Impact of Clinical Pharmacist Interventions on Economic Outcomes in a Cardiology Setting in Qatar

Daoud Al-Badriyeh, PhD[a], Rasha Kaddoura, PharmD[b], Fatima AlMaraghi, PharmD[b], Ahmed Homosy, MSc[c], Moza Al Hail, PGCert[d], Wessam El-Kassem, PharmD[d], Palli Valappila Abdul Rouf, PhD[d], Abdalla Fadul, MD[e], Ahmed Mahfouz, MD[b], Sumaya Alsaadi Alyafei, PharmD[b], and Dina Abushanab, MSc[d*]

From the [a] College of Pharmacy, QU Health, Qatar University, Doha, Qatar, [b] Department of Pharmacy, Heart Hospital, Hamad Medical Corporation, Doha, Qatar, [c] Department of Pharmacy, Al-Wakra Hospital, Hamad Medical Corporation, Doha, Qatar, [d] Department of Pharmacy, Hamad Bin Khalifa Medical City, Hamad Medical Corporation, Doha, Qatar and [e] Department of Medicine, Hamad Medical Corporation, Doha, Qatar.

Abstract: We sought to investigate the economic impact of preventing adverse events in a cardiology setting in Qatar as an effect of the clinical pharmacist as an intervention. This is a retrospective study of interventions by clinical pharmacists within an adult cardiology setting in a public healthcare setting (i.e Hamad Medical Corporation). The study included interventions that took place in March 2018, July 15, 2018 to August 15, 2018, and January 2019. The economic impact was measured via calculating the total benefit, defined as the sum of the cost savings and the cost avoidance. Sensitivity analyses were adopted to confirm the robustness of the results. The pharmacist

Funding: This work was supported by the Medical Research Center, Hamad Medical Corporation [grant number (MRC-01-19-110)].
*Corresponding author: Dina Abushanab, MSc, Department of Pharmacy, Hamad Bin Khalifa Medical City, Hamad Medical Corporation, Doha, Qatar. Tel: +974 40260755. E-mail: dabushanab@hamad.qa

Curr Probl Cardiol 2023;48:101838
0146-2806/$ – see front matter
https://doi.org/10.1016/j.cpcardiol.2023.101838

intervened in 262 patients, resulting in 845 interventions, with appropriate therapy (58.6%) and dosing/administration (30.2%) being the most frequent categories of reported interventions. Cost savings and cost avoidance resulted in QAR-11,536 (USD-3169) and QAR1,607,484 (USD 441,616), respectively, yielding a total benefit of QAR1,595,948 (USD 438,447) per 3 months and QAR6,383,792 (USD 1,753,789) per a year. (Curr Probl Cardiol 2023;48:101838.)

Introduction

Cardiovascular diseases (CVD) remain the leading cause of mortality worldwide, accounting for approximately 18 million deaths annually.[1] The global prevalence of CVD has also risen steadily over the last decades; for example, from 271 million in 1990 to 523 million in 2019.[2,3] In response to the high prevalence of CVD, multidisciplinary management involving a clinical pharmacist has been recommended to enhance patients' outcomes and reduce the overall healthcare cost.[4-10] The scope of clinical pharmacy practice has evolved substantially in recent decades to meet patients' needs, target more complex groups of patients, and ensure the cost-effective use of medicines through engaging in direct patient care and collaborating with healthcare professionals.[4-10] The role of clinical pharmacist interventions in hospitalized patients has been at the center of attention and interest. Clinical interventions have been shown to optimize medication use, promote rational prescribing, prevent adverse drug events (ADEs) that often contribute to a prolonged hospital stay and, consequently, result in a substantial decrease in healthcare cost.[4,5,7-10] While some studies have evaluated the role of pharmacists working with physicians in a variety of clinical practice settings, such as nephrology, critical care, neurology, and cancer,[11-21] and have shown positive economic outcomes due to implementing clinical interventions, studies that evaluated the economic impact of pharmacists' interventions in an adult cardiology setting are currently sparse. As inappropriate medication prescribing is associated with a substantial impact on patients and the healthcare system, and with the immensely increasing overall healthcare costs, especially in the setting of CVD, it has become imperative to evaluate the value of any medical service. Furthermore, with increasingly stretched health system budgets, healthcare services need to plan for efficient resource allocation and demonstrate that they remain cost saving through continually proving the economic benefit of

such services. Moreover, in order to ensure the sustainability of practices, such as resource utilization and staffing at practice sites, healthcare systems must demonstrate the return on investments made in their services. Within this context, the objective of this study was to evaluate the economic impact of interventions against medication-related problems (MRPs), implemented by clinical pharmacists, in the main public adult cardiology setting in Qatar.

Materials and Methods

Design and Setting

A retrospective observational study including clinical pharmacy interventions of adult hospitalized patients with CVD was carried out at Heart Hospital (HH) over 3-month periods (between March 1st and March 31st, 2018; July 15th and August 15th, 2018; and January 1st to January 31st, 2019). HH is known as the leading contributor of secondary and tertiary healthcare provision of cardiology services, with 139 beds, at Hamad Medical Corporation (HMC) in Qatar.[22] Information on clinical pharmacy interventions was extracted from a pharmacy intervention sheet in an Electronic Medical Record (EMR) system and was recorded in a standardized Excel sheet. When data was not available through the pharmacy sheet, the medical records for the respective patients were reviewed to obtain the missing data.

Ethics Approval

The study was approved by the Medical Research Center of HMC in September 2019 (MRC-01-19-110).

Study Population

Accepted interventions to any patient managed in the general cardiology, critical care, emergency wards, or heart failure clinic at HH during the study period, and documented during the study period, were eligible for inclusion. Interventions were excluded if rejected by the physicians or performed by pharmacists who do not directly communicate with clinical pharmacists assigned to a particular clinical ward.

