Pharmaceutical Sciences Asia

Pharm Sci Asia 2022; 49(1), 106-113

DOI:10.29090/psa.2022.01.21.096

Research Article

# Pharmacist-led interventions to reduce drug-related problems in prescribing for Vietnamese outpatients

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## ABSTRACT

Drug-related problems (DRPs) can lead to adverse outcomes and increase the risk of hospitalization. Pharmacist interventions can help to reduce these problems. We aimed to evaluate the effect of pharmacist-led interventions on DRPs in prescribing for outpatients and determine the risk factors of these DRPs. We conducted a before-and-after intervention study on prescribing process for outpatients from a hospital in Vietnam. We collected prescriptions from the hospital's electronic prescription system. Clinical pharmacists determined DRPs following (1) medication leaflets, (2) guidelines of the Vietnam Ministry of Health, (3) Vietnamese National Drug Formulary. We checked drug-drug interactions using Drugs.com. Interventions, including a workshop on DRPs, providing information sheets, and reminding physicians about DRPs, were conducted by researchers in collaboration with clinical pharmacists in the study hospital. In the pre-intervention phase, we analyzed 3352 prescriptions. The number of prescriptions with at least 1 DRP was 88.8%. In the post-intervention, we analyzed 2685 prescriptions. The number of prescriptions with at least 1 DRP decreased from 88.8% to 74.9% ($p$<0.001). Pharmacist interventions are effective on DRPs in drug indications ($p$<0.001), dosage ($p$<0.001), frequency of use ($p$<0.001), time of taking medications ($p$<0.001). There was no significant improvement in DRPs of the time of taking drugs compared with meals and drug-drug interaction after interventions. The number of DRP increases with the number of drugs prescribed ($p$<0.001). In conclusion, pharmacist-led interventions reduced the proportion of prescriptions with DRPs. Prescribing 5 or more medications increased the risk of DRPs occurrence.

**Keywords:**
Drug-related problems, Outpatients, Prescribing, Pharmacist-led interventions

## 1. INTRODUCTION

Inappropriate prescribing reduces the quality of treatment and leads to a waste of resources[1]. The World Health Organization estimates that more than half of all drugs are prescribed, dispensed, or sold inappropriately, and that half of all patients do not take them correctly[2]. Drug-related problems can increase the risk of side effects, drug interactions, antimicrobial resistance, increase costs for treatment (in terms of both direct medication costs and indirect medication costs), and pressure the insurance budget society. According to the studies, about 50% to 80% of drug-related problems may be preventable[3]. In particular, clinical pharmacists help identify, treat and have a crucial role in preventing drug-related problems through specific interventions. The pharmacist's contribution to improving the quality of medication use and patient safety can be assessed directly or indirectly by determining the number of drug-related problems being managed/prevented or by cost-effective treatment[4].

All over the world, many studies are showing the critical role of pharmacists in identifying and managing drug-related problems in prescribing[5-6]. In Sweden, pharmacists' recommendations on DRPs might positively influence physicians' prescribing quality and contribute to better and safer drug therapy for patients[5]. In addition, Japanese pharmacists also had an essential role in providing medication safety, with potential cost savings[6].

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In Vietnam, studies evaluating the importance of clinical pharmacists' interventions are more and more focused; however, studies assessing the impact of clinical pharmacists' interventions on drug-related problems, especially in outpatients, are still limited. This study aimed to evaluate the effects of clinical pharmacists' interventions on drug-related problems in prescribing for outpatients at a hospital in Vietnam.

## 2. MATERIALS AND METHODS

### 2.1. Study population and setting

Outpatient prescriptions at a G2 hospital (250 beds) in Can Tho from March 1, 2019, to March 15, 2019 (pre-intervention) and from August 1, 2019, to August 15, 2019 (post-intervention).

#### *2.1.1. Inclusion criteria*

We included all outpatient prescriptions of 18 years of age, and older patients get a medical examination at General Internal Medicine, Ear-Nose-Throat, Orthopedic clinics.

