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# Implementation of Pharmaceutical Practice Guidelines by a Project Model Based

## Clinical and Economic Impact

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**Abstract:** All around the world a few studies have been found on the effect of guideline implementation on direct medications' expenditure. The goal of this study was to evaluate cost savings of guideline implementation among patients who had to receive 3 costly medications including albumin, enoxaparin, and pantoprazole in a tertiary hospital in Shiraz, Iran.

An 8-month prospective study was performed in 2 groups; group 1 as an observational group (control group) in 4 months from June to September 2014 and group 2 as an interventional group from October 2014 to January 2015.

For group 1 the pattern of costly medications usage was determined without any intervention. For group 2, after guideline implementation, the economic impact was evaluated by making comparisons between the data achieved from the 2 groups.

A total of 12,680 patients were evaluated during this study (6470 in group 1; 6210 in group 2). The reduction in the total value of costly administered drugs was 56% after guideline implementation. Such reduction in inappropriate prescribing accounts for the saving of 85,625 United States dollars (USD) monthly and estimated 1,027,500 USD annually.

Guideline implementation could improve the adherence of evidence-based drug utilization and resulted in significant cost savings in a major teaching medical center via a decrease in inappropriate prescribing of costly medications.

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**Abbreviations**: GI = Gastrointestinal, HIS = hospital information system, LOS = Length of hospital stay, PPI = Proton pump inhibitor, USD = United States dollar, VTE = venous thromboembolic events.

## INTRODUCTION

Due to increasing concern about unjustifiable variations in clinical practice for the same condition, clinical practice guidelines have attracted worldwide attention with the aim of improving people's health, and a desire to make the best use of available health resources.[1]

Carefully constructed practice guidelines can decrease the unnecessary use of costly medications. This concept has generated unprecedented interest across all medical specialties in the past decade.[2,3]

A major concern is implementations of these guidelines to ensure that they are incorporated in clinical practice and are actually used in clinical decision making.[4] Implementation of guidelines prevent medication errors significantly, improve appropriateness of prescription, and lead to significant cost saving.[5] The application of evidence-based practices will maximize benefit to the patient by achieving optimum treatment outcomes while reducing cost and decreasing possible risks due to side effects and drug interactions.[6]

Since there are a limited number of studies in assessing the implementation of clinical practice guidelines for decreasing drug expenditure,[7] we designed this study to examine the influence of guideline implementation on decreasing inappropriate use and consequently direct drug cost in a tertiary referral hospital. Decrease in patients' medical expenditure and rationalizing the administration of medicine were 2 dedicated goals of this project.

## MATERIALS AND METHODS

In May 2014, a consensus was developed in Shahid Faghihi Hospital regarding the need to control costly medications' use. This hospital is a teaching referral hospital with 350 beds, affiliated to Shiraz University of Medical Sciences. The approval to this study was obtained from the institutional review board and HSR committee, office of vice chancellor for development of management and resources of Shiraz university of medical sciences (93-01-26-8297). Commenced in June 2014, an automated hospital information system (HIS) was used to identify the top costly medications in the mentioned hospital.

### Calculating Costs

At first it seemed necessary to compute the costs of drugs according to the prices at which they were obtained from the Department of Pharmacy. The only thing that was taken into consideration was the hospital's acquisition expenditures, while the nursing or pharmacy labor costs associated with costly drugs use were not included.

## Practice Guideline Implementation

The drugs which were targeted for practice guidelines implementation were those with largest budget (>10,000 USD/month) and wide use in the whole wards of hospital including albumin, pantoprazole, and enoxaparin.

An expert panel of different specialists (including internist, gastroenterologist, cardiologist, surgeon, neurologist, and clinical pharmacist) was formed to choose updated international consensus guidelines in literature that best matched local condition for the mentioned drugs.

Having selected international consensus guidelines for albumin,[8] enoxaparine,[9–11] and pantoprazole,[12] preprinted order forms were developed accordingly for these drugs.

