Economic Impact and Cost Benefit of the Inpatient Clinical Pharmacist Interventions in Cancer Care Units

Dina Abushanab

Hamad Medical Corporation

Amaal Gulied

Hamad Medical Corporation

Anas Hamad

Hamad Medical Corporation

Palli Valappila Abdul Rouf

Hamad Medical Corporation

Moza Al Hail

Hamad Medical Corporation

Wessam El Kassem

Hamad Medical Corporation

Maguy El Hajj

Qatar University College of Pharmacy

Daoud Al-Badriyeh (✉ daoud.a@qu.edu.qa)

Qatar University <https://orcid.org/0000-0001-7791-954X>

Research Article

Keywords: Clinical pharmacist intervention, cancer, economic benefit, cost-benefit, cost saving, cost avoidance, adverse drug event

Posted Date: January 4th, 2022

DOI: <https://doi.org/10.21203/rs.3.rs-1180212/v1>

License: © ⓘ This work is licensed under a Creative Commons Attribution 4.0 International License.

[Read Full License](#)

Title page**Title:**

Economic impact and cost benefit of the inpatient clinical pharmacist interventions in cancer care units

Authors

Dina Abushanab¹, Amaal Gulied², Anas Hamad², Palli Valappila Abdul Rouf¹, Moza Al Hail¹, Wessam El-Kassem¹, Maguy Saffouh El Hajj³, Daoud Al-Badriyeh³

Affiliations

¹Pharmacy Department, Hamad Bin Khalifa Medical City, Hamad Medical Corporation, Doha, Qatar

²Pharmacy Department, National Center for Cancer Care & Research, Hamad Medical Corporation, Doha, Qatar

³College of Pharmacy, QU Health, Qatar University, Doha, Qatar

Corresponding author:

Daoud Al-Badriyeh, PhD, Health Economics and Outcomes Research, College of Pharmacy, QU Health, Qatar University, Doha 2713, Qatar. Tel: +974 4403 5591. Fax: +974 4403 5551. Email: daoud.a@qu.edu.qa. ORCID: <https://orcid.org/0000-0001-7791-954X>

Number of words (manuscript): 3,410

Number of words (abstract): 248

Abstract

Background: Clinical pharmacists play a key role in ensuring the optimum use of cancer medicines. Yet, the economic benefit of this role has never been assessed in Qatar.

Aim: To evaluate the overall economic impact of clinical pharmacist interventions in the main cancer care setting in Qatar.

Methods: From the public healthcare perspective, this was an analysis of the total economic benefit and a cost-benefit analysis of the clinical pharmacy interventions. As a study sample size, patient records in March 2018, July/August 2018, and January 2019 were retrospectively reviewed at the National Center for Cancer Care & Research (NCCCR), Qatar. The total benefit from interventions was the total of the cost avoidance due to preventable adverse drug events (ADEs) plus the cost savings associated with therapeutic interventions. The interventions cost was based on salary and increased cost due to therapeutic interventions. The cost-benefit analysis results were presented via net benefit and benefit-to-cost ratio measures.

Results: Total of 1,352 interventions occurred during the 3-month follow-up period. The total benefit was QAR 196,010,360 (USD53,834,206), constituting cost avoidance of QAR 194,764,534 (USD 53,492,040) and cost savings of QAR 1,245,826 (USD 342,166), mostly due to recommending additional medications and the medication dose reduction. The benefit-to-cost ratio was 174:1 and the annual net benefit was QAR 779,539,440 (USD 214,100,351). Sensitivity analyses confirmed the robustness of results.

Conclusion: The clinical pharmacist intervention is a cost-beneficial practice in the NCCCR setting, associated with ADEs prevention and substantial economic benefits, including relative to the interventions cost.

Keywords: Clinical pharmacist intervention, cancer, economic benefit, cost-benefit, cost saving, cost avoidance, adverse drug event

Impact of findings on practice statements:

- The clinical interventions performed by clinical pharmacists successfully prevent adverse drug events (ADEs) that are associated with substantial net benefit, adding to QAR 779,539,440 (USD 214,100,351) per year, with an associated long-term return to investment at a rate of 174:1.
- Our results suggest that the intervention role of clinical pharmacists should be expanded, given that the majority of interventions prevented ADEs, generating cost savings. Also demonstrated, in parallel to the clinical pharmacist interventions, is the potential need for continuous education on cancer therapies and an improved implantation of clinical pathways.

Introduction

The irrational use of medication is a foremost worldwide public health problem, with a considerable impact on clinical, humanistic, and economic outcomes [1]. The World Health Organization estimated that over 50% of all medications are associated with drug-related problems (DRPs), which is described as 'an event including drug therapy which can actually and potentially interfere with optimal health outcomes' [2–4].

