REVIEWS

Rational medicine prescription interventions in various countries: a systematic review

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A – Study Design, **B** – Data Collection, **C** – Statistical Analysis, **D** – Data Interpretation, **E** – Manuscript Preparation, **F** – Literature Search, **G** – Funds Collection

Summary **Background.** Rationalization is one of the first priorities in medicine for the logical prescription of medication; it is necessary to consider the individual's clinical condition, with the right dosage, during the appropriate period of time, and to impose the lowest possible cost to the patient and society. The proper and rational prescription of medicine is an important factor in securing community health. Obviously, the inappropriate use of medicine can lead to unfortunate consequences, such as patient dissatisfaction.
Objectives. This study aimed to investigate interventions which have been carried out about the logical prescription of medicine around the world.
Material and methods. This study is a systematic review study. All databases from inside and outside Iran – including PubMed, Scopus, Web of Science, Google scholar, Sid and Iran Medex – were searched. Articles from 2000 to 2017 were investigated and, ultimately, the articles were extracted and analyzed using the thematic analysis technique.
Results. From among 8,139 articles, 28 were selected. They referred to performance-based payment, performance feedback to physicians and education.
Conclusions. The implementation of interventions is an effective way to change physicians' behavior and to rationalize the prescription of medicine. The authorities are recommended to take more care in this regard.
Key words: policy, reimbursement mechanism, reimbursement incentive.

Background

According to the WHO, rational prescription of medication means prescribing a drug which is appropriate for the specific conditions of the patient, with the lowest possible dosage and duration, with the lowest possible cost to the patient. Improper drug prescription is considered a worldwide problem since it can result in decreased rates of treatment success, the incidence of a larger number of side effects, increased drug resistance, failure of the patient to accept medication and heavy costs exerted on the patient in particular and on the healthcare economy in general [1].

A failure to understand the rational prescription of drugs and medication may have adverse consequences, such as patient dissatisfaction, a damaged relationship between a patient and his or her physician, elongation and increased acuteness of the illness, the creation of dangerous side effects, an increased likelihood of hospitalization and ultimately increased healthcare costs for patients, public organizations and the country as a whole [2].

Research shows that more than half of the medications prescribed around the world are inappropriately prescribed, distributed or sold. In developed countries, 10–20 percent of the healthcare budget is spent on medications, while in developing countries, 20–40 percent is spent on prescription drugs [3].

Studies indicate that the amount of medicine prescribed does not follow a logical pattern and that it remains high [4–9]. In many countries, antibiotics represent 30% to 50% of medicine prescription among therapy-related factors. Despite the fact that antibiotics are necessary to treat bacterial infections and that the failure to use them can in some cases threaten the patient's life, studies show that 30–60 percent of prescriptions are inaccurate. These mistakes originate from physicians and distributers or from self-medication [4].

Several studies show that 5.1 to 5.43 percent of inpatients and 2 to 50 percent of outpatients are affected by undesirable medicine. Other results indicate that unwanted side effects of medicine can lead to longer hospitalization [6].

It should be noted that medicines, despite their vital role for patients, have side effects and sometimes dangerous impacts, which only highlights the importance of controlling the overuse of medicine. Therefore, both the economic role of medicine and its severe and deadly effects force us to create serious and comprehensive plans at the national and international levels to restrict the use of medication. Some countries have found appropriate solutions by controlling costs in various sectors, such as production, import, distribution or prescription [10].

Appropriate policy options – and consequently, the rational prescription of medicine – have significant impacts on in-

dividual, economic, social and cultural aspects. At the patient level, it leads to effective and successful treatment, a reduction in treatment duration and length of stay in hospital, a reduction in treatment costs, increased safety and, ultimately, patient satisfaction. We created a systematic study to investigate appropriate interventions that have been conducted in other countries in order to rationalize the prescription of medicines.

Objectives

This study aimed to investigate interventions about the logical prescription of medicine carried out around the world.