The forms were presented to all faculty members, resident physicians and nurses who were involved in the administration of the target drugs, and their final comments were invited. To maximize physicians' adherence to the guidelines and evaluate their fidelity, several strategies[13] were employed including:

- the application of computer decision support program according to order forms;
- periodic audit and feedback based on one-on-one consulting and telephone calls; and
- interactive educational meetings.

In our study pool, demographic data, including age, sex, and admission wards, were obtained for each patient. It should be noted that the total number of albumin, enoxaparin, and pantoprazole that were administered for each patient during their hospital stay were recorded.

A control survey was performed in group 1 (pre-guideline implementation group) during the first 4 months to determine the appropriateness of target drug use in different wards based on selected guidelines.

At the start of guideline implementation, during the second 4 months in group 2, the hospital pharmacy began distributing target drugs according to the practice guidelines by confirmation of clinical pharmacist except in emergencies.

## Outcome Analysis

The preliminary purpose of this study was to decrease inappropriate utilization of costly medications after the implementation of the clinical-based guidelines. Secondary purpose included the differences in making significant impact on cost between 2 groups in pre and postguideline implementation phases.

Specific outcome criteria such as venous thromboembolic events (VTE), gastrointestinal (GI) bleeding, length of hospital stay (LOS), and mortality rate were evaluated at the end.

## Statistical Analysis

Chi-squared test and *t* test were applied for continuous and nominal data, where appropriate. Independent sample test was employed when appropriate, to compare the differences between pre and post-intervention. The results were compiled with SPSS version 20.0 (Systat Software, Inc., Chicago, IL), and descriptive statistics were analyzed. $P_v < 0.05$ were considered significant.

## RESULTS

## Patients' Size and Characteristics

A total of 12,680 patients were included in the 8-month study period, with 6470 and 6210 subjects representing the group 1 (pre-guideline implementation group) and group 2 (post-guidelinegroup 2 (postguideline implementation group), respectively. The mean (standard deviation, SD) age of the patients was 49.35 (6.30) years and 52.48% were female. No significant differences in age and sex distribution were found between the 2 groups (Table 1).

## Drug Utilization Review

The drugs that we targeted consisted of albumin, enoxaparin, and pantoprazole which represented only 5.81% of total number of hospital drugs; however, the sum of their cost accounted for 30.0% of the total pharmaceutical budget with an average of 152,000 USD/month (Table 2).

In order to determine the appropriateness of the target drugs use in different wards, we surveyed the prescriptions during 4 months in group 1. The results showed that 51.2% of albumin, 26% of enoxaparin, and 67% of pantoprazole administrations were inappropriate.

**TABLE 1.** Patient's Characteristics

| Variable | Group 1 | Group 2 | *P* Value |
|---|---|---|---|
| N | 6470 | 6210 | 0.95 |
| Age (yr ± SD) | 48.8 (5.4) | 49.9 (7.2) | 0.10 |
| Female, N (%) | 3364 (52.00) | 3291 (53.0) | 0.12 |
| Male, N (%) | 3106 (48.00) | 2919 (47.03) | 0.12 |
| | | | |
| Distribution in hospital wards, N (%) | | | |
| Intensive care unit | 561 (8.67) | 537 (8.65) | 0.93 |
| General surgery | 2455 (37.94) | 2347 (37.79) | 0.88 |
| Gynecology | 658 (10.17) | 681 (10.97) | 0.17 |
| Internal | 762 (11.78) | 728 (11.72) | 0.33 |
| Dermatology | 214 (3.31) | 219 (3.53) | 0.24 |
| Neurology | 528 (8.16) | 458 (7.37) | 0.11 |
| CCU | 377 (5.83) | 328 (5.28) | 0.36 |
| Cardio surgery | 915 (14.14) | 912 (14.69) | 0.37 |

CCU = coronary care unit, Group 1 = pre-guideline implementation, Group 2: post-guideline implementation, SD = standard deviation.

