on medications to reach almost \$1.3 trillion in 2018, which is a 30% increment over 2013 (Aitken et al., 2014). The increased price of medication affects the sustainability of the health insurance system (Ueki et al., 2022), so the initiative to investigate and monitor the medical costs is crucial to prevent medication wastage. This has become a global issue and can potentially influence the cost associated with medication disposal (Ebrahim et al., 2019). On top of that, waste-reducing actions taken by pharmacists, such as improving stock management, improving the pharmaceutical preparation process, increasing dispensing expertise, and redispensing unused medications, may help to ensure the long-term viability of the healthcare system, where sustainable supply and use of medication can be achieved (Smale et al., 2021). It has also been reported that the reasons of returning unused medications to the pharmacy include public awareness regarding environmental risks

posed by inappropriate disposal (Arkaravichien et al., 2014; Ong et al., 2020).

In Malaysia, more than 80% of the study population in Selangor were aware of the issue of medication wastage and its effects on patients and the economy (Hassali & Shakeel, 2020). Ibrahim and colleagues were the first investigated the extent of medication wastage by Malaysian consumers in 1996, where they collected 451 types of leftover medications from 101 houses (Ibrahim, Awang, Razak, 1997). In 2016, a single public hospital in Malaysia has allocated approximately RM 62 million for medications, indicating that medications accounted for a significant portion of a hospital's revenue and expenditure (Sim et al., 2018). The Malaysian Ministry of Health claimed that between 2014 and 2016, RM 2 million was spent on the disposal of spoiled medications, which included medications from government hospitals' "medication take-back" services (Rahim, 2016). There have been several reports of medication waste in hospitals in Malaysia. For instance, at Hospital Tuanku Jaafar Seremban, the total cost was RM 4,362.28, and the average wastage per patient was RM 42.35 (Hassali et al., 2012). An analysis of unused medications can help to identify patients who are stockpiling their medications, which could result in unnecessary health care costs, so intervention can be made to address this issue. Therefore, this study aimed to examine the types and costs of medications returned by outpatients at a teaching hospital in Pahang, Malaysia.

Methodology

This study received ethical approval from the International Islamic University Malaysia (IIUM) Research Ethics Committee (IREC) (ID NO. IREC 2021-205).

This study was performed in the outpatient pharmacy department at Sultan Ahmad Shah Medical Centre (SASMEC) @IIUM between January 2021 and December 2021 (a cross-sectional study). Pharmacists collected returned medications, and data were recorded in the system. The data included patient registration number, age, gender, drug name, strength, dosage form, date of returned medications and quantities. Each drug was counted as one dosage unit regardless of the dosage form (e.g. pills, pens, syrup).

For the current study, data were collected from the electronic medical record based on the list of returned medications at the outpatient pharmacy. Only medications with SASMEC patients' labels were included, excluding items from external sources. All the returned medications were considered as waste and could not be re-used for other patients (Alhamad et al., 2017). The medications were classified according to the classification index of the British National Formulary. The data were analysed using Microsoft Excel version 16.52 programme. The cost associated with returned medications was calculated descriptively, referring to the latest cost price of the respective medications and per unit according to the dosage

form (e.g. price per pill/tablet, pen, bottle). The Ringgit Malaysia (RM) amount that is stated throughout this manuscript refers to per unit of dosage form.

Results

A total of 134 patients (mean \pm SD age: 63 \pm 13 years) returned their medications at the outpatient pharmacy throughout the study period. Female patients were higher (52%) than males (48%), with most of the participants (99%) were elderly (60 years and above). A total of 11,054 units of returned medications were collected throughout 2021, with an average per patient of 82 units. The medications that were excluded were 22 units because they were from other sources like other private clinics or hospitals; thus, they were not under the cost that was covered by SASMEC @IIUM. The total number of returned expired medications were 883 units. The average wastage was 921 units per month, consisting of pills, devices (inhalers, insulin pens), bottles, and plastic containers. The top six quantities of returned medications were calcium carbonate, metformin, perindopril, prazosin, atorvastatin, and celecoxib (Table 1). Table 2 shows the top six highest costs of returned medications, and most of them were devices. Overall, endocrine group contributed to the highest cost of returned medications, although the percentage quantities were lower than the cardiovascular group (Table 3). The most common pharmacological group of all returned medications was the cardiovascular medications (Table 3).

Table 1: Top six returned medications with the highest quantities at the outpatient pharmacy.

Item	Quantity	RM
Calcium carbonate 500mg tab	2,070	103.50
Metformin 500mg tab	1,998	159.84
Perindopril 4mg tab	649	39.46
Prazosin 2mg tab	475	20.93
Atorvastatin 40mg tab	405	57.31
Celecoxib 20 mg tab	362	818.48

Table 2: Top six returned medications with the highest cost at outpatient pharmacy.

