# THE POTENTIAL CONTRIBUTION OF CLINICAL PHARMACISTS TO QUALITY USE OF MEDICINES IN GERIATRIC PATIENTS IN VIETNAM

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**STATEMENT OF ORIGINALITY**

*I hereby certify that the work embodied in the thesis is my own work, conducted under normal supervision. The thesis contains no material which has been accepted, or is being examined, for the award of any other degree or diploma in any university or other tertiary institution and, to the best of my knowledge and belief, contains no material previously published or written by another person, except where due reference has been made. I give consent to the final version of my thesis being made available worldwide when deposited in the University's Digital Repository, subject to the provisions of the Copyright Act 1968 and any approved embargo.*

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*I hereby certify that the work embodied in this thesis contains published paper/s/scholarly work of which I am a joint author. I have included as part of the thesis a written declaration endorsed in writing by my supervisor, attesting to my contribution to the joint publication/s/scholarly work.*

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*By signing below I confirm that Thi Xuan Phuong DONG contributed designing studies, collecting and analysing data, writing and editing manuscripts to the paper/ publication entitled:*

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## OTHER PUBLICATIONS DURING PH.D. CANDIDATURE

1. Trinh HT, Nguyen HTL, Pham VTT, Ba HL, **Dong TXP**, Cao TTB, Nguyen HTH, Brien JA (2018). Hospital clinical pharmacy services in Vietnam. International Journal of Clinical Pharmacy. 2018 Oct;40(5):1144-1153.
2. Dinh LA, **Dong TXP**, Pham TTV, Nguyen SN. Drug-related problems in outpatients' prescriptions in chronic medications in a central hospital. Vietnam Medical Journal. 2020May; 490(1): 273-242. [in Vietnamese]
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## CONFERENCE PRESENTATION (POSTER)

1. Pham TTV, **Dong TXP**, Vu TT, Li SC. Applying the 2015 updated Beers criteria to assess potentially inappropriate medication in elderly patient at discharge: A geriatric hospital-based study. Asian PharmNET II Conference, Kuala Lumpur, Malaysia, November 2017.

## GLOSSARY OF ABBREVIATIONS AND ACRONYMS

| | |
|---|---|
| 95% CI | 95% Confidence Interval |
| ADE | Adverse Drug Events |
| ADR | Adverse Drug Reactions |
| ADL | Activities of Daily Living |
| ASHP | American Society of Health-System Pharmacists |
| ATC | Anatomical Therapeutic Chemical |
| BPMH | Best Possible Medication History |
| CCI | Charlson Co-morbidity Index |
| CPI | Clinical Pharmacist Intervention |
| CPS | Clinical Pharmacy Services |
| DTC | Drug and Therapeutic Committee |
| DMSA | Department of Medical Services Administration |
| DRPs | Drug-Related Problem |
| EBM | Evidence-Based Medicine |
| FTE | Full-time Equivalent |
| HREC | Human Research Ethics Committee |
| MAI | Medical Appropriateness Index |
| MD | Medication Discrepancies |
| MedRec | Medication Reconciliation |
| MOH | Ministry of Health |
| OR | Odds Ratio |

| | |
|---|---|
| ORadj | Adjusted Odds Ratio |
| pADE | potential Adverse Drug Events |
| PCNE | Pharmaceutical Care Network Europe |
| PIM | Potentially Inappropriate Medication |
| PIP | Potentially Inappropriate Prescribing |
| PPO | Potentially Prescribing Omission |
| SD | Standard Deviation |
| SOP | Standard Operation Procedure |
| START | Screening Tool to Alert to Right Treatment |
| STOPP | Screening Tool of Older People's Prescriptions |
| QUM | Quality Use of Medicine |
| TDF | Theoretical Domains Framework |
| UMD | Unintentional Medication Discrepancies |
| WHO | World Health Organization |

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## THESIS SUMMARY

The thesis consists of eight chapters divided into four main parts (A-D), providing evidence on pharmacist-led interventions that have contributed to improving the quality of drug use in geriatric patients in Vietnamese hospitals. Chapter titles and each link in the four-part layout of the thesis are shown in Figure 0.1.

Part A consists of three chapters (1, 2 and 3), providing an overview of the context and purpose of the study. Chapter 1 provides a literature review about aspects of drug use in the elderly and the practice of pharmacists to help improve the quality of drug use in this population. More specifically, Chapter 1 provides a background as to why the elderly would be at high risk for drug-related problems and the extent of these problems among older adults around the world. This chapter also briefly introduces the concepts of clinical pharmacy and pharmaceutical care, as well as provides an overview of pharmacist-initiated interventions to improve and resolve these drug-related problems in elderly inpatients. Chapters 2 and 3 present a quantitative study and a qualitative study to provide information of the status of clinical pharmacy implementation in Vietnam (Chapter 2) as well as barriers and facilitators in implementing clinical pharmacy activities in Vietnamese hospitals (Chapter 3). These two chapters show that clinical pharmacy in Vietnam has been implemented in a limited way with barriers from human resources, policies as well as awareness of stakeholders. The results of these two chapters also show aspects that need improvement in practice implementation and suggest measures to overcome those barriers of implementation.

Part B consists of two chapters (4 and 5) that aim to evaluate the current situation of drug use in geriatric inpatients in Vietnamese hospitals. It focuses on two types of common drug-

related problems among this patient group, namely, unintentional medication discrepancies (Chapter 4) and potentially inappropriate prescribing (Chapter 5). Results from these two studies confirm that the prevalence of drug-related problems in geriatric inpatients is relatively high, which is similar to the situation in other countries. The results also show the less-than-ideal situation in the current practice of inpatient prescribing in Vietnamese hospitals for the elderly where clinical pharmacists can contribute to improving the quality of prescribing.

Part C is the central part of the thesis, with two chapters (6 and 7) that provide evidence of the potential role of pharmacists in improving the quality of prescribing in geriatric inpatients by reducing drug-related problems described in Chapters 4 and 5. Chapter 6 presents a before-and-after study showing the effectiveness of pharmacist interventions in enhancing the quality of drug management practice in inpatients. Chapter 7 provides details of an implementation study that evaluates the effectiveness of clinical pharmacy services in detecting and resolving inappropriate prescriptions among inpatients. These studies demonstrate the role of pharmacists in improving the quality of patient prescriptions by improving medication continuum at the time of admission (minimising unintentional discrepancies – Chapter 6) and detecting and solving drug-related problems in prescribing (Chapter 7) in geriatric inpatients.

This thesis demonstrates how to effectively use the limited available hospital pharmacist resources to improve the quality use of medicines in the geriatric population in Vietnam and countries with similar healthcare systems. Furthermore, given the theoretical framework proposed by Australia's National Strategy for Quality Use of Medicine, the overall project is an example of a strategy of utilising the professional expertise of pharmacists to solving the problem of suboptimal medication use (1). This can be illustrated graphically with actions at the different levels of the quality use of medicines' pyramid. At Level 1, "*the awareness level*,"

Chapters 4 and 5 are expected to provide evidence about the suboptimal prescribing in geriatric inpatients as a serious public health issue. At Level 2, "*the knowledge and skills level*," Chapters 2 and 3 will allow hospital pharmacists to discuss the issue and possible solutions. Finally, at Level 3 "*the action and evaluation level*", feasible solutions are developed, implemented, and incorporated into routine clinical hospital practice in Vietnam (Chapter 6 and Chapter 7).

In conclusion, this thesis shows that pharmacists are still able to effectively improve the quality use of medicines in Vietnam through strategically implemented clinical pharmacy activities, despite the lack of human resources and many other barriers in implementation. Pharmacists can achieve this with minimum disruption to the routine clinical workflow and resource requirement, but also make a significant contribution to improving the quality of drug prescribing in high-risk patients. This will provide an example for the pharmacy profession in other jurisdictions where human and other resources are highly constrained, like Vietnam.

**PART A. INTRODUCTION**

Chapter 1. Overview of prescribing issues in geriatric patients and potential contribution of clinical pharmacists

Chapter 2. Implementing clinical pharmacy activities in hospital settings in Vietnam: Current status from a national survey

Chapter 3. Barriers and facilitators of implementing clinical pharmacy services in Vietnamese hospitals from the perspective of pharmacists: An exploratory qualitative study

**PART B. CURRENT SITUATION OF DRUG USE IN GERIATRIC INPATIENTS IN VIETNAMESE HOSPITALS**

Chapter 4. Unintentional medication discrepancies at admission of elderly inpatients in Vietnam: Frequence, Risk Factors and Potential Clinical Impact

Chapter 5. Prevalence and Risk Factors of Potentially Inappropriate Prescribing in Elderly Inpatients in Geriatric Hospitals in Vietnam according to STOPP/START version 2

**PART C. POTENTIAL CONTRIBUTION OF CLINICAL PHARMACISTS**

Chapter 6. The impact of pharmacist-initiated educational intervention on improving medication reconciliation practice in geriatric inpatients during hospital admission in Vietnam

Chapter 7. Implementation and evaluation of clinical pharmacy services on improving quality of prescribing in geriatric inpatients in Vietnam: an example in a low resources setting

**PART D. DISCUSSION AND CONCLUSION**

Chapter 8. Discussion, conclusion and future work

**Figure 0.1. Structure and flow chart of the thesis**

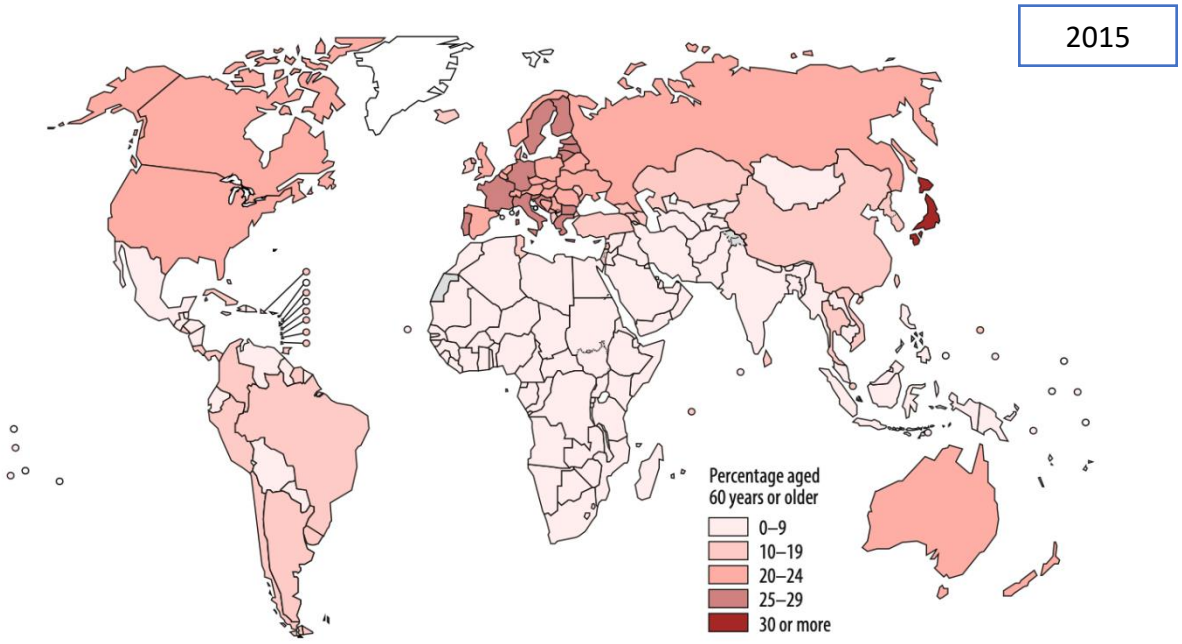
# PART A. INTRODUCTION

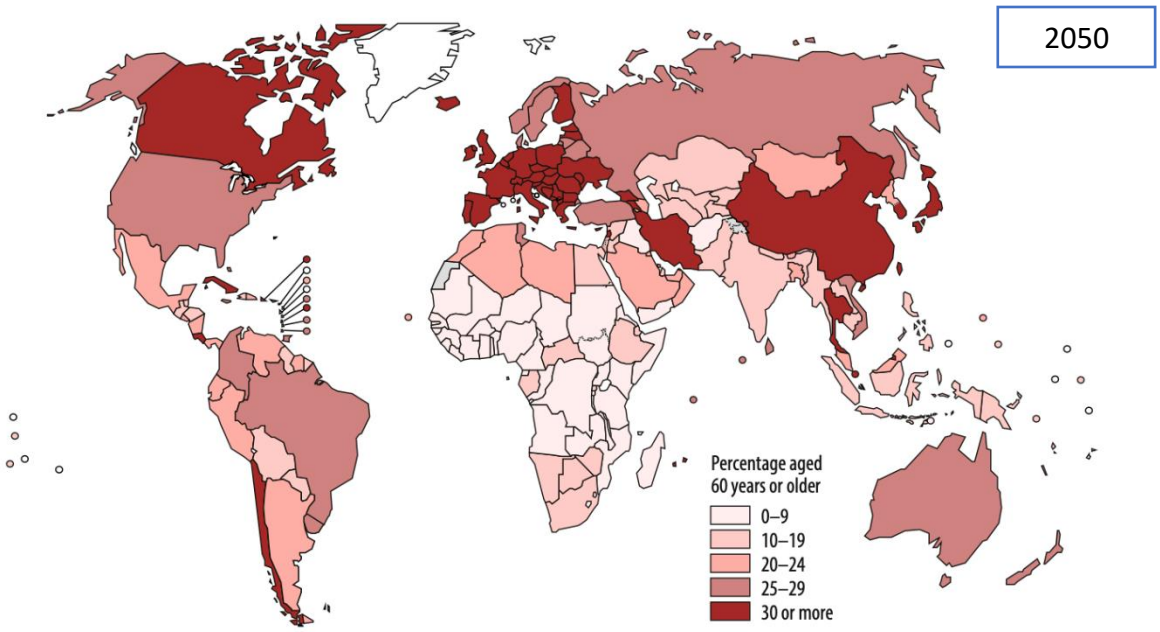
# Chapter 1. Overview of prescribing issues in the geriatric population and potential contribution of clinical pharmacists

# 1 Aging and Health

## 1.1 Epidemiology of aging

Population aging is a global phenomenon that impacts the healthcare systems of many countries. According to data from the World Health Organization, the proportion and absolute number of older people are rising substantially worldwide. With 565 million people, the world's population that are over 60 years old accounted for 7.6% of the total population in 2015. Many countries around the world, particularly those in Europe, North America, and Southeast Asia, are expected to have an elderly population of over 30% of their overall population by 2050 (2) (Figure 1.1).





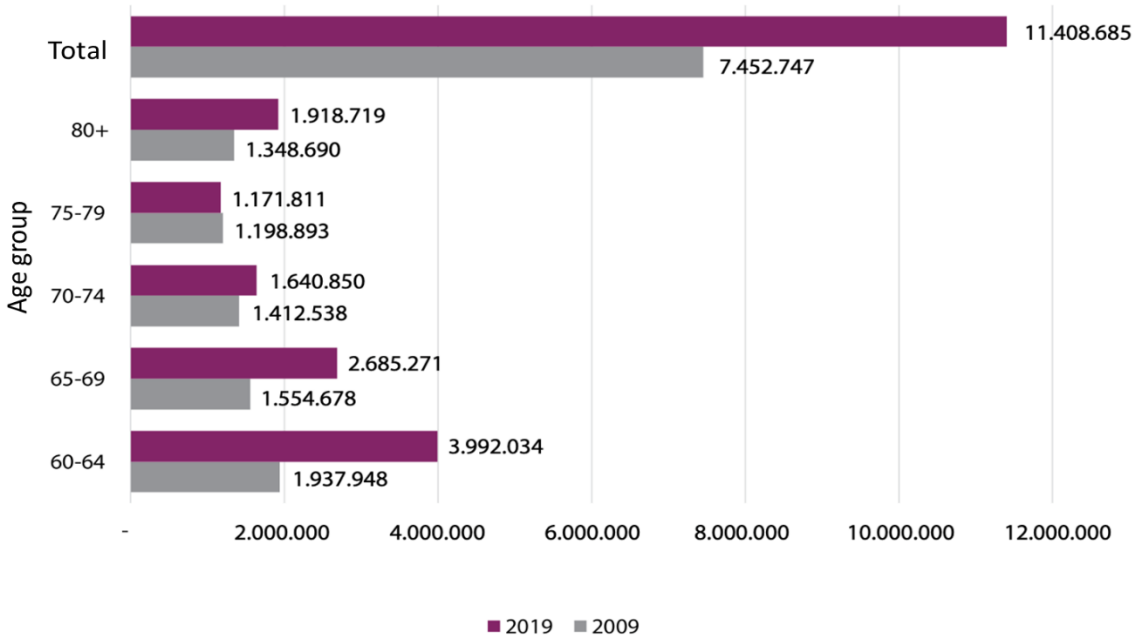

*Source: WHO (2015) World report on aging and health.*

***Figure 1.1. Proportion of population aged 60 years or older, by country, in 2015 and 2050***

Similarly, in Vietnam, the proportion of people aged 60 years and older is fast increasing. With 11.41 million individuals, the geriatric population in Vietnam now accounts for 11.86% of the total population, which is much higher compared to 2009 (8.68%) (Figure 1.2). As a result, Vietnam has joined the rank of countries with an aging population. By 2049, it is expected that the population over 60 years will account for 28.44% of the total population (3).