**TABLE 2.** Costly Drugs (Average Monthly Data) in Group 1 (Pre-guideline Implementation Group)

| Drugs | Cost of Drug (USD) Mean (SD) | Portion of Drug Number From Total Number of Hospital Drugs, % | Portion of Drug Cost From Total Pharmaceutical Budget, % |
|---|---|---|---|
| Albumin | 85,001.66 (926.21) | 1.94 | 5.19 |
| Enoxaparin | 7968.13 (19.27) | 3.20 | 1.94 |
| Pantoprazole | 27,090.11 (144.61) | 0.67 | 22.87 |
| Total | 151,693 (839.52) | 5.81 | 30.00 |

SD = standard deviation, USD = United States dollars.

**TABLE 3.** Comparison of Monthly Pharmaceutical Expenditure in Both Groups

| | Cost (USD) Mean (SD) | | Total Number of Unit Drug Used | | | |
|---|---|---|---|---|---|---|
| Drugs | Group 1 | Group 2 | Group 1 | Group 2 | Reduction of Unit Drug Used, % | $P_v$ |
| Albumin | 85,001.66 (926.21) | 49,028.82 (257.26) | 7106 | 4501 | 36 | <0.0001 |
| Enoxaparin | 7968.13 (19.27) | 5188.42 (45.26) | 4412 | 2952 | 33 | <0.0001 |
| Pantoprazole | 27,090.11 (144.61) | 15,459.42 (433.30) | 17,310 | 10,325 | 40 | <0.0001 |
| Total | 151,693 (839.52) | 66,068 (531.25) | 28,828 | 17,778 | 38 | <0.0001 |

Group 1 = pre-guideline implementation, Group 2 = post-guideline implementation, SD = standard deviation, USD = United States dollars.

## Pharmaceutical Savings as a Result of Practice Guidelines

In group 2, from October 2014 to January 2015, 2732 requests were made for these drugs. From which, 59.7% (1630/2732) were in accordance with guideline, whereas the other 40.3% (1102/2732) were the subject of intervention so the administration continuance were ceased and a feedback was given to the related physician in each case. The reduction in total number of drugs were 36%, 33%, and 40% in albumin, enoxaparin, and pantoprazole, respectively (Table 3, $P_v < 0.0001$).

The effects of practice guidelines on the monthly costs of the target drugs are shown in Table 3. (Costs are calculated in USD and they are not adjusted to inflation.)

Mean baseline pharmaceutical costs of the 3 target drugs were calculated to be $151,693 \pm 839.52$ USD/month, from June to September 2014 in group 1. After the implementation of practice guidelines, the pharmaceutical costs per month have been reduced to $66,068 \pm 531.25$ USD from October 2014 to January 2015 in group 2 ($P_v < 0.0001$; Table 3).

The estimated total annual costs of group 1 and group 2 were 1,820,316 USD and 792,816 USD, respectively, which translates into an estimated annual cost saving of 1,027,500 USD (85,625 USD/month).

Overall, in group 1 we had 1156 orders of the target drugs per month of which approximately 53.2% were inappropriate according to the guidelines. In group 2, after guideline implementation, the inappropriate administration was reduced to 34.2 % (683 orders monthly) that makes a significant difference ($P_v < 0/0001$). So the finding suggests that by implementation of guidelines the number of inappropriate drug orders can be significantly reduced and led to 65.8% physician's adherence to guidelines (Figure 1).

## Outcome Analysis

The reason for the overuse of the mentioned drugs is the physicians' attempt to decrease the incidence of GI bleeding, VTE, and post-surgery recovery time by correction of patients' hypo-albuminemia and consequently shortening LOS. Hence, in order to determine the consequence of reducing the target drugs overuse, we also proceeded to survey VTE, GI bleeding, VTE, raw, and pure death rate in groups 1 and 2.

