Saudi Journal of Health Systems Research

Research Article

Saudi J Health Syst Res 2023;3:162–168
DOI: 10.1159/000534011

Received: February 22, 2023
Accepted: September 4, 2023
Published online: October 20, 2023

# Dose Rounding and Cost Reduction of Anticancer Agents at King Fahad Medical City, Saudi Arabia: A 1-Year Feasibility Study

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**Keywords**
Dose rounding · Cancer therapy · Cost saving · Chemotherapy

**Abstract**
***Introduction:*** The exponential increase in the price of anticancer drugs has warranted looking for a cost-saving measure to counter their price rise. We aim to study the impact of dose rounding of biological and anticancer agents within a range of 10% of the ordered dose. ***Method:*** The study involved patients treated with anticancer agents between January 2018 and December 2018 at King Fahad Medical City's (KFMC) comprehensive cancer center. An anticancer medication database was created for data collection and processing. All the eligible orders were processed by hematology and oncology physicians. A performance improvement methodology was used. The dose rounding was based on the patient's preprinted order and the nearest available vial size. The potential impact on cost was measured in Saudi Riyals (SAR). Descriptive statistics were applied for data analysis and interpretation of the results. ***Results:*** A total of 26 anticancer medications were used for treating cancer patients, and 208 prescriptions were found to be eligible for dose rounding. Brentuximab was among the drugs, showing the highest cost saving at an estimated 20,600 SAR. In addition to reducing wastage and cost of medications, 7 min were saved per preparation episode in the post-intervention period. ***Conclusion:*** Data reflected that dose rounding of chemotherapy and biological agents up to a limit of 10% is a feasible approach and could potentially save extra cost and wastage of medications in the comprehensive cancer center of KFMC.



## Introduction

Cancer has now become the leading cause of mortality worldwide, irrespective of income level. With the exponential increase in population, there is a proportionate increase in cancer cases and associated deaths [1]. As per an estimate, cancer led to approximately 9.6 million deaths globally in 2018 [2]. One in every six deaths was attributed to cancer, and low- and middle-income countries accounted for 70% of all the deaths caused by it [2]. Cancer is now the fastest-growing deadly disease in the Middle East region [3]. The Middle East and Asia constitute around two-thirds of the world's population, and they have the most significant regional concentration of low- and middle-income countries. Extensive

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demographic and epidemiologic transitions make these regions susceptible to experiencing a substantial rise in cancer-related mortalities [4].

Depending upon the type of cancer, different treatment options are employed, including surgery, radiotherapy, chemotherapy, immunotherapy, hormone therapy, and molecular-targeted therapy. However, in most cases, a combination of treatments, such as surgery, chemotherapy, or radiation therapy, is required [5]. Chemotherapy medications are a class of drugs that target cells at different cell cycle phases. Since cancer cells proliferate more quickly than normal cells, they serve as a better target for chemotherapy medications. Chemotherapy drugs can be classified based on their mode of action, chemical structure, and relationship with other drugs [6]. The infusion of costly biological anticancer agents and oral chemotherapy has led to a significant and exponential rise in the cost of cancer treatment over the years [7]. The speakers at a workshop conducted by the Institute of Medicine's National Cancer Policy Forum on "Delivering Affordable Cancer Care in the 21st Century" in October 2012 comprehended that a rise in the cost of emerging cancer therapies and the introduction of technological advancement rendered cancer treatment unaffordable with no evidence of improved outcomes among cancer patients [8, 9]. The exponential increase in the price of anticancer drugs and accompanying expenditure has raised concerns regarding the overuse of drugs. It has warranted looking for a cost-saving measure to counter the price rise [10].

Another implication of this high cost is that it has made therapeutic recommendations and cancer management more difficult [11]. Measures, such as government direct price control (Greece, France, and Spain), risk-sharing policy (Italy), and value-based pricing schemes (UK and Germany), have yet to result in favorable outcomes [12]. In such a situation, implementing low-cost measures such as drug waste reduction and human resource optimization could be an ideal choice to restrict and reduce drug spending. The most common form of drug wastage includes inevitable and/or disproportionate clearance of partly used ampules, vials, and syringes [13].