Material and methods

Search strategy

This systematic review aimed to investigate interventions which were carried out between 2000 and 2017 and promoted the logical prescription of medicine.

Keywords such as ((Inappropriate Prescription [mesh] OR Inappropriate OR Irrational OR illogical) AND (drug prescription [mesh] OR Prescription OR treatment OR order) AND (Prescription Drug Misuse [mesh] OR Drug) AND (Intervention OR policy OR strategy OR plan OR program)) were searched in the databases of Web of Science, PubMed, Scopus and EMBASE.

A sample search strategy for Pub Med is as follows: ((Inappropriate Prescription [mesh] OR Inappropriate [title/abstract] OR Irrational [title/abstract] OR illogical [title/abstract]) AND (drug prescription [mesh] OR Prescription OR treatment OR order) AND (Prescription Drug Misuse [mesh] OR Drug) AND (Intervention [Title/Abstract] OR policy [Title/Abstract] OR strategy [Title/Abstract] OR plan [Title/Abstract] OR program [Title/Abstract]))) Filters: Publication date from 2000/01/01 to 2017/12/01; Humans.

Eligibility criteria

Inclusion criteria
The inclusion criteria for selecting articles are:
1 – publication date between 2000 and 2017 and
2 – English or Persian language.

Exclusion criteria

The exclusion criteria included:
1 – letters to the editor,
2 – articles presented at conferences,
3 – clinical topics and
4 – articles without an English abstract.

Review process

Our search was conducted in each database by using the search strategy above. Articles with duplicate titles were removed from the review process and the inclusion and exclusion criteria were applied. To find the most relevant papers, the title, abstract and full text of the articles were checked. Resource management software (Endnote X6) was used to remove duplicate cases and to organize and evaluate the abstract titles.

Quality assessment

The selected articles were evaluated by a checklist for analytical-descriptive studies (STROBE) and articles which were not of the required quality were excluded from the study.

Data extraction

After reviewing the articles' quality, 28 articles were eventually studied. These papers were analyzed by the thematic technique.

Results

Summary of the articles reviewed

A total of 28 articles were included in this study. Figure 1 shows the process of reviewing and selecting the papers.
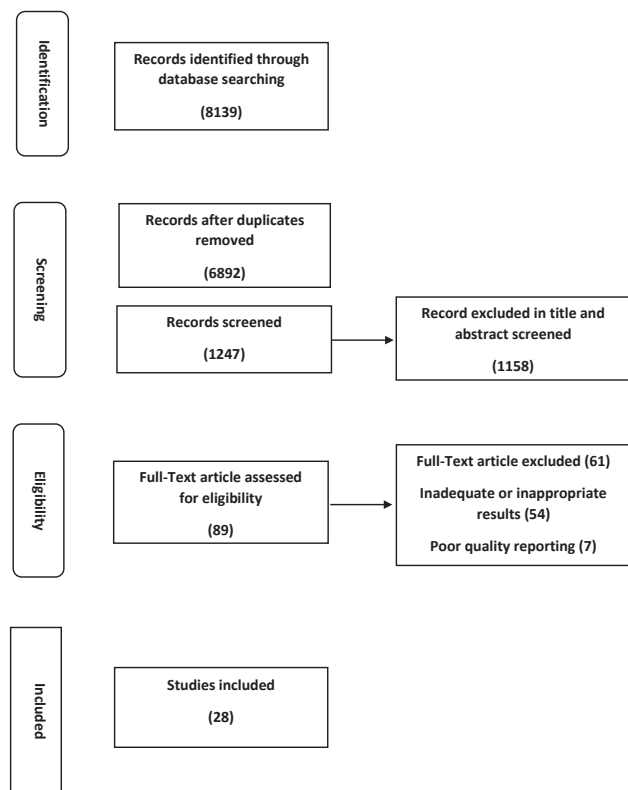

Figure 1. PRISMA flow diagram of the study

The majority of the studies were performed before 2010 (62%) and came from the continent of Asia (28%). In terms of research methodology (86%), the majority were interventional and 14% were retrospective.