Item	Quantity	RM
Novorapid® insulin	95	2,653.00
Levemir® insulin	65	2,600.00
Clexane 40mg injection	77	1,463.00
Celecoxib 200mg tab	362	818.48
Novomix® insulin	26	719.68
Tramadol 37.5mg and paracetamol 325mg tab	342	519.26

Table 3: Percentage distribution of pharmacological groups with

quantity and cost.

Pharmacological classes	Percentage of Medication Quantities (%)	Percentage of Medication Cost (%)
Cardiovascular	32.5	19.24
Respiratory	1.1	2.16
Immuno and Malignant	1.8	1.42
Anti-Infectives	0.1	2.16
Central Nervous System	4.4	2.8
Peripheral Nervous System	5.2	4.44
Endocrine System	26	48.67
Musculoskeletal	11.9	10.37
Genito-urinary	1.4	0.85
Eye-ear	4.4	5.13
Gastrointestinal	5.1	1.1
Nutrition	6.2	1.69

Discussion

Our observations indicated that the return of unused medications was the most common among the elderly population. In the United States, medication wastage was amounted to more than USD1 billion among the elderly population (over the age of 65 years old), accounting for 2.3% of total medication costs (Morgan, 2001; El-Hamamsy, 2011). This might occur because the percentage of the elderly population has increased gradually in developed societies (Chiatti et al., 2012). It was estimated that Americans aged 65 and above to nearly double over the next three decades, rising from 48 million to 88 million by 2050 (National Institutes of Health, 2016). The health and economic burden of the elderly population was related to undesirable medication effects, improper drug prescribing, and poor adherence, all of which resulted in huge cost of unused medications (Chiatti et al., 2012).

We report in the current study about the types, quantities and costs associated with returned medications that were collected at the outpatient pharmacy at a teaching hospital in Pahang state. A total of 11, 054 units of medications were returned in 2021, with an average per month of 921 units consisting of various dosage forms. From this, the total cost of the returned medication was RM 13,594.90, with an average of RM 1,132.90 per month. In comparison, a government hospital in a different state Negeri Sembilan reported a higher number of pills returned to outpatient pharmacy between June and November 2007, which was 131,098 pills, with an average of 21,850 pills per month (Hassali et al., 2012). The total cost of medications reported in a government hospital in Negeri Sembilan between June and November 2007 was RM 59,566.50. The average wastage for each month was RM 9,927.75 The estimated total cost of the wastage for that year was RM

119,133.00 (Hassali et al., 2012). A different study in Oman reported that 1,171 medications were returned to the pharmacy (mean per patient: 3.1 medications) (Al-Siyabi & Al-Riyami, 2007). Our findings indicate a relatively lower return rate of returned medications by the outpatients at SASMEC @IIUM.

The present study also found that calcium carbonate, metformin, perindopril, prazosin, atorvastatin, and celecoxib were the top six highest in quantities of returned medications at the outpatient pharmacy. On the contrary, Hassali et al. (2012) have reported that the highest quantities of medications returned to the pharmacy within five months were isosorbide dinitrate 10 mg tab, metformin 500 mg tab, lovastatin 20 mg tab, frusemide 40 mg tab, trimetazidine 20 mg tab and potassium chloride 600 mg tab. In Egypt, the top five medications returned to 20 community pharmacies were antibiotics, gastrointestinal, cardiovascular system, respiratory system and nervous system medications (El-Hamamsy, 2011). Among the reasons reported by El-Hamamsy (2011) were because the patient felt better or died, and medications reached the expiry date. In Australia, 60% of the returned medications were Pharmaceutical Benefits Scheme (PBS) medications, which were subsidised prescription medications (Bettington et al., 2018). The top-six PBS-listed medications in Australia in 2016 were paracetamol, salbutamol, glyceryl trinitrate, cefalexin, metoclopramide and doxycycline (Wheeler et al., 2016). Most of them were considered "if necessary" medications for acute diseases such as nausea, acute infections, asthma, and angina attacks (Bettington et al., 2018).

Metformin was among the common medications of returned medications in our study. This could be due to non-adherence issues with the frequency to take metformin three times daily (Hassali et al., 2012). Similar results were reported where diabetic patients who took oral hypoglycemic agents tend to have adherence rates of 74.8% for once-a-day doses and 38% for three times daily doses (Paes & Barker, 1997; Hassali et al., 2012). One-daily dosing was a strategy of reducing regimen complexity and thereby increasing adherence rate (Roca, Lapuebla, & Vidal-Tegedor, 2005; Kuna et al., 2006; Laliberte et al., 2013; Hernández Arroyo et al., 2016; Oh et al., 2020). Therefore, simplifying the dosing regimen to a once-daily dosage might be the most effective strategy to improve patient adherence (Ma et al., 2010; Rubio et al., 2010; Fabbiani et al., 2014; Elnaem et al., 2020).