Dose rounding is one of those strategies that has been considered to reduce cost and wastage without impacting the clinical efficacy of the drugs [14]. Dose rounding seems more relevant for prescriptions supplied in single-use vials as a preservative-free formulation [15]. Interestingly, in one institution, dose rounding has become a part of clinical practice to avoid wastage through partially used vials [16]. There are a limited number of studies have been conducted both internationally and locally. Consideration of the nearest vial size for dose rounding is gaining popularity as a means of reducing drug waste, ensuring accuracy in drug preparation, and limiting overall healthcare expenditure [15]. In routine clinical care, around ≤10% of the ordered dose is considered acceptable with no effect on the safety or efficacy of the therapy [15].

The skyrocketing price of cancer drugs has become a universal phenomenon nowadays. As per the report published in 2009 by the Canadian Cancer Society, newer anticancer drugs cost around 65,000 Canadian Dollars per course of treatment [17]. Apart from spending on research, a reason for the high cost of cancer treatment can be attributed to drug wastage [18]. The international guideline allows doses to be rounded (banded) for 5–10%. This has no negative impact on the patient and is safe [10].

Estimation of cost saving was based on the cost of the available vial size, the initial dose of the drug, and the price after dose rounding. Trastuzumab is available in 440 mg vials, which cost approximately 7,296 Saudi Riyals (SAR); the records showed that an initial dose of 444 mg was prescribed, which cost around 14,592 SAR (since two vials were used). In such a situation, rounding to 440 mg could save 7,296 SAR per dose by opening only one vial at a time instead of two. It was found that dose rounding up to a limit of 10% was feasible for chemotherapy and biological drugs and could save extra costs and wastage of medications. The dose rounding of vinblastine from 8.4 mg to 8 mg did not result in any cost saving. Still, for bortezomib, dose rounding from 2.1 mg to 2 mg resulted in a saving of 162 SAR, indicating that cost saving is dependent on dose rounding and the category of the drug being used at a particular strength. Brentuximab, with a dose rounding within 10%, showed the highest cost saving among all the prescription drugs. Analysis of the prescriptions before the project started reflected that cost saving from dose rounding per year could range from 800,000 to 1,000,000 SAR. Within 6 months, cost saving was evaluated to be around 360,000 SAR. Assuming that the same number of patients was being served under the same protocol, the institution might save about two times the cost saved in the study period. Since King Fahad Medical City (KFMC) typically has an increase of approximately 10–15% in patients annually, it was anticipated that savings per year could be around 800,000 SAR.

The vial size and administered dose are the possible causes for variation in the number of leftover medications in the vial. This packaging of expensive infused drugs in quantities larger than needed is the cause of the wastage of medicines [19]. In this regard, it has been said that a