Clinical Pharmacy Interventions

Clinical pharmacist interventions were defined as any action by a pharmacist that directly resulted in a change to patient management or

therapy.[23] Pharmacist interventions were grouped into 14 main categories as per the clinical intervention sheet embedded in Cerner, and these are: the addition of another medication; discontinuation of medication; switching to alternative medication; addition of a prophylactic agent during hospitalization; change in medication route; change in medication strength; change in medication duration; change in medication dose; change in medication frequency; therapeutic drug monitoring (TDM); addition of a lab test; addition of a diagnostic test; addition of a culture test; and addition of a vaccine.

Expert Panel

A panel of 5 healthcare professionals (3 clinical pharmacists, 1 pharmacy resident, and 1 physician) was involved in predicting the likelihood of ADEs without clinical pharmacy interventions. Using the Nesbit et al method,[24] the clinical panel estimated the probabilities of ADEs that may occur in the absence of interventions, which were: 0 (none), 0.01 (very low), 0.1 (low), 0.4 (medium), or 0.6 (high).[24] Table 1 provides a brief summary of ADE probabilities by Nesbit et al. An average probability estimate was then calculated between the panel members. The physician was to validate the likelihood of ADEs estimated by clinical pharmacist members.

Table 1. Description of adverse drug event probability according to Nesbit et al. method*

Probability of ADE category	Probability score	Description
None	0	Information requested
Very low	0.01	For problem orders such as clarifications, missing information, or missing strengths)
Low	0.1	For preventing a potentially significant reaction, eg, 2-4× normal dose, ineffective dose to produce therapeutic effect, or potential for therapeutic failure/toxicity due to incorrect schedule/route, duplicated therapy
Medium	0.4	For preventing a potentially serious reaction, eg, allergy to an ordered drug, missing allergy information, 4-10× normal dose, no adjustment for renal or hepatic failure
High	0.6	For preventing a potentially fatal or severe reaction, eg, 10× normal dose, narrow therapeutic index, life-threatening reaction)

*ADE, adverse drug event

Economic Outcome Measures

The outcomes of this study were to estimate the total benefit, cost saving, and cost avoidance associated with clinical pharmacy interventions. All outcomes were calculated over 3-month and 1-year periods. To estimate the total benefit of clinical pharmacists' interventions, the sum of cost savings and cost avoidance was considered:[39,40]

- Cost savings: defined as the overall reduced cost of therapy due to the clinical pharmacist intervention. A negative reduction in the cost of therapy implies that the increase in cost of therapy outweighs the reduction in cost of therapy. The increase or decrease in cost of therapy was calculated by contrasting the cost of full-course therapy that took place after clinical pharmacy intervention against the cost of actual therapy that took place before clinical pharmacy intervention.
- Cost avoidance: defined as the cost of ADEs avoided due to the interventions. The cost avoidance was calculated for each intervention by multiplying the probability of avoided ADE by the cost of an ADE. Here, we assumed that each ADE might cause additional 2 days of stay in the hospital.[21]
- In this analysis, a 3-month prescription refills cost was considered for chronic disease medications, while for acute diseases, we followed the duration reported as per the national HMC protocols or as written in the prescription by the physicians.

Perspective and Resource Utilization

From the perspective of HH, only direct medical costs associated with the interventions were considered. Hospitalization costs, including pharmaceuticals, laboratory tests, diagnostic procedures, and hospitalization stay, were obtained from the pharmacy and finance departments at HMC. All costs were adjusted to 2022 using the Qatari Health Consumer Price Index[25] and were presented in Qatari Riyal (QAR) and United States Dollar (USD) (1 USD is equal to 3.65).

Sample Size

The selection of the study population was decided by successful examples in the literature,[26-31] with patient recruitment predicated on a duration-based approach rather than a sample size. However, because the

performance evaluation takes place every year in HH between January and February, some staff may over document interventions during this period and, hence, the documentation of interventions by clinical pharmacists may be affected by the annual evaluation. Therefore, a decision was made by the study team to select clinical interventions that were documented immediately on the first month after the performance evaluation, the last month of the year before the performance evaluation, and the middle month of the year. Importantly, given that such studies are primarily concerned with cost estimation, rather than hypothesis testing, such as clinical research, the underpowered sample size of the study does not compromise its utility in guiding decision-makers seeking to address the financial requirements of healthcare systems.[15-17]

Data Snalysis

Findings of the patient demographics were imported from Microsoft Excel Spreadsheet to Statistical Package for the Social Sciences (SPSS) version 28 software. Continuous variables were presented as means ± standard deviation (SD) and categorical variables were displayed as frequencies and percentages. To determine the significant difference among the 3 groups: (i) March, 2018, (ii) July 15, 2018 to August 15, 2018, and (iii) January, 2019, 1-way analysis of variance (ANOVA) (if normally distributed with continuous data), Kruskal−Wallis tests (if not normally distributed with continuous data), and chi-square tests (categorical data) were considered. A P value of ≤ 0.05 implied a statistical significance.

Sensitivity Analysis

To test study assumptions and the effect of uncertainty around key input parameters, we performed a number of sensitivity analyses. For a univariate sensitivity analysis, we used a ±20% variation range of the base case cost of the ADE. For the probabilistic sensitivity analysis (PSA), an uncertainty range of ±15% of the base case was used for the probabilities of avoided ADEs. All analyses were performed using triangular-type distribution, ranning 1000 iterations of a Monte Carlo simulation. Cost-effectiveness acceptability curves (CEACs) were generated to present the outcomes graphically. All analyses were performed using @Risk-5.7 (Palisade Corporation, NY).

Results

Characteristics of Patients

A total of 845 interventions in 262 patients with CVD were reported by clinical pharmacists. Of these, 441 interventions were reported in 139 patients in March 2018, 277 interventions in 108 patients in July-August 2018, and 127 interventions in 15 patients in January 2019. Most of the patients were male (n = 158, 60.3%) and the mean age was 60.9 ± 13.1 years. Additionally, most interventions were reported among Arab patients (n =197, 75.2%), followed by Asian (n =61, 23.3%), and were hospitalized in the general cardiology (n =209, 79.4%), followed by emergency care unit (n =31, 11.8%). No statistically significant differences were observed between the study groups except concerning gender. Further details regarding patients' characteristics are shown in Table 2.