Managing cancer patients is complex, and patients are more susceptible to developing DRPs due to narrow therapeutic index of some cancer medications with a high incidence of toxicity[5,6]. Drug–disease and drug-drug interactions among chemotherapy agents and daily treatments, or adjuvant regimens, may also cause severe adverse drug events (ADEs), defined as 'injuries resulting from the use of a drug' [4], and extend hospital stay with a substantial economic burden [7].

The pharmacist role has grown substantially from primarily focusing on the operational activities of the pharmacy profession to being involved in direct patient care[7]. The clinical pharmacist intervention is one of the most critical approaches used to avoid ADEs in practices. The actions developed by the clinical pharmacists through reviewing medication orders and intervening when needed are tremendously significant. These actions include but are not limited to identifying and managing DRPs, ensuring better utilization of medications, to eventually reduce the risk of unfavorable ADEs, which in turn reduces the healthcare costs [8]. Indeed, previous studies reporting pharmacists' participation in the cancer setting have demonstrated improved quality of care [9–11]. However, recruiting clinical pharmacists as well as implementing the interventions themselves can come with added costs that may offset any cost savings produced by the prevention of ADEs.

Aim

In this study, therefore, we sought to perform a first-time evaluation of the economic impact and cost-benefit of the clinical pharmacist interventions for DRPs in the cancer care units at the National Center for Cancer Care and Research (NCCCR) in Qatar.

Ethics approval

The study was approved by the Medical Research Center, HMC (MRC-01-19-110).

Methods

Study setting

The study was conducted at the NCCCR in Hamad Medical Corporation (HMC), the main provider of secondary and tertiary healthcare in Qatar. NCCCR is the leading cancer hospital in Qatar, with 91 beds, and it offers a range of specialized services [12].

Study design

The study is a retrospective review of clinical pharmacist interventions, defined as any action by a pharmacist that directly resulted in a change to patient management or therapy [13]. All clinical interventions were directly obtained via the clinical intervention sheet, which is included in each patient record in the Cerner electronic medical database. When relevant data was not found in the clinical intervention sheet, data was directly obtained from the Cerner medical record of the patient.

Study population

The targeted clinical pharmacist interventions in this study were based on those performed in patients admitted to the inpatient wards in the oncology, hematology, urgent care, and palliative care units. The

study sample was based on interventions that occurred among hospitalized patients in inpatient wards during a 3-month sample size period (in March 2018, from July 15 to August 15, 2018, and in January 2019).

Inclusion criteria:

- Clinical pharmacist interventions during a 3 month follow-up period (in March 2018, from July 15 to August 15, 2018, and in January 2019).
- All the interventions that were performed by clinical pharmacists or clinical pharmacist specialists.
- All interventional recommendations to physicians that were based on evidence. To note, clinical pharmacists have to include evidence in support of their interventions for consideration by physicians before approving the interventions.
- The interventional recommendations that were accepted by the physicians.

Exclusion criteria:

- Interventions documented by the operational pharmacists.

Outcome

The main outcome of this study was to evaluate the cost-benefit of preventable ADEs through interventions by clinical pharmacists. Preventable ADEs occur due to a medication error that reaches the patient and result in any degree of harm [14]. The 'cost' is defined as the cost of hiring the clinical pharmacist as well as any increase in the cost of the course of therapy because of an intervention. The 'benefit' is the economic value of ADEs avoided because of interventions as well as any decrease in the cost of the course of therapy because of an intervention.

Economic evaluation

Cost of intervention

The cost of the intervention was calculated based on the sum of the salary of clinical pharmacists, added to any increased cost of therapy associated with the administration of intervention. The basic monthly salary of a clinical pharmacy in Qatar is estimated to be around QAR20,000 (USD5,493). For the current study, however, calculations were based on an overestimated monthly salary of QAR30,000 (USD8,239). Details of the cost of interventions calculations can be seen in Supplementary Information S1. As per the duration of study follow up, the cost of intervention over 3 months was calculated.

Cost savings

Cost savings based on the clinical pharmacist interventions were the reduced cost of therapy associated with therapy changes due to the intervention. Details of the cost savings calculations can be seen in Supplementary Information S1. As per the duration of study follow up, the cost saving over 3 months was calculated.

Cost avoidance

Cost avoidance was the cost avoided by eliminating the occurrence of ADEs as a consequence of the clinical pharmacist interventions [15]. Based on the method of Nesbit et al., the likelihood of an ADE in the absence of the intervention was determined at 0 (none), 0.01 (very low), 0.1 (low), 0.4 (medium), or 0.6 (high). The description of Nesbit et al. method is shown in Supplementary Information S2. The cost of an ADE was calculated based on the conservative assumption that an ADE will lead to an additional 2 days of hospital stay in the relevant unit, which is consistent with previous studies [16]. Further details of the cost avoidance calculations can be seen in Supplementary Information S1. As per the duration of study follow up, the cost avoidance over 3 months was calculated.