The incidence of VTE was 1.31% (85/6470) in group 1 and 1.16% (72/6210) in group 2, while the difference was not statistically significant ($P_v = 0.49$). GI bleeding incidence was measured to be 0.61 % (40/6470) and 0.51% (32/6210) in groups 1 and 2, respectively. The results demonstrated a slight decrease in the incidence GI bleeding in group 2; however, it was not statistically significant as well ($P_v = 0.52$).

LOS (mean $\pm$ SD) was $11.43 \pm 6.64$ days in group 1 versus $11.79 \pm 6.57$ days in group 2 ($P_v = 0.95$).

In total number of patients surveyed, there was no statistically significant relationship between either LOS of the 2 groups ($P_v > 0.05$) or the raw and pure death rates ($P_v > 0.05$) (Table 4).

## DISCUSSION

This is the first study from Iran which evaluates the budget saving effect of a guideline implementation for selected costly medications. It should be noted that in healthcare systems, drug expenditure is one of the largest components of the entire hospital operating budget, and increases continuously at a faster pace than other healthcare expenditures.[14] Hence, drug costs remain as an area of focus for cost containment initiatives and clinical practice guidelines that attract significant attention of hospital managers.[15]

Inappropriate use of drugs is reported with varying degrees depending on the drug type and institution. According to a report from Food and Drug Organization of Health Ministry in 2008 in Iran, the highest cost paid for a single drug which was used in hospitals was devoted to albumin.[16] Results from our study showed that based on guideline, 51.2% of albumin prescriptions had not been appropriately administered.

In the past few years, some studies in human albumin usage have been carried out in a number of countries. The studies revealed that 50% to 70% of prescriptions were inappropriate, imposing a substantial burden of costs to their healthcare system.[17–19]

Enoxaparin is a low-molecular weight heparin, which is widely used as curative or preventive treatment of the thromboembolic disorders.[20] The present study showed that 26% of
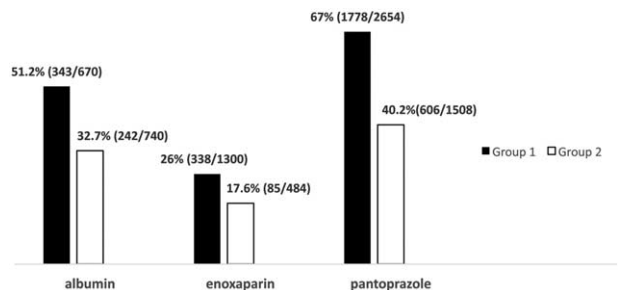


**FIGURE 1.** Trend of inappropriate orders for target drugs (%) before and after the employment of an evidence-based drug utilization management program. Group 1 = preguideline implementation, Group 2 = postguideline implementation.

**TABLE 4.** Comparison of Outcomes Before and After Practice Guidelines Implementation

| Intervention | Group 1 | Group 2 | $P_v$ |
|---|---|---|---|
| The incidence of VTE, % (N) | 1.31 (85/6470) | 1.16 (72/6210) | 0.49 |
| The incidence of GI bleeding, % (N) | 0.61 (40/6470) | 0.51 (32/6210) | 0.52 |
| LOS mean (SD) | 11.43 (6.64) | 11.79 (6.57) | 0.95 |
| Raw death, % | 1.30 | 1.35 | 0.75 |
| Pure death, % | 1.18 | 1.24 | 0.71 |

GI = gastrointestinal, Group 1 = preguideline implementation, Group 2 = postguideline implementation, LOS = length of hospital stay, SD = standard deviation, VTE = venous thromboembolic events.

enoxaparin administration had been inappropriate. Similar result has been obtained from another comparable study that was performed on enoxaparin prescription for elderly patients, showing that a total of 28.7% of which were inappropriate.[21]

In the group 1 of our study, 67% of pantoprazole administrations were inappropriate according to the guidelines. The improper administration of proton pump inhibitors (PPIs) including pantoprazole has been shown in other studies as well. Batuwitage et al[22] reported inappropriate PPI use in 54% of patients treated with PPIs in a primary care situation. Another study showed that up to 55% of patients for whom PPIs were administered were over-prescribed.[23]