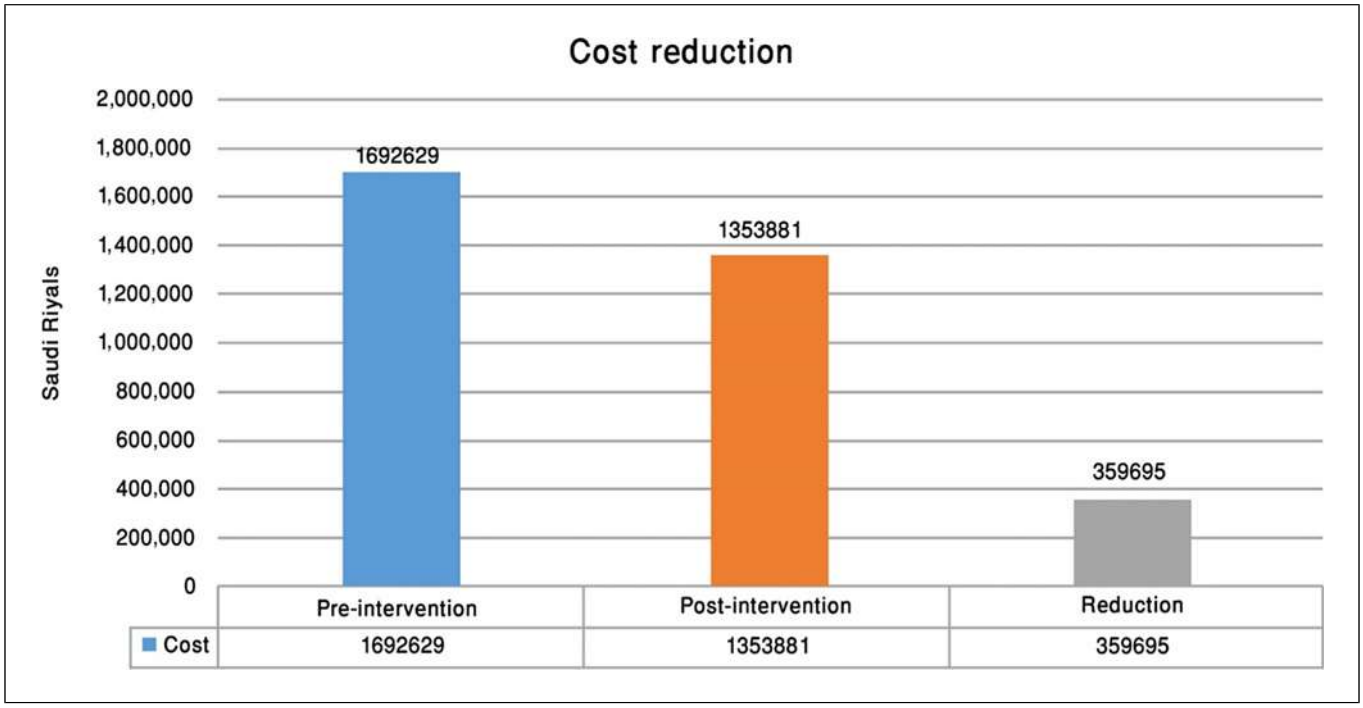


**Fig. 1.** Cumulative cost reduction post-intervention in SAR.

policy implementation targeting the reduction of wastage may substantially reduce the expenditure on pharmacies and provide cost-benefit [18].

Chemotherapy medications account for the highest cost of KFMC's total medication budget. Baseline data at the beginning of the project's implementation revealed a potential for dose rounding. Of the 340 chemotherapy orders that were audited during January 2018, the number of medications found to be eligible for rounding was 85 drugs. However, none had any dose rounding. As per estimation, this led to a wastage of approximately 200,000 SAR. This study aimed to reduce drug wastage and expenditure by effectively implementing a new methodology of dose rounding of biological and anticancer agents within a 10% limit of the ordered dose.

## Methods

*Study Settings*

The study was conducted at the comprehensive cancer center of KFMC Saudi Arabia, from January to December 2018. Adult patients were admitted to the cancer center for diagnostic workups and to receive treatment, including radiation therapy, palliative care, chemotherapy, hematological, and oncological therapies, and for the management of complications. It also contributes significantly to developing a national strategy for cancer treatment with the ministry of health.

All the anticancer drugs that hematology and oncology physicians prescribed during the study period were eligible. The non-eligible order included pediatric patients less than 2 years old and the prescription for the non-anticancer drugs.

*Study Design*

The study used pre- and post-intervention designs. A performance improvement model called FOCUS-PDCA was used throughout the study where FOCUS-PDCA means finding, organizing, clarifying, understanding, and selecting. PDCA stands for planning-doing-checking results-acting [20]. The FOCUS-PDCA is a multistep management method used for process improvement and is implemented by healthcare organizations to guide their improvement efforts. This method is used for improving the processes and find solutions for various problems through several stages, F: finding an opportunity for improvement (medication delay), O: organizing a multidisciplinary team that understands the process, C: clarifying the current process, U: understanding the problem and reasons for process change, S: selection of an aspect of the process in need of improvement [21].

*Study Intervention*

Initially, a multidisciplinary team consisting of a medical director, oncologists, pharmacists, and the quality team was involved with the intervention cycle. The team then started to determine, understand the existing problems, and select the desired outcome(s). The high cost of anticancer medications requiring dose rounding was identified.

The physicians and pharmacy team engage in and evaluate the feasibility of implementing the new dose rounding processes.

Evidence-based practice for such intervention was discussed, and policy development for dose rounding within the 10% limit of the prescribed dose was created. We also worked with them to incorporate the dose rounding workflow into the preprinted anticancer therapy drug order sheet and pharmacy documentation records. Additional critical stakeholder engagement in the process was provided by the nurses in the unit who checked and administered the anticancer drugs. A standard pathway with explicit instruction for dose rounding anticancer drugs was also implemented to ease the process of implementation for healthcare providers.

Educational support was provided continuously to the team members throughout the intervention's implementation. Dose rounding guidance was incorporated into the revised anticancer therapy policy and procedures. Dose calculations were performed for all the orders received from the healthcare providers. As agreed, a limit of up to 10% was applied during dose rounding of the ordered dose of biological and anticancer medications.