Cost-benefit analysis

Results of the cost-benefit analysis were presented in terms of the total benefit, the benefit-to-cost ratio, and the net benefit of the intervention, which was calculated in 3-monthly and annual values. Cost is the cost of the interventions, while the total monetary value of the benefit of the interventions was calculated as the sum of the cost savings and the cost avoidance associated with the interventions.

Expert panel

In accordance with the Nesbit et al. method, an expert panel was used to identify the probabilities of ADEs in the absence of interventions [15]. The panel was of four clinical pharmacists who have over 5 years of clinical experience in the area of cancer and its therapies, whereby each provided an estimate of the likelihood of an ADE in the absence of an intervention. The average ADE probability in the absence of each of the interventions was calculated.

Perspective

The study was conducted from the perspective of the public NCCCR hospital. Thus, only direct medical costs were considered in the analysis.

Cost inputs

The monetary values of resources were calculated, where the cost of medications, non-medication-based resources such as laboratory and diagnostic tests, and hospital stay were obtained via the pharmacy and the finance and costing departments at HMC. The salary values of clinical pharmacists and clinical pharmacy specialists were derived from the human resources of HMC. All costs were adjusted to the financial year 2021, utilizing the Qatari health Consumer Price Index [17], and were presented in Qatari Riyal (QAR) and the United States Dollar (USD).

Sample size

All clinical pharmacist interventions documented during the 3-month follow-up period of the study were included in the analysis. This study is not comparative and there are no relevant sample size calculations for the purpose of analysis. There is also no standardization in relation to the sample size used in similar literature studies as this is based on a variety of factors, including size of setting and prevalence of the underlying conditions. Unlike clinical research, economic evaluations like the current one are not concerned with hypothesis testing, but they are about making a cost estimation. Here, even if an economic evaluation is underpowered, it still provides important information that guides decision making [18–20].

To enhance how representative the sample size of the population is, the sample size was based on the first month after the annual staff performance evaluation in NCCCR, the last month in the year before the annual performance evaluation, and the middle month of the year. This is as it is always possible that how vigilant pharmacists are and the prevalence of interventions by clinical pharmacists are affected during the institutional review process of the performance of the clinical pharmacists. There is no evidence of such a pattern in the clinical pharmacy practices, and this sampling is only precautionary.

Statistical Analysis

Data were tabulated for each patient and analyzed using the IBM SPSS (Statistical Package for the Social Sciences) version-24. The data were presented as numerical and percentage measures for categorical variables and as mean and standard deviation measures for continuous variables. Kruskal–Wallis and Chi-Square tests were used to detect any significant differences among the three sample size groups, i.e. March 2018, July/August 2018, and January 2019.

Sensitivity analysis

One-way and multivariate sensitivity analyses were used to assess the impact of uncertainty in the base-case values of variables in relation to the costs and ADEs probabilities, to enhance the robustness/generalizability of the study conclusion.

One-way sensitivity analysis was performed to target values of individual uncertain input variables to analyze the effect of uncertainty on the study conclusion. Targeted uncertain inputs included the clinical pharmacist salary and the cost of the ADE, using an assigned $\pm 20\%$ uncertainty range.

Multivariate uncertainty analysis was performed by targeting several underlying uncertain probabilistic inputs in the economic model before re-running the model several times, for a distribution of the model results to be generated. Here, the probabilistic inputs of interest were the probabilities of the avoided ADEs set by the expert panel, using an assigned $\pm 15\%$ uncertainty range for any probability.

Both sensitivity analyses were conducted via Monte Carlo simulation (1000 iterations), using @Risk-5.7 (Palisade Corporation, NY).

Results

Characteristics of patients and interventions

A total of 1,352 interventions in 1,352 patients occurred during the study follow-up period. The mean patient age was 47 years. Among the study population, 59.39% were male. Interventions that were related to oncology comprised majority of interventions (73.52%), followed by hematology interventions (15.31%).

Overall, as per the categorization of interventions in the patient clinical intervention sheet, the most common interventions by the clinical pharmacists were related to the appropriateness of therapy (78.1%),

followed by interventions related to dosing and administration (16.2%), contraindication and safety (3.18%), drug interaction (1.48%), and duplicate therapy (1.04%).

There were no significant differences between the study groups except with regards to the ward type (Table 1).

Supplementary Information S3 presents a summary of the categories of the interventions types, including study examples, and the associated average probability of avoided ADEs as per category.

Economic analysis

Cost of intervention

Based on interventions performed in the current study, a clinical pharmacist performed an average of 250 interventions over the 3-month study period. Based on total number of interventions in the current study, 6 clinical pharmacists were needed, where the overall salary of the clinical pharmacists was calculated to be QAR180,000 (USD49,437). For the added cost associated with therapeutic interventions for the DRPs over a 3-month period, this was QAR945,500 (USD259,681). The total cost of the intervention over the 3-month study period is, therefore, adding to QAR1,125,500 (USD309,118). The added cost with interventions as per different intervention type categories can be seen in Table 2.