#### *2.1.2. Exclusion criteria*

We excluded prescriptions for pregnant women, prescriptions of the same patient to follow-up examination in the same month.

### 2.2. Methods

#### *2.2.1. Study design*

We conducted a before-and-after intervention study.

#### *2.2.2. Sample size*

The single proportion formula was used to estimate the required sample size by considering the following assumptions: the proportion of DRP 50.2%[7], a 95% confidence level, and a 2% margin of error. However, the research team collected prescriptions for 15 days from all doctors attending the clinics. Hence, the expected number of prescriptions in the study period was higher than the sample size in the calculation, specifically, 3352 pre and 2685 post-intervention phases.

#### *2.2.3. Data collection and analysis*

We collected prescriptions from the hospital's electronic prescription system. Three pharmacists determined DRPs in the following order of priority: (1) summary of product characteristics; (2) Vietnamese National Drug Formulary 2015[8]; and (3) treatment guidelines of Vietnam Ministry of Health[9]. We checked drug-drug interactions using Drugs.com[10]. DRPs include:

(1) DRPs for drug indications: no drug treatment despite existing indication, no indication for the drug, drug within guidelines but otherwise contraindicated.
(2) DRPs for dosage: dosage too high and too low according to indication/guidelines (24 hours).
(3) DRPs for frequency of use: frequency of use too high and too low according to indication/guidelines (24 hours)
(4) DRPs for the time of taking drugs: the time of taking medications per day (morning, afternoon, evening) and time of taking drugs compared with meals (before, during, and after meals).
(5) Drug-drug interaction: serious drug-drug interactions according to Drugs.com.

#### *2.2.4. Intervention procedure*

Clinical pharmacists performed interventions on DRPs in prescribing for outpatients. The intervention subjects were doctors at the study hospital clinics. Interventions included:

(1) Organizing a clinical pharmacy reporting session at the study hospital. Clinical pharmacists presented an oral presentation on DRPs' determination results in the pre-intervention phase for 15 minutes.

(2) Information sheets about DRPs: The sheets contented of describing specific drugs for each case of DRPs; and giving directions for solving each type of DRP: recommend the correct information based on three references (summary of product characteristics, Vietnamese National Drug Formulary 2015, treatment guidelines of Vietnam Ministry of Health). We also gave examples of some cases of prescribing not according to indication/guidelines. Information sheets were placed at the doctor's desk (the most convenient place to follow). Through the permission of the Department of Examination and Treatment, researchers inform doctors about the information sheets' contents during the meeting at the department.

(3) Clinical pharmacists discussed and reminded doctors about the Information Sheets' contents and intervened on specific prescriptions. Clinical pharmacists discussed with each doctor once a week during the intervention period July 8, 2019, to July 31, 2019.

#### *2.2.5. Statistical analysis*

We analyzed data using SPSS software version 20.0. We described qualitative variables as frequencies and percentages and quantitative variables as means±standard deviations. We compared pre- and post-intervention differences by statistical analysis with

95% confidence and multivariate logistic regression analysis to test relevance between the occurrence of DRP and patient characteristics. The difference was statistically significant with $p<0.05$.

## 3. RESULTS

We analyzed 3,352 prescriptions in the pre-intervention phase (from March 1, 2019, to March 15, 2019) and 2,685 prescriptions in the post-intervention phase (from August 1, 2019, to August 15, 2019). The patient characteristics are shown in Table 1. There were differences between patient's characteristics pre and post interventions.

Researchers collaborating with clinical pharmacists in the study hospital carried out interventions, including a workshop on DRPs in the indication, providing information sheets, and reminding physicians of DRPs. The results are shown in Table 2. The number of prescriptions with at least 1 DRP decreased from 88.8% to 74.9% ($p<0.001$). Most DRPs had a statistically significant decrease compared to pre interventions ($p<0.05$), except for the time of taking drugs compared with meals and drug-drug interaction. Some drugs with high rates of DRPs in pre- and post-interventions are shown in Table 3.