Characteristics of Interventions

The most abundant categories of reported interventions were the appropriate therapy (58.6%) and dosing/administration (30.2%). The most documented intervention relating to the appropriate therapy category was an additional therapy required (45.3%), whereas optimum dose was frequently reported under the dosing/administration category (78.4%). The contraindication and safety category constituted 8.4% of interventions, duplicate therapy constituted 1.5%, and 1.3% was of drug interactions.

A summary of the categories of the interventions with examples from the study population, in addition to the associated average probability of avoided ADEs, as per category, can be seen in Table 3.

Economic Outcomes

Cost Saving. The overall added cost with interventions for the MRPs over a 3-month period was calculated to be QAR 160,563 (USD 44,111). In this study, the interventions that contributed to the added cost the most were the addition of another medication and change in medication dose (ie, incorrect dose, increased or decreased dose), while the change in medication duration (ie, increased or decreased duration) and change in medication frequency (ie, increased or decreased frequency) were the categories that contributed to the added cost least. Table 4 presents the results of added cost with each type of intervention categories.

Table 2. Patients demographics among the study periods

	Total (n = 262)	March 2018 (n = 139)	July-August 2018 (n = 108)	January 2019 (n = 15)	P value*
Gender, average ± standard deviation or frequency (%)					
Male	158 (60.31)	80 (57.55)	68 (62.96)	10 (66.67)	0.001
Female	104 (39.69)	59 (42.45)	40 (37.04)	5 (33.33)	
Age	60.9 ± 13.05	69.84 ± 10.82	62.16 ± 11.60	69.13 ± 15.44	0.05
Weight	86.01 ± 23.89	90.93 ± 23.93	96.23 ± 24.18	79.73 ± 10.33	0.06
Nationality, average ± standard deviation or frequency (%)					
Arab	197 (75.19)	137 (98.56)	45 (41.67)	15 (100)	0.09
Asian (non-Arab)	61 (23.28)	2 (1.44)	59 (54.63)	0 (0)	
Others	4 (1.53)	0 (0)	4 (3.70)	0 (0)	
Ward type, average ± standard deviation or frequency (%)					
General cardiology	209 (79.39)	104 (74.82)	94 (87.04)	11 (73.33)	0.05
Emergency	31 (11.83)	25 (17.99)	2 (1.85)	4 (26.67)	
Critical care	16 (6.11)	7 (5.04)	9 (8.33)	0 (0)	
Heart failure Clinic	6 (2.29)	3 (2.16)	3 (2.78)	0 (0)	

*Statistical difference among study periods.

Table 3. Description of the probability of avoided adverse drug event and categories of resources associated with the clinical pharmacy interventions, including examples

Probability of avoided adverse drug event	Categories of intervention resources with examples
0.01	Switching to an alternative medication. **Example** Patient admitted for elective coronary artery bypass graft. The patient was on esomeprazole 40 mg orally daily. The clinical pharmacist recommended to switch to lansoprazole 30 mg oral daily.
0.1	Discontinuation of a medication, addition of another medication, switching to alternative medication, change in medication dose, change in medication route, addition of lab test, change in medication frequency, therapeutic drug monitoring. **Example** Patient had a prescription of ferrous sulfate 190 mg orally daily due to anemia. The patient was also receiving iron intravenously (ferric carboxymaltose 1500 mg (total dose was 500 and 1000 weekly), therefore, the pharmacist recommended to discontinue the medication.
0.2	Discontinuation of a medication, addition of another medication, switching to alternative medication, change in medication duration, change in medication route, change in medication frequency, change in medication strength, change in medication dose, addition of lab test. **Example** Patient with hypertension on isosorbide dinitrate 40 mg orally twice daily. The pharmacist recommended to increase the dose to 40 mg oral 3 times daily to optimize the regimen.
0.3	Discontinuation of a medication, addition of another medication, switching to alternative medication, change in medication dose, addition of a lab test, requesting a TDM, change in medication route. *Example:* Patient with coronary artery disease and low magnesium level (0.61 mmol/L). Hence, the pharmacist recommended to add magnesium sulfate 10% 2 g in 100 ml normal saline intravenous once.
0.4	Discontinuation of a medication, addition of another medication, switching to alternative medication; change in medication dose, requesting therapeutic drug monitoring. **Example** Patient with congestive heart failure and had symptoms of lethargy and confusion. The patient was on digoxin 0.125 mg orally daily, thus the pharmacist requested digoxin serum level monitoring.
0.5	Discontinuation of a medication, addition of another medication, switching to alternative medication, change in medication dose, change in medication duration, requesting

(*continued*)

Table 3. (*continued*)

Probability of avoided adverse drug event	Categories of intervention resources with examples
	therapeutic drug monitoring, requesting a lab test, change in medication frequency. **Example** Patient with hypertension and heart failure and had high serum creatinine, on furosemide 40 mg orally twice daily. The pharmacist recommended to decrease the frequency to once daily due to increased serum creatinine.
0.6	Discontinuation of a medication and requesting therapeutic drug monitoring **Example** Patient with hypertension on lisinopril 2.5/1.25 mg orally daily and sacubitril/valsartan 49mg/51mg orally twice daily. The pharmacist recommended to discontinue lisinopril as both medications from the same pharmacological class.

The overall reduced cost due to the interventions was QAR 149,027 (USD 40,941). Of which, discontinuation of a medication and change in medication dose (ie, incorrect dose, increased or decreased dose) contributed to the reduced cost the most, whereas the change in medication duration (ie, increased or decreased duration) contributed to the reduced cost the least. Table 4 presents the results of cost saving associated with each type of intervention category.

The overall cost saving, therefore, which is the overall reduction in the cost of resources used, was calculated to be QAR -11,536 (USD −3169).