Cost saving

The overall cost saving was QAR1,245,826 (USD 342,166). Cost saving as per different intervention type categories can be seen in Table 2.

Cost avoidance

An average probability of 0.03 was calculated for each of 3 interventions, an average of 0.1 was calculated for each of 541 interventions, an average of 0.2 was calculated for each of 406 interventions, an average of 0.3 for each of 347 interventions, an average of 0.4 for each of 46 interventions, and an average of 0.5 is the estimated probability with each of 9 interventions. The overall cost avoidance due to the

218 interventions over a 3-month period was QAR194,764,534 (USD53,492,040). Table 2 summarizes cost
219 avoidance associated with each type of intervention category.

220 *Cost-benefit analysis*

221 The total benefit due to the interventions over a 3-month period was QAR196,010,360 (USD 53,834,206).
222 The benefit-to-cost ratio was 174:1, where for every QAR1 (USD0.27) invested into the clinical pharmacist
223 interventions approach, a QAR174 (USD48) of benefit is generated. The net benefit was QAR 194,884,860
224 (USD53,525,089) per 3 months and QAR779,539,440 (USD214,100,351) per 1 year of intervention
225 practices. Overall costs and cost-benefit calculations are summarized in Table 3.

226 **Sensitivity analysis**

227 The outcome of the economic model was insensitive to uncertainty in the clinical pharmacist salary and
228 in the cost of the ADE.

229 Multivariate sensitivity analysis demonstrated that there is a 100% probability that the pharmacist
230 intervention is associated with positive a 3-monthly net benefit and total benefit (Fig.1a) and an annual
231 net benefit (Fig. 1b). Furthermore, as illustrated in Fig. 1c, the analysis showed that there is a 100%
232 probability that the pharmacist intervention is associated with an >1 benefit to cost ratio.

233 Input uncertainties and sampling distributions used in the one-way and multivariate sensitivity analyses,
234 and the details of their outcomes, are shown in Table 4.

235 A regression Tornado analysis revealed that the main driver of the outcome was the cost of ADE, followed
236 by the 0.3 probability of avoided ADE (Fig. 2).

237

238 **Discussion**

This study was conducted for the purpose of evaluating the cost-benefit of managing DRPs of cancer units at NCCCR for the prevention of ADEs among hospitalized cancer patients in Qatar. This is the first cost-benefit study of clinical pharmacist interventions in Qatar. Our study revealed that clinical pharmacist interventions could significantly reduce the incidence of ADEs, which may result in a net benefit of QAR779,539,440 (USD214,100,351). The majority of the DRPs were related to the appropriateness of therapy, followed by DRPs related to dosing and administration.

Apart from the economic impact of cancer pharmacy interventions in optimizing outpatient practices, there are few published studies on the economic impact of clinical pharmacy interventions in the inpatient clinical cancer setting. Gregori et al. recently suggested that the total cost saving of inpatient cancer pharmacy interventions contributed to €175,563 for a total of 1,970 interventions, corresponding to an average cost avoidance of €390,480. Similar to our results, the cost of ADE was the key driver affecting the outcome [9]. This study, however, was prospective and only included oncology and hematology interventions among patients receiving first injectable chemotherapy and/or immunotherapy regimen. Also different from our study, in the retrospective study by Zecchini et al., the cost saving of inpatient cancer pharmacy interventions was only evaluated for injectable cancer medications, which led to €15,096 for a total of 237 interventions, limited relative to results in our study where we evaluated all cancer medications regardless of the antineoplastic dosage form [10]. In a prospective, pilot study at an inpatient ambulatory oncology unit in the United States, by Randolph et al., only the cost avoidance of DRPs was evaluated, calculating an annual cost avoidance of USD282,741 per pharmacist, resulting in a net benefit of USD138,441 (19).

The probability of preventable ADE was determined using the Nesbit et al. method, which provides the best source to estimate the probability of avoidable ADEs [15,16,18,19,21], which was based on average scores provided by the four clinical pharmacists. Most of the estimated probability scores were low, which is consistent with relevant literature studies adopting the same methods [19,22,23].

263 The estimated cost saving was calculated conservatively based on the 90-day prescription refills cost of
264 the intervened chronic medications and as per the prescriber order or the local protocol for acute medical
265 conditions. Regardless of the DRPs and how they vary in severity and duration, they are uniformly
266 compared based on the value of the ADEs associated with them. While the literature reported that ADEs
267 might cause more than two days of hospital admission (i.e. 4.6 days) [23], the estimated cost avoidance
268 was calculated conservatively by considering only two additional days of hospital stay if ADEs occurred.
269 Considering longer hospital stays in the current study will only further increase the economic benefit of
270 the interventions.