From a public health perspective, population aging places a greater emphasis on promoting healthy aging and improving the quality of life of individuals in their remaining years. The most critical objectives in the care of older individuals are maintaining independence and avoiding the necessity of hospitalisation. However, intrinsic capacity (i.e., the sum of their physical and mental capacities) tends to deteriorate with age, whilst health problems become more chronic

and complex. Functional loss or disability is a common cause of eventual institutionalisation in older people, particularly those over 75 years old. According to data from the 2019 Population and Housing Census in Vietnam, 35.73% of the elderly had difficulty with at least one body function (such as hearing, seeing, walking, etc.), compared to only 2.24% of children aged 6-15 years and 4.39% of adults aged 16-59 years. This substantially higher prevalence of functional disability in the older population highlights the need to devote more resources to addressing issues connected to functional disability in older people.




*Source: 2019 Population and Housing Census in Vietnam*

***Figure 1.2. Distribution of elderly population according to age group in Vietnam, 2019 - 2009***

In addition, chronic diseases such as heart failure, hypertension, stroke, asthma, and diabetes are becoming more common as people get older. According to a study on the Vietnamese elderly population, 72.4% of them had at least one chronic condition (4, 5). As a

result, older people consume more healthcare resources including prescription medications than any other age group. Chronic diseases or impairments are also the primary causes of disability and death in older adults.

## 1.2 Health characteristics of the elderly population

The following section describes the health characteristics among the elderly that predispose them to suffer from adverse events from managing their health conditions. Age-related physiological changes and multi-morbidity are key health-related features of the elderly population.

### *1.2.1 Age-related physiological changes*

Changes in the biochemical constitution of tissues, reduced capacity of body systems, lower ability to adjust to physiologic stress, and increased sensitivity to disease are natural physiological changes that occur as people age (6-8). In terms of *pharmacokinetics*, the four basic processes (including absorption, distribution, metabolism, and elimination) are significantly altered in the elderly when compared to healthy young adults (6, 9, 10) (Table 1.1). The deterioration in renal function, which leads to a decrease in drug clearance, is arguably the most important pharmacokinetic change (9). As a result, if the dose of drugs that are predominantly renally cleared are not adjusted appropriately, there is a risk of adverse drug reactions (ADRs) from drug accumulation.

**Table 1.1. Age-associated changes in drug pharmacokinetics**

| Pharmacokinetic phase | Pharmacokinetic Parameters |
|---|---|
| Absorption | ▪ Unchanged passive diffusion and no change in bioavailability for most drugs<br>▪ ↓ Active transport and ↓ bioavailability for some drugs<br>▪ ↓ First-pass metabolism and ↑ bioavailability for some medicines and ↓ bioavailability for some prodrugs |
| Distribution | ▪ ↓ Volume of distribution and ↑ plasma concentration of water-soluble drugs<br>▪ ↑ Volume of distribution and ↑ terminal disposition half-life ($t_{1/2}$) for lipid-soluble drugs |
| Hepatic metabolism | ▪ ↓ Clearance and ↑ $t_{1/2}$ for some drugs with poor hepatic extraction capacity-limited metabolism, phase I metabolism may be affected more than phase II<br>▪ ↓ Clearance and ↑ $t_{1/2}$ for medications with high hepatic extraction ratios flow-limited metabolism |
| Renal excretion | ▪ ↓ Clearance and ↑ $t_{1/2}$ for renally eliminated drugs and active metabolites |

*Footnote: Adapted from Hilmer et al. (7), Shi and Klotz (11), and Corsonello et al. (12) – Source: Pharmacotherapy – A pathophysiologic Approach*

The change in drug response due to age-related changes is also a major concern in terms of pharmacodynamics. Pharmacodynamic changes with age have been shown to be challenging to predict. These changes could occur at the receptor level (e.g., different drug concentrations at the receptor, receptor numbers or affinity), at the signal-transduction level, or the level of aging-related altered homeostatic systems (13). Pharmacodynamic variations between young and older persons may be attributable to changed sensitivity (i.e., a higher change in effect for a given change in drug concentration). It could also be related to changes in baseline performance or differing drug concentrations at the site of action (12). In general, most organ systems in the elderly are more fragile compared to those of younger persons, which implies that they are more sensitive to the side effects of medicines.

### *1.2.2 Multi-morbidity*

Multi-morbidity, or the prevalence of many chronic diseases or ailments simultaneously, is more common in the elderly. According to a systematic review of the literature including 48 articles between 1990 and 2010, the prevalence of multi-morbidity in older adults changes from 55 to 98% (14). The increasing prevalence of multi-morbidity with age has also been documented in other studies. For example, multi-morbidity was reported in 81.5% of populations over 85 years old compared to 62% of those 65–74 years old and 50% of those under 65 years old (15). Another study found multi-morbidity to be three times more common in people over the age of 85 years in comparison to people under 70 years old (16).

Clinically, multi-morbidity worsens disease load, impairments in function, and quality of life and increases the risk substantially more than the sum of the individual illnesses. This is due to interactions between the medical conditions and the medications used to treat the various illnesses as well as the medicines themselves (14). These often require extra health management. Consequently, multi-morbidity is associated with greater rates of healthcare utilisation expenses (14).

Furthermore, treatment of older adults with multi-morbidity is complex for a variety of reasons. Standard clinical treatment guidelines typically only provide recommendations for a specific condition, and information on potential comorbidities is not included (17, 18). As aforementioned, the use of polypharmacy places the patient at increased risk of drug-drug interactions and adverse drug reactions (19), even though each medication may be appropriate for treating the individual disease. Last but not least, most clinical trials generally exclude older

people entirely, despite their altered physiology requiring special attention, and the elderly are most likely to be the common users of the new drugs (20). This causes a lack of evidence of proper treatment in the elderly and severely limits the application of evidence-based medicine (EBM) on optimising treatment outcomes in this population (21).

### *1.2.3 Polypharmacy*

As mentioned above, polypharmacy in older adults is a common consequence of multi-morbidity. There are many definitions for polypharmacy, depending on the patient population and study setting (22). One commonly used definition is the use of five or more drugs simultaneous, which is the definition used in this thesis. The prevalence of polypharmacy in the elderly is substantially high and increasing worldwide in community settings (23, 24), nursing facilities, and hospital settings (25, 26). Clinically, polypharmacy has been strongly associated with the risk of ADRs, medication non-adherence, falls, cognitive impairment, and increased healthcare costs (23). Besides the requirement of treatment for multi-morbidity, which is usually reasonable, there are some circumstances where elderly patients receive more medications than needed. For example, if older patients use medications prescribed by a variety of physicians, they are at increased risk of accumulating "layers of medication treatment". Prescribing cascades, the events in which an adverse effect is misinterpreted as a new medical problem and lead to the prescription of additional drugs, are other common concerns in elderly patients (27).

### *1.2.4 Risk of Adverse Drug Reactions (ADRs)*

Due to age-related physiological changes, the high prevalence of polypharmacy, and multiple comorbid conditions mentioned above, elderly patients are at a higher risk of ADRs, drug-drug

interactions, drug-disease interactions, and medication errors (16, 28, 29). Adverse drug events are not only more frequent but are also more severe in the elderly than in the younger population. A recent systematic review showed that ADRs occurred in 10.7% of hospitalised elderly patients, while this figure was only 6.3% in young patients (30). A hospital-based prospective cohort study conducted in 1000 elderly patients in 2013 in Pakistan showed that polypharmacy (≥5 drugs) occurred in 70% of the study population, with 10.5% having also suffered from ADRs. The risk of ADRs in patients taking polypharmacy was 2.3 fold higher (95% CI: 1.4-3.9) compared to patients taking less medications (31, 32). The risk of ADRs in the elderly was estimated at 6% when taking two drugs simultaneously, and this increased up to 50% when five concurrent drugs were used and up to 100% with eight or more drugs (32). A prospective cohort study found that outpatients taking five or more drugs increased the risk of ADRs by 88% compared to those taking less than five drugs (33). Regarding the consequence of increased risk of ADRs, Maher et al. established a clear association between polypharmacy and negative clinical outcomes (28). In addition, Zacharyet al. also showed that older veterans who took more than five drugs increased their risk of hospitalisation 4-fold compared to those taking less medications (34).

## 2 Drug – Related Problems and prescribing issues in elderly inpatients

### 2.1 Definition of Drug – Related Problem

In 1990, a definition of the term Drug Related Problem (DRP) was put forth by Linda Strand to describe the categorisation and description of clinical problems related to the use of drugs. According to this definition, "A Drug-Related Problem is an event or circumstance involving drug therapy that actually or potentially interferes with desired health outcomes. A DRP exists when a patient experiences or is likely to experience either a disease or symptom having an

actual or suspected relationship with drug therapy" (19). Similarly, the Pharmaceutical Society of Australia defines a DRP as "an event or circumstance involving drug treatment that actually or potentially interferes with the patient experiencing an optimum outcome of medical care" (35).

## 2.2 Classification of drug-related problems

Several research groups and organizations have developed their own systems for the classification of DRPs, such as The Pharmaceutical Care Network Europe (PCNE) (36), The American Society of Health-System Pharmacists (37), and Pharmaceutical Society of Australia (35). These classifications have been utilised as a process indicator in studies of pharmaceutical care outcomes as well as to explain the nature, prevalence, and characteristics of DRPs. It is also designed to assist healthcare workers to keep track of DRP data during the pharmaceutical care process. DRP categorisation can be used as a starting point for building a systematic procedure that allows pharmacists to make a major contribution to positive patient outcomes.

In clinical practice, DRPs might appear at any point during the medication use process. As a result, the PCNE divides DRPs into three categories: prescription, dispensing, and use (related to patients). This thesis focuses on the group of DRPs related to prescribing in geriatric inpatients and uses the PCNE classification as a basis for recording DRPs during the implementation study.

## 2.3 DRP in prescribing for geriatric patients

Prescribing is defined the process of deciding which and how medications are to be used, with the prescription being the means to communicate these decisions (38). Prescribing in older patients is recognised as a difficult and time-consuming task, and ample evidence of DRPs in prescribing among geriatric patients in hospital have been reported (39-41). Several commonly

used terms to describe poor prescription issues include “DRP in prescribing”, “Potentially Inappropriate Prescribing”, and “Prescribing errors (Medication Error in Prescribing)”. Despite the lack of agreement on the definitions of these categories, the term DRP in prescription might be considered the broadest term, covering most aspects of the other terminologies. According to the PCNE classification (36), prescribing DRPs can be divided into four groups: choice of active ingredient, dose, dosage form, and duration of treatment (Table 1.2).

**Table 1.2. PCNE classification of Drug-Related Problems (DRPs) in prescribing (36)**

| Primary Domain | Code | Cause |
|---|---|---|
| **1. Drug selection**<br><br>The cause of the (potential) DRP is related to the selection of the drug (by patient or health professional) | C1.1 | Inappropriate drug according to guidelines/formulary |
| | C1.2 | No indication for drug |
| | C1.3 | Inappropriate combination of drugs, or drugs and herbal |
| | C1.4 | medications, or drugs and dietary supplements<br>Inappropriate duplication of therapeutic group or active ingredient |
| | C1.5 | No or incomplete drug treatment in spite of existing indication |
| | C1.6 | Too many different drugs/active ingredients prescribed for indication |
| **2. Drug form**<br><br>The cause of the DRP is related to the selection of the drug form | C2.1 | Inappropriate drug form/formulation (for this patient) |
| **3. Dose selection**<br><br>The cause of the DRP is related to the selection of the dose or dosage | C3.1 | Drug dose too low |
| | C3.2 | Drug dose of a single active ingredient too high |
| | C3.3 | Dosage regimen not frequent enough |
| | C3.4 | Dosage regimen too frequent |
| | C3.5 | Dose timing instructions wrong, unclear or missing |

| | | |
|---|---|---|
| **4. Treatment duration** The cause of the DRP is related to the duration of treatment | C4.1<br><br>C4.2 | Duration of treatment too short<br><br>Duration of treatment too long |

The second term **"**inappropriate prescribing" or "potentially inappropriate prescribing" refers to a variety of suboptimal prescribing practices (42), such as under-prescribing, over-prescribing and mis-prescribing.

Under-prescribing can be caused by a lack of sufficient geriatric pharmacotherapy training of the prescribing doctors (43), or by a behavior known as ageism, which is the refusal to prescribe a prescription or increase a dose only because the patient is elderly (44). Overprescribing is frequently caused by inadequate re-evaluation of medication therapy over time, with the result that medications are prescribed even when the indication for their use no longer exists. When a patient with a known medical indication is prescribed a prescription that is hazardous or ineffective, or a suboptimal dose, formulation, or dosing interval, this is known as mis-prescribing. Inappropriate prescription might also result from a lack of communication among clinicians working in various contexts (43, 44).

### *2.3.1 Tools to assess "Potentially Inappropriate Prescribing"*

There are currently a variety of screening techniques available to determine whether prescribing in the elderly is suitable. These are commonly classified into two categories: "implicit" or open tools, which are based on clinical assessment, and "explicit" or closed tools, which are based on standards/criteria.

*Implicit tools (judgment-based)*

The Medical Appropriateness Index (MAI) score is the most widely used implicit tool today. Hanlon et al. published MAI for the first time in 1992 (45). This tool assesses prescribing appropriateness based on ten criteria: indications, efficacy, dosage, administration (correct and practical), drug-drug interactions, disease-drug interactions, duration of treatment, duplication with other drugs, and treatment costs. MAI is widely regarded as the most complete and valuable open evaluation tool available. It covers every aspect of prescribing and can be used with any medicine or condition in any clinical context. However, applying MAI takes a long time (about 10 minutes for each medicine) and does not address the issue of under-prescribing. As a result, MAI is mostly used in research investigations and is hard to apply in clinical practice (46).

*Explicit tools (criteria-based)*

Many organizations throughout the world have developed screening tools to help make prescribing more appropriate over the last few decades. Several systematic reviews showed that there were 14 to 42 tools available being used to evaluate these prescribing patterns in elderly patients (47-49). The most often utilised tools in study and practice to date are Beers (50), STOPP/START (51), EU(7)-PIM (52), and FORTA (Fit fOR The Aged) list (53). Most of the tools are built on literature review and expert consensus using the Delphi method. A systematic review about all potentially inappropriate medications for older persons included in prescribing criteria published in 2015 (47) showed that the most common potentially inappropriate medications in the elderly according to these tools are benzodiazepines, NSAIDs, antihistamines, and antipsychotics.

### *2.3.2 Prevalence and consequence of PIP in elderly people*

A number of recent systematic reviews have shown that inappropriate prescribing practices in the elderly are common around the world. Using several explicit screening tools for potentially inappropriate prescribing, many studies have also shown a high prevalence of inappropriate prescriptions in the elderly in primary setting (54), secondary setting (39, 55-61), and nursing homes (62) with negative outcomes (39, 63). It is generally acknowledged that inappropriate prescribing in the elderly causes significant morbidity and is recognised as a serious public health concern.

### *2.3.3 Medication errors in transition of care – unintentional medication discrepancies*

Medication discrepancies, defined as inconsistencies between two or more patients' medication lists, that occur during the transition between healthcare facilities, such as on admission, transfer, and discharge (64). These discrepancies, particularly those that are unintended, can frequently lead to avoidable medication errors and can be hazardous to patients (65, 66). They are likely to occur when medication changes are not communicated between care settings or responsible healthcare professionals. These discrepancies are the cause of prescribing errors such as treatment omissions, incorrect doses, and incorrect dosage forms. They are generally due to technical gaps in the patient's treatment transition process, rather than a clinical prescribing decision. Because of their high risk of suffering drug-related problems, medication discrepancies have been extensively studied in geriatric patients. Medication discrepancies during care transitions have been reported in this population at a rate ranging from 49.5% to 81.9% (67-70).