Cost Avoidance. The probability of ADEs in the absence of interventions, with an average of 0.01, was calculated for each of 8 interventions, avoided ADEe probability with an average of 0.1 was calculated for each of 93 interventions, an average of 0.2 was calculated for each of 242 interventions, an average of 0.3 was calculated for each of 310 interventions, an average of 0.4 was calculated for each of 116 interventions, an average of 0.5 was calculated for each of 69 interventions, an average of 0.6 was calculated for each of 7 interventions. The overall cost avoidance due to the interventions over a 3-month period was QAR 1,607,484 (USD 441,616). Table 4 summarizes the cost avoidance associated with each type of intervention categories.

Table 5 summarizes the total benefit associated with each category of clinical pharmacist interventions.

Table 4. Added cost, reduced cost, and avoided cost associated with each category of clinical pharmacist intervention*

Type of interventions	Overall added cost with interventions, QAR (USD)	Overall reduced cost with interventions, QAR (USD)	Overall cost avoidance, QAR (USD)
Addition of another medication	89,397 (24,559)	0	573,997 (157,691
Discontinuation of a medication	0	81,419 (22,368)	402,559 (110,593)
Switching to alternative medication	712 (196)	19,732 (5421)	77,748 (21,359)
Change in medication route	994 (273)	4,460 (1225)	31,493 (8652)
Therapeutic drug monitoring	4,560 (1253)	0	25,911 (7118)
Change in medication dose	59,766 (16,419)	41,970 (11,530)	399,267 (109,689)
Change in medication frequency	345 (95)	1,408 (387)	20,847 (5727)
Change in medication duration	158 (43.4)	38 (10)	5,923 (1627)
Addition of a diagnostic test	489 (134)	0	1,925 (529)
Addition of a lab test	4,142 (1138)	0	67,813 (18,630)
Total	160,563 (44,111)	149,027 (40,941)	1,607,484 (441,616)

*QAR, Qatari Riyal; USD, United States Dollar (1 USD = 3.65 QAR).

Table 5. Total benefit analysis outcomes*

Outcome	Value, QAR (USD)
Overall added cost with therapy interventions per 3 months	160,563 (44,111)
Overall reduced cost with therapy interventions per 3 months	149,027 (40,941)
Overall cost saving per 3 months	−11,536 (3,169)
Overall cost avoidance per 3 months	1,607,484 (441,616)
Total benefit per 3 months	1,595,948 (438,447)
Projected total benefit per 1 year	6,383,792 (1,753,789)

*QAR, Qatari Riyal; USD, United States Dollar (1 USD = 3.65 QAR).

Sensitivity Analysis

The results of the univariate analysis indicated robustness against the uncertainty in the cost of the ADE, where the mean of total benefit was QAR 6,383,792 (USD 1,753,789), 95% CI QAR 3,993,029 to 6,487,353 (USD 1,096,986-1,782,240), over 1-year, and QAR 1,595,948 (USD 438,447), 95% CI QAR 1,000,126 to 1,619,734 (USD 274,760-444,982), over 3-month (Fig 1 and 2). PSA showed that there is a 100% probability that the interventions performed by the clinical pharmacists are associated with positive total economic benefits over a 3-month, with a mean of QAR 1,377,966 (USD 378,562), 95% CI QAR 1,364,805 to 1,389,721 (USD 374,946-381,791). Extrapolating to an annual total economic benefits, a mean of QAR 5,511,864 (USD 1,514,248), 95% CI 5,465,688 to 5,511,864 (USD 1,501,563-1,514,248) was calculated (Fig 3 and 4). A regression Tornado analysis indicated that the cost of ADE and the avoided ADEs at a 0.2 probability were the key drivers behind the

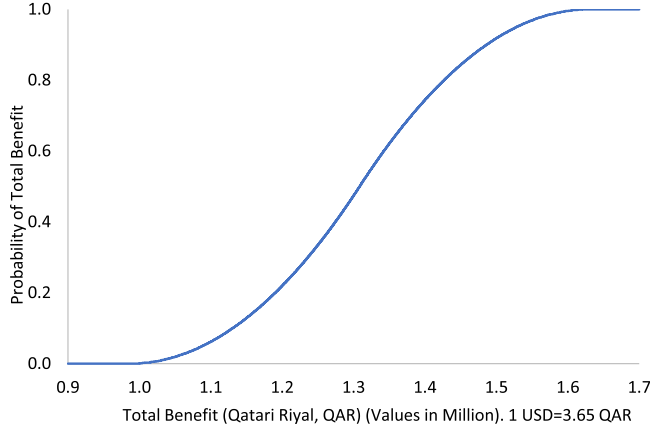

Figure 1. Total benefit probability curve over a 3-month period (1-way sensitivity analysis). (Color version of figure is available online.)

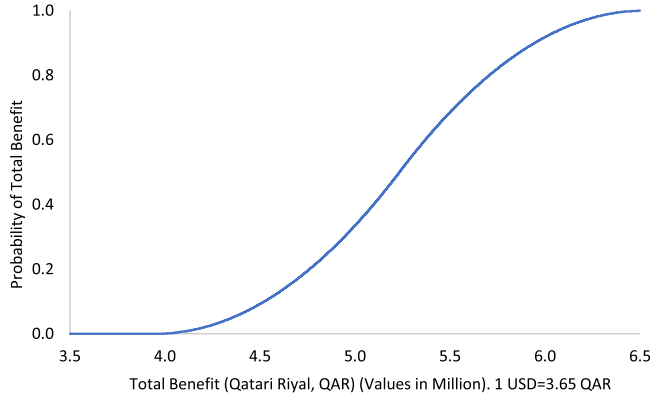

Figure 2. Total benefit probability curve over a 1-year period (1-way sensitivity analysis). (Color version of figure is available online.)

outcome, while avoided ADEs with a 0.01 probability was the least influencing factor (Fig 5).

Table 6 reports the outcomes of sensitivity analyses with their uncertainty distributions.