271 In agreement with one previous study [24], the most frequent type of DRPs intercepted by clinical
272 pharmacists was related to inappropriate therapy, which made 78% of interventions. The addition of
273 another medication and decreasing medication doses were the main resource use changes that resulted
274 in cost saving and cost avoidance. The dose of most antineoplastic drugs is mainly based on the calculated
275 body surface area, which should be recalculated based on weight change. This may be missed by
276 physicians [25]. Another example was related to adding antiemetics to prevent chemotherapy-induced
277 nausea and vomiting, which remain the main issue for many cancer patients [26]. Also an example is the
278 leucovorin rescue, which was added to all patients receiving the high dose methotrexate to prevent
279 toxicity [27].

280 Our study demonstrated the importance of individualized therapy, especially in relation to the adjustment
281 of dose. Some of our study population is comprised of critically ill patients where the incidence of renal
282 disease is frequently high, and the dose adjustment of medications is required [28]. This type of
283 intervention resulted in a total cost saving of QAR22,088 (USD6,066) and cost avoidance of
284 QAR23,772,983 (USD652,924).

285 Discontinuation of inappropriate or unnecessary medicine also comprised a high percentage (~22%) of
286 interventions. It led to cost saving of QAR364,987 (USD100,243) and a cost avoidance of QAR 180,101,227
287 (USD49,464,783). This is consistent with the literature, where, for example, LaPointe et al. showed over
288 35% of interventions to be due to wrong medications [29].

289 Clinical pharmacists also play an important role in disease-related problems. Indeed, the deployment of
290 clinical pharmacists in clinical rounds led in our study to recommend interventions related to laboratory
291 testing such as therapeutic drug monitoring, diagnostic, and culture tests, which resulted in a cost saving
292 of QAR23,807 (USD6,539) and a cost avoidance of QAR45,025,307 (USD12,366,192).

293 This study is not without limitations. The cost-benefit might be over or underestimated due to the nature
294 of the retrospective study design, which has the inherent limitation of missing data, especially as daily
295 reporting of interventions is not mandatory. Furthermore, the clinical outcome of patients, wherein
296 clinical pharmacists intervened, were only analyzed using the probabilities of avoidable ADEs, which may
297 not reflect the real impact of interventions beyond the ADEs. In addition, the cost of ADEs was calculated
298 with the assumption that it is equal among the different ADEs, universally associated with an additional
299 two days of hospital stay. As already discussed in methods, however, this is justified, especially since it is
300 impossible to follow up patients until the end of intervention consequences that never took place. Also,
301 in our study, a 3-month follow-up duration may not accurately represent the real economic benefits over
302 one year. However, given how the 3-month follow up was selected as a sample size, as already discussed
303 above, and given the lack of significant differences in patient characteristics between the 3 months of the
304 follow-up duration, there is no reason to assume that the remaining months of the year will differ and
305 that results from the study's 3-month follow-up cannot be extrapolated to calculate an annual benefit.
306 Finally, while the comprehensive one-way and multivariate sensitivity analyses performed would
307 considerably increase the robustness and generalizability of results beyond the study setting, our results

308 will need to be considered with caution by other settings, given that the resource utilization and costs can
309 considerably differ.

310 Given that the NCCCR is only one of several specialized hospitals under the HMC in Qatar, among which
311 the nature and quantity of interventions considerably vary, similar evaluations to the current one would
312 ideally be also required to better understand the impact of the pharmacy interventions in the different
313 HMC inpatient clinical settings.

314

315 **Conclusion**

316 Based on the study assumptions and setting, the clinical interventions performed by clinical pharmacists
317 successfully prevent ADEs that are associated with substantial net benefit with an associated long-term
318 return to investment. These results suggest that the intervention role of clinical pharmacists should be
319 expanded, given that the majority of interventions prevented ADEs, generating cost savings. Also
320 demonstrated, in parallel to the clinical pharmacist interventions, is the potential need for continuous
321 education on cancer therapies and an improved implantation of clinical pathways.