The multivariate logistic regression analysis results on the relationship between the survey variables and the occurrence of DRP in the prescription were shown in Table 4. Post-intervention prescriptions had a lower risk of DRPs than before ($p<0.001$). Prescriptions of female; patients under 65 years of age; patients with health insurance had a higher chance of DRP than other patient groups ($p=0.025$; $p=0.001$; $p<0.001$). Patients using 5 or more drugs had a 4 times higher risk of DRP than patients using fewer drugs ($p<0.001$).

## 4. DISCUSSION

### 4.1. Drug-related problems in pre- and post-interventions

#### *4.1.1. Prescriptions with at least 1 DRP*

The proportion of prescriptions with at least 1 DRP was high before the intervention phase in our study

**Table 1.** Patient characteristics in pre- and post- interventions.

| Characteristics | | Pre-interventions (n, %) (N=3,352) | Post-interventions (n, %) (N=2,685) | *p*-value |
|---|---|---|---|---|
| Age (mean±SD) | | 49.59±16.32 | 52.56±14.95 | <0.001 |
| | <65 years old | 2,677 (79.9%) | 2,080 (77.5%) | 0.024 |
| | ≥65 years old | 675 (20.1%) | 605 (22.6%) | |
| Gender | Male | 1,194 (41.6%) | 1,044 (38.9%) | 0.033 |
| | Female | 1,958 (58.4%) | 1,641 (61.1%) | |
| Health insurance | No | 1,353 (40.4%) | 507 (18.9%) | <0.001 |
| | Yes | 1,999 (59.6%) | 2,178 (81.1%) | |
| Number of drugs (mean±SD) | | 4.5±1.78 | 3.98±2.23 | |
| | <5 drugs | 1,781 (53.1%) | 1,700 (63.3%) | <0.001 |
| | ≥5 drugs | 1,571 (46.9%) | 985 (36.7%) | |

**Table 2.** Drug-related problems in pre- and post- interventions.

| Drug-related problem | Pre-intervention (n, %) (N=3,352) | Post-intervention (n, %) (N=2,685) | OR | 95% CI (OR) | *p*-value |
|---|---|---|---|---|---|
| Prescriptions with at least 1 DRP | 2,975 (88.8%) | 2,010 (74.9%) | 0.377 | 0.329-0.433 | <0.001 |
| Drug indications | 1,792 (53.5%) | 774 (28.8%) | 2.836 | 2.547-3.158 | <0.001 |
| Drug within guidelines but otherwise contraindicated | 50 (1.5%) | 33 (1.2%) | 1.217 | 0.782-1.894 | 0.384 |
| No drug treatment in spite of existing indication | 24 (0.7%) | 15 (0.6%) | 0.779 | 0.408-1.487 | 0.448 |
| No indication for drug | 1,768 (52.7%) | 749 (27.9%) | 2.885 | 2.589-3.215 | <0.001 |
| Frequency of use | 1,396 (41.6%) | 821 (30.6%) | 1.620 | 1.456-1.803 | <0.001 |
| Frequency of use too low | 1,105 (33.0%) | 624 (23.2%) | 1.624 | 1.448-1.822 | <0.001 |
| Frequency of use too high | 470 (14.0%) | 306 (11.4%) | 1.268 | 1.087-1.479 | 0.002 |
| Dosage | 1,332 (39.7%) | 763 (28.4%) | 1.661 | 1.490-1.852 | <0.001 |
| Dosage too low | 1,132 (33.8%) | 700 (26.1%) | 1.446 | 1.293-1.617 | <0.001 |
| Dosage too high | 356 (10.6%) | 106 (4.0%) | 2.891 | 2.313-3.614 | <0.001 |
| Time of taking drugs | 1,472 (43.9%) | 918 (34.2%) | 1.507 | 1.357-1.674 | <0.001 |
| Time of taking drugs compared with meals | 1,607 (47.9%) | 1,311 (48.8%) | 0.965 | 0.872-1.068 | 0.494 |
| Drug-drug interactions | 123 (3.7%) | 116 (4.3%) | 0.037 | 0.031-0.044 | 0.197 |