## 3 Clinical pharmacy and its role in improving the quality of prescribing in geriatric patients

### 3.1 Definition of clinical pharmacy and pharmaceutical care

The concept of clinical pharmacy was first proposed in the United States in the 1960s in response to a societal need to enhance the use of medicines. The goal of clinical pharmacy practice is to encourage rational drug use, which would result in enhanced health, well-being, and illness prevention, as well as an overall improvement in the quality of life for patients. To implement clinical pharmacy practice, pharmacists who have received specialised advanced education and training and who possess the necessary clinical competences are required to practice in team-based, direct patient care settings (71, 72).

The concept of pharmaceutical care, described by the American Society of Health-System Pharmacists (ASHP) as the pharmacist's mission, is closely related with the concept of clinical pharmacy. Accordingly, "pharmaceutical care is the direct, responsible provision of medication-related care for the purpose of achieving definite outcomes that improve a patient's quality of life" (37). Another consensus definition of pharmaceutical care was suggested by the Pharmaceutical Care Network Europe (PCNE) in 2013: "Pharmaceutical Care is the pharmacologist/pharmacist's contribution to the care of individuals in order to optimise medicines use and improve health outcomes"(73). Pharmaceutical care, according to both definitions, has the same objective of clinical pharmacy and is viewed as a professional practice rather than a health science. It describes a method for clinical pharmacists to better organise their activities. The notion of clinical pharmacy clarifies the process component of pharmacists' involvement in pharmaceutical care and increases the academic foundation of pharmaceutical care (71).

Consequently, clinical pharmacists' roles in hospitals have evolved over time, with a greater emphasis on collaborative treatment and patient involvement. Clinical pharmacy services

for inpatients have been shown to be beneficial in terms of clinical outcomes, patient-related outcomes, and economic outcomes in previous research. This includes reducing the number of drug-related issues, hospital stays, expenses, adverse drug events, readmission rates, and drug-related admissions (74-78). A recent systematic review and meta-analysis conducted in 2020 including 42 intervention studies (controlled trials) re-confirmed the impact of clinical pharmacists on the clinical effects following pharmaceutical care for patients, including reducing systolic blood pressure and diastolic blood pressure and shortening hospitalisation days (79). Currently, clinical pharmacy services are well established and implemented in many countries, particularly in North America, Europe, and Australia; and clinical pharmacists are considered an integral part of the multidisciplinary healthcare team to improving the quality use of medicines.

## 3.2 The role of clinical pharmacists in improving quality of prescribing for elderly patients in hospital settings.

The efficacy of multiple strategies for improving quality of prescribing has been examined, and studies have shown that pharmacists play a key role in minimising prescribing-related DRPs (80-83). The following sections provide evidence of the positive effect of clinical pharmacist interventions to improving the quality of prescribing and optimisation of treatment in geriatric inpatients, with a focus on three key intervention types: medication reconciliation, medication review, and pharmacist-led educational interventions.

### *3.2.1 Medication reconciliation*

*Definition*

Medication reconciliation is a practice that aims to intercept medication discrepancies at all transitions in care (84). Many organisations have demonstrated that implementing medication

reconciliation at all interfaces of care is an effective and necessary strategy for identifying and resolving medication discrepancies, thus ensuring patient safety (84-86). Currently, medication reconciliation has become a standard healthcare practice recommended by the WHO (87) and many countries (88-91). According to the WHO, "medication reconciliation is the formal process in which health care professionals partner with patients to ensure accurate and complete medication information transfer at interfaces of care" (84). Medication reconciliation is a process that can be divided into three main steps: (i) Verification (collection of the patient's medication history); (ii) Clarification (ensuring the medications and dosages are appropriate); and (iii) Reconciliation (documentation of changes in the orders).

*Impact of pharmacist-led medication reconciliation in elderly inpatients.*

Many studies have shown that pharmacists are health care professionals with the most appropriate skills and knowledge to perform medication reconciliation (92, 93). The elderly population have always been the focus of medication reconciliation, due to their high prevalence of suffering from multi-morbidity and utilisation of polypharmacy. As mentioned in the previous section, the time of transition of care from community to hospital setting is prone to prescribing errors due to unintentional medication discrepancies. Therefore, many studies discussed below have demonstrated the role of pharmacists in implementing medication reconciliation for elderly patients during hospital admission and discharge. Some of the clinical benefits are listed briefly as follows.

- ***Improving accuracy***: Some studies have found that pharmacists made fewer errors compared to physicians when completing medication reconciliation, thereby improving the accuracy of patients' medication history (94, 95).

- ***Reducing prescribing errors***: Pharmacist-led medication reconciliation has proven successful in identifying and reducing most prescribing discrepancies in patients (66).
- ***Improving clinical outcomes***: A systematic review involving 17 studies (8 RCTs) conducted in 2016 showed that pharmacist-led medication reconciliation service led to significant reduction in adverse drug event-related hospital revisits, emergency department visits, and hospital readmissions by 67%, 28% and 19%, respectively (96).
- ***Economic outcomes:*** Medication reconciliation is also associated with significant financial savings. In a prospective study conducted In USA, pharmacist-led medication reconciliation resulted in $42,300 in cost avoidance in 77 patients. Financial savings were calculated based on cost avoidance for the treatment of potential ADRs avoided by the patient receiving medication reconciliation services, after correction for the pharmacist's salary performing the activity (98). In an ad hoc retrospective comparison conducted in USA in 2010, the financial savings per 100 patients who received medication reconciliation was estimated as $35,000. Financial savings were calculated from 14-day readmission data, which indicated a statistically significant reduction in readmissions. (97).

*Medication reconciliation practice in Vietnam*

In Vietnam, obtaining the medication history from patients is the responsibility of doctors, nurses, and clinical pharmacists during ward rounds. However, the concept of medication reconciliation is still very new and has not been mentioned in any government documents or specialised professional practice standard guidelines. Currently, there is no standard operating procedure for medication reconciliation in Vietnam. This is further attested by a literature search performed by our research team, which found no studies on this topic performed in Vietnam

before the time of conducting the research project as presented in this thesis. Hence, the prevalence and clinical impact of medication discrepancies remain unknown as a potential clinical problem in Vietnam. Without this information, it is difficult to request the healthcare administrators to allocate appropriate resources to rectify this problem.

### *3.2.2 Medication review*

*Definition*

The official definition by the Pharmaceutical Care Network Europe (PCNE) for medication review in all settings was introduced in 2016 as follows: "Medication review is a structured evaluation of a patient's medicines with the aim of optimising medicines use and improving health outcomes. This entails detecting drug-related problems and recommending interventions" (36).

*Classification of medication review*

Due to differences in the available information, different types of medication review may uncover distinct DRPs. PCNE separates medication reviews into three categories based on the information that will be used and the forms of DRP that can be identified accordingly (Figure 1.3). Using pharmacy claims data or pharmacy medication histories, a type 1 medication review looks for concerns such inappropriate dosing, drug–drug interactions, and therapeutic duplication. The medication history, clinical data, and information from the patient interview are all required for an advanced medication review (type 3). This data can also be used to identify additional DRPs, such as a medicine without an indication or an inappropriate dose form.

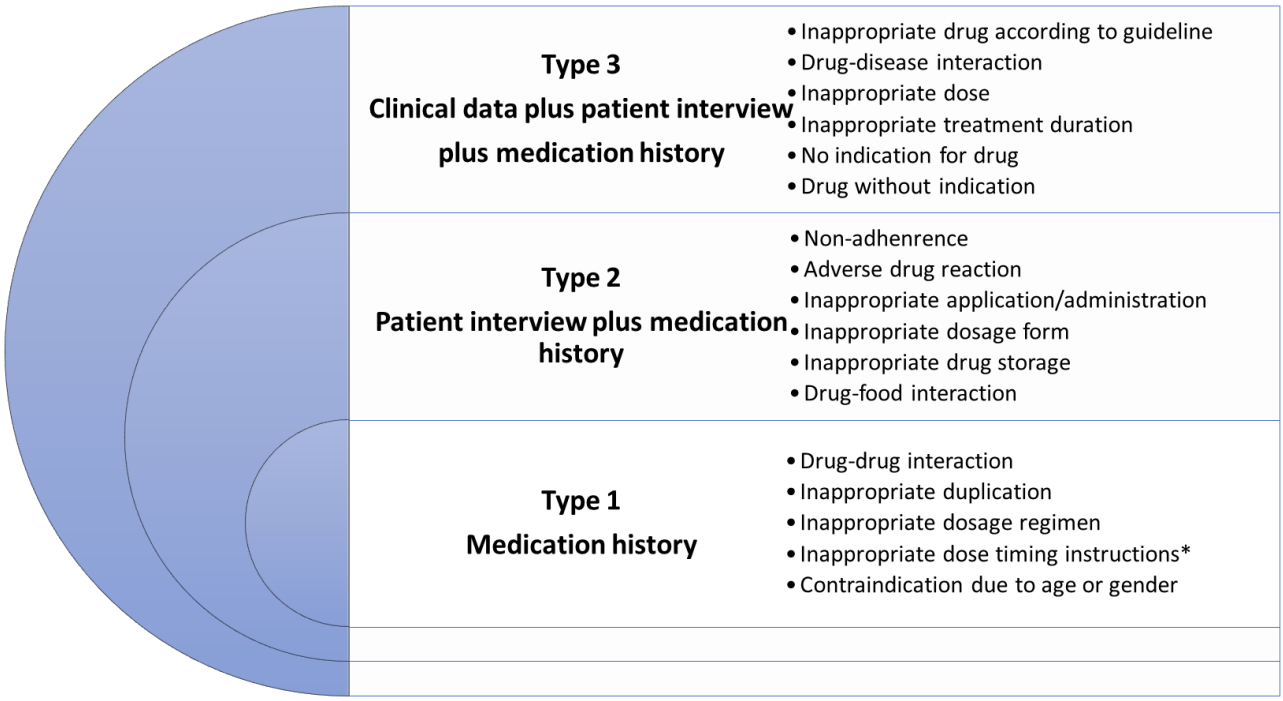



***Figure 1.3. Types of medication review according to Pharmaceutical Care Network Europe***

*The impact of pharmacist-led medication review*

Much research has examined the impact of clinical pharmacists on improving prescription quality in the elderly, using various outcomes. Recently, researchers have focused on characterising intermediate outcomes using the number of prescribing related DRP identified by pharmacists and intervention acceptance rate by physicians (99-101). Several studies used the Medication Appropriateness Index scale to assess the degree of improvement in prescribing appropriateness with the participation of clinical pharmacists (99, 102). Other studies were conducted to measure the effectiveness of pharmacist-led medication review using clinical outcomes such as mortality, emergency department visit, and length of hospital stay (103-106). In all these studies, pharmacists took medication histories at admission, performed medication reviews and patient counseling during the hospital stay, and communicated with patients and primary care practitioners upon discharge. The findings showed that the participation of clinical

pharmacists in a multidisciplinary team enhanced the Medication Appropriateness Index (MAI) and improved all clinical outcomes indicators (103-106). Similarly, studies that used other available assessment tools, such as Beers and STOPP/START, to evaluate prescribing in the elderly also identified a decrease in the prescribing rate of PIPs with intervention by pharmacists (80-82).

### *3.2.3 Pharmacist-initiated education*

Another type of interventions that pharmacists can perform to reduce prescribing problems in patients is to provide training for other healthcare professionals (107). Several systematic reviews have demonstrated the impact of educational interventions particularly on the quality of prescription. For example, Ross and Loke conducted a systematic review in 2009 including 22 intervention studies (controlled trials and before-after-studies) to evaluate if educational interventions could improve the quality of prescribing by medical students and junior practitioners (108). Ten of the eleven controlled trials and four before-and-after trials included in the review showed improvements in participants' performance in written scen

arios or clinical exam stations. The WHO Good Prescribing Guide (109), according to a systematic assessment of educational interventions to improve prescribing, has shown efficacy in worldwide settings across a wide spectrum of students at various levels (110). Recently, a with 12 studies systematic review conducted by *Jaam et al*. in 2021 about pharmacist educational interventions for nurses and physicians found that providing appropriate training can significantly reduce medication errors, including prescribing errors. The results from the meta-analysis support the implementation of training interventions to improve the quality of drug use in patients (107).

# 4 Potential contribution of clinical pharmacists to the Quality Use of Medicines in geriatric patients in Vietnam

Although Vietnam adopted the concept of clinical pharmacy in the 1990s, clinical pharmacy services were not defined in any official government document until 2011. However, throughout the last decade, several official government documents have been issued. Specifically, the Vietnam Ministry of Health (MOH) has produced "circulars" since 1997, which are legal regulations for the Drug and Therapeutic Committee (DTC) (111), medicine information centres in hospitals (112), and medicine information in marketing and communication (113). Based on these regulations, hospitals commenced implementation of pharmacy activities related to medicine information, thereby supporting the DTC to improve the quality of medicine use in Vietnam.

In December 2012, the first legal regulation of Vietnam MOH in clinical pharmacy – the "Circular No. 31 for clinical pharmacy service" (114) – officially defined the roles of clinical pharmacists in hospital settings. Clinical departments in hospitals were guided to cooperate with their departments of pharmacy to provide clinical pharmacy activities. This was the first legal framework for clinical pharmacy in hospitals in Vietnam and highlighted the expectation of increase in clinical pharmacists' contribution in the healthcare system. However, the contributions of the activities of hospital pharmacists as an integrated part of the multidisciplinary team in improving quality use of medicine have not been widely evaluated in Vietnam up to now. Without this information on the status of practice, it is difficult to plan how

to effectively implement more clinical pharmacy services in hospitals to improve healthcare delivery and quality of care in Vietnam.

In general, all the conducted studies emphasise the importance of safe and effective prescribing to minimise Adverse Drug Events (ADE) and DRPs in geriatric patients, as they increase the risk of morbidity and mortality for patients as well as increase health system expenditures. These reviews recommend that all DRPs be subjected to risk assessment. Numerous initiatives, including education and training as well as academic detailing have been examined with the goal of increasing the safety and appropriateness of prescribing for this vulnerable population. There are established benefits to expanding the role of clinical pharmacists in hospitals to improve medication management across a number of settings. While there is evidence of the benefits of clinical pharmacist-led interventions globally, there is less evidence of their impact on the quality of prescribing in elderly patients in Vietnam.

## Hypothesis

The overall hypothesis of this thesis is that pharmacist-led interventions would lead to significant improvements in the quality of medicine prescribing in geriatric inpatients in Vietnamese hospitals.

## Aims

1. To ascertain the status of clinical pharmacy activities performed within the Vietnamese hospital setting.
2. To determine the barriers and facilitators associated with implementing clinical pharmacy services (i.e., pharmaceutical care activities) in Vietnamese hospitals.

3. To evaluate the prevalence and risk factor of some Drug-Related Problems (potentially inappropriate prescribing and unintentional medication discrepancies) in prescribing in geriatric inpatients in Vietnamese healthcare settings.
4. To develop and evaluate the impact of pharmacist–initiated interventions on improving the quality of prescribing for geriatric inpatients.

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# Chapter 2. Implementing Clinical Pharmacy Activities in Hospital Setting in Vietnam: Current Status from a National Survey

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**Abstract**

**Background**: Clinical pharmacy activities have evolved over the past decades contributing to all stages of the patient care process, especially in the hospital setting. However, these practice roles may differ to a significant extent depending on the healthcare policy of countries. In Vietnam, the magnitude of adopting clinical pharmacy activities in hospital settings throughout the country is still unknown since these activities have been implemented. This study aimed to ascertain the current status of clinical pharmacy activities performed within the Vietnamese hospital setting.

**Methods:** A nation-wide survey was conducted from December 2017 to January 2018. Two online questionnaires, one for the Heads of Pharmacy Department and one for clinical pharmacists, were designed based on the national legal regulations about implementing clinical pharmacy activities in the hospital setting. These questionnaires were sent to all hospitals and healthcare facilities with a department of pharmacy.