Discussion

In response to the growing prevalence of CVD, several studies and societies such as the American Heart Association, the Heart Failure Society of America and American College of Clinical Pharmacy Cardiology Practice and Research Network, and the National Lipid Association recommend a multidisciplinary healthcare team approach to manage patients

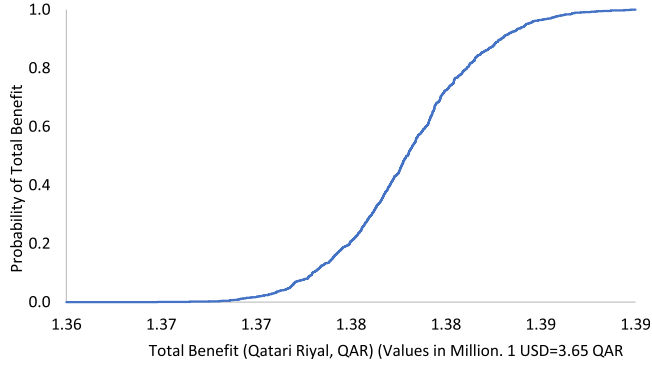

Figure 3. Total benefit probability curve over a 3-month period (probabilistic sensitivity analysis). (Color version of figure is available online.)

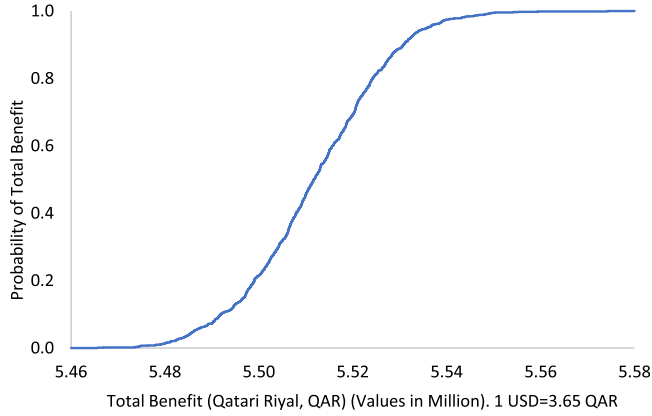

Figure 4. Total benefit probability curve over a 1-year period (probabilistic sensitivity analysis). (Color version of figure is available online.)

with CVD, which involve clinical pharmacists that have the potentials to improve outcomes, enhance medication adherence, and reduce the overall healthcare cost.[2,4-10]

Preventing ADEs among patients with CVD is a burdensome situation, and errors are likely to occur unless a systematic multidisciplinary strategy is followed. Studies have shown that ADEs from inappropriate medication prescribing, occurring during CVD management, arise frequently and cause high rates of morbidity and mortality.[32,33] Importantly, while a substantial decrease in ADEs during CVD management has been reported when pharmacists are part of the healthcare team, there is a lack of solid evidence showing the economic impact of interventions in the prevention of ADEs through a clinical pharmacist intervention in a cardiology practice setting.[4-10] In this study, our analysis focused on quantifying the economic aspect of this study by estimating the cost saving and cost avoidance, which would be reflected in the institution's financial performance. Through our data analysis, it was discovered that an overall cost saving of QAR −11,536 (USD 3169) and total cost-avoidance of QAR 1,607,484 (USD 441,616) were generated from 845 interventions by clinical pharmacists practising in the cardiology wards, translating to a total benefit of 1,595,948 (USD 438,447) over a 3-month period and a total annual benefit of QAR 6,383,792 (USD 1,753,789). We also showed that the discontinuation of a medication that is no longer needed and the change in medication dose (ie, incorrect dose, increased or decreased dose) were the interventions associated with the greatest cost reduction, while the addition of another medication and the change in medication dose were the interventions associated with the greatest cost increase.

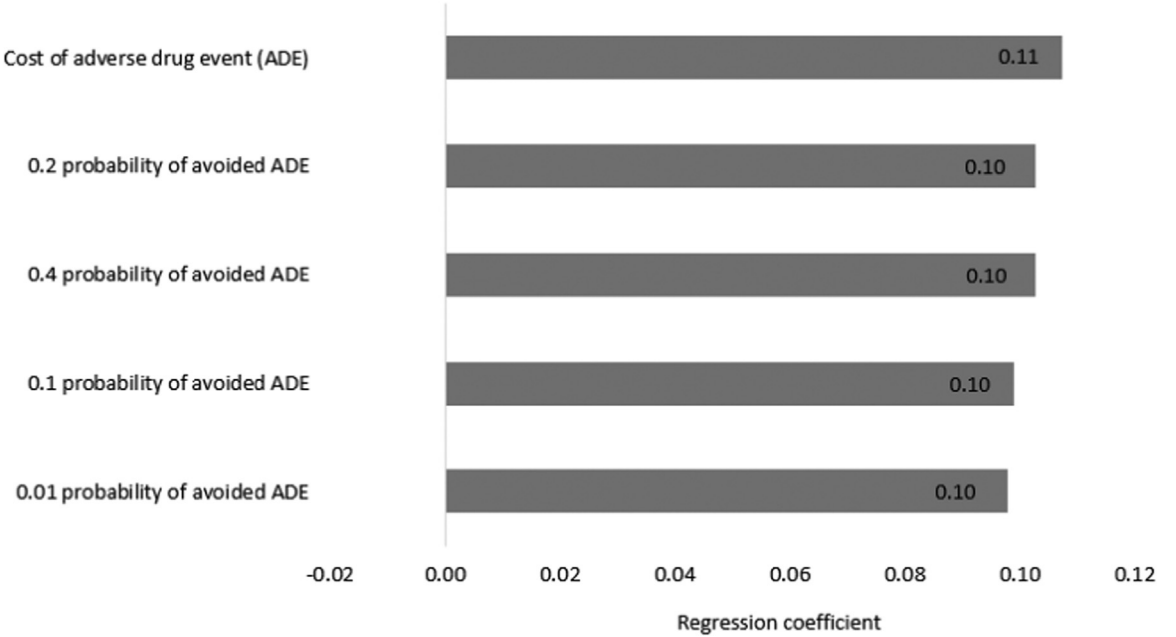

Figure 5. A regression tornado diagram of model inputs and their effect on the outcome