The summaries of each article related to the interventions about logical prescription of medicine in the world are shown in Table 1.

Table 1. Summary of data extracted from the selected articles to investigate interventions about the logical prescription of medicine around the world (2000–2017)

No. (Reference No.)	Author	Setting	Year of publication	Methods	Intervention	Funding
1 [11]	Amiri, M	Iran	2015	This study was a descriptive-analytical study. The effect of prescription patterns and medicine price were investigated on prescribing injection medicines in Iran. 91994667 copies number of 36 cities in Iran was evaluated in 2011. A logarithm regression model was used to investigate relationships.	Increased prices for injectable drugs.	The percentage of injection medicines in Yazd (27%) was the lowest percent of usage; in Ilam (57%) was the highest use. There was no significant relationship between price and medicine prescription ($p \leq 5\%$).
2 [12]	Brown and Earnhart	Indiana	2004	This study was a retrospective case series.	An ACE (Acute Care for Elders) team pharmacist consulted all patients.	Upon admission, 10.1% were prescribed inappropriate medicines compared with 2.02% on discharge ($p < 0.02$).
3 [13]	Batuwitage et al.	Swansea	2007	This study was a prospective study with 271 in the intervention group and 66 controls.	The results of pre-intervention audits were discussed and the findings were sent to all GPs, along with NICE (National Institute of Health and Clinical Excellence) guidelines.	No effect was found on the proportion of patients taking proton pump inhibitors at the time of hospital admission or on the appropriateness of prescription in the community.
4 [7]	Chen, M	China	2014	8,258 prescriptions in 2007 and 8,278 prescriptions in 2010 were compared together in a before-and-after study on the Essential Medicines program in China. In order to assess the effect, a program of difference analysis was conducted in prescription change.	• Preparing a list of basic medications in each area; • Determining the price of drugs through negotiating with drug manufacturers and sellers; • Determining the price of 296 out of 307 drugs on the government's list of basic medications; Supplying medications in villages by the cooperative system of the village and prescriptions from Primary Care Providers.	The total changes of indicators were not significantly different. There were significant differences for different illnesses. The number of medicines decreased in outpatients. The prescription cost of medicines decreased in each prescription.
5 [14]	Crotty et al.	Australia	2004	This study was a randomized, controlled trial with a sample size of 154 Residents.	Two multidisciplinary case conferences (including a geriatrician, GP, pharmacist and residential care staff).	Medication appropriateness improved in the intervention group (MAI mean change 4.1 [95% CI 2.1– 6.1]) compared with the control group (MAI mean change 0.4 [95% CI -0.4–1.2]; $p < 0.001$).
6 [15]	Crotty et al.	Australia	2004	This study was a randomized, controlled trial with an intervention group of 56 and a control of 54.	Medication management transfer summary and medication review by a community pharmacist followed by a case conference.	At 8-week follow-up, the mean MAI (Medication Appropriateness Index) was significantly lower in the intervention group than in the control group (2.5 [95% CI 1.4–3.7] vs 6.5 [95% CI 3.9–9.1]; $p = 0.007$).