**Results**: A total of 560 Heads of Pharmacy and 574 clinical pharmacists participated in the study, representing a response rate of 41.2%. Among the participating hospitals, *non-patient specific* activities were implemented widely across all hospital classes, with pharmacovigilance, medication information, and standard operating procedures development implemented in ≥88% of all hospitals. In contrast, there was a significant variation in the level of implementation of *patient-specific activities* among hospital classes. with *activities* such as medication counseling, monitoring of adverse drug reactions, and obtaining patient medication histories provided at a considerably lower level in between 49 and 57% of hospitals.

**Conclusion**: Clinical pharmacy activities have been initiated in most of the surveyed hospitals. In general, clinical pharmacy is more established in higher-class hospitals in Vietnam. However,

the current implementation status is focused on non-patient-specific activities, while patient-oriented activities remained insufficiently established.

**Keywords:** clinical pharmacy, pharmacy practice, national survey, Vietnam

# 1 Background

Clinical pharmacy is a health science discipline in which pharmacists provide pharmaceutical care that optimizes medication therapy and promotes health, wellness, and disease prevention (1). Clinical pharmacy services have been widely proven to reduce adverse drug reactions (ADRs) and hospital readmissions, improve medication adherence and appropriateness, and enhance clinical outcomes for patients (2, 3). With this practice mode, the responsibilities of pharmacists are no longer limited to drug manufacturing and supply. Instead, their role has significantly expanded to incorporate a number of clinical pharmacy services across various clinical settings, including in many patient care areas in hospitals (1, 4, 5). While clinical pharmacy services are well-established in many developed countries (6, 7), these practice roles may differ to a significant extent depending on the healthcare policy and resources in other countries (8-10).

In Vietnam, a lower-middle-income country in Southeast Asia, with a high-pressure healthcare system and a low ratio of healthcare workers per capita, the extent of clinical pharmacy development in healthcare facilities is still not fully explored. For almost 30 years, the Ministry of Health (MOH) in Vietnam has issued consecutive “circulars” and “decisions” related to clinical pharmacy areas. Examples of these documents include Pharmacy and Therapeutic Committees (1997), Medicines Information Centers in Hospitals (2003) (11), and MOH’s Regulation Circular 31 (2012) – the latter was the first legal framework for implementing clinical pharmacy in Vietnamese hospitals (12). Most recently, clinical pharmacy was defined explicitly in the updated Pharmaceutical Law (2016) (13), and included administrative rules related to clinical pharmacy. The actions of the health authorities demonstrate that clinical pharmacy is

becoming more important and is gradually recognized and accepted in hospitals and by clinical leaders in Vietnam.

Along with significant policy changes, clinical pharmacy education and training in Vietnam have improved since the 2010s. Pharmacy schools began changing their curricula to include a greater emphasis on the patient and clinical practice. The 2007–2012 project "Strengthening the training quality of clinical pharmacists in Vietnam," in which six Vietnamese schools of pharmacy collaborated with Dutch, Thai, and Indonesian institutions, has integrated clinical pharmacy as a specialization into existing pharmacy programs. In 2012, the Ministry of Education and Training issued BPharm curriculum reform (14), which required pharmacy schools to provide a specialization in clinical pharmacy. This was a step in preparing well-trained human resources for implementing clinical pharmacy activities in hospitals.

Following these initiatives, clinical pharmacy services have been provided diversely across Vietnamese hospitals, depending on their needs, workforce, and facilities. These services were broadly described in a few small-scale studies with limited information detailed. These recent studies on the clinical pharmacy services in Hanoi and Ho Chi Minh City (two of the biggest cities in Vietnam) (15-17) reported that the most described clinical pharmacy activities were non-patient specific activities, with the most common being the provision of drug information, participation in pharmacovigilance activities, and research of medication usage. Direct-patient care activities were limited and varied widely among hospitals. These studies also highlighted that the main obstacles faced by most hospitals were insufficient workforce and lack of qualified clinical pharmacists (15, 16).

Nevertheless, it should be noted that these studies were only limited to one city (15, 16). Therefore the results cannot be extrapolated to identify clinical pharmacy services across the

country after promulgating and implementing the official regulations. To evaluate the impact of the legal requirements, there is a need to perform a more comprehensive study to provide more generalizable information about the current status of the practice of clinical pharmacy in Vietnamese hospitals.

**Aim**

The aim of this study was to assess the workforce involved in providing clinical pharmacy activities in Vietnamese hospitals and to describe the current extent of clinical pharmacy activities performed within the hospital setting. The differences in clinical pharmacy activities between the hospital classes were also compared in this study. The key reason for conducting the study was to understand the necessary future changes required and support strategies needed in Vietnamese hospitals to improve the implementation of clinical pharmacy services

## 2 Methods

### 2.1 Study design and setting

This study was a part of a project supported by the Department of Medical Services Administration (DMSA) from the Ministry of Health (MOH) to investigate the current status of clinical pharmacy services and medication information services in Vietnamese hospitals. The project was conducted in the context of the development of the Decree of Clinical Pharmacy and the National Guideline of Clinical Pharmacy Services to be released to understand the extent of implementation of clinical pharmacy services throughout the whole country. The study methods have previously been published in another article about medication information services by the research group (18). In brief, a national cross-sectional survey was conducted in Vietnam, a

middle-income country in Southeast Asia with a population of 92.7 million. All hospitals with a pharmacy department were invited to this study, with a total number of 1359 according to the Health Statistics Yearbook 2017 (19).

### 2.2 Definition of hospital class

According to the regulations of the Ministry of Health of Vietnam, all hospitals are categorized in descending order of available medical specialties and size of the hospital as Special Class, Class 1, Class 2, Class 3, or Class 4 based on the following predefined criteria (20-22) – (i) location, function, mission, (ii) scale and content of operation, (iii) technical expertise, infrastructure, and (iv) medical equipment. However, there is no precise definition for each hospital class. The classification of hospitals is the basis for technical classification and development orientation of hospital activities over time, including clinical pharmacy activities. Therefore, the extent of clinical pharmacy implementation was analyzed based on hospital classes in this study.

### 2.3 Design of the questionnaires

According to the clinical pharmacy regulations of the Ministry of Health (11, 12, 23), the activities of clinical pharmacists in the hospital setting are organized into two main categories:

- *Non-patient specific activities* including participation in hospital committees, development of guidelines and protocols for medication use, development of treatment guidelines in collaboration with medical and nursing teams in the departments involved, participation in pharmacovigilance activities, participation in pharmacy research, and provision of medication information to healthcare professional staff.

- *Patient-specific activities (i.e., pharmaceutical care activities or patient-centered care activities)* comprised of the patient-related stream (e.g., obtaining medication history and medication counseling for patients) and the treatment-related stream (e.g., ward rounds, medication reviews, and working with physicians in the optimization of therapy).

Therefore, two separate questionnaires were developed to explore the current extent of each group of activities implemented in Vietnamese hospitals. The first questionnaire *(Part 1 Survey – Supplementary file 1),* which was to be completed by the Head of the Pharmacy Department of each hospital, consisted of multiple-choice questions to solicit workforce information and extent of non-patient specific activities. The second questionnaire *(Part 2 Survey – Supplementary file 2)*, which aimed to obtain the extent of *patient-specific activities* provided by clinical pharmacists, was answered by all clinical pharmacists willing to participate. The survey questionnaires were designed corresponding to the clinical pharmacy activities required by Circular No. 31 and clinical pharmacy literature (15, 24). Although there was no formal validation, the questionnaires were reviewed and pilot-tested for eliminating errors and user-friendliness by five clinical pharmacists in Hanoi hospitals. Four members of the research team and two clinical pharmacists from a public hospital in Hanoi checked face and content validity of the draft questionnaires before they were finalized and the online platforms were created.

### 2.4 Data collection

Data collection for the questionnaires was supported and facilitated by the Vietnamese Department of Medical Services Administration (DMSA) from the Ministry of Health (MoH). First, an invitation letter was sent to all hospitals under the administration of the MoH as well as other Ministries/Branches and the People Committees – including all 63 Provincial Health

Bureaus. Furthermore, the Provincial Health Bureaus were asked to send the invitation letter to the board of directors of all hospitals under their direct administration. The hospitals that accepted to participate in the study then used the link of the Online Form attached to the invitation letter to answer the survey. Online forms (created using Google Form®) were available from December 2017 to January 2018. The first questionnaire was responded by the Heads of the Pharmacy Department, with each hospital providing only one response. The second questionnaire was responded by all clinical pharmacists willing to participate. The questionnaires of the survey were developed and distributed in Vietnamese.

### 2.5 Data analysis

After receiving the results, the data were then analyzed using Stata 13.0. All data were described as percentage (categorical data) or mean with standard deviation (data with normal distribution) or median with interquartile range (data with non-normal distribution), where appropriate. The workforce characteristics and current status of clinical pharmacy activities were compared among hospitals by class. The Likert scale (25) was employed to assess the extent of provision of clinical pharmacy activities, with 1 = never/don't have; 2 = rarely; 3 = sometimes; 4 = usually; 5 = always. To compare the level of implementation between hospital classes, the Kruskal–Wallis test (for non-normally distributed quantitative variables), the Chi-square test, and Fisher's Exact test (for categorical variables) were applied, followed by post hoc pairwise comparisons.

### Ethics approval

This study was approved and supported by the Department of Medical Services Administration (DMSA) from the Ministry of Health in Vietnam. All respondents agreed to participate in the

study by completing and returning an online questionnaire. The name of the participants and their organizations were anonymous.

## 3 Results

### 3.1 Number of responses

From December 2017 to January 2018, we received 621 responses from the Heads of the Pharmacy Departments in hospitals for the first questionnaire and 596 responses from clinical pharmacists for the second questionnaire. After removing duplicate responses, responses from community centers without beds, control and prevention centers (due to a lack of pharmacy department), there were 560 and 570 eligible responses for the first and second questionnaire, respectively. The overall response rate of the first questionnaire was 41.2% from 1359 invited hospitals. The profile of the participating hospitals has been described in our previous publication (18).

### 3.2 Demographic profile of participating hospitals

The rate of response was highest from national hospitals (57.4%) and lowest (14.8%) from private hospitals (Table 2.1). Most of the participated hospitals are general (71.4%), public (95.2%), and not affiliated with a university (98.9%). The majority of the responses was obtained from the North and the Mekong Delta area (a part of the Southern area of Vietnam) at 63.0 % and 25.6%, respectively.

**Table 2.1. Profile of participating hospitals**

| *Hospital Information* | | *Number of responses N (%)* | *Total number of hospitals*† | *Response rate* |
|---|---|---|---|---|
| Hospital level (n=560) | National | 27 (4.8) | 47 | 57.4 |
| | Provincial | 211 (37.7) | 419 | 50.4 |
| | District | 285 (50.9) | 684 | 41.7 |
| | Private | 27 (4.8) | 182 | 14.8 |
| | From other Ministries/Branches | 10 (1.8) | 27 | 37.0 |
| Hospital class (n=560) | Special class | 3 (0.5) | NA‡ | |
| | Class 1 | 59 (10.5) | NA | |
| | Class 2 | 179 (32.0) | NA | |
| | Class 3 | 308 (55.0) | NA | |
| | Class 4 | 11 (2.0) | NA | |
| Hospital types (n = 560) | General | 400 (71.4) | NA | |
| | Specialized | 160 (28.6) | NA | |
| Hospital funding (n=560) | Public | 533 (95.2) | 1177 | 45.3 |
| | Private | 27 (4.8) | 182 | 14.8 |
| Area (n=560) | Red river delta | 124 (22.1) | 303 | 40.9 |
| | Northern midlands and mountainous | 114 (20.4) | 221 | 51.6 |
| | North central and south central coast | 114 (20.4) | 345 | 33.0 |
| | Central highlands | 36 (6.4) | 90 | 40.0 |
| | Southeast | 29 (5.2) | 191 | 15.2 |
| | Mekong river delta | 143 (25.5) | 209 | 68.4 |
| Nominal beds (n=560) | ≤100 | 204 (36.4) | NA | |
| | 101-500 | 304 (54.30 | NA | |
| | 501-1000 | 40(7.1) | NA | |
| | 1001-1500 | 9 (1.6) | NA | |
| | >1500 | 3 (0.5) | NA | |

†The number was extracted from the Health Statistics Year Book 2015 (published in 2017) of Ministry of Health (19).
‡ NA: Data were not available

### *3.3* Clinical pharmacy workforce in the participating hospitals

The workforce of the participating hospitals and pharmacy departments was analyzed by hospital class (Table 2.2). The data indicates that the number of physicians, pharmacists and pharmacists in clinical pharmacy per 100 beds of Special Class and Class 1 hospitals were significantly lower in comparison to Class 2 and Class 3. An opposite trend was observed in the number of nurses per 100 beds. However, the numbers of full-time equivalent (FTE) clinical pharmacists per 100 beds were not significantly different among all hospital classes (p=0.057, Kruskal-Wallis rank-sum test). The number of clinical pharmacists in all hospital classes was significantly lower compared to the number of physicians and nurses. The median number of pharmacists in the Clinical Pharmacy division was 1.8 and the number of FTE was 0.4, which indicates that most pharmacists held part-time positions.

**Table 2.2. Clinical pharmacy workforce in the participating hospitals (n = 560)**

| **Characteristics (number/100 beds)** | **Special class* (N=3)** | **Class 1* (N=59)** | **Class 2 * (N=179)** | **Class 3* (N=308)** | **Class 4* (N=11)** | **Total* (N=560)** | **P-value** |
|---|---|---|---|---|---|---|---|
| Pharmacists | 0.8 (0.9 – 1.0) | 1.5 (1.0 – 1.8) | 1.9 (1.3 – 2.8) | 2.6 (1.7 – 4.2) | 2.0 (1.5 – 4.2) | 1.9 (1.2– 3.0) | < 0.001 |
| Pharmacy technicians | 1.9 (1.8 – 2.5) | 2.6 (1.6 – 3.6) | 4.0 (2.7 – 5.8) | 5.8 (3.3 – 8.3) | 7.5 (3.7 – 15.0) | 4.0 (2.5 – 6.0) | < 0.001 |
| Physicians | 19.2 (11.1 – 29.8) | 24.2 (19.4 – 29.7) | 20.8 (16.4 – 27.4) | 21.6 (16.6 – 29.4) | 23.3 (20.0 – 34.3) | 21.8 (16.7 – 28.9) | 0.09 |
| Nurses | 83.1 (62.0 – 95.9) | 55.2 (45.5 – 64.4) | 45.3 (34.9 – 59.2) | 36.0 (27.2 – 50.0) | 33.3 (30.0 – 44.0) | 41.1 (30.0 – 57.1) | < 0.001 |
| Pharmacists in clinical pharmacy | 0.3 (0.3 – 0.4) | 0.6 (0.4 – 0.8) | 1.0 (0.6 – 1.6) | 1.3 (0.8 – 2.0) | 0 (0 – 1) | 1.8 (1.0 – 2.7) | < 0.001 |
| FTE clinical pharmacists /100 beds | 0.2 (0.1 – 0.2) | 0.3 (0.2 – 0.5) | 0.3 (0.2 – 0.7) | 0.5 (0.2 – 0.9) | 0 (0 – 1) | 0.4 (0.2 – 0.8) | 0.057 |

** Median (IQR)*

### 3.4 Establishment of Clinical Pharmacy Division

The majority of the participating hospitals have established Clinical Pharmacy Divisions (78.8%) (Table 2.3), with a small number of hospitals did not have any established clinical pharmacy activities (3.0%).

**Table 2.3. Establishment of Clinical Pharmacy Division**

| Status | Special class (N=3) | Class 1 (N=59) | Class 2 (N=179) | Class 3 (N=308) | Class 4 (N=11) | Total (N=560) |
|---|---|---|---|---|---|---|
| Officially established | 3 (100%) | 56 (94.9%) | 148 (82.7%) | 229 (74.4%) | 5 (45.5%) | 441 (78.8%) |
| Not established, but still provides clinical pharmacy activities | 0 (0%) | 2 (3.4%) | 21 (11.7%) | 57 (18.5%) | 2 (18.2%) | 82 (14.6%) |
| Not established with no clinical pharmacy activity | 0 (0%) | 1 (1.7%) | 2 (1.1%) | 12 (3.9%) | 2 (18.2%) | 17 (3.0%) |
| Others | 0 (0%) | 0 (0%) | 8 (4.5%) | 10 (3.2%) | 2 (18.2%) | 20 (3.6%) |

### 3.5 Non-patient specific activities of clinical pharmacists

Figure 2.1 shows the types of *non-patient-specific activities* of clinical pharmacists and highlights the differences in the extent of activities according to the hospital class. The activities of clinical pharmacists that were provided on a regular basis ("Usually" and "Always" responses) in most hospitals are participation in pharmacovigilance activities (89.3%), developing Standard Operating Procedures (SOPs) in hospitals (88.0%), providing medication information for healthcare professional staff (88.0%), and participation in hospital committees (83.0%). The participation of clinical pharmacists in developing medication use protocols and pharmacy research were carried out in fewer hospitals, with 71.8% and 43.4% of responses, respectively.