Table 6. Outcomes of sensitivity analyses with their uncertainty distributions*

Variable	Point estimate, QAR (USD)	Variation range	Total benefit per 1 year	Total benefit per 3 mo
One-way sensitivity analysis				
Cost of adverse drug event	2961 (813)	Triangular distribution, QAR 2369, 2961 3554 (USD 651, 813, 976)	Mean QAR 6,383,792 (USD 1,753,789), 95% CI QAR 3,993,029 to 6,487,353 (USD 1,096,986-1,782,240)	Mean QAR 1,595,948 (USD 438,447), 95% CI QAR 1,000,126-1,619,734 (USD 274,760-444,982)
Multivariate uncertainty analysis				
Very low probability for ADE	0.01	Triangular Distribution (0.009,0.01,0.012)	Mean QAR 5,511,864 (USD 1,514,248), 95% CI QAR 5,465,688 to 5,511,864 (USD 1,501,563-1,514,248)	Mean QAR 1,377,966 (USD 378,562), 95% CI QAR 1,364,805 to 1,389,721 (USD 374,946-381,791)
Low probability for ADE	0.1	Triangular distribution (0.09,0.1,0.12)		
Low to moderate probability for avoided ADE	0.2	Triangular distribution (0.17,0.2,0.23)		
Low to moderate probability for avoided ADE	0.3	Triangular distribution (0.26,0.3,0.35)		
Moderate probability for avoided ADE	0.4	Triangular distribution (0.34,0.4,0.46)		
Moderate to high probability for avoided ADE	0.5	Triangular distribution (0.43,0.5,0.58)		
High probability for avoided ADE	0.6	Triangular distribution (0.51,0.6,0.69)		

*CI, confidence interval; QAR, Qatari Riyal; USD, United States Dollar.

Looking into the literature, and despite that there are multiple studies that showed the clinical and economic impact of pharmacy intervention in non-cardiology settings, such as nephrology, critical care, neurology, and cancer,[11-21] studies that estimate the economic impact of clinical pharmacy interventions against MRPs in the cardiology practice setting is currently lacking. Hence, potential discrepancies between our findings and previous investigations are found, which could relate to differences in the study population, setting, or the specific resource utilization considered. Our findings are consistent with those reported in studies by Lesar et al.[34] and Miranda et al.,[35] which were in the medical, obstetric-gynecologic, surgical, or emergency departments, where most of the interventions were related to the appropriateness of therapy, including adding or discontinuing medication and adjusting a dosing regimen in. Cazarim et al.[20] also reported that the most commonly reported interventions in a neurology unit were related to the dosing of medications with an annual added USD 1158 cost of interventions and a cost avoidance of USD 25,536 from a Brazilian public health care system.

Given the nature of the HH setting investigated in this study, it was expected that the majority of the medical conditions would be of cardiovascular nature. Hence, the most commonly witnessed class of medications, for which interventions were documented, was CVD medications. This did not directly align with findings from other studies since this was the first study to outline pharmacy interventions in a specialized heart hospital setting, where cardiovascular agents contributed to many interventions after anti-infective agents in Patel et al.[36] study. This is expected since cardiovascular agents are considered one of the most classes worldwide.

Our study also highlights TDM as one of several clinical pharmacist roles in a cardiology setting. ADEs prevention achieved through TDM represent the fourth largest amount of added cost among the intervention categories, with QAR 4560 (USD 1253). The use of multiple agents with a narrow therapeutic index, in patients with CVD with altered pharmacokinetics and pharmacodynamics, places these patients at greater risk for complications and adverse events.[37] The substantial impact pharmacists have on ADE prevention aligns with findings from a clinical trial that reported a 66% relative risk reduction in ADEs due to the presence of a clinical pharmacist on rounds.[38]

There are common practices that are often performed per multidisciplinary guidelines which can reduce ADEs and overall hospital costs. For example, clinical pharmacists in cardiology wards commonly convert more expensive intravenous medications to oral dosage forms with

similar efficacy or discontinue prophylactic medications when they are no longer required. In this study, the change in medication route contributed to QAR 4460 (USD 1225) reduction in cost.

It is worth highlighting the crucial role of clinical pharmacists in conducting medication reconciliation at the time of admission and discharge, where this is the typical practice demonstrated in HH and all hospitals under HMC, and this is further supported by the fact that the most frequently occurring interventions were attributed to the addition or discontinuation of medications as well as dosing adjustments. This is essential since it immensely aids in the therapeutic regimen planned for the patient during their hospital stay, and it is considered one of the most efficient strategies utilized to ensure that the appropriate medications are considered while avoiding any consequent unwanted patient harm.

Our study provides healthcare providers with evidence in relation to the main contributing factors of cost associated with DRPs among the diverse Qatari population and, therefore, provides a better differential understanding of the burden of these, beyond the clinical and humanistic aspects. The findings suggest that the intervention role of clinical pharmacists should also be utilized in other settings at HMC, Qatar, given that the majority of interventions-prevented ADEs, presumably generate cost savings. Also demonstrated, in parallel to the clinical pharmacist interventions, is the potential need for continuous education on cardiovascular therapies and improved implantation of clinical pathways.

This study has several noteworthy limitations. Mainly, the retrospective study nature allows for a possibility of bias, such as recall bias pertaining to the reporting of interventions. In addition, the interventions that were included in the study were not subject to content quality auditing since it was assumed that the content verification would be completed by the clinical pharmacist placing the intervention and the prescribing physician who needed to approve it. We also limited our study to 3 time periods of approximately 1 month each in relation to the performance appraisal process for clinical pharmacists at HMC. This may introduce a risk of bias and underestimate/overestimate the actual economic impact of clinical pharmacy interventions. Also, the ADE probabilities assessment was an evidence- and experience-based evaluation by local healthcare experts committee and could include a component of subjectivity and evaluation bias. Moreover, our study was conducted in a single healthcare center, making it difficult to extrapolate the data to other cardiology settings because of differences in CVD prevalence, patients' characteristics, and resource utilization. Finally, in our study we assumed that

each ADE may lead to additional 2 days of stay in the hospital,[21] which may not reflect the real avoided cost of the ADE.