**Table 3.** The five most common drugs with DRPs.

| Drug | Pre-intervention (n/N,%) | Post-intervention (n/N,%) | *p*-value |
|---|---|---|---|
| No indication for drugs | | | |
| Sulpiride | 358/362 (98.9%) | 53/53 (100%) | 1.000 |
| Magnesium+Vitamin B6 | 353/381 (92.7%) | 149/192 (77.6%) | <0.001 |
| Calcitriol | 307/337 (91.1%) | 29/92 (31.5%) | <0.001 |
| Eperisone | 183/445 (41.1%) | 67/279 (24.0%) | <0.001 |
| Esomeprazole | 161/868 (18.5%) | 107/507 (21.1%) | 0.248 |
| Drug within guidelines but otherwise contraindicated | | | |
| Celecoxib | 25/819 (3.1%) | 13/440 (3.0%) | 0.923 |
| Acarbose | 13/97 (13.4%) | 0/127 (0%) | <0.001 |
| Metformin | 5/285 (1.8%) | 4/358 (1.1%) | 0.519 |
| Atorvastatin | 3/300 (1.0%) | 2/460 (0.4%) | 0.308 |
| Etoricoxib | 1/102 (1.0%) | 0/4 (0%) | 0.923 |
| Dosage too low | | | |
| Itopride | 153/159 (96.2%) | 143/156 (91.7%) | 0.089 |
| Rebamipide | 114/138 (82.6%) | 25/34 (73.5%) | 0.228 |
| Bromhexine | 112/159 (70.4%) | 31/32 (96.9%) | 0.002 |
| Mephenesin | 105/108 (97.2%) | 11/108 (10.2%) | <0.001 |
| Trimebutine | 85/222 (38.3%) | 93/102 (91.2%) | <0.001 |
| Dosage too high | | | |
| Rabeprazole | 109/156 (69.9%) | 13/96 (17.1%) | <0.001 |
| Omeprazole | 86/436 (19.7%) | 7/134 (5.2%) | <0.001 |
| Desloratadine | 67/112 (59.8%) | 13/35 (37.1%) | 0.019 |
| Fluticasone furoate | 39/52 (75.0%) | 0/0 | |
| Amoxicillin-Sulbactam | 20/23 (87.0%) | 20/23 (87.0%) | 1.000 |
| Frequency of use too low | | | |
| Itopride | 153/159 (96.2%) | 143/156 (91.7%) | 0.089 |
| Rebamipide | 117/138 (84.8%) | 25/34 (73.5%) | 0.121 |
| Bromhexine | 117/159 (73.6%) | 31/32 (96.9%) | 0.004 |
| Mephenesin | 108/108 (100%) | 11/108 (10.2%) | <0.001 |
| Trimebutine | 90/222 (40.5%) | 93/102 (91.2%) | <0.001 |
| Frequency of use too high | | | |
| Omeprazole | 113/436 (25.9%) | 24/134 (17.9%) | 0.058 |
| Rabeprazole | 109/156 (69.9%) | 14/76 (17.1%) | <0.001 |
| Desloratadine | 67/112 (59.8%) | 13/35 (37.1%) | 0.019 |
| Bisoprolol | 44/316 (13.9%) | 38/465 (8.2%) | 0.010 |
| Fluticasone furoate | 42/52 (80.8%) | 0/0 | 0.058 |
| Time of taking medications per day (morning, afternoon, evening) | | | |
| Itopride | 153/159 (96.4%) | 143/156 (91.7%) | 0.089 |
| Rebamipide | 118/138 (85.5%) | 25/34 (73.5%) | 0.095 |
| Bromhexine | 117/159 (73.6%) | 31/32 (96.9%) | 0.004 |
| Diosmin+hesperidin | 112/165 (67.9%) | 129/129 (100%) | <0.001 |
| Rabeprazole | 109/156 (69.9%) | 13/76 (17.1%) | <0.001 |
| Time of taking drugs with meals (before, during, and after meals) | | | |
| Esomeprazole | 298/707 (42.1%) | 225/450 (56.2%) | <0.001 |
| Omeprazole | 244/436 (56.0%) | 51/134 (38.1%) | <0.001 |
| Gliclazide | 188/207 (90.8%) | 204/243 (84.0%) | 0.030 |
| Metformin | 141/276 (51.1%) | 193/347 (55.6%) | 0.260 |
| Methylprednisolone | 175/288 (60.8%) | 132/182 (72.5%) | 0.009 |
| Serious drug-drug interactions | | | |
| Clopidogrel-Esomeprazole | 39 (1.2%) | 50 (1.9%) | 0.104 |
| Clopidogrel-Omeprazole | 27 (0.8%) | 14 (0.5%) | 0.089 |
| Clopidogrel-Rabeprazole | 13 (0.4%) | 33 (1.2%) | <0.001 |
| Amitriptyline-Escitalopram | 7 (0.2%) | 0 | 0.008 |
| Ciprofloxacin-Methylprednisolone | 6 (0.2%) | 2 (0.1%) | 0.024 |