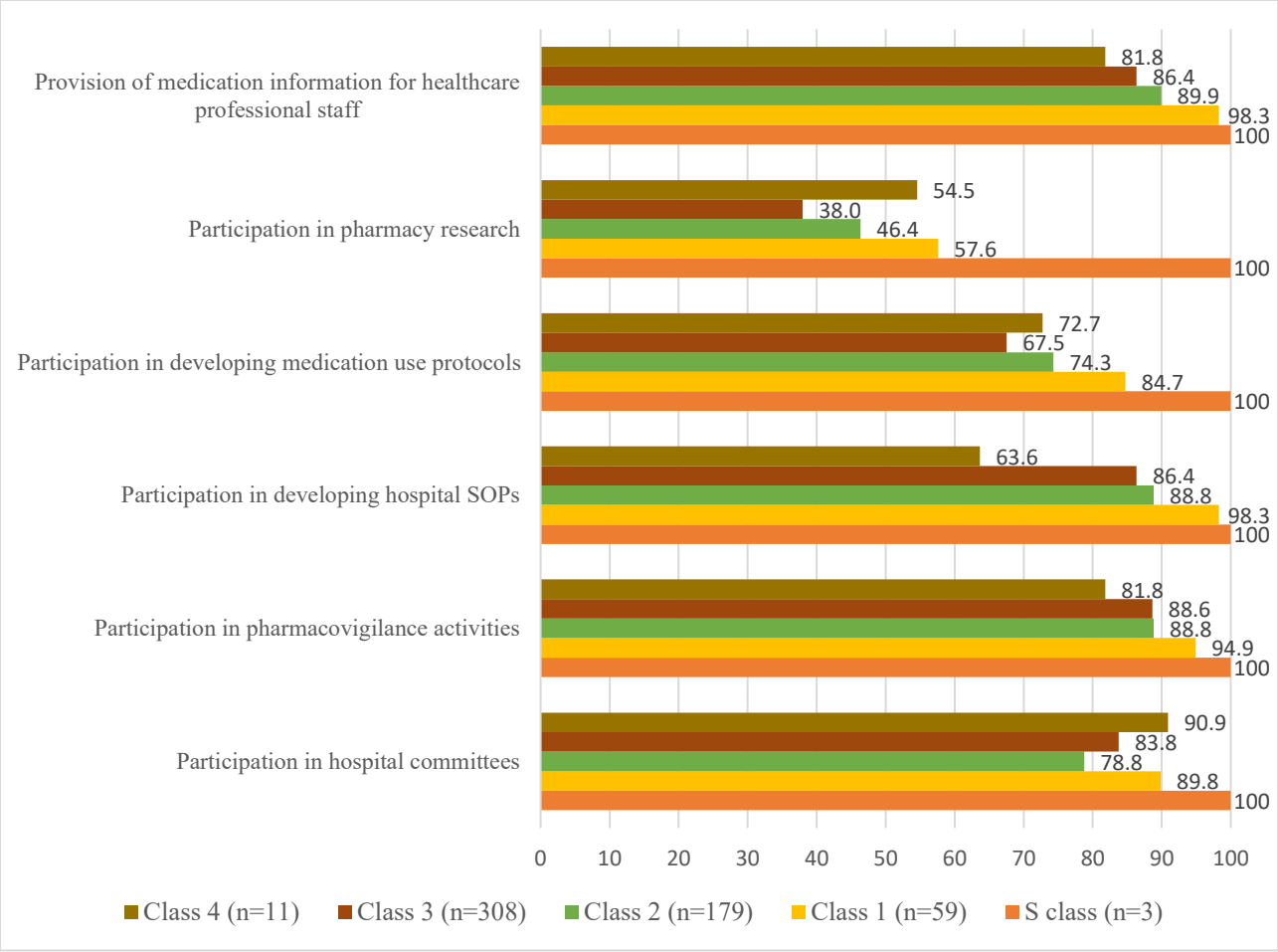


**Figure 2.1. The extent of non-patient specific activities of clinical pharmacists**

### *3.6* Patient-specific activities of clinical pharmacists

According to Circular 31, *patient-specific* or *patient–centered care activities* are expected to be performed by clinical pharmacists during their ward activities. However, despite the high extent of non-patient-specific activities, only 39.9% of clinical pharmacists reported that *patient-centered activities* were officially implemented in their hospitals (Figure 2.2). The implementation rate was significantly different between Special Class hospitals (100%) and other hospital classes (less than 63.4%). More than one-third (35.9%) of hospitals were in the pilot period of implementation. In addition, the average time that clinical pharmacists spent on these activities were approximately 5.8 hours per week (Figure 2.2).

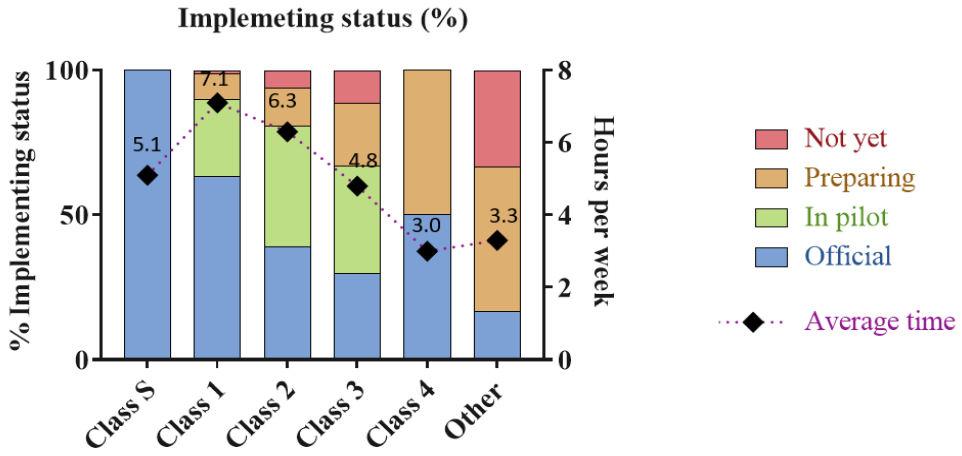


**Figure 2.2. Current status of implementing patient-specific activities**

Clinical pharmacists reported that they frequently participated in ward rounds and medication reviews for patients (64.8%) and provided medication counselling services for patients and nurses (55.7%) (Figure 2.3). However, only 20.6% of clinical pharmacists collaborated with physicians to rationalize patients' therapeutic regimens. The results also demonstrate a significant difference in the level of implementation of patient-centered activities among hospital classes, which was reflected across all aspects of the activities (Fisher's Exact test, $p < 0.05$) (Figure 2.3).

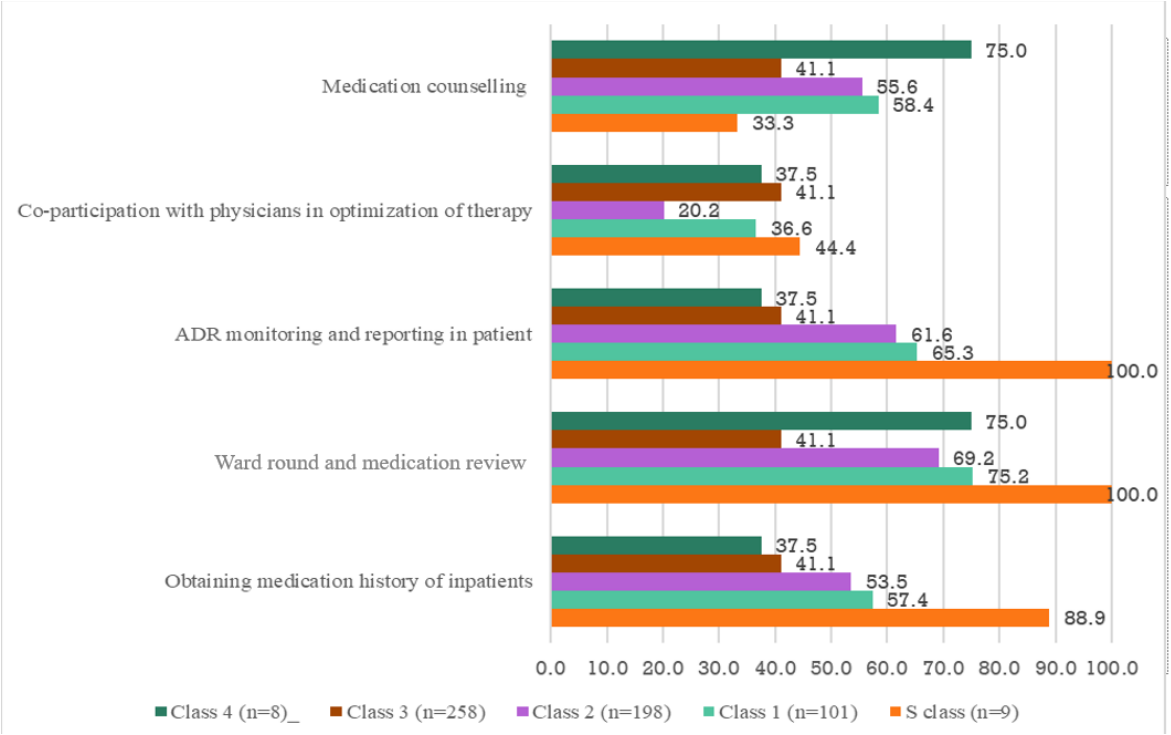


**Figure 2.3. The extent of patient specific activities of clinical pharmacists**

## 4 Discussion

To the best of our knowledge, this is the first comprehensive national survey of clinical pharmacy activities in the hospital setting in Vietnam. The response rate from the hospitals was acceptable (41.2%), with the highest response from Class 2 and Class 3 hospitals. The low response rates was seen in some areas and in private hospitals. The potential reason for that was that invitations to participate in the study were sent via the internal portal systems of the Ministry of Health and the Department of Health of each province and include all hospitals in Vietnam. As the private hospitals are not funded nor under the direct operational control of these ministries, both government ministries would have less influence on them. This could explain why the private sector's response rate was so low. However, due to the low number and smaller size of private hospitals among all medical facilities in Vietnam, their low response rate may not have a significant impact on the survey participant's representativeness. The diverse characteristics of the participating hospitals in terms of geographical location, hospital class, and type of institute (public/private) suggest that the results reflect the current pattern of clinical pharmacy activities in Vietnam. Hence, the results from this study are expected to provide helpful information for developing the National Decree of Clinical Pharmacy and the National Guideline of Implementing Clinical Pharmacy Services in Vietnamese hospitals.

The survey results highlighted a severe shortage of human resources for clinical pharmacy activities in hospital settings across all classes in Vietnam, with only 0.4 FTE clinical pharmacists per 100 beds. The number of clinical pharmacists in all hospital classes was also significantly lower compared to the number of physicians and nurses (1.8 versus 21.8 and 41.1, respectively). The constraint of limited resources has led to Vietnamese hospitals focusing their resources on the implementation of *non-patient-specific* activities. Consequently, pharmaceutical

care (*patient-specific*) activities have not been well established in many hospitals. Significant differences in the availability of clinical pharmacy activities were also reported across the hospital classes, with a much higher level and extent of activities available in "higher class" hospitals.

The workforce indicators from the survey may reflect limitations in the implementation extent of the clinical pharmacy activities in Vietnamese hospitals. To provide core CPS (including medication information, ADR management, medication review, and medication reconciliation on hospital admission), a minimum number of three clinical pharmacists per hospital has been recommended by some professional associations and mandated by the law in some countries (10, 26). Based on this recommendation, only a few Vietnamese hospitals in the Special Class category achieved the standard. The human resource issue for clinical pharmacy activities in Vietnamese hospitals has barely improved during the last several years. Previous studies have reported 0.36 FTE clinical pharmacists per 100 beds from an earlier survey in Hanoi (15) and 0.67 FTE clinical pharmacists per 100 beds in Ho Chi Minh City (16).

To account for the current low level of human resources for clinical pharmacy activities in Vietnam, several issues should be considered. There is no explicit legal requirement for the minimum number of clinical pharmacists as well as the core clinical pharmacy tasks in Vietnam (12, 13). In addition, clinical pharmacy in hospitals is still in the initial development stages in Vietnam. The lack of research conducted in Vietnam to provide evidence of direct positive benefit, especially financial benefit from clinical pharmacy activities to the hospitals, may impede the expansion of these activities.

Congruent with the low human resources available, our survey showed that current clinical pharmacy activities in Vietnam focused primarily on process-related services in all hospital

classes. *Non-patient specific services* are defined as pharmacists' activities that are not directly related to patient care but have a significant impact on improving the quality use of medicines for patients. These activities include participating in policy development (e.g., participation in hospital committees, developing SOP and medication use protocols), research, and feedback. The participation of pharmacists in these activities demonstrates the shift in the pharmacist's role from dispensing and supplying drugs to taking part in ensuring and improving the quality use of medicine. These particular activities can be undertaken by a small number of clinical pharmacists, which may be why *non-patient-specific activities* were considered the priority activities of clinical pharmacists in Vietnam and were highly implemented in Vietnamese hospitals irrespective of hospital class.

Furthermore, the results from the study indicated a limited level of implementation of *patient-specific activities* provided by clinical pharmacists in Vietnamese hospitals. Only ~40% of clinical pharmacists reported that *patient-specific activities* were officially implemented in their hospitals, despite the legal recommendation of Circular Number 31. A possible explanation is that Circular Number 31 is not considered a mandatory requirement that hospitals have to follow. Therefore, different hospitals would have different implementation plans and resources depending on their roadmap for developing clinical pharmacy services. Furthermore, our findings showed that clinical pharmacists in Vietnam only spend an average of 5.8 hours per week performing these duties, which is significantly different from the clinical pharmacy models in developed countries. With such a limited amount of time dedicated to *patient-specific activities*, medication counseling (57%), ADR monitoring and reporting (57.5%), and obtaining medication history of inpatients (49%) were reported to be the most commonly performed activities by the clinical pharmacists. Meanwhile, the core activity of pharmaceutical care (co-

participation with physicians in optimization of therapy) was performed regularly by only one-fifth of the participating clinical pharmacists. It should be noted that the “usually” and “always” responses in the survey regarding the core activities need to be interpreted relative to the low average time (5.8 hours per week) that the clinical pharmacists had on the ward.

Furthermore, there is a significant difference in the level of implementation of patient-centered activities among hospital classes. As implementation of activities in Vietnamese hospitals could be affected by many factors, the difference between human resources and the extent of implementation of clinical pharmacy activities among groups of hospitals is expected. Higher-class hospitals on a larger scale will have a greater number of clinical pharmacy personnel as well as better trained human resources, which are the foundation for implementing clinical pharmacy activities. Furthermore, higher-class hospitals are usually affiliated with universities, an important source that contribute expertise to implement these activities.

Barriers to the implementation of pharmaceutical care services in some countries, including developing countries similar to Vietnam, have been reported in studies from Brazil (27, 28), Nigeria (29), Lebanon(30), Kuwait (31), Portugal (32), and China (33). A systematic review conducted by Onozato et al. (34) also identified the multifactorial nature surrounding the implementation process of clinical pharmacy services in hospitals, with the most cited influencing factors related to the pharmacists, healthcare team, local hospital, and national organization. More specifically, the major barriers related to the pharmacists were their mindset, hard to shifting the role, lack of readiness, and inadequate clinical education/training (27, 32). Barriers at the organizational level include insufficient human resources, difficulty in collaboration between pharmacists and other healthcare staff, lack of support by hospital leaders, and lack of awareness by other healthcare staff (31, 32). Our present study suggests that these

identified barriers may also apply in the Vietnamese context, including limited human resources (discussed above), inadequate clinical training and the lack of an official Standard of Practice for clinical pharmacy activities. Along with a lack of human resources, another significant issue in Vietnam is a dearth of clinical pharmacist training. In a 2011 survey of 137 clinical pharmacists, nearly 40% indicated that they were not trained in clinical aspects of pharmacy in college and only 58% reported participating in continuing education courses (35). Additionally, the lack of an official Standard of Practice for the provision of *patient-specific activities* in the whole country may be one of the main reasons these activities have not been implemented systematically. However, further studies are needed with larger numbers of interviewees to comprehensively understand the barriers to pharmaceutical care activities in the Vietnamese hospital setting.