Over the past few years inappropriate PPI usage has contributed to an increase in healthcare costs. In some reports similar to our results, pantoprazole ranked among the ''Top-10'' costly drugs which consumed the largest part of total medication costs.[22,23]

Due to limited healthcare resources, the appropriate use of existing fund seems to be crucial. Introducing guideline restrictions to prescribers at the point of order entry may reduce the number of inappropriate administrations. It is generally believed that implementing a restrictive policy on prescription of costly medications can avoid unnecessary administrations and complications and more people can be served. Since monitoring all pharmaceuticals that are used in hospital is next to impossible and also unnecessary, it is important to determine most costly medications with high impact on the budget.

It seems necessary to find proper strategies to propagate and implement evidence-based guidelines in order to improve physicians' performance and increase their adherence to these guidelines.[24–27]

Hence, we used a combination of different methods such as preprinted order forms, local experts' opinion as well as audit and feedback to optimize the compliance of the healthcare workers.[26]

In our setting, such interventions led to 65.8% physicians' adherence to guidelines and consequently inappropriate drug use showed significant decrease in group 2 (Figure 1).

The findings also suggest a declining trend of the target drug orders that in turn reflects the physicians' education after the establishment of the institutional guidelines (Figure 1).

Different modalities with the aim of increasing adherence to institutional guidelines have previously demonstrated favorable outcomes.[28,29] Fraser et al[30] showed that suggestions from a team of experts (an infectious disease fellow and a clinical pharmacist)

including changes in antibiotic choice, dosing, or administration route reduced antibiotic charges per patient for nearly 400 USD in adult in-patients receiving parenteral antibiotics.

In another study by Gentry et al,[31] implementation of antibiotic control program yielded a total cost saving of 291,885 USD (30.8% reduction) in a teaching hospital in the United States.

At the Hartford Hospital, the investigators reported a total cost avoidance of 777,462 USD over 4 years by a pharmacy-managed anemia protocol implementation in an outpatient dialysis setting.[32]

In the present study, by implementing the practice guidelines, major cost savings (56%) was produced via limiting the inappropriate use of costly drugs (Table 3) without any adverse impact on the clinical outcomes (Table 4).

In our tertiary hospital, we saved 85,595 USD/month by simply implementing guidelines for only 3 medications. If we assume that the same profile of drug usage continues, the magnitude of annually saving would be 1 million USD for only 1 hospital.

One of the major causes that the physicians stated for overprescribing the target drugs was that they were extremely cautious about their patients. In other words, there was a presumption that if guidelines criteria were implemented, it would put the patients at the risk of VTE, GI bleeding, or also lengthy surgery recovery and consequently lead to increasing LOS. However, our results showed that when administration is fully in accordance with guideline criteria, it does not increase the risk of aforesaid incidents, since there was no statistically relation between the incidences of VTE, GI bleeding, LOS, and death rates of the 2 groups ($P$ value $> 0.05$).

Contrary to the physicians' belief; LOS did not increase by declining drug administrations, besides a significant cost saving was achieved via the reduction of inappropriate and overuse of these drugs (Table 3).

In fact, the results implied that drugs overuse not only did not provide any excessive benefit, but also can potentially put the patients at risk of side effects and imposed a burden of unnecessary costs on them.

Interestingly in spite of the fact that our intervention mostly included declining drug administrations, LOS ($P = 0.95$) and mortality rate ($P = 0.75$) was not different when comparing the 2 groups before and after guideline implementation.

The main limitation of this study was failing to account the nursing or pharmacy labor costs associated with costly drugs use.

## CONCLUSIONS

In conclusion, institutionalizing practice guidelines can lead to a significant decrease in the cost and proper use of drugs. Based on the results, implementing a drug-utilization management program, could improve the adherence of evidence-based drug utilization which would in turn result in 1 million USD savings annually only for 3 drugs. Therefore, it is recommended that institutions consider implementing such management programs in order to reduce inappropriate drug usage and decrease their costs.

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