Finally, action was taken for further improvement of the process based on the outcome. The dose-rounding approach achieved cost containment in this improvement intervention.

*Data Collection and Processing*

An anticancer medication Excel database was used for data collection and processing. The information entered into the anticancer medication database was as follows: date of order, patient ID, name of the drug – also, drug dose, cost (hospital cost in SAR), preparation time for initial and amount rounding orders. Data were recorded daily.

Preprinted order of anticancer medication was used and reviewed to collect the required data. The data collection form was developed and piloted by the expert in the oncology clinical pharmacist and quality expert before starting the data collection process. The data were collected by a team comprising individuals from the administration, quality improvement, pharmacy, and oncology.

For determination of cost avoidance, vial size was calculated by the pharmacy via rounding of the prescribed dose to the nearest available vial size (up or down) based on the order and patient condition. For instance, the pharmacy's available vial size of trastuzumab is 440 mg. If the prescribed dose was 460 mg, and the amount was rounded to 440 mg, usage of fresh vials could be prevented. Therefore, the cost avoidance was the cost of another vial of 440 mg, which otherwise would have led to a cost increment in the absence of dose rounding.

Oncologists usually calculate the doses of chemotherapy and biologic-targeted therapy to the nearest milligrams based on the patient's body weight and body surface area. However, the possibility of the patient's body size matching the amount of drug included in the vials is improbable; there is always some leftover medicine in the vials in each treatment session. The dose rounded was limited to up to 10%, as agreed and applied during team discussion before starting the intervention implementation of dose rounding of the ordered dose of biological and anticancer medications.

Likewise, timesaving per preparation episode post-intervention was measured using a stopwatch. A comparison was made by monitoring the time for preparation of each dose between the pre- and post-implementation period based on pharmacy data collection records. This was achieved under the supervision of pharmacists maintaining pharmacy records.

*Data Analysis*

Descriptive statistics were performed on rounding the doses of chemotherapy and biological agents, and the results were presented in terms of percentages, averages, and numbers. The cost of drugs was calculated in SAR. Rounding of dose (up or down) was based on patients' preprinted orders. For example, a dose of 108 mg strength was rounded to 100 mg, with a dose reduction of 7.4%.

## Results

During the project implementation period, it was found that a total number of 26 anticancer medications were used for treating patients with various cancers at comprehensive cancer center. Of all the oncology prescriptions, including chemotherapy and biologic therapy, 208 were eligible for dose rounding per the criteria set forth. The number of drugs was highest for irinotecan (33), followed by cetuximab (26), rituximab (23), and trastuzumab emtansine (19) (Table 1). Among all the prescription medications, brentuximab (at initial doses of 111 mg and 153 mg rounded to 100 mg and 150 mg, respectively) showed the highest cost saving at an estimated amount of 20,600 SAR, followed by trastuzumab emtansine (at initial doses of 205 mg, 208 mg, 210 mg, 212 mg, and 219 mg rounded to 200 mg) with an estimated cost saving of 15,000 SAR, and trastuzumab (at initial doses of 444 mg and 447.6 mg rounded to 440 mg) with an estimated cost saving of 7,296 SAR (Table 1). In contrast, among all the prescription drugs, vinblastine (at an initial dose of 8.4 mg rounded to 8 mg) showed no cost reduction and savings of only 0.2 SAR at an initial dose of 9.96 mg rounded to 10 mg.

Dose rounding of chemotherapy and biological drugs to approximately an amount within 10% of the prescribed dose is a feasible approach for reducing cost and drug waste. In the case of brentuximab, the dose reduction for the initial dose of 111 mg was 10%, and for an initial amount of 153 mg was 1.96%. A dose reduction of 4.76% for vinblastine (rounding from 8.4 mg to 8 mg) did not result in any cost saving, but a dose reduction of 4.76% for bortezomib (rounding from 2.1 mg to 2 mg) resulted in a cost saving of 162 SAR.

Based on the analysis, it was estimated that a cost saving of approximately 360,000 SAR at 6 months post-intervention was feasible at KFMC (Fig. 1). In addition to the reduction in wastage and cost of medications, on an average of 7 min, time was saved per preparation episode in the post-intervention period (Fig. 2).