Regarding the strengths and limitations of our study, this is the first national survey focused on clinical pharmacy practice in the hospital setting in which all hospitals in Vietnam were invited to participate. Circular 31 and Pharmaceutical Law 2016 related to clinical pharmacy activities were employed to design the survey questionnaires, thus allowing the elicitation of the impact of these legal requirements on current clinical pharmacy activities in Vietnam. Nevertheless, the survey results should be considered in the context of the study limitations. Firstly, it was a self-administered survey where the respondents could have potentially misunderstood the questions but did not have the opportunity to clarify with the researcher. The study used the Likert scale with relative frequency, which also could lead to different understanding by the respondents. Furthermore, there may be some self-selection bias leading to overestimation as clinical pharmacists who are more confident in practicing pharmaceutical care may be more willing to participate. Finally, the explanation for some of the

barriers affecting the extent of clinical pharmacy activities was hypothesized by the research team. Therefore, further studies focusing on the difficulties and advantages of the implementation of clinical pharmacy activities in Vietnam are required to confirm our suggested explanations.

## 5 Conclusion

The study provided an overview of the current status of clinical pharmacy activities in Vietnamese hospitals. These activities were implemented at a much lower level in Vietnam than developed countries. In general, the extent of implementation of clinical pharmacy activities varied based on the type of activity and classification of the hospital in Vietnam. The extent of these activities was more established in higher class hospitals with a larger number of clinical pharmacists. In addition, the current implementation status focused more on *non-patient specific* activities, while *patient-specific* activities remained insufficiently established in Vietnam. Therefore further research focusing on the enablers and barriers to the implementation of clinical pharmacy services from the perspective of stakeholders is required to provide a more comprehensive understanding and solutions for better practice.

## ABBREVIATIONS

ADRs: Adverse Drug Reactions

MOH: Ministry of Health

DMSA: Department of Medical Services Administration

FTE: Full-time Equivalent

## DECLARATIONS

**Ethics approval and consent to participate**: As a nationwide study, this study has been reviewed and approved by the Review Board of the Department of Medical Services Administration, Ministry of Health, Vietnam. Ethics approval was provided by the Ethics Committee of the Department of Medical Services Administration, Ministry of Health. Informed consent were obtained online from all respondents before answering and returning an online questionnaire. The name of participants and their organizations were anonymous. The study was performed in accordance with relevant guidelines and regulations.

**Consent for publication**: Not applicable

**Availability of data and material:** All data generated and analyzed during the current study are available from the corresponding author on reasonable request.

**Competing interests:** The authors declare that they have no competing interests

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The author contributions are presented as follow:

- **Phuong Thi Xuan Dong**: Conceptualization, Methodology, Data collection, Formal analysis, Writing – Original Draft, Writing – Review & Editing.
- Hieu Trung Trinh: Conceptualization, Methodology, Data collection, Writing – Review & Editing
- Duy Huu Nguyen: Formal analysis, Writing – Original Draft, Writing – Review & Editing
- Son Tu Nguyen: Writing – Original Draft, Writing – Review & Editing
- Van Thi Thuy Pham: Conceptualization, Methodology, Writing – Review & Editing.
- Ha Bich Ngo:: Investigation, Resources, Writing - Review & Editing.
- Susan Hua: Conceptualization, Methodology, Writing – Review & Editing, Supervision
- Shu Chuen Li: Conceptualization, Methodology, Writing – Review & Editing, Supervision,
- Huong Thi Lien Nguyen: Conceptualization, Methodology, Writing – Review & Editing, Project administration.
- All authors read and approved the final manuscript.

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**Appendix**

## SUPPLEMENT DATA

***Table S1.*** *Extent of non-patient specific activities of clinical pharmacists*

| Activities | Frequency of "Usually/Always" responses (%) | | | | | | |
|---|---|---|---|---|---|---|---|
| | ***Special Class (n=3)*** | ***Class 1 (n=59)*** | ***Class 2 (n=179)*** | ***Class 3 (n=308)*** | ***Class 4 (n=11)*** | ***Total (n=560)*** | ***P value*** |
| Participation in hospital committees | 3 (100.0) | 53 (89.9) | 141 (78.8) | 258 (83.8) | 10 (90.9) | 465 (83.0) | 0.30 |
| Participation in pharmacovigilance activities | 3 (100.0) | 56 (94.9) | 159 (88.8) | 273 (88.6) | 9 (81.8) | 500 (89.3) | 0.49 |
| Participation in developing hospital SOPs | 3 (100.0) | 58 (98.3) | 159 (88.8) | 266 (86.4) | 7 (63.6) | 493 (88.0) | 0.047 |
| Participation in developing medication use protocols | 3 (100.0) | 50 (84.7) | 133 (74.3) | 208 (67.5) | 8 (72.7) | 402 (71.8) | 0.047 |
| Participation in pharmacy research | 3 (100.0) | 34 (57.6) | 83 (46.4) | 117 (38.0) | 6 (54.5) | 243 (43.4) | 0.007 |
| Provision of medication information for healthcare professional staff | 3 (100) | 58 (98.3) | 161 (89.9) | 266 (86.4) | 9 (81.8) | 493 (88.0) | 0.04 |

***Table S2.*** *Current status of implementing patient-specific activities*

| ***Characteristics*** | ***Special Class (n=9)*** | ***Class 1 (n=101)*** | ***Class 2 (n=198)*** | ***Class 3 (n=258)*** | ***Class 4 (n=2)*** | ***Others (N=6)*** | ***Total (N=574)*** |
|---|---|---|---|---|---|---|---|
| **Status of implementation** | | | | | | | |
| *Not implementing yet* | - | 1 (1.0) | 12 (6.1) | 29 (11.2) | - | 2 (33.3) | 44 (7.7) |
| *Preparing to implement* | - | 9 (8.9) | 26 (13.1) | 56 (21.7) | 1 (50.0) | 3 (50.0) | 95 (16.6) |
| *In pilot period of implementation* | - | 27 (26.7) | 83 (41.9) | 96 (37.2) | - | - | 206 (35.9) |
| *Officially implementing* | 9 (100.0) | 64 (63.4) | 77 (38.9) | 77 (29.8) | 1 (50.0) | 1 (16.7) | 229 (39.9) |
| **Average time per week (hour)** | **5.1 (2.1)** | **7.1 (5.0)** | **6.3 (5.6)** | **4.8 (4.9)** | **3 (1.4)** | **3.3 (3.7)** | **5.8 (5.2)** |

***Table S3.*** *Extent of patient specific activities of clinical pharmacists*

| ***Activities*** | ***Frequency of "Usually" or "Always" responses (%)*** | | | | | | | ***P value*** |
|---|---|---|---|---|---|---|---|---|
| | ***Special Class (n=9)*** | ***Class 1 (n=101 )*** | ***Class 2 (n=198 )*** | ***Class 3 (n=258 )*** | ***Class 4 (n=2)*** | ***Others (n=6)*** | ***Total (n=574 )*** | |
| Obtaining medication history of inpatients/Medication reconciliation | 8 (88.9) | 58 (57.4) | 106 (53.5) | 106 (41.1) | 0 (0) | 3 (50.0) | 281 (49.0) | 0.0006 |
| Ward round and medication review | 9 (100.0) | 76 (75.2) | 137 (69.2) | 144 (55.8) | 1 (50.0) | 5 (83.3) | 372 (64.8) | <0.0001 |
| ADR monitoring and reporting in patient | 9 (100.0) | 66 (65.3) | 122 (61.6) | 130 (50.4) | 0 (0) | 3 (50.0) | 330 (57.5) | 0.0007 |
| Co-participation with physicians in optimization of therapy | 4 (44.4) | 37 (36.6) | 40 (20.2) | 34 (13.2) | 0 (0) | 3 (50.0) | 118 (20.6) | <0.0001 |
| Medication counselling | 3 (33.3) | 59 (58.4) | 110 (55.6) | 142 (55.0) | 1 (50.0) | 5 (83.3) | 320 (55.7) | 0.0007 |

*(The number in parenthesis under the hospital class represents the pharmacists that responded to the questionnaire)*

**Supplementary file 1**

**Part 1. Workforce and Non-patients Specific Activities**

**(for the Head of Department of Pharmacy)**

**Section 1. General information and workforce**

1.1. Name of hospital

1.2. Hospital location (province)

1.3. Level of hospital

A. National hospital
B. Regional hospital
C. Provincial hospital
D. Other: …….

1.4. Class of hospital

A. Special class
B. Class 1
C. Class 2
D. Class 3
E. Other:……..

1.5. Type of hospital:

A. General hospital
B. Specialize hospital
C. Other:……..

1.6. Sources of funding

A. Private
B. Public
C. Other:……

1.7. Affiliations

A. Belong to a university
B. Not belong to a university

1.8. Number of nominated beds in last year: ……..

1.9. Number of pharmacists in hospital:……

1.10. Number of doctors in hospital: …….

1.11. Number of nurses in hopital: ……..

1.12. Number of pharmacy technicians in hospital: …….

**Section 2. The establishment of Clinical Pharmacy (CP) Division**

2.1. The status of the establishment of CP division in hospital:

A. Official established
B. Not established, but still provides clinical pharmacy activities
C. Not established with no clinical pharmacy activity
D. Other

2.2. Number of pharmacist in the CP division?…….

2.3. Number of doctor in the CP division?.....

2.4. Number of FTE pharmacist in the CP division?…….

2.5. Number of pharmacist meeting requirement criteria accroding to Circular No.31 in the CP division?…….

**Section 3. The extent of non patient specific activities**

3.1. What is the extent of the clinical pharmacy unit/team's participation in the following committees' activities in your hospital? Please choose the relevant ones.

(with 1 = never/don't have; 2 = rarely; 3 = sometimes; 4 = usually; 5 = always; NA: do not know)

| **Committee** | **The extent of participant** | | | | | |
|---|---|---|---|---|---|---|
| The Pharmacy and Therapeutic Committee | **1** | **2** | **3** | **4** | **5** | **NA** |
| The Science and Technology Committee | **1** | **2** | **3** | **4** | **5** | **NA** |
| Infection Control Group | **1** | **2** | **3** | **4** | **5** | **NA** |
| Patient Safety Group | **1** | **2** | **3** | **4** | **5** | **NA** |
| Quality Assurance Group | **1** | **2** | **3** | **4** | **5** | **NA** |
| Quality Assurance Group | **1** | **2** | **3** | **4** | **5** | **NA** |
| Nutrition Group | **1** | **2** | **3** | **4** | **5** | **NA** |
| Hygiene Management Group | **1** | **2** | **3** | **4** | **5** | **NA** |
| Other:…… | **1** | **2** | **3** | **4** | **5** | **NA** |

3.2. What is the extent of clinical pharmacists' involvement in building or revising the hospital formulary? Please choose all relevant options.
(with 1 = never/don't have; 2 = rarely; 3 = sometimes; 4 = usually; 5 = always, NA: do not know)

| **Activities** | **The exent of activities** | | | | | |
|---|---|---|---|---|---|---|
| Provide evidence to compare efficacy and safety of drugs in/with hospital formulary | **1** | **2** | **3** | **4** | **5** | **NA** |
| Provide evidence to compare the cost benefit of drugs in/with hospital formular | **1** | **2** | **3** | **4** | **5** | **NA** |
| Evaluate, control the duplication of generic drugs | **1** | **2** | **3** | **4** | **5** | **NA** |
| Other: | **1** | **2** | **3** | **4** | **5** | **NA** |

3.3. What is the extent of clinical pharmacists' participation in building the following medication use protocols and therapeutic guidelines? Please choose all relevant options.
(with 1 = never/don't have; 2 = rarely; 3 = sometimes; 4 = usually; 5 = always, NA: do not know)

| **Activities** | **The exent of activities** | | | | | |
|---|---|---|---|---|---|---|
| Building the process of medication information in hospital | **1** | **2** | **3** | **4** | **5** | **NA** |
| Building ADR monitoring protocol | **1** | **2** | **3** | **4** | **5** | **NA** |
| Building Medication Error monitoring protocol | **1** | **2** | **3** | **4** | **5** | **NA** |
| Building hospital therapeutic guidelines | **1** | **2** | **3** | **4** | **5** | **NA** |
| Building hospital technical processes | **1** | **2** | **3** | **4** | **5** | **NA** |
| Others…….. | **1** | **2** | **3** | **4** | **5** | **NA** |

3.4. What is the extent of clinical pharmacists' participation in building medication monitoring protocols for following drug groups?
(1 = never/don't have; 2 = rarely; 3 = sometimes; 4 = usually; 5 = always, NA: do not know)

| Group of medicine | The exent of participant | | | | | |
|---|---|---|---|---|---|---|
| Narrow therapeutic window medicines | **1** | **2** | **3** | **4** | **5** | **NA** |
| Medicine with serious ADRs | **1** | **2** | **3** | **4** | **5** | **NA** |
| Antibiotics | **1** | **2** | **3** | **4** | **5** | **NA** |
| Prophylatic Antibiotics | **1** | **2** | **3** | **4** | **5** | **NA** |
| Medicines with special precaution for infusion in pediatric | **1** | **2** | **3** | **4** | **5** | **NA** |
| Medicines with special precaution for infusion in oncology | **1** | **2** | **3** | **4** | **5** | **NA** |
| Medicines with Special precaution for storage condition | **1** | **2** | **3** | **4** | **5** | **NA** |
| Medicines with Therapeutic drug monitoring (TDM) | **1** | **2** | **3** | **4** | **5** | **NA** |
| Other | **1** | **2** | **3** | **4** | **5** | **NA** |

3.5. What is the extent of clinical pharmacists' participation in the following research activities in the hospital?

(with 1 = never/don't have; 2 = rarely; 3 = sometimes; 4 = usually; 5 = always, NA: do not know)

| Research activities | The exent of activities | | | | | |
|---|---|---|---|---|---|---|
| Drug Usage evaluation research | **1** | **2** | **3** | **4** | **5** | **NA** |
| Quality Improvement research in Pharmacy Practice | **1** | **2** | **3** | **4** | **5** | **NA** |
| Clinical Trials | **1** | **2** | **3** | **4** | **5** | **NA** |
| Protocol-Adherence Research | **1** | **2** | **3** | **4** | **5** | **NA** |
| Other | **1** | **2** | **3** | **4** | **5** | **NA** |

3.6. What is the extent of clinical pharmacists' provision of medication information for healthcare professional staff in the hospital?

(with 1 = never/don't have; 2 = rarely; 3 = sometimes; 4 = usually; 5 = always, NA: do not know)

| Activities | The exent of activities | | | | | |
|---|---|---|---|---|---|---|
| Providing MI for HCPs via paper documents to clinical wards | **1** | **2** | **3** | **4** | **5** | **NA** |
| Updating MI for HCPs via grand rounds in hospital | **1** | **2** | **3** | **4** | **5** | **NA** |
| Providing MI for HCPs via pharmacy bulletins/posters in the hospital | **1** | **2** | **3** | **4** | **5** | **NA** |
| Updating MI for clinical wards via LAN | **1** | **2** | **3** | **4** | **5** | **NA** |
| Updating MI for HCPs via scientific conferences/seminars in hospitals* | **1** | **2** | **3** | **4** | **5** | **NA** |

3.7. What is the extent of clinical pharmacists' participant in the pharmacovigilance activities? (with 1 = never/don't have; 2 = rarely; 3 = sometimes; 4 = usually; 5 = always, NA: do not know)

| Activities | The exent of activities | | | | | |
|---|---|---|---|---|---|---|
| Being coordinator in reporting ADRs of hospital | **1** | **2** | **3** | **4** | **5** | **NA** |
| Participating in monitoring and supervise ADRs in hospitals | **1** | **2** | **3** | **4** | **5** | **NA** |

**Supplementary file 2.**

**Questionnaire of the national survey**

**Part 2 – Patient – specific activities**

**(for the clinical pharmacists)**

**Section 1. General information of hospital**

1. Name of hospital
2. Hospital location (province)
3. Level of hospital
    A. National hospital
    B. Regional hospital
    C. Provincial hospital
    D. Other…….
4. Class of hospital
    A. Special class
    B. Class 1
    C. Class 2
    D. Class 3
    E. Other:……..
5. Type of hospital
    A. General hospital
    B. Specialize hospital
    C. Other:……..
6. Sources of funding
    A. Private
    B. Public
    C. Other:……
7. Affiliations
    A. Belong to a university
    B. Not belong to a university

**Section 2. The extent of patient-specific activities**

2.1. In your hospital, what is the status of clinical pharmacy services in clinical wards?

A. Have been officially implemented
B. In the pilot period of implementation
C. Have not been implemented yet, but we have prepared for these actitivites
D. Other:…….