Analgesics were found to be commonly returned medications in our study. Analgesics indicated for chronic and acute pain were commonly prescribed in excessive amounts (Bettington et al., 2018). For example, a study has highlighted that between 42% and 71% of opioid tablets prescribed after surgery remain unused (Bicket et al., 2017). This could happen due to unawareness of healthcare providers about unused analgesics (Chou et al., 2016). In

hospital settings, the development of evidence-based prescription recommendations is complicated by diverse patient groups and treatment types (Bicket et al., 2017). However, prescribing smaller quantities was not recommended even though it was a commonly proposed intervention to prevent medication wastage. This is due to non-adherence towards the medication and leads to more frequent dispensing and prescribing that later can increase the costs instead (Bettington et al., 2018). Future research on economic analysis can be explored to overcome this issue.

In our study, cardiovascular medications were the most common pharmacological group of all returned medications (32.5%). It was similar to a study that reported cardiovascular medications were the highest quantity (24%) of returned medications (Al-Siyabi & Al-Riyami, 2007). It has been reported previously that patients did not believe in the necessity of statins (40%), some of them were not convinced (48%), and did not sure of statin's efficacy (47%), did not believe that statins can prevent cardiovascular disease (49%) or believed that the efficacy of the statin is limited (71%) (Wouters et al., 2016). There were concerns about side effects associated with statins including ache, stiffness, muscle pain, swelling, or joint inflammation (Newman et al., 2019). In our study, atorvastatin was prescribed once a day, and it depends on the patient to take it at any time, but there was a possibility that the patient took it at night, leading to non-adherence. The lack of convenience in taking medication might become the barrier to patient's adherence. For example, lovastatin that was suggested to be taken at night, contributed to patients' non-adherence since they tended to forget to take the medication (Hassali et al., 2012). Non-adherence to anti-hypertensive medications could be the cause of wastage, as it was reported globally ranging from 10% to 80% (Wijekoon et al., 2020).

Our study showed that the endocrine category of medications contributed to the highest cost (48.67%) due to the high cost of insulin pen. Nevertheless, a previous study has reported that anti-infective group had the highest cost (61%) due to the expensive price of anti-viral drugs (Valaciclovir) (Al-Siyabi & Al-Riyami, 2007). A study in Australia found that cardiovascular group medications possessed the highest cost of disposed medications which amounted to about AUD 2923 (Guirguis, 2010). The highest cost of specific category of medications depicted the large quantities of returned medications, and its high utilised especially among the elderly (Jørgensen et al., 2001).

In addition, the high cost of the medications contributes to the high wastage cost even though the quantity is small. We found that the quantity of returned Novorapid® insulin was 95 pens, but it contributed to the highest cost which was RM 2,653.00, followed by Levemir® insulin (RM 2,600.00), and Clexane 40 mg injection (RM 1,463.00). The quantities of these three medications were much lower than tablet Celecoxib 200 mg,

tablet Tramadol 37.5 mg, and tablet paracetamol 325 mg. On the other hand, another study demonstrated that the highest cost of medication wastage was contributed by tablet Donepezil 5 mg with RM 6,129.00 with 690 units, compared to 1920 tablets of amlodipine 5 mg, with the cost of RM 1,996.00 (Hassali et al., 2012). It has been highlighted that the four main factors of medication wastage were the diagnosis (37.4%), perceived ineffectiveness (22.6%), change of prescriptions (15.8%) and perceived adverse effects (14.4%) (Morgan, 2001; Hassali et al., 2012).

From an economic perspective, the behaviour of patients when using subsidised and non-subsidised medication could vary in particular to compliance. In Brunei, the health care system was mainly subsidised, and medication wastage has been reported to be high as it affected the increment of Brunei's Government health expenditure by about 3.5% from 2013 to 2016 (Nurolaini, 2016). In Malaysia, a study found that self-paying patients had better medication adherence (63.8%) than subsidised patients (50%) (Aziz et al., 2018). On the contrary, a different study reported different findings where subsidised patients had high adherence rates of 84.6%, compared to patients who paid 50% of medication cost (adherence rate of 71.6%), patients who paid for 75% of medication cost (adherence rate of 72.3%) and patients who fully paid the medication cost (adherence rate of 79.2%) (Batavia et al., 2010; Aziz et al., 2018). Nevertheless, among the self-paying patients, the adherence rate was higher in patients who paid more (Batavia et al., 2010). In our study, subsidy or discount was available for pensioners, students, and staff of IIUM, which might influence non-adherence to a certain extent. It is the limitation of our study that this information was not investigated. Future studies exploring this aspect would be able to develop tailored cost-effective strategies for different categories of outpatients to reduce the cost of unused medications.

Conclusion

The most returned medications at our outpatient hospital setting were from the cardiovascular group, followed by endocrine group and musculoskeletal group. The highest cost for returned medications was the endocrine group, followed by cardiovascular group and musculoskeletal group. Future studies should explore modifiable factors that contribute to the unused medications returned to the pharmacy.

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Conflict of Interest

All the authors declare no conflict of interest.

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