**Table 1.** Cost saving per dose for different chemotherapeutic agents

| Chemotherapy name | *N*/total | Initial orders | | Rounding orders | | Cost saving, SAR |
|---|---|---|---|---|---|---|
| | | initial dose, mg | cost, SAR | rounding dose, mg | cost, SAR | |
| Bevacizumab | 11/208 | 308.5–1,170 | 4,176–16,657 | 300–1,200 | 4,737–16,242 | 0–1,943 |
| Bleomycin | 1/208 | 16 | 188 | 15 | 94 | 94 |
| Bortezomib | 1/208 | 2.1 | 3,408 | 2 | 3,246 | 162 |
| Brentuximab | 5/208 | 75.6–153 | 31,147–82,400 | 75–150 | 30,000–61,800 | 1,147–20,600 |
| Cabazitaxel | 1/208 | 41.75 | 4,998 | 40 | 4,788 | 210 |
| Capecitabine | 1/208 | 1,150 | 523 | 1,200 | 546 | 23 |
| Cetuximab | 26/208 | 395–920 | 1,152–11,844 | 400–900 | 864–11,844 | 288–1,316 |
| Cisplatin | 4/208 | 62.4–67 | 41.18–44.22 | 60–65 | 39.6–42.9 | 0.66–2.64 |
| Cyclophosphamide | 5/208 | 584–1,237.5 | 24.65–62.6 | 500–1,240 | 24.55–51.74 | 0.08–14.6 |
| Dacarbazine | 3/208 | 562.5–626.25 | 156–208 | 550–600 | 143–156 | 13–52 |
| Daratumumab | 1/208 | 880 | 21,368 | 800 | 14,168 | 7,200 |
| Docetaxel | 13/208 | 83–148.5 | 2,369–3,662 | 80–150 | 1,831–3,433 | 6–1,831 |
| Doxorubicin | 4/208 | 44.75–79 | 28.46–125 | 44–80 | 27.98–100 | 0.48–93.2 |
| Erwina L-asparaginase | 1/208 | 11,800 units | 7,000 | 10,000 units | 3,500 | 3,500 |
| Fluorouracil | 1/208 | 352.5 | 54 | 350 | 18.9 | 35.1 |
| Gemcitabine | 6/208 | 1,188–2,136 | 447–805 | 1,190–2,140 | 448–806 | 0–157 |
| Irinotecan | 33/208 | 202–336 | 604.8–1,152 | 200–300 | 576–864 | 28.8–288 |
| Liposomal doxorubicin | 6/208 | 62.4–66 | 1,152–7,704 | 60 | 864–5,778 | 288–1,926 |
| Oxaliplatin | 13/208 | 92.5–244 | 347–1,125 | 90–240 | 337–798 | 6–375 |
| Paclitaxel | 9/208 | 52.5–337 | 94.5–1,080 | 50–337 | 90–606 | 1.5–540 |
| Panitumumab | 7/208 | 210–528 | 1,152–12,529 | 200–500 | 864–11,865.9 | 2,373.46–9,492.72 |
| Pemetrexed | 3/208 | 725–950 | 1,152 | 700–900 | 864 | 288 |
| Rituximab | 23/208 | 560–1,025 | 1,152–10,469 | 500–1,000 | 864–10,688 | 82–1,336 |
| Trastuzumab | 6/208 | 205–447.6 | 3,399–14,592 | 200–440 | 3,136–7,296 | 8–7,296 |
| Trastuzumab + emtansine | 19/208 | 198–262.8 | 1,152–45,000 | 200–265 | 864–45,000 | 0–15,000 |
| Vinblastine | 5/208 | 8.4–10.5 | 37.3–77.8 | 8–10 | 38.9 | 0–38.9 |

*N*, numbers of prescriptions.

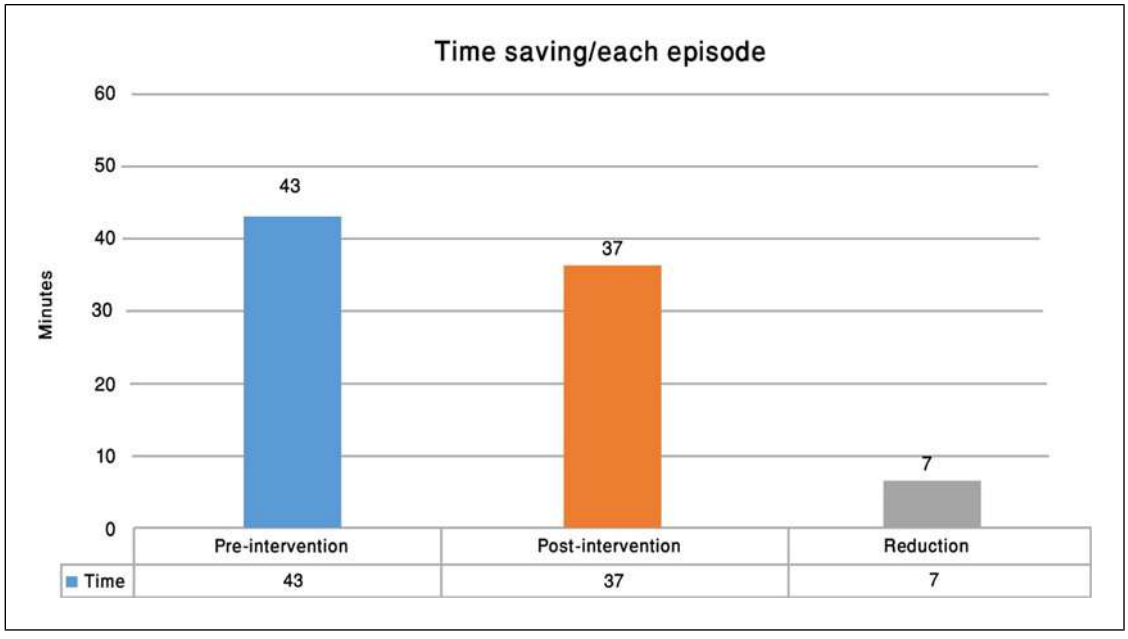


**Fig. 2.** Average time saved per episode in minutes.

## Discussion

Drug waste is defined as the consequence of inappropriate disposal of unused or partially used drug vials, ampoules, or syringes [7]. Although experience is limited and most studies focus on other therapeutic areas, drug inefficiency may result in a significant economic loss [7, 10]. In this study, we have looked at minimizing costs through oncology medication preparation procedures.

The results of this study were similar to a previous study [11], which observed that drugs such as trastuzumab, cetuximab, docetaxel, gemcitabine, oxaliplatin, and pemetrexed, were involved in substantial cost wastage. After implementing a waste containment strategy, a significant reduction of 45% in drug waste expenditure was achieved [11]. Another study also reported that 42% of 126 orders for biologic anticancer agents could generate a saving of approximately USD 24,434 within 3 months if subjected to dose rounding [19].

In addition to cost saving, the present study revealed that the dose-rounding strategy saved an average time of 7 min per preparation episode. It has been shown that the standardization of infliximab dose rounding resulted in reduced time consumption for order verification on an average of 8–10 min [16].

Before dose rounding, elements such as the ability to use multiple-dose vials for multiple patients and the risk of toxicity to patients should be taken into consideration. With the possibility of implementing a new electronic medical record system, dose rounding should be a part of the routine ordering process. The institution should be required to establish a plan for automatic dose rounding, the maximum allowable percentage for rounding, and the procedures for operationalizing and documenting any modifications to the initially prescribed dose. Periodic audits would be ideal for assessing the implementation of the dose-rounding methodology as a part of the sustainability plan. As a result of this project, KFMC could improve its local system and reduce drug wastage and cost at the same time.

*Limitation*

One of the limitations of this study was the need for an electronic system for calculating costs. For analysis purposes, data were fed manually using an Excel sheet, which might have resulted in any possible bias.

## Conclusion

This study confirmed that routine dose rounding of biological and anticancer agents within ±10% range is a feasible approach to restrict cost and wastage associated with the high cost of biological and anticancer drugs. This will ultimately lead to substantial cost savings and reduced drug wastage at KFMC.


## Acknowledgments

We would like to thank the research center at King Fahad Medical City for its support and contribution.


## Statement of Ethics

Ethical approval was obtained from the Institutional Review Board at King Fahad Medical City (Ref: 19-518Q). All the data were professionally transcribed, stored securely, and accessed only by the authors to preserve confidentiality and anonymity as per requirements. Patient consents were not required as this study was based on publicly available data.

## Conflict of Interest Statement

The authors declare no conflict of interest.


## Funding Sources

No funding was received.


## Author Contributions

A.H.: conceptualization, designing, investigation and drafting; N.A.: conceptualization, designing, and reviewing; I.A. and A.A.: data collection; R.O. and F.A.: acquisition and technical assistance; and M.A.: conceptualization and reviewing.

## Data Availability Statement

All data generated or analyzed during this study are included in this article. Further inquiries can be directed to the corresponding author.

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