2.2. What is the extent of your clinical activities in each of clinical ward below? Please choose all relevant options.

(1 = never/don't have; 2 = rarely; 3 = sometimes; 4 = usually; 5 = always)

| **Ward** | **1** | **2** | **3** | **4** | **5** | **Others** |
|---|---|---|---|---|---|---|
| Critical Care | **1** | **2** | **3** | **4** | **5** | |
| Poison Control | **1** | **2** | **3** | **4** | **5** | |
| Infections | **1** | **2** | **3** | **4** | **5** | |
| Gynecology/Nephrology | **1** | **2** | **3** | **4** | **5** | |
| Gatroenterology | **1** | **2** | **3** | **4** | **5** | |
| Cardiology | **1** | **2** | **3** | **4** | **5** | |
| Oncology | **1** | **2** | **3** | **4** | **5** | |
| Radiology | **1** | **2** | **3** | **4** | **5** | |
| Geriatric | **1** | **2** | **3** | **4** | **5** | |
| Pediatric | **1** | **2** | **3** | **4** | **5** | |
| Endocrinology | **1** | **2** | **3** | **4** | **5** | |

2.3. Please estimate the average (and the min-max) time of your clinical activities per weeks. For examples, 12 hours/week (min 2h – max 20h)

……..

2.4. What is the availability of criteria of patient in the clinical ward that you choose to take care?

A. Using the official criteria for target patients
B. Available criteria for target patients but not using

C. Not available

If the answer is A, could you please list some of criteria?

……

If the answer is B, why do you not use them?

……..

2.5. In clinical wards, which following activities that you provide for patients and healthcare staffs?

(you can choose many options) :

(1 = never/don't have; 2 = rarely; 3 = sometimes; 4 = usually; 5 = always)

| **Activities** | **1** | **2** | **3** | **4** | **5** | **Other** |
|---|---|---|---|---|---|---|
| Obtaining medication history of inpatients/medication reconciliation | **1** | **2** | **3** | **4** | **5** | |
| Medication review | **1** | **2** | **3** | **4** | **5** | |
| ADR monitoring and reporting in patient | **1** | **2** | **3** | **4** | **5** | |
| Co-participation with physicians in optimization of therapy | **1** | **2** | **3** | **4** | **5** | |
| Medication counselling | **1** | **2** | **3** | **4** | **5** | |

2.6. Related to Medication reconciliation activities (obtaining medication history), how do you do following activities (you can choose many options) :

(1 = never/don't have; 2 = rarely; 3 = sometimes; 4 = usually; 5 = always)

| **Activities** | **1** | **2** | **3** | **4** | **5** | **Other** |
|---|---|---|---|---|---|---|
| *Information that you obtain from patients* | | | | | | |
| Medication history | **1** | **2** | **3** | **4** | **5** | |
| Medical history | **1** | **2** | **3** | **4** | **5** | |
| Allergic history | **1** | **2** | **3** | **4** | **5** | |
| Medication adherence | **1** | **2** | **3** | **4** | **5** | |
| *The sources that you use to obtain medication history* | | | | | | |

| | | | | | | |
|---|---|---|---|---|---|---|
| Paper-based medical records | **1** | **2** | **3** | **4** | **5** | |
| Electronic-based medical records | **1** | **2** | **3** | **4** | **5** | |
| Interviewing patients and relatives | **1** | **2** | **3** | **4** | **5** | |

2.7. Related to medication review and ward round, which following activities that you have done (you can choose many options) for patients:

(1 = never/don't have; 2 = rarely; 3 = sometimes; 4 = usually; 5 = always)

| **Activities** | **1** | **2** | **3** | **4** | **5** | **Others** |
|---|---|---|---|---|---|---|
| Check indications | **1** | **2** | **3** | **4** | **5** | |
| Check contra-indications | **1** | **2** | **3** | **4** | **5** | |
| Evaluate medicines choice | **1** | **2** | **3** | **4** | **5** | |
| Evaluate dosage for each medicine | **1** | **2** | **3** | **4** | **5** | |
| Evaluate administration route for each medicine | **1** | **2** | **3** | **4** | **5** | |
| Evaluate administration time for each medicine | **1** | **2** | **3** | **4** | **5** | |
| Evaluate the interval time for each medicine | **1** | **2** | **3** | **4** | **5** | |
| Note the information relevant to adverse drug reactions, drug allergy | **1** | **2** | **3** | **4** | **5** | |
| Check drug interactions | **1** | **2** | **3** | **4** | **5** | |
| At this time, none of above has been done | **1** | **2** | **3** | **4** | **5** | |
| Other: | | | | | | |

2.8. During the treatment, which following activities that clinical pharmacists have done in collaboration with physicians to optimize patients' therapy (you can choose many options):

(1 = never/don't have; 2 = rarely; 3 = sometimes; 4 = usually; 5 = always)

| **Activities** | **1** | **2** | **3** | **4** | **5** | **Other** |
|---|---|---|---|---|---|---|

| | | | | | | |
|---|---|---|---|---|---|---|
| Identify possible drug-related problems | **1** | **2** | **3** | **4** | **5** | |
| Set the therapy goals and propose solutions for problems with physicians | **1** | **2** | **3** | **4** | **5** | |
| Follow patients'status based on clinical symtoms | **1** | **2** | **3** | **4** | **5** | |
| Monitor changes in laboratory tests' results | **1** | **2** | **3** | **4** | **5** | |
| Suggest doing additional laboratory tests if needed | **1** | **2** | **3** | **4** | **5** | |
| Monitor ADRs and drugs' toxicity | **1** | **2** | **3** | **4** | **5** | |
| Suggest the interventions with physicians | **1** | **2** | **3** | **4** | **5** | |
| At this time, none of above has been done | **1** | **2** | **3** | **4** | **5** | |
| Other: | | | | | | |

2.9. Related to medication conselling, how often do you provide each of following activitied?

| **Actitivities** | **1** | **2** | **3** | **4** | **5** | **Other** |
|---|---|---|---|---|---|---|
| Advice for nurses on how to admisnister medicines | **1** | **2** | **3** | **4** | **5** | |
| Advice for inpatients on how to take medicine properly during hospital stay | **1** | **2** | **3** | **4** | **5** | |
| Advice for inpatients on how to take medicine properly at discharge | **1** | **2** | **3** | **4** | **5** | |
| Advice for outpatients on how to take medicine properly | **1** | **2** | **3** | **4** | **5** | |
| Other: …… | | | | | | |

14. Which following medication groups and how often do clinical pharmacists counsel for healthcare professionals in clinical wards:

(1 = never/don't have; 2 = rarely; 3 = sometimes; 4 = usually; 5 = always)

| **Committee** | **1** | **2** | **3** | **4** | **5** | **Other** |
|---|---|---|---|---|---|---|
| Antibiotics | **1** | **2** | **3** | **4** | **5** | |
| Central nervous system agents | **1** | **2** | **3** | **4** | **5** | |
| Anticoagulant agents | **1** | **2** | **3** | **4** | **5** | |
| Immunodepressants (cyscloporin, tacrolimus..) | **1** | **2** | **3** | **4** | **5** | |
| Total parenteral nutrition | **1** | **2** | **3** | **4** | **5** | |
| Antineoplastic | **1** | **2** | **3** | **4** | **5** | |
| Anti-diabetes medicines | **1** | **2** | **3** | **4** | **5** | |
| Cardiovascular medicines | **1** | **2** | **3** | **4** | **5** | |
| Other | | | | | | |

2.10. Which following methods do you document the clinical pharmacy intervention (You can choose many options):

A. Not documented
B. Paper-based documentation using official forms
C. Paper-based documentation without official forms
D. Computer-based documentation, using software i.e Excel
E. Internet-based documentation (i.e Google Form)
F. Specialized software for documentation
G. Others……

# Chapter 3. Barriers and Facilitators of Implementing Clinical Pharmacy Services in Vietnamese Hospitals from the Perspective of Pharmacists: An Exploratory Qualitative Study

*(Will be submitted to BMC Health Services Research)*

**Abstract**

**Introduction** In Vietnam, clinical pharmacy services (CPS) have been initially implemented in healthcare facilities, following the issuance of governing legal regulations. However, research indicates that the extent of activity implementation has been limited and varied significantly amongst healthcare facilities.

**Aims.** To explore the barriers and facilitators of implementing clinical pharmacy services in Vietnamese hospitals.

**Methods**. Individual interviews with clinical pharmacists and pharmacy managers in Vietnamese hospitals were conducted using a guide based on the Theoretical Domains Framework (TDF). All interviews were taped, transcribed verbatim, and the content deductively analyzed using TDF domains. After that, the TDF domains were integrated and classified with COM-B model (Capability, Opportunity, and Motivation).

**Results.** Whilst it was reported that clinical pharmacists believed in the benefits of their activities for patients and feel happy while providing the services (Motivation – facilitators), most of the interviewees thought they needed to have more clinical experience and specialized knowledge for collaborating with physicians (barriers). National regulations and support from the hospital board of directors were considered facilitators, allowing for service implementation. However, service delivery was hampered by a lack of workforce, documents, and national standard operating procedures (Opportunity).

**Conclusion**. This is the first study in Vietnam to use the TDF and COM-B model to evaluate the facilitators and barriers to CPS. It is possible to use these findings as a basis for future efforts to improve the delivery of these services in Vietnam.

# 1 Introduction

Clinical pharmacy is a patient-centered and outcomes-oriented practice that requires pharmacists to work together with patients and other healthcare providers to promote health, to prevent disease, and to assess, monitor, initiate, and modify medication use to assure safe and effective drug therapy regimens. Studies have reported that the implementation of Clinical Pharmacy Services (CPS) can minimize medication errors, reduce hospital costs, and improve pharmacotherapy outcomes for patients (1-7). Hence, the provision of CPS such as medication information, medication reconciliation, medication review of pharmacotherapy follow-up, and patient counselling are advocated and promoted by the World Health Organization (WHO) and across many countries worldwide (4, 8-11).

The concept of clinical pharmacy and pharmaceutical care have been introduced in Vietnam for almost 30 years. Since 2012, legal regulations related to these services were officially issued by the Ministry of Health (MOH), including Regulation Circular 31 in 2012 (12) and Pharmaceutical Law in 2016 (13). These initiatives by the authorities reveal that clinical pharmacy and pharmaceutical care care services are seen as essential and have been steadily acknowledged and approved by clinical leaders and decision-makers in hospitals. As a result of these activities, Vietnamese hospitals provide CPS in a variety of ways that are based on their needs as well as available human resource and facilities. A few small-scale studies have provided generalized descriptions of these services (14-16). For example, recent research on CPS in Hanoi and Ho Chi Minh City (two of the biggest cities in Vietnam) (14-16) reported that the most described CPS were non-patient specific activities, with the most common being the provision of drug information, participation in pharmacovigilance activities, and research on medication usage. Direct-patient care activities were limited and varied widely among hospitals (14, 15).

Our previous study (Chapter 2) evaluated the current status of implementing CPS across the whole country of Vietnam. However, due to the quantitative nature of the study design, it was unable to determine how and why these characteristics influenced CPS availability. Furthermore, it was difficult to investigate the behavioral elements and external contexts that may influence the quality and availability of CPS such as legislation, leadership attitudes, and workplace cultures. Therefore, the goal of this study was to investigate the external and internal enablers and barriers to providing CPS in Vietnamese hospitals in greater depth. In particular, the aim of this study was to explore the barriers and facilitators of implementing pharmaceutical care services in Vietnamese hospitals from the perspective of clinical pharmacists and managers of Departments of Pharmacy. Insight into the perceptions of concerned health care professionals are important to enhancing the successful implementation and quality of these activities in Vietnam.

## 2 Methods

### 2.1 Participants

Head of Departments of Pharmacy, Division of Clinical Pharmacy, and clinical pharmacists at Vietnamese hospitals with experience in pharmaceutical care services were invited to participate in an in-depth, semi-structured interview. This mode of data collection is thought to be the most appropriate since it allows participants to freely express their personal opinions and impressions, while openly discussing and exchanging information with others.

### 2.2 Recruitment

To recruit representative individuals, the maximum variation sampling technique and stratified sampling technique was used. Based on the geographical characteristics of Vietnam,

cities/provinces representative of three socio-economic regions of Vietnam were selected, including Hanoi (North of Vietnam), Nghe An (Middle of Vietnam), Danang (Middle of Vietnam), Hue (Middle of Vietnam), and Ho Chi Minh City (South of Vietnam). Within each city/province, the research team selected targeted hospitals based on the hospital type (general or specialized) and hospital class. In Vietnam, hospitals and health facilities are classified by the Ministry of Health into several categories (i.e., special, class 1, class 2, and class 3) based on their scale, administration, and level of technical expertise. The research team then sent an invitation letter to the Board of Directors of the selected institutions to introduce the research team and explain the goal of the study. Following that, a member of the research team called the various Head of Pharmacy Departments, Chief of Clinical Pharmacy Divisions, and clinical pharmacists to invite them to participate in the study. When agreement to participate was attained, two researchers would meet or telephone the participants for the interviews after setting an appointment.

### 2.3 Sample size

To determine the sample size for this qualitative study, the approach by Francis et al was applied (17). The initial number of hospitals was 15, with a total of 30 people expected to take part. Before ensuring that thematic saturation had been attained, the stopping criterion were reviewed after each two consecutive interviews.

### 2.4 Interview process

All participants who agreed to an interview would have a face-to-face or phone interview at their respective hospitals' interview rooms. Before the interviews, a researcher (Thi Xuan Phuong

Dong) would acquire a signed written consent form from the participants. The interviews were conducted in Vietnamese and taped for transcribing purposes.

### 2.5 Developing the questions

Questions for the interview were developed based on the Theoretical Domain Framework (TDF) (18). The TDF is an evidence-based framework that can be used to identify barriers and enablers of behavior change in clinical practice (18, 19). It includes the following 14 domains related to behavior change: Knowledge; Skills; Professional role and identity; Belief about capabilities; Optimism; Beliefs about consequences; Memory attention and decision process; Environmental context and resources; Social influences; Emotion; Reinforcement; Intentions; Behaviour regulation; and Goals. This framework was selected as it has been extensively employed to explore difficulties to change in clinical practice and to develop interventions (20, 21). The interview guide, including proposed questions, is presented in Appendix 1.

The TDF approach to creating interventions for behavior change has been incorporated into the Behaviour Change Wheel. The Behaviour Change Wheel is a tool that summarizes the desired behavior in terms of its capability, opportunity, and motivational factors (COM-B). For behavior change to occur, an individual must possess capability, motivation, and opportunity according to the COM-B model (22). The fourteen TDF domains have been separately mapped onto COM-B segments. This is beneficial for the design of future behavior change strategies, as each source of behavior identified in the COM-B system has been connected to effective behavior modification interventions. Consequently, if barriers and facilitators for a target behavior are assessed using the TDF, they can be mapped to the COM-B system, which can then be used to identify appropriate behavior change interventions in an effort to systematically alter

the behavior. A Head of Pharmacy Department and a clinical pharmacist in a national hospital examined and pilot-tested the questions to ensure face and content validity, ease of comprehension, suitability of the interview duration, and feasibility of the interview methodology

### 2.6 Data analysis

The collected data were inputted and analyzed using QSR Nvivo software. All recordings were transcribed ad verbatim by the research group. The transcripts were analyzed using TDF analysis and deductive analysis. These transcripts were independently analyzed using pre-defined domains in TDF and COM-B model to investigate the behavioral perspectives of Head of Clinical Pharmacy, Chief of Clinical Pharmacy Divisions and clinical pharmacists.

The first three interviews were coded with theme identified. After the research team reached consensus that they were satisfied with the coding and theme identification methods, the remaining transcripts were analysed.

## 3 Results

### 3.1 Study participants

This study included 28 clinical pharmacists and managers of pharmacy departments from 15 hospitals. Each participant completed the entire interview. The interview lasted between 23 and 56 minutes. Table 3.1 details the characteristics of the participants and their affiliated hospitals. The results show that the majority of participants were female (75%) and nearly four fifths of participants (22/28) had a higher graduate degree.