Conclusion

Incorporating a clinical pharmacist in a multidisciplinary cardiology team, to intervene against MRPs, resulted in significant public health financial benefits, with a total economic benefits of QAR 1,595,948 (USD 438,447) per 3 months and QAR 6,383,792 (USD 1,753,789) per year periods. While the economic impact of clinical pharmacy intervention is crucial, it is not the only aspect that should be taken into consideration. The impact that the intervention has on clinical as well as humanistic outcomes is also of great importance and must be considered in future studies of the complete influence.

Author Contributions

DA contributed to the study conception and design, led data validation, data analysis and interpretation, and wrote the first draft of manuscript. DB led the study conceptualization and design, contributed to data analysis and interpretation. RK, FM, and AH contributed to the data collection. MA, PA, WE, AM, and SA facilitated the planning and carrying out of the study. All authors contributed to the final version of the manuscript.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Acknowledgment

We would like to thank all the clinical pharmacists who contributed to the documentation of the interventions. "*Open Access funding provided by the Qatar National Library*".

REFERENCES

1. Roth GA, Mensah GA, Johnson CO, et al. Global burden of cardiovascular diseases and risk factors, 1990-2019: update from the gbd 2019 study. *J Am Coll Cardiol* 2020;76(25):2982–3021. https://doi.org/10.1016/j.jacc.2020.11.010.

2. McClellan M, Brown N, Califf RM, Warner JJ. Call to action: urgent challenges in cardiovascular disease: a presidential advisory from the american heart association. *Circulation* 2019;139(9):e44–54. https://doi.org/10.1161/CIR.0000000000000652.
3. Virani SS, Alonso A, Benjamin EJ, et al. Heart disease and stroke statistics-2020 update: a report from the american heart association. *Circulation* 2020;141(9):e139–596. https://doi.org/10.1161/CIR.0000000000000757.
4. Dunn SP, Birtcher KK, Beavers CJ, et al. The role of the clinical pharmacist in the care of patients with cardiovascular disease. *J Am Coll Cardiol* 2015;66(19):2129–39. https://doi.org/10.1016/j.jacc.2015.09.025.
5. Milfred-LaForest SK, Chow SL, DiDomenico RJ, et al. Clinical pharmacy services in heart failure: an opinion paper from the Heart Failure Society of America and American College of Clinical Pharmacy Cardiology Practice and Research Network. *Pharmacotherapy* 2013;33(5):529–48. https://doi.org/10.1002/phar.1295.
6. Jacobson TA, Maki KC, Orringer CE, et al. National lipid association recommendations for patient-centered management of dyslipidemia: part 2. *J Clin Lipidol* 2015;9 (suppl 6):S1–122.e1. https://doi.org/10.1016/j.jacl.2015.09.002.
7. Omboni S, Caserini M. Effectiveness of pharmacist's intervention in the management of cardiovascular diseases. *Open Hear* 2018;5(1):e000687. https://doi.org/10.1136/openhrt-2017-000687.
8. Shapiro MD, Fazio S. Setting the agenda for preventive cardiology. *Circ Res* 2017;121(3):211–3. https://doi.org/10.1161/CIRCRESAHA.117.311390.
9. Ripley TL, Adamson PB, Hennebry TA, Van Tuyl JS, Harrison DL, Rathbun RC. Collaborative practice model between cardiologists and clinical pharmacists for management of patients with cardiovascular disease in an outpatient clinic. *Ann Pharmacother* 2014;48(3):412–9. https://doi.org/10.1177/1060028013515432.
10. Ripley TL, Hennebry TA, Sanders TN, Harrison D, Rathbun RC. Impact of a clinical pharmacist on a cardiovascular surrogate endpoint: a pilot study. *Pharm Pract (Granada)* 2012;10(3):173–9. https://doi.org/10.4321/s1886-36552012000300008.
11. de Grégori J, Pistre P, Boutet M, et al. Clinical and economic impact of pharmacist interventions in an ambulatory hematology-oncology department. *J Oncol Pharm Pract* 2020;26(5):1172–9. https://doi.org/10.1177/1078155220915763.
12. Zecchini C, Vo T-H, Chanoine S, et al. Clinical, economic and organizational impact of pharmacist interventions on injectable antineoplastic prescriptions: a prospective observational study. *BMC Health Serv Res* 2020;20(1):113. https://doi.org/10.1186/s12913-020-4963-7.
13. Schumock GT, Butler MG, Meek PD, Vermeulen LC, Arondekar B V, Bauman JL. Evidence of the economic benefit of clinical pharmacy services: 1996-2000. *Pharmacotherapy* 2003;23(1):113–32. https://doi.org/10.1592/phco.23.1.113.31910.
14. Randolph LA, Walker CK, Nguyen AT, Zachariah SR. Impact of pharmacist interventions on cost avoidance in an ambulatory cancer center. *J Oncol Pharm Pract* 2018;24(1):3–8. https://doi.org/10.1177/1078155216671189.
15. Dean B, Schachter M, Vincent C, Barber N. Causes of prescribing errors in hospital inpatients: a prospective study. *Lancet* 2002;359(9315):1373–8. https://doi.org/10.1016/S0140-6736(02)08350-2.