322

References

1. le Grand A, Hogerzeil H V, Haaijer-Ruskamp FM. Intervention research in rational use of drugs: a review. *Health Policy Plan. England*; 1999;14:89–102. <https://doi10.1093/heapol/14.2.89>
2. Foroughinia F, Tazarehie SR, Petramfar P. Detecting and managing drug-related problems in the neurology ward of a tertiary care teaching hospital in Iran: A clinical pharmacist's intervention. *J Res Pharm Pract.* 2016;5:285–9. <https://doi10.4103/2279-042X.192455>
3. Geneva. World Health Organization (WHO). The role of education in the rational use of medication. 2006.
4. Bailey C, Peddie D, Wickham ME, et al. Adverse drug event reporting systems: a systematic review. *Br J Clin Pharmacol.* 2016;82:17–29. <https://doi10.1111/bcp.12944>
5. Chopra D, Rehan HS, Sharma V, et al. Chemotherapy-induced adverse drug reactions in oncology patients: A prospective observational survey. *Indian J Med Paediatr Oncol Off J Indian Soc Med Paediatr Oncol.* 2016;37:42–6. <https://doi10.4103/0971-5851.177015>
6. Monestime S, Page R, Jordan WM, et al. Prevalence and predictors of patients reporting adverse drug reactions to health care providers during oral targeted cancer treatment. *J Am Pharm Assoc.* 2021;61:53–9. <https://doi.org/10.1016/j.japh.2020.09.001>
7. Blouin RA, Adams ML. The Role of the Pharmacist in Health Care: Expanding and Evolving. *N C Med J. United States*; 2017;78:165–7. <https://doi10.18043/ncm.78.3.165>
8. Al-Qudah RA, Al-Badriyeh D, Al-Ali FM, et al. Cost-benefit analysis of clinical pharmacist intervention in preventing adverse drug events in the general chronic diseases outpatients. *J Eval Clin Pract. England*; 2020;26:115–24. <https://doi10.1111/jep.13209>
9. 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 Off Publ Int Soc Oncol Pharm Pract. England*; 2020;26:1172–9. <https://doi.org/10.1177/1078155220915763>

10. 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;20:113. <https://doi.org/10.1186/s12913-020-4963-7>

11. Delpeuch A, Leveque D, Gourieux B, et al. Impact of clinical pharmacy services in a hematology/oncology inpatient setting. *Anticancer Res. Greece*; 2015;35:457–60.

12. Mohsen H, Haddad P, Allam A, et al. Patterns in place of cancer death in the State of Qatar: a population-based study. *PLoS One. Public Library of Science*; 2014;9:e109615–e109615. <https://doi.org/10.1371/journal.pone.0109615>

13. 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;57:513–21. <https://doi.org/10.1046/j.1365-2125.2003.02029.x>

14. Garrouste-Orgeas M, Philippart F, Bruel C, et al. Overview of medical errors and adverse events. *Ann Intensive Care. Springer*; 2012;2:2. <https://doi.org/10.1186/2110-5820-2-2>

15. Nesbit TW, Shermock KM, Bobek MB, et al. Implementation and pharmacoeconomic analysis of a clinical staff pharmacist practice model. *Am J Heal Pharm AJHP Off J Am Soc Heal Pharm. England*; 2001;58:784–90. <https://doi.org/10.1093/ajhp/58.9.784>

16. Chen C-C, Hsiao F-Y, Shen L-J, et al. The cost-saving effect and prevention of medication errors by clinical pharmacist intervention in a nephrology unit. *Medicine (Baltimore).* 2017;96:e7883. <https://doi.org/10.1097/MD.0000000000007883>

17. Qatar Inflation Rate. 2021. Available from: <https://tradingeconomics.com/qatar/inflation-cpi>.

367 Accessed 15 October 2021

368 18. Sebaaly J, Parsons LB, Pilch NAW, et al. Clinical and Financial Impact of Pharmacist Involvement in
369 Discharge Medication Reconciliation at an Academic Medical Center: A Prospective Pilot Study. *Hosp*
370 *Pharm.* 2015;50:505–13. <https://doi.org/10.1310/hpj5006-505>

371 19. Gallagher J, Byrne S, Woods N, et al. Cost-outcome description of clinical pharmacist interventions in
372 a university teaching hospital. *BMC Health Serv Res.* 2014;14:177. [https://doi.org/10.1186/1472-6963-14-](https://doi.org/10.1186/1472-6963-14-177)
373 177

374 20. Branham AR, Katz AJ, Moose JS, et al. Retrospective analysis of estimated cost avoidance following
375 pharmacist-provided medication therapy management services. *J Pharm Pract. United States;*
376 2013;26:420–7. <https://doi.org/10.1177/0897190012465992>

377 21. Hirsch JD, Bounthavong M, Arjmand A, et al. Estimated Cost-Effectiveness, Cost Benefit, and Risk
378 Reduction Associated with an Endocrinologist-Pharmacist Diabetes Intense Medical Management
379 “Tune-Up” Clinic. *J Manag care Spec Pharm. United States;* 2017;23:318–26.
380 <https://doi.org/10.18553/jmcp.2017.23.3.318>

381 22. Han J-M, Ah Y-M, Suh SY, et al. Clinical and economic impact of pharmacists’ intervention in a large
382 volume chemotherapy preparation unit. *Int J Clin Pharm. Netherlands;* 2016;38:1124–32.
383 <https://doi.org/10.1007/s11096-016-0339-9>

384 23. Bates DW, Spell N, Cullen DJ, et al. The costs of adverse drug events in hospitalized patients. Adverse
385 Drug Events Prevention Study Group. *JAMA. United States;* 1997;277:307–11.