**Table 3.1. Participant characteristics**

| Characteristics | Number of participants | % |
|---|---|---|
| **Hospitals characteristics (n=15)** | | |
| ***Hospital level*** | | |
| Central | 7 | 46.7 |
| Provincial | 7 | 46.7 |
| District | 1 | 6.6 |
| ***Hospital class*** | | |
| Special | 4 | 26.7 |
| Class 1 | 10 | 66.7 |
| Class 2 | 1 | 6.6 |
| ***Hospital location*** | | |
| North | 8 | 53.3 |
| Middle | 3 | 20.0 |
| South | 4 | 26.7 |
| ***Type of hospitals*** | | |
| General | 10 | 66.7 |
| Specialized | 5 | 33.3 |
| **Interviewee characteristics (n=28)** | | |
| ***Gender, female*** | 21 | 75.0 |
| ***Position*** | | |
| Manager | 15 | 53.6 |
| Clinical pharmacist | 13 | 46.4 |
| ***Highest academic degree*** | | |
| Bachelor of Pharmacy | 7 | 25.0 |
| Master of Pharmacy | 17 | 60.7 |
| Other Postgraduate qualifications in Pharmacy | 4 | 14.3 |

### 3.2 Barriers to clinical pharmacy services implementation

There were many themes that emerged as barriers to pharmacists implementing CPS (Table 3.2). The themes of the barriers mirrored all three components of the COM-B system (capability, opportunity, and motivation).

***Workforce (Capability)***

According to pharmacy managers, human resource constraints were the most significant impediment to the implementation of clinical pharmacy activities on a large scale, particularly clinical pharmacy activities for individualized patients. Below is an example of a representative comment from one of the participants.

- "*The human resources available [for clinical pharmacy activities] are only two people, and they have not been assigned to the clinical departments. They only provide consultations to clinical departments when requested.*" (Pharmacy manager 6)

Pharmacists also stated that most of the clinical pharmacists work part-time in that capacity, which means they must complete other pharmaceutical activities, reducing the time available for patient-centered care. Many pharmacists believe that the backbone activities of the Faculty of Pharmacy are still acquisition and dispensing drugs. As a result, provision of CPS remains at a lower priority level. Comments from three participants regarding this topic are stated below.

- "*Officially, clinical pharmacy division has four pharmacists; however, the pharmacists are often part-time. In this case, they often devote most of their time to other activities [less time for clinical pharmacy activities]*." (Pharmacy manager 1)
- *"It is sometimes necessary to reduce CPS time in order to perform more important tasks. For example, sometimes you must spend time working at medication bidding while spending less*

*time in the clinical department. The [pharmacy] department leader has requested that I prioritize my work, so I must comply. Do what is more urgent first.* (Clinical pharmacist 2)

- *"[Due to a scarcity of human resources] So in the past, I used to struggle as I need to do everything from A to Z. Sometimes I was in the middle of doing a task, the director gave me another job that I had to complete first. Only then can I come back [to the previous tasks], it was still unfinished, nothing can be done."* (Pharmacy manager 5)

***Knowledge and Skills (Capability)***

Many clinical pharmacists felt that they were only confident in specific areas of pharmacotherapy knowledge (which they have extensive reading and experience). When they enter the clinical department and provide patient-centered activities, they have to gain a wider range of knowledge about clinical examination, diseases and medication regimens, necessitating additional reading and research. Examples of participants statements are below.

- *"If we're talking about antibiotics, I'm confident in my knowledge level because I've read extensively on the subject. Other issues, however, are uncertain"* (Clinical pharmacist 7)
- "*Many times, I don't dare to answer the doctor's questions right away; instead, I'll go back and double-check the reference literature before reporting back to the doctor. Because if I respond directly but the information is incorrect, it will be harmful to the patient, so I must go back and double-check*" (Clinical pharmacist 2)

Most pharmacists believe that their lack of confidence in their abilities stems from the pharmacy training program failing to meet the requirements of practice. An undergraduate program focused on the integration of knowledge and practical skills would improve their clinical pharmacy practice expertise. Two examples of participants statements are below.

- *"In terms of ability, I have to admit that I had not been properly trained in the past. I'm also studying medicine, but my knowledge is mixed, so I don't have an orientation or an in-depth education in clinical pharmacy.* (Clinical pharmacist 9)
- *Then I gradually realized that my training program was primarily theoretical [...] But when I started work, I was surprised because I was working with physicians. They were confident because they had been trained in real practice. While pharmacy students study theory, I only study the process of applying knowledge to practice."* (Pharmacy manager 5).

Clinical pharmacists also expressed their desire to improve their competencies (knowledge and skills) through attending continuing professional education and training. Although they have been encouraged to participate in continuing professional education, it is currently still insufficient.

***Emotion (Motivation)***

Clinical pharmacists also expressed being afraid to interact with doctors as a barrier to implementing CPS, particularly for junior clinical pharmacists that have recently attained their Bachelor of Pharmacy degree. This is a direct result of the clinical pharmacists' lack of confidence in their treatment-related competency as well as knowledge and skills. Below is an example of a representative comment from one of the participants.

- "*Since working as a clinical pharmacist, I have cried three times following my interaction with the doctors, as they said that my work was terrible. This makes me very upset and stressed. I feel like there are mornings when I wake up and don't want to go to work."* (Pharmacy manager 5)

***Cognitive and interpersonal skills (Psychological Capability)***

Due to CPS being newly initiated in Vietnam, there has an absence of detailed guidelines for implementing these services. Standard Operation Procedures (SOP) are frequently self-developed by the Division of Clinical Pharmacy but some of them have not been implemented in practice on a routine basis. Representative examples of statements from two participants are below.

- *“"Clinical pharmacy regulatory documents, such as Circular 31, only specify general operational requirements, with no detailed implementation guidelines.” (Pharmacy manager 1)*
- *“[About SOP] some things remain only on paper, such as the intervention form, which was built in accordance with the form in Australia, and the drug-related problem classification, but no one uses them in clinical practice. Surely, there are some important procedures that everyone still follows, but there are some other SOPs that are inconvenient for people to use."* (Clinical pharmacist 5)

***Professional role and identity (Reflective Motivation)***

Clinical pharmacists felt that the other healthcare staff do not fully comprehend the role of clinical pharmacists, thereby contributing to the lack of collaboration. This was seen primarily in hospitals with recent implementation of CPS. Many physicians are unfamiliar with the concepts of clinical pharmacist and pharmaceutical care. For a long time, physicians in Vietnam have been solely responsible for prescribing medications for patients, making it difficult for them to accept the review of and advice on medications from a second party (in this case, clinical pharmacists). Examples of these statements are below.

- *"When I go to the ward, everyone from the doctors to the nurses only see pharmacy as the people who supply and sell drugs. Even when I work with the department, people think I come to check their work.* (Clinical pharmacist 9)
- *It must be accepted that the number of doctors who understand what clinical pharmacists do in hospitals is limited*. (Pharmacy manager 1)
- *"Physicians, they are "ego'' individuals confident in their work. That is why it is so difficult for us to collaborate with them. They will find any way to undermine me as long as they believe I am "attacking" them and finding their mistakes."* (Pharmacy manager 5)

***Environmental Context and Resources (Opportunity)***

Many interviewees believe that clinical pharmacy activities are specialized and require more effort from pharmacists, necessitating the addition of more payment mechanisms and policies. Despite current practice, the majority of the hospitals surveyed do not have such a mechanism. An example of a representative statement from the participants is below:

- *"As a wish, I hope to have more financial support, encouragement, and income as a clinical pharmacist. This job is more difficult to perform than other activities. More time is required. When people go home in other departments, their work is finished, but when I go home, I still have to read and answer questions. That's what I believe."* (Clinical pharmacist 2)

***Professional role and identity (Reflective Motivation)***

Some pharmacy managers admitted that there is currently a lack of studies/reviews to determine the efficacy of CPS in their hospitals, especially in economics aspect. This can have a number of

negative consequences, the most significant is that it is impossible to recommend the hospital to hire more staff for clinical pharmacy activities.

- *"The hospital director is open to hire more clinical pharmacists. However, my hospital is preparing to be financially self-sufficient, so any additional recruitment must demonstrate that this position will have benefit. However, lack of studies/summary on CPS effectiveness have been conducted to date."* (Pharmacy manager 5)
- *"The reason for being unable to recruit people is [...], you must first determine whether the work is effective before hiring them. It is extremely difficult to summarize the effectiveness of CPS, especially in terms of cost"* (Pharmacy manager 1)

***Reinforcement (Automatic Motivation)***

The lack of reporting and monitoring system for the quality of CPS activities, which are still regarded "additional" activities, is another barrier that keeps clinical pharmacists from being motivated to implement them. An example of a representative statement is below.

- *"There is currently no mechanism for reprimand and punishment, nor is there a target for clinical pharmacy. You don't know if you meet the department's target; it's up to the faculty leader to decide. This reduces my stress, but the same time it also reduces my motivation to do more work for clinical pharmacy activities."* (Clinical pharmacist 2)

**Table 3.2. Barriers of implementing pharmaceutical care services**

| COM-B Category | TDF Domain | Themes |
|---|---|---|
| Capability | ▪ Psychological (knowledge, cognitive and interpersonal skills, memory, attention and decision processes, behaviour regulation) | ▪ Most interviewees did not consider that they had enough competencies in pharmacotherapy knowledge to perform CPS, particularly when optimizing treatment for specialized conditions and critical ill patients.<br>▪ University training provided insufficient knowledge and skills to meet job requirements and continuing professional education classes were not regularly attended.<br>▪ Documents and standard operating procedures (SOP) to support practice are ambiguous. |
| Opportunity | ▪ Physical (Environmental context and resources)<br>▪ Social (social influences) | ▪ In addition to CPS, clinical pharmacists must also perform a variety of other tasks, which are sometimes regarded as more important.<br>▪ The opportunity to study to raise clinical pharmacists' knowledge and skills is insufficient. |
| Motivation | ▪ Reflective (goals, intention, beliefs about consequence, social/professional role and identity, beliefs about capabilities, optimism)<br>▪ Automatic (reinforcement, emotion) | ▪ The role of clinical pharmacists has been somehow misunderstood by other healthcare practitioners.<br>▪ There is lack of studies demonstrating the function of clinical pharmacists and the benefits of pharmaceutical care activities, particularly in terms of economic outcomes. As a result, the hospital's Board of Directors frequently reject the hiring of additional staff for these services.<br>▪ The lack of reporting and monitoring system for the quality of services might sometimes detract from desire to carry them out. |

### 3.3 Facilitators to clinical pharmacy services implementation

Table 3.3 provides a summary of themes that are regarded as facilitators for CPS.

***Belief in capability (Motivation)***

The majority of pharmacists interviewed indicated that they had the capability and disposition to self-study and enhance their qualifications in order to execute activities in the clinical area. An example of a representative statement is below.

*"I must constantly update and improve; I cannot claim to be qualified from the beginning I need to see the doctor, and whatever I don't know, I'll study and look up myself. I am quite confident when it comes to searching for information and self-studying because I have been doing it on a daily basis for a long time"* (Clinical pharmacist 9)

***Goals, intentions, emotion, and beliefs about consequences (Motivations)***

When providing pharmaceutical care activities for patients and other healthcare personnel, all pharmacists reported feeling useful and happy. They believed that these actions promote drug adherence, decrease adverse drug reactions (ADR), and increase the likelihood of recognizing medication-related issues. However, because they were overburdened with multiple responsibilities, the clinical pharmacists occasionally felt strained when completing multiple chores simultaneously. Examples of representative statements from the participants are below.

- *"I discovered that what I do makes a difference for patients and the doctor also changed their perspective on prescribing medicines based on my input. However, I believe I should limit my tasks to a few areas to be more effective due to a lack of human resources and having other responsibilities. When I am distracted with other tasks, the efficiency is low"* (Clinical pharmacist 2)

- *"This is what I call passion. I learned a lot about diseases and drugs. This is my job; as I gain more knowledge, I will gain confidence and be able to do more. Is it a motivator to grow, learn, and improve?"* (Clinical pharmacist 2)
- *"I try to be satisfied with my work at all times. There are patients who are overjoyed when the pharmacist comes to inquire about their illness; there are issues that the patient cannot discuss with the doctor but can discuss with the pharmacist; this makes me very happy."* (Clinical pharmacist 6)

***Environmental context and resources (Opportunity)***

Legal regulations, according to all interviewees, paved the way for CPS in hospitals. Most pharmacists also reported that hospital directors and pharmacy department heads strongly supported the implementation of CPS. Examples of these statements are below.

- *"I believe that policy is the most important aspect. Actually, Circular 31 was created to orientate us a lot, and we all know how much it help us in persuading the hospital directors to implement CPS [...]. Clinical pharmacy activities were also integrated in many relevant documents, such as Pharmaceutical Activities Circulars, Drug and Treatment Council Circulars, Hospital Antibiotic Management Guidelines [...] which aid us in carrying out these activities*." (Pharmacy manager 5)
- *"The director's mindset is important in implementing clinical pharmacy activities; they are willing to try new things and are very supportive of CPS. […] Regarding the working environment and the board of directors' policies, everything is very favorable for us to demonstrate our roles to other clinical departments*." (Pharmacy manager 5)

The interviewees also reported the positive shift in physician recognition of the role of clinical pharmacists as well as the evolution of its effectiveness over time. This shift appeared to be more noticeable among younger physicians. Examples of these statements are below.

- *"Working with the doctor was difficult a few years ago, but now almost all doctors work well with the clinical pharmacy team." (Pharmacy manager 1)*
- *"We are creating a colistin usage protocol in hospitals. Doctors considering the use of colistin will immediately come to me to see if the dose they are prescribing is correct, and if I have any additional advice*." (Clinical pharmacist 2)
- *"I've seen some young doctors who are very open and willing to discuss drug-related issues with me. I've also provided new treatment guidelines and they have asked me questions. Going on ward round with young doctors is easier because of this. Some more experienced physicians may not want to discuss the unimportant Drug-Related Problems; I frequently focus on more significant issues. I guess we'll have to wait a little longer to discuss the minor issues with these physicians."* (Clinical pharmacist 6)

**Table 3.3. Facilitators of implementing pharmaceutical care services**

| COM-B Category | TDF Domain | Themes |
|---|---|---|
| Capability | ▪ Psychological (knowledge, cognitive and interpersonal skills, memory, attention and decision processes, behavior regulation) | ▪ Most of the pharmacists interviewed stated that they had the ability and a positive attitude to self-study and improve their qualifications to perform tasks in the clinical department. |
| Opportunity | ▪ Physical<br>▪ Environmental context and resources<br>▪ Social (social influences) | ▪ By means of legal documents, clinical pharmaceutical actions are made mandatory.<br>▪ CPS received strong policy support from hospital and pharmacy administration.<br>▪ The positive shift in physician recognition of the role of clinical pharmacists as well as the evolution of its effectiveness over time. |
| Motivation | ▪ Reflective (goals, intention, beliefs about consequence, social/professional role and identity, beliefs about capabilities, optimism)<br>▪ Automatic (reinforcement, emotion) | ▪ The majority of interviewed pharmacists believed in the efficacy of CPS, believing that the activities they performed provided numerous benefits to patients. Consequently, pharmacists noted that they enjoyed and were motivated by their work. |

# 4 Discussion

To the best of our knowledge, this is the only study that has used TDF to explore the barriers and facilitators of implementing CPS in Vietnam. Using the TDF framework permits a deeper examination of factors that may be pertinent to the implementation of CPS activities using various interview instruments. Clinical interventions like CPS need to first identify what pharmacists perceive as barriers to their implementation. For effective implementation, the barriers should be removed or modified where possible and/or the facilitators should be increased accordingly.

In the present study, we attempted to collect data from a diverse range of voices in the targeted population to ensure sample representativeness. With stratified sampling, participants in the study were recruited with a wide range of characteristics such as age, gender, education, experience, and so on. The participant group was expected to represent the clinical pharmacist population in Vietnam. Therefore, the results of this study are expected to reflect the factors that currently affect CPS implementation across the nation, which can be used as a foundation for future solutions to enhance this activity. This study identified various themes pertaining to the barriers and facilitators of CPS implementation, spanning the three COM-B behavior source components. Despite receiving support from the legal framework, the findings of this study showed that the following factors could impede the development, implementation, and delivery of