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No. (Reference No.)	Author	Setting	Year of publication	Methods	Intervention	Funding
7 [16]	Fischer, K	Germany	2018	This study was a retrospective study. The data on 440 physicians from three regions of Germany from 2005 to 2011 were collected. Using the delayed dependent variable regression model, the effects of the medication budget on the prescriptions of physicians were analyzed.	Increasing the medication budget.	There is a significant relationship between using drugs and prescribing generic medication ($p = 0.0246$). Moreover, there is a significant relationship between using the medication budget and the number of medications on the prescription $p \leq 0.001$. Furthermore, there is a significant relationship between increasing the medication budget and improper prescription.
8 [8]	Fürst, J	Slovenia	2015	This article is a retrospective and interventional before-and-after study. The population included all physicians between 1995 and 2012.	Interventions including a two-day symposium about antibiotics held annually for general physicians, limitations on physicians prescribing special antibiotics, holding workshops at primary care centers, distributing guidelines based on treatment of infectious diseases by general physicians, providing medicine bulletins, holding a workshop about the logical prescription of medicine, limiting prescriptions of some antibiotics, preparing a brochure on the correct use of medicines to all people, preparing a booklet with subject "My child has a fever" for people, and a series of engineering activities (containing management and organizational interventions) such as determining the number of qualitative indicators of prescriptions for doctors, including the maximum number of prescriptive antibiotics among the physician's prescriptions, an assessment of physicians' performance and presentation of feedback and observation of their performance and other colleagues. A financial mechanism containing financial incentives for the doctors who move along with determined goals and at the other side financial penalties for the doctors who ignore these cases.	Antibiotics consumption has decreased 2–9 percent from 1999 to 2012 annually and 31 percent overall. Among 10 antibiotics, decreased consumption was found in 7 cases; in addition, the cost of antibiotics decreased by 53 percent.
9 [17]	Garjani, A	Iran	2009	More than 50 prescriptions of 51 general physicians were collected. In order to evaluate the prescriptions, they were given to a focus group. The issues with these prescriptions were explained for the intervention group in a class discussion.	Training class.	The average number of medicines before the intervention was 82.3%; the percentage of injections of antibiotics was 8.40% and the percentage of injecting of injections medicine was 58%.

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No. (Reference No.)	Author	Setting	Year of publication	Methods	Intervention	Funding
10 [18]	Gong, Y	China	2015	376,700 prescriptions were collected from primary care providers from 2007 to 2011. The method used in this study was studying the difference before and after prescribing.	Essential medicines in China.	After implementation of essential medicine in China, the number of medicines in each prescription declined to 2%.
11 [19]	Helin Salmi-vaara, A	Finland	2003	A rational medicine prescription program was implemented in Finland in 1990 with the purpose of changing physicians' behavior. This program included elements such as continual medical training, implementation of medical guidelines, presentation of information and provision of prescription feedback to doctors. Its effect was investigated in 2001.	Continual medical training, implementation of medical guidelines.	The effect of a rational medicine prescription program in Finland was effective in rationalizing prescription.
12 [20]	Kafle, K	Nepal	2005	Three areas were randomly selected and the interventions were administered.	Educational intervention (holding training classes and distributing pamphlets among physicians), management interventions (group discussions among physicians and evaluating prescription issues and their solutions, monitoring the prescriptions of physicians and giving feedback to them).	Educational interventions were only effective in improving one indicator: management interventions. (Group discussions were effective in improving 7 indicators and in monitoring type was effective in improving one indicator.) In the private sector, however, educational interventions were effective in improving three indicators and management interventions in improving one indicator.
13 [21]	Krska et al.	Scotland	2001	This study was a randomized, controlled trial with 168 intervention subjects and 164 controls.	Resolution of pharmaceutical care issues and health-related quality of life.	An inappropriate dosage regimen was found in 5.7% of the intervention group and was resolved in 78.3% cases, whereas in the control group an inappropriate dosage regimen was found in 6.5% and was resolved in only 17.9% cases ($p < 0.0001$).
14 [22]	Lau et al.	Ireland	2004	This study investigated 1,588 intervention subjects and 1,814 controls.	Weekly onsite availability of a consultant pharmacist.	No significant relationship between potentially inappropriate medication and weekly onsite availability of consultant pharmacist was found: for the intervention group, (OR 0.96 [95% CI 0.81–1.14]) and for control group, (OR 1.00 [95% CI 1.00–1.00]).
15 [23]	Lionis, C	Cyprus, France, Greece, Malta and Turkey	2014	This training intervention was conducted in 5 European countries. General practitioners were selected and randomly divided into two groups.	The intervention included a one-day and intensive curriculum, training table of daily supervisions done by trained experts from the participants' workplace, and sending messages and e-mails to participants for 4 consecutive weeks. The training method was in the form of pre-test and post-test.	Physicians' tendency to irrationally prescribe medicines in the intervention groups were less than in the control group.

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No. (Reference No.)	Author	Setting	Year of publication	Methods	Intervention	Funding
16 [24]	Pimlott et al.	Canada	2003	This study was a randomized controlled design with an intervention sample of 168 and a control sample of 206.	Mailed packages of feedback about participants' prescriptions together with evidence-based educational material.	Long-acting BZD prescriptions decreased by 0.7% in the intervention group and increased by 1.1% in the control group ($p = 0.036$), which was clinically insignificant.
17 [25]	Rahme et al.	USA	2005	This retrospective assessment of prescriptions had 167 in the intervention group and 82 in the control group.	Three interventions: small group workshop; decision tree reflecting the current evidence-based guidelines; and small group plus decision tree.	The probability of improvement in the workshop and decision groups over the controls was 94% (OR 1.5 [95% CI 0.9–2.3]), compared with 74% (OR 1.3 [95% CI 0.6–2.4]) in the workshop group and 55% (OR 1.1 [95% CI 0.6–1.6]) in the decision-tree group.
18 [26]	Raebel et al.	USA	2007	This study was a randomized controlled trial with an intervention group of 29,840 and a usual care group of 29,840.	Medication alert to pharmacist regarding inappropriate prescription.	Newly dispensed prescriptions for inappropriate medications were 1.8% for the intervention group and 2.2% in the usual care group ($p = 0.002$).
19 [27]	Saltvedt et al.	Norway	2005	This study was a randomized trial with a sample population of 254 patients.	Multidisciplinary geriatric team care including a geriatrician.	13 (10%) GEMU patients and 12 (9%) medical ward patients prescribed inappropriate medications at admission compared with (4%) GEMU patients and 7 (6%) medical ward patients at discharge (statistically insignificant differences).
20 [28]	Schmader et al.	USA	2004	This study was a randomized controlled trial with an intervention group of 430 and a control group of 404.	Multidisciplinary geriatric team care including a geriatrician, social worker and nurse for inpatients and outpatients.	A GEMU (geriatric evaluation and management unit) was associated with significant reductions ($p < 0.05$) in the number of unnecessary drugs, MAI score and the number of inappropriate drugs.
21 [29]	Rhoads and Thai	USA	2003	This study was a prospective case series with a sample of 456 physicians.	A consultant pharmacist identified potentially inappropriate medications and faxed recommendation letters to physicians.	31.6% prescribed one or more routine or as-required medications considered potentially inappropriate. Of these, 16.7% were discontinued after pharmacist recommendations. The overall return rate of all faxed recommendations was 88.7%.
22 [30]	San et al.	China	2014	This was a prospective study. It was conducted on two groups of health centers in 2 cities that were randomly selected. Their payment method was based on reward and service unit. In one of the payment centers, payment method was administered instead of global method and in the other a combination of global and performance-based payments was used, so that 20% of payments were given to providers if they followed indicators about rationale prescription of medicine.	Pay for performance.	The combination of performance-based payment methods and global method were effective more than only global payment in the quality of drug prescription by doctors.

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No. (Reference No.)	Author	Setting	Year of publication	Methods	Intervention	Funding
23 [31]	Tamblyn et al.	Canadian	2003	This study had a cluster randomized control design. The intervention group had 6,284 subjects, the control group 6,276.	Physicians were provided with a computerized decision support system.	The number of new inappropriate prescriptions was significantly lower than in the control group [RR = 0.82 (95% CI 0.69–0.98)].
24 [32]	Wessell et al.	Carolina	2008	This study was a prospective study with 124,802 patients.	Three-step intervention: quarterly practice performance reports; biannual onsite visits; and, finally, annual meetings.	The adjusted absolute annual decline for the comprehensive categories of "always inappropriate" medications was 0.018% ($p = 0.03$) and for "rarely appropriate" medications was 0.113% ($p = 0.001$).
25 [33]	Wang et al.	China	2014	20 primary care centers in China were divided into two groups of control and intervention. The study was a quasi-experimental study. Differences in the difference method and logistic regression testing were used to determine the effect of intervention.	The performance of the intervention group regarding medicine prescription was clearly reported among physicians and related clinics. The rate of medicine prescription in both groups was compared before and after the intervention. (Physicians' performance was printed on bulletins, journals and newspapers. The bulletins were placed in the outpatient clinic to be viewed by patients and physicians, and magazines and newsletters were placed on counters in outpatient centers).	4 months after the intervention, a 4% reduction in the prescription of injection medicines was observed among physicians of the intervention group.
26 [19]	Helin-Salmi-vaara et al.	Netherlands	2004	This study was a randomized, controlled trial of 12 groups including 100 general practitioners and pharmacists which were studied. Interventions were included.	Training sessions with comprehensive educational instruction, monitoring and feedback of medicine prescription behaviors.	89% of general physicians participated in this study. At the beginning of the study, there was no significant difference in the rate of antibiotic prescription in the intervention and control groups (27% vs. 29%). After 9 months, however, the rate of prescription in the intervention group decreased to 23%, while it increased to 37% in the control group.
27 [34]	Gerber, J	America	2013	This study was conducted in a hospital which was related to 29 primary child care facilities. A total of 162 physicians participated in this study, which were divided into two groups of control and intervention.	Intervention was done by one of the specialist physicians in the form of a 1-hour training session and feedback was given to the trained physicians privately (through e-mail) once every 4 months about the manner of their prescription.	In the intervention group, prescription of a Broad-Spectrum antibiotic decreased from 8.26% to 3.14% and in control group it decreased from 6.22% to 4.28%. In the intervention group, off-guideline prescriptions in patients who suffered from pneumonia decreased from 7.15% to 2.4% and in the control group it decreased from 1.17% to 3.16%; in patients with acute sinusitis prescription decreased from 9.38% to 8.18% in the intervention group and from 40% to 30% in the control group.

Table 1. Summary of data extracted from the selected articles to investigate interventions about the logical prescription of medicine around the world (2000–2017)

No. (Reference No.)	Author	Setting	Year of publication	Methods	Intervention	Funding
28 [35]	Zhang et al.	China	2014	20 urban hospitals and 274 physicians were divided into intervention and control groups. The chi-squared test and t-test were used to investigate the effect of public report on prescribing the prescribing information on the rational medicine prescription.	In the intervention group, the costs of each prescription, the percentage of antibiotics and injection medicines for each prescription were distinguished separately for hospitals and doctors and they were exposed to view by physicians and patients monthly. Data were collected 4 months before and after intervention.	The percentage of prescriptions with antibiotics and injection drugs were 63% and 71%, respectively. There was a significant difference between the control and the intervention groups regarding the percentage of prescriptions containing injection drugs ($p \leq 0.05$).

Discussion

In the present study, a total of 28 articles were investigated based on measures for rationalizing medicine prescription in other countries.

The results of the present study indicate that training is effective in changing the behavior of physicians relying on rational medicine prescription. A study by Teppo et al. indicated that training for primary care physicians is crucial and effective for early diagnosis of disease [36]. Also, the results of studies by Legare et al. [37], are consistent with the results of this study.

The results of studies by Bloom [38] and Berdage et al. [39] demonstrated that training is not solitarily effective on behavioral change, though these results are inconsistent with the results of this study.

Its seems that training, learner participation in educational discussions and the presentation of practical solutions in educational sections are effective. As the results of Valaitis study also show, educational workshops are more effective than traditional lectures in improving physicians' skills and promoting patient health [40]. Another factor which affects the results of the training is the training level, skill and experience of the educator. Likewise, it seems that the number of learners and their level of interest in learning, the time when classes are held and the number of hours in the educational classroom are important in this regard.

The results obtained in this study showed that performance-based payment is effective on behavioral change of physicians, as is rational prescription of medicine. In a study by Li et al., they found that in hospitals which implemented performance-based pay, the quantity of care and the length of patient treatment are higher than in hospitals that have not implemented performance-based pay [41]. This study and the results obtained by Damberg and Fang are in line with the results of the current study. Werner et al. indicated that performance-based pay does not lead to higher quality of nurses' performance in nursing homes [42, 43].

It seems that background and cultural factors, including characteristics of physicians and the level of regulation, have an impact on healthcare systems, in terms of the implementation of performance-based pay, as does the environment. It also seems that in systems where performance-based pay has an impact on the performance of physicians, other interventions may act as confounding factors – such as applying regulations, reminders and reminding to doctors, implementing guidelines and presenting performance feedback to them – which can double the effect of performance-based pay.

Moreover, it seems that the amount and type of financial incentives are important in this regard. A study by Park and Werner shows that large financial incentives have a greater impact on performance-based pay [44]. It seems in some cases the goals that are set are very ideal and unreachable; therefore, although the rewards are significant, it is obvious that individuals are not motivated to achieve these goals.

Based on this study, rewarding is effective on changing the behavior of physicians. The results of Al-Enezi's et al. study indicated that external rewards do not work because nurses have a high perception of inequality [45].

In general, one of the most important issues in human resource management is a reward system that has a motivational effect on employees' behaviors, satisfaction and organizational effectiveness [46]. Rewards are divided into internal and external categories. External rewards are awarded from the outside and are further divided into financial and non-financial categories; internal rewards are organized and derived from the individual themselves and from the successes achieved.

Creamer studied why rewards are not effective in motivating employees and found that the reasons are an emphasis on cash rewards and pay bonuses that do not have a motivating effect, a delay between performance and rewards and offering similar rewards at frequent intervals [47].

Robbins, in his research, argued that when a person knows that the parity and equality principle is not observed or not applied to him/her or when there is no logical relationship between his reward and his performance, or when his/her remuneration does not meet his/her individual needs, it is likely that this person is not performing properly and will leave the organization [48].

The results of our study indicate that feedback and presenting feedback to physicians were helpful in changing their behavior and in fact in improving the rational prescription of medicine. The results of studies by Price-Haywood et al. [49] and Mostofian et al. [50] are consistent with the results of the current study.

Tavarez's et al. study showed that performance feedback to pediatric emergency physicians over a three-month period did not affect patient suffering from diarrhea and vomiting [51]. The results of these studies are not consistent with the results of this study.

It seems that background characteristics of the environment, such as the level of the staff's attention and belief in feedback are less effective on the results obtained. The results from Sargeant's et al. study indicated that the reaction, vision and imagination of physicians to multistage feedback is influenced by the effect of the reaction on their performance [52].

Similarly, the characteristics of service providers such as presenting feedback and the accuracy rate of feedback given to the staff are effective on giving them the feedback. Setting policies on presenting feedback to physicians in order to im-

prove their performance can be effective, but existing problems – the interests or aspirations of the people who are subjected to these policies – may also change, requiring new policies to address them [53].

Conclusions

1. Physicians and community members should be informed of the dangers and conditions of irrational drug prescription.
2. Pharmacists should be engaged as an important control lever in reviewing doctors' prescription and feedback.
3. Management practices should be applied, including monitoring of the performance of doctors.
4. A performance-based payment system should be implemented.
5. The system of family doctors and their prescriptions should be practiced.
6. Encouragement and punishment should be used to rationalize an appropriate monitoring function of drug prescription.

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