386 24. Allard J, Carthey J, Cope J, et al. Medication errors: causes, prevention and reduction. *Br J Haematol.*
387 *England;* 2002;116:255–65. <https://doi.org/10.1046/j.1365-2141.2002.03272>.

388 25. Body surface area for adjustment of drug dose. *Drug Ther Bull [Internet].* 2010;48:33 LP – 36.

389 Available from: <http://dtb.bmj.com/content/48/3/33.abstract><https://doi.org/10.1136/dtb.2010.01.0002>

390 26. Gupta K, Walton R, Kataria SP. Chemotherapy-Induced Nausea and Vomiting: Pathogenesis,
391 Recommendations, and New Trends. *Cancer Treat Res Commun.* 2021;26:100278.
392 <https://doi.org/10.1016/j.ctarc.2020.100278>

393 27. Howard SC, McCormick J, Pui C-H, et al. Preventing and Managing Toxicities of High-Dose
394 Methotrexate. *Oncologist.* 2016/08/05. AlphaMed Press; 2016;21:1471–82.
395 <https://doi.org/10.1634/theoncologist.2015-0164>

396 28. Wilkins RG, Faragher EB. Acute renal failure in an intensive care unit: incidence, prediction and
397 outcome. *Anaesthesia.* England; 1983;38:628–34. <https://doi.org/10.1111/j.1365-2044.1983.tb12153.x>

398 29. LaPointe NMA, Jollis JG. Medication errors in hospitalized cardiovascular patients. *Arch Intern Med.*
399 United States; 2003;163:1461–6. <https://doi.org/10.1001/archinte.163.12.1461>

400

401

402

403

404

405

406

407

408

Fig.1a Net and Total Benefits (Million Qatari Riyal, QAR). 1 USD = 3.65 QAR

Fig.1b Net Benefit (Million Qatari Riyal, QAR). 1 USD = 3.65 QAR

Fig.1c Benefit To Cost Ratio

Figure 1. Probability curves of economic impact results

415 Figure 2. A regression tornado diagram of elements and their effect on the outcome

416

417 Table 1. Patients' demographics among the study periods

		March 2018	July-August 2018	January 2019	P value
		(n=463)	(n=309)	(n=580)	
Variable	Average (± standard deviation) / frequency (%)				
Gender					
Male	803 (59.39%)	258 (55.72)	188 (60.84)	355 (61.21)	0.16
Female	549 (40.6%)	205 (44.28)	121 (39.16)	225 (38.79)	
Age	47 ± 16.19	49.39 ± 15.12	48.15 ± 15.7	44.61 ± 16.93	0.21
Weight	70.17 ± 19.77	72.17 ± 21.38	68.79 ± 17.64	69.27 ± 21.21	0.11
Nationality					
Arab	690 (51.04%)	237 (51.19)	166 (53.72)	286 (49.31)	0.17
Asian (non-Arab)	567 (41.94%)	194 (41.9)	114 (36.89)	258 (44.48)	
African (non-Arab)	36 (2.66%)	10 (2.16)	14 (4.53)	12 (2.07)	
Others	59 (4.36%)	22 (4.75)	15 (4.85)	24 (4.14)	
Ward type					
Oncology	994 (73.52%)	358 (77.32)	176 (56.96)	460 (79.31)	0.003

Hematology	207 (15.31%)	67 (14.47)	65 (21.04)	62 (10.69)	
Palliative care	149 (11.02%)	36 (7.78)	65 (21.04)	47 (8.1)	
Critical care	2 (0.15%)	2 (0.43)	3 (0.97)	11 (1.9)	

418

419 Table 2. Added cost, cost saving, and cost avoidance for clinical pharmacist intervention types.

Type of interventions	Overall added cost with interventions, QAR (USD)	Overall saving, QAR (USD)	Overall cost avoidance, QAR (USD)
Addition of another medication	1,560,419 (428,569)	0	35,052,450 (9,627,148)
Discontinuation of a medication	109,924 (30,191)	23,807 (6,539)	45,025,307 (12,366,192)
Switching to alternative medication	206,805 (56,799)	190,799 (52,403)	18,202,132 (4,999,212)
Addition of a prophylactic agent during hospitalization	599,698 (164,707)	0	31,875,257 (8,754,533)
Change in medication route	156 (43)	16,732 (4,595)	2,421,641 (665,103)
Change in medication strength	0	2,488 (683)	47,357 (13,007)
Therapeutic drug monitoring	900 (247)	0	5,191,999 (1,425,981)
Change in medication dose	9,568 (2,628)	13,890 (3,815)	13,302,882 (3,653,634)
Change in medication duration	4,589 (1,260)	2,162 (594)	4,378,328 (1,202,507)
Change in medication frequency	765 (210)	6,036 (1,658)	6,091,773 (1,673,104)
Addition of a lab test	4,286 (1,177)	0	13,957,264 (3,833,360)
Addition of a diagnostic test	1,638 (450)	0	1,571,376 (431,578)