**Table 4.** Determinants of drug-related problems in prescriptions.

| Determinants of DRPs | | Odds ratio (OR) | 95% CI | *p*-value |
|---|---|---|---|---|
| Intervention | No (pre-intervention) | 1.000 | | |
| | Yes (post-interventions) | 0.362 | 0.312-0.419 | <0.001 |
| Age | <65 years old | 1.000 | | |
| | ≥65 years old | 0.752 | 0.631-0.896 | 0.001 |
| Gender | Female | 1.000 | | |
| | Male | 0.850 | 0.738-0.980 | 0,025 |
| Health insurance | No | 1.000 | | |
| | Yes | 1.812 | 1.557-2.109 | <0.001 |
| Number of drugs | <5 drugs | 1.000 | | |
| | ≥5 drugs | 3.978 | 3.334-4.746 | <0.001 |

(88.8%). DRPs were also seen with high proportions in Xiao-Feng Ni et al.'s systematic review of 27 studies worldwide (approximately 70%)[11]. Pharmacist-led interventions significantly reduce DRPs to 74.9% ($p$<0.001) in our studies. Other studies show the essential role of clinical pharmacists in improving prescribing quality in Germany[12], France[13], and other countries[11].

*4.1.2. DRPs for drug indications*

DRPs for drug indications had the highest proportion of prescriptions' DRPs (53.5%). This result was similar to Hue Yu Wang et al. (2017) study at a medical center outpatient clinic in Taiwan (50.2%)[7] but higher than in prescribing for pediatric outpatients in Vietnam (35.6%)[14].

In the post-intervention phase, the percentage of prescriptions with DRPs for drug indications reduced from 53.5% to 28.8% ($p$<0.001). Among them, no indication for the drug was the DRP that the doctors were most concerned about. Indicating unnecessary drugs did not increase the effectiveness of treatment and might occur drug interactions/adverse events for the patient[15]. Besides, indicating unnecessary drugs also increased treatment costs[15-16] and affected the health insurance fund. Therefore, the intervention on this DRP (no indication for drug) was recorded to be effective (decreased from 52.7% to 27.9% with $p$<0.001). Research results of Vina A. Sagita et al. (2018) on evaluating a clinical pharmacist intervention on clinical and drug-related problems among coronary heart disease inpatients at a general hospital in Indonesia showed that the intervention significantly reduced the rate of problems related to drug indications, from 37.5% before intervention to 4.5% after intervention ($p$<0.05)[17]. The post-intervention efficacy in our study was lower than the result of Vina A. Sagita et al. This may be because our study population was outpatient. People conducting the intervention were not clinical pharmacists working in the research hospital (although there was still a collaboration), so the time of contact and communication with the prescribers were limited.