16. Lewis PJ, Dornan T, Taylor D, Tully MP, Wass V, Ashcroft DM. Prevalence, incidence and nature of prescribing errors in hospital inpatients: a systematic review. *Drug Saf* 2009;32(5):379–89. https://doi.org/10.2165/00002018-200932050-00002.
17. Franklin BD, McLeod M, Barber N. Comment on "prevalence, incidence and nature of prescribing errors in hospital inpatients: a systematic review. *Drug Saf* 2010;33 (2):163–6. https://doi.org/10.2165/11319080-000000000-00000.
18. American Society of Health-System Pharmacists. ASHP guidelines: minimum standard for pharmacies in hospitals. *Am J Health-Syst Pharm* 2013;70:1619–30. https://doi.org/10.1093/ajhp/52.23.2711.
19. Kaboli PJ, Hoth AB, McClimon BJ, Schnipper JL. Clinical pharmacists and inpatient medical care: a systematic review. *Arch Intern Med* 2006;166(9):955–64. https://doi.org/10.1001/archinte.166.9.955.
20. Cazarim M de S, Rodrigues JPV, Calcini PS, Einarson TR, Pereira LRL. Cost-benefit analysis of pharmacist interventions over 36 months in a university hospital. *Rev Saude Publica* 2020;54:94. https://doi.org/10.11606/s1518-8787.2020054001895.
21. Chen C-C, Hsiao F-Y, Shen L-J, Wu C-C. The cost-saving effect and prevention of medication errors by clinical pharmacist intervention in a nephrology unit. *Medicine (Baltimore)* 2017;96(34):e7883. https://doi.org/10.1097/MD.0000000000007883.
22. Hamad Medical Corporation. Accessed October 20, 2022. Available at: https://www.hamad.qa/EN/Pages/default.aspx
23. Dooley MJ, Allen KM, Doecke CJ, et al. A prospective multicentre study of pharmacist initiated changes to drug therapy and patient management in acute care government funded hospitals. *Br J Clin Pharmacol* 2004;57(4):513–21. https://doi.org/10.1046/j.1365-2125.2003.02029.x.
24. Nesbit TW, Shermock KM, Bobek MB, et al. Implementation and pharmacoeconomic analysis of a clinical staff pharmacist practice model. *Am J Heal Pharm* 2001;58(9):784–90. https://doi.org/10.1093/ajhp/58.9.784.
25. Qatar: Inflation rate from 1986 to 2026*. Accessed January 6, 2022Available at: https://www.statista.com/statistics/379995/inflation-rate-in-qatar/.
26. Malani AN, Richards PG, Kapila S, Otto MH, Czerwinski J, Singal B. Clinical and economic outcomes from a community hospital's antimicrobial stewardship program. *Am J Infect Control* 2013;41(2):145–8. https://doi.org/10.1016/j.ajic.2012.02.021.
27. Sebaaly J, Parsons LB, Pilch NAW, Bullington W, Hayes GL, Easterling H. Clinical and financial impact of pharmacist involvement in discharge medication reconciliation at an academic medical center: a prospective pilot study. *Hosp Pharm* 2015;50 (6):505–13. https://doi.org/10.1310/hpj5006-505.
28. Gallagher J, Byrne S, Woods N, Lynch D, McCarthy S. Cost-outcome description of clinical pharmacist interventions in a university teaching hospital. *BMC Health Serv Res* 2014;14:177. https://doi.org/10.1186/1472-6963-14-177.
29. Branham AR, Katz AJ, Moose JS, Ferreri SP, Farley JF, Marciniak MW. Retrospective analysis of estimated cost avoidance following pharmacist-provided medication therapy management services. *J Pharm Pract* 2013;26(4):420–7. https://doi.org/10.1177/0897190012465992.

30. Miyamoto GC, Ben ÂJ, Bosmans JE, et al. Interpretation of trial-based economic evaluations of musculoskeletal physical therapy interventions. *Brazilian J Phys Ther* 2021;25(5):514–29. https://doi.org/10.1016/j.bjpt.2021.06.011.
31. Al MJ, van Hout BA, Michel BC, Rutten FF. Sample size calculation in economic evaluations. *Health Econ* 1998;7(4):327–35. https://doi.org/10.1002/(sici)1099-1050(199806)7:4<327::aid-hec342>3.0.co;2-u.
32. Hallas J, Haghfelt T, Gram LF, Grodum E, Damsbo N. Drug related admissions to a cardiology department; frequency and avoidability. *J Intern Med* 1990;228(4):379–84. https://doi.org/10.1111/j.1365-2796.1990.tb00249.x.
33. Roughead EE, Gilbert AL, Primrose JG, Sansom LN. Drug-related hospital admissions: a review of Australian studies published 1988-1996. *Med J Aust* 1998;168(8):405–8. https://doi.org/10.5694/j.1326-5377.1998.tb138996.x.
34. Lesar TS, Briceland L, Stein DS. Factors related to errors in medication prescribing. *JAMA* 1997;277(4):312–7.
35. Miranda TMM, Petriccione S, Ferracini FT, Borges Filho WM. Interventions performed by the clinical pharmacist in the emergency department. *Einstein (Sao Paulo)* 2012;10(1):74–8. https://doi.org/10.1590/s1679-45082012000100015.
36. Patel N, Desai M, Shah S, Patel P, Gandhi A. A study of medication errors in a tertiary care hospital. *Perspect Clin Res* 2016;7(4):168–73. https://doi.org/10.4103/2229-3485.192039.
37. Yin J, Li X, Li F, Lu Y, Zeng S, Zhu F. Identification of the key target profiles underlying the drugs of narrow therapeutic index for treating cancer and cardiovascular disease. *Comput Struct Biotechnol J* 2021;19:2318–28. https://doi.org/10.1016/j.csbj.2021.04.035.
38. Leape LL, Cullen DJ, Clapp MD, et al. Pharmacist participation on physician rounds and adverse drug events in the intensive care unit. *JAMA* 1999;282(3):267–70. https://doi.org/10.1001/jama.282.3.267.
39. Abushanab D, Atchan M, Elajez R, Elshafei M, Abdelbari A, Al Hail M, et al. Economic impact of clinical pharmacist interventions in a general tertiary hospital in Qatar. *PLoS One* 2023;18(6):e0286419. https://doi.org/10.1371/journal.pone.0286419. PMID: 37262042; PMCID: PMC10234553.
40. Abushanab D, Gulied A, Hamad A, Abu-Tineh M, Abdul Rouf PV, Al Hail M, et al. Cost savings and cost avoidance with the inpatient clinical pharmacist interventions in a tertiary cancer care hospital. *J Oncol Pharm Pract*. 2023:10781552231160275. https://doi.org/10.1177/10781552231160275. Epub ahead of print. PMID: 36946146.