Addition of a culture test	480 (132)	0	968,657 (266,041)
Addition of a vaccine	0	0	0

*QAR: Qatari Riyal, USD: United States Dollar

Table 3. Outcomes of cost-benefit analysis

Outcome	Value, QAR (USD)
Salary of the clinical pharmacists per 3 months	180,000 (49,437)
The added cost with therapy interventions per 3 months	945,500 (259,681)
Overall cost of intervention per 3 months	1,125,500 (309,118)
Overall cost saving per 3 months	1,245,826 (342,166)
Overall cost avoidance per 3 months	194,764,534 (53,492,040)
Net benefit per 3-month	194,884,860 (53,525,088)
Net benefit per 1-year	779,539,440 (214,100,351)
Benefit-to-cost ratio	174:1
Total benefit per 3 months	196,010,360 (53,834,206)

*QAR: Qatari Riyal, USD: United States Dollar

429 Table 4. Uncertainty distributions used for one-way and probabilistic sensitivity analysis, and their
 430 outcomes

Variable	Point estimate, QAR (USD)	Variation range, QAR (USD)	Net benefit per 1 year range, QAR (USD)	Benefit to cost ratio	Total benefit per 3-month, QAR (USD)
One-way sensitivity analysis					
Salary of clinical pharmacist	30,000 (8,239)	Triangular distribution (QAR 24,000,30,000,36,000) (USD 6,592, 8,239, 9,887)	Mean: 779,539,440 (USD 214,100,351), 95% CI 779,401,581 to 779,678,323 (USD 214,062,488 to 214,138,495)	Mean: 174, 95% CI 169 to 180	Mean: 196,011,842 (USD 53,834,613), 95% CI 157,971,465 to 234,026,797 (USD 43,386,831 to 64,275,413)
Cost of adverse drug event	9,359 (2,570)	Triangular distribution (QAR 8,423,9,359,10,295) (USD 2313, 2,570, 2,828)	Mean: 779,552,059 (USD 214,103,817), 95% CI 626,969,446 to 934,425,777	Mean: 174, 95% CI 141 to 208	Mean: 196,008,409 (USD 53,833,670), 95% CI 158,165,714 to 233,236,517 (USD

			(USD 172,197,033 to 256,639,853)		43,440,182 to 64,058,363)
Multivariate uncertainty analysis					
Very low probability for ADE	0.03	Triangular distribution (0.025,0.03,0.035)	Mean: 843,766,754	Mean: 188, 95% CI 155 to 231	Mean: 212,096,666 (USD 58,252,30), 95% CI 171,962,981 to 257,301,517 (USD 47,229,598 to 70,667,810)
Low probability for ADE	0.1	Triangular distribution (0.09,0.1,0.11)	(USD 231,740,370),		
Low to moderate probability for ADE	0.2	Triangular distribution (0.17,0.2,0.23)	95% CI 838,336,934 to		
Low to moderate probability for ADE	0.3	Triangular distribution (0.26,0.3,0.35)	848,401,062 (USD		
Moderate probability for ADE	0.4	Triangular distribution (0.35,0.4,0.46)	230,249,071 to 233,013,182)		
Moderate to high probability for ADE	0.5	Triangular distribution (0.43,0.5,0.58)			

431 *QAR: Qatari Riyal, USD: United States Dollar, CI: confidence interval

432

433

434

435

436

437 **Statements and Declarations**

438 **Acknowledgements**

439 None.

440 **Funding**

441 This work was supported by Medical Research Center, Hamad Medical Corporation [grant number (MRC-
442 01-19-110)].

443 **Competing Interests**

444 The authors have no relevant financial or non-financial conflicting interests to disclose.

445

446 **Author Contributions**

447 DA contributed to the study conception and design, data validation, data analysis and interpretation, and
448 wrote the first draft of manuscript. DB led the study conception and design, and contributed to data
449 analysis and interpretation. AG contributed to the data collection. AH, PA, MA, WE, and ME facilitated the
450 planning and carrying out of the study. All authors contributed to the final version of manuscript.

451

452 **Ethics approval**

453 This study was performed in line with the principles of the Declaration of Helsinki. Approval was granted
454 by the Medical Research Center, Hamad Medical Corporation (MRC-01-19-110).

455 **Consent to participate**

456 None.

457

458

Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- [SupplementaryInformationS1.pdf](#)
- [SupplementaryInformationS2.pdf](#)
- [SupplementaryInformationS3.pdf](#)