Meanwhile, DRP about drug within guidelines but otherwise contraindicated and DRP about no drug treatment despite existing indication did not decrease post-intervention significantly (although these rates before intervention were relatively low). This showed that these problems were not concerned by doctors. The reason for no drug treatment despite existing indications may be that the doctor prescribed a lack of medicine compared to the diagnosis, or the disease was diagnosed. Still, it was unnecessary to use the drug, or the patient already had medication, and doctors recorded in diagnosis to note when prescribing other drugs. In addition, prescribing drugs with contraindications still did not improve after the intervention; this may be that doctors often focused on treating the diseases and paid little attention to specific contraindications.

*4.1.3. DRPs for dosage and frequency of use*

The percentage of prescriptions with inappropriate dosage and frequency of use was relatively high, 45.14% and 47.74%, respectively. These results were lower than the study of Iman et al. (2017) on "Treatment-related problems for outpatients with chronic diseases in Jordan" with DRP about inappropriate dosage according to indication/guidelines was 50.3%[18]. Dose-related DRP might have been more common in patients treating chronic diseases.

The percentage of DRPs in inappropriate dosage and frequency of use decreased after the intervention (from 39.7% to 28.4% for DRP in dosage ($p$<0.001) and from 41.6% to 30.6% for DRP in the frequency of use ($p$<0.001)). In particular, dosage/frequency of use was too high and too low according to indication/guidelines were significantly reduced. Although the research team intervened by providing general information and specific information sheets about drugs for a short period, the doctors still noted and remembered some of the errors. With these results, the intervention on these DRPs was considered adequate ($p$<0.001) and significant. For example, the DRP-reducing interventions on a too high dosage could save patients' safety and cost savings.

*4.1.4. DRPs for the time of taking drugs*

According to indication/guidelines, the time of taking drugs per day (morning, afternoon, evening) and time of taking drugs with meals (before, during, and after meals) inappropriately were more than 40% of prescriptions with DRPs. When prescribing, doctors often overlooked these (this was recorded when we reminded/intervened directly with each doctor). The proportion is higher than in Vietnamese patients with coronary artery diseases (23.3%)[19].

The percentage of DRP for the time of taking drugs per day inappropriately according to indication/ guidelines significantly decreased after the intervention (from 43.9% to 34.2%, $p<0.001$). This DRP usually occurs in some typical drugs. In particular, some drugs had relatively easy-to-remember times of use per day (for example, antihypertensive drugs were typically taken in the morning, statin drugs were usually taken in the evening). On the other hand, information about the time of taking drugs compared with meals (before, during, or after a meal) seemed harder to remember. It was a possible reason for the result after interventions this DRP not decreasing significantly ($p>0.05$). However, the degree of DRPs' influence on treatment outcome had not been documented in this study. To ensure optimal therapeutic efficacy for patients, more specific forms of information or reminders doctors to limit DRPs for the time of taking drugs compared with meals.

*4.1.5. Major drug-drug interactions*

The proportion of major drug-drug interactions in our study (3.7%) is lower than other studies in Germany (22.9%)[12]. The difference might be due to only major interactions being counted in our study. This DRP rate did not improve significantly after the intervention ($p>0.05$). This was probably because the drug interactions we reported (serious drug-drug interactions) were largely "monitored closely", such as the interaction between amitriptyline and escitalopram or ciprofloxacin and methylprednisolone. Only a few cases recommended contraindication to combine, for example, omeprazole, esomeprazole, and rabeprazole with clopidogrel. Therefore, when prescribing these drugs with drug interactions, the doctors might have weighed the benefits of treatment and consequences of drug interactions and made an appropriate follow-up plan. Specifically, when considering the detail of the interactions, we found that the interaction between amitriptyline and escitalopram was no longer after the intervention; meanwhile, the interaction between clopidogrel and PPIs was still high because the consequence of this interaction on clinical practice was still debated. In a recent study (Przespolewski ER et al., 2018) which evaluated the effect of six proton pump inhibitors on the antiplatelet effects of clopidogrel, the authors did not demonstrate the significant interaction between PPIs and clopidogrel in healthy volunteers[20].

### 4.2. Determinants of drug-related problems

Our study found that the intervention reduced the risk of DRPs ($p<0.001$). Prescriptions of female patients; patients under 65 years of age; patients with health insurance had a higher risk of DRP than another group ($p=0.025$; $p=0.001$; $p<0.001$). However, Koh et al.'s research (2005) stated that there was no relationship of age or gender to the occurrence of DRPs[21]. More than 70% of the population in Vietnam had health insurance; however, older people, people with one or more chronic diseases, had a higher frequency of using health services[17,22], so these factors could affect the DRP outcomes. Further studies need to analyze more clearly to find the real dominant causes.

We also recorded the number of drugs in the prescription related to the occurrence of DRPs ($p<0.001$), and this result was similar to many studies around the world[3,15-16,21]. Prescribing many drugs simultaneously, in particular, patients using 5 or more drugs got four times higher risk of DRPs than patients who used fewer ones ($p<0.001$) because each drug could occur one or more various types of DRPs.

### 4.3. Strengths and limitations

This is one of the first studies of pharmacist interventions on drug-related problems for outpatients in Viet Nam, and the study is designed with a large sample size. Assessment of drug-related problems in prescriptions based on three approved resources for health insurance reimbursement. The interventions are feasible/ easy to do in a hospital. We chose 15 days to collect prescriptions from all doctors at the clinics to ensure the balance between before and after interventions. Moreover, the multivariate analysis also includes factors with differences that can influence to process of data. In the clinical aspect, this study can be conducted in hospital efficiently and be supported by doctors because of Circular No. 30/2018/TT-BYT dated October 30, 2018, of the Ministry of Health on promulgation of the list of modern medicines, biologicals, radiopharmaceuticals and tracers covered by health insurance, insurance coverage ratio and payment conditions thereof, clinical pharmacists quickly check and apply study results by pasting/noting common DRPs at their desks to shorten the time to check prescriptions. If the study is used widely, it might improve efficiency, safety, and treatment costs for outpatients. In the scientific aspect, the study opens up many following directions to deepen/ evaluate the impact of DRPs in the clinic and/or conducts researches on integrating into prescribing software alerting DRPs.

Besides, the study also has some limitations.

The study did not evaluate the seasonal impact on the research results. In addition, it did not clearly show information about the patient's primary disease, did not evaluate medication prescribed between pre-intervention and post-intervention, and explain how similar conditions and drug patterns between groups. However, in general, the routine application of prescribing control interventions is also significant in prescription management. Researchers have not yet collected specific information to explain the reason why doctors prescribe a lack of drugs. This research only analyzed prescriptions, so the information was not enough to clarify the impact of kidney or liver dysfunction on prescribing. The consequences of DRPs on the patient's health and outcomes have not been considered. The mechanism of rotation in the clinic also gets influences on effects of interventions in the study.

## 5. CONCLUSIONS

Pharmacist-led interventions significantly reduced the proportion of prescriptions with DRPs, from 88.8% to 74.9% ($p$<0.001). Prescribing 5 or more medications increased the risk of DRPs compared to prescribing fewer drugs. Clinical pharmacists should be involved in controlling prescriptions for outpatients in clinical practice to improve prescribing safety, efficacy, and appropriateness.

## 6. ACKNOWLEDGEMENT

We would like to express our sincere gratitude to Can Tho University of Medicine and Pharmacy Hospital for allowing us to conduct this study.

### Conflict of interest

The authors declare that there are no conflict of interest.

### Funding

None to declare.

### Ethics approval

The study was approved by the Research Review Committee of the University of Medicine and Pharmacy at Ho Chi Minh City and accepted for performing at the study hospital in Vietnam in 2018 No. 1765/QD-DHYD.

### Article info:

Received June 1, 2021
Received in revised form September 22, 2021
Accepted October 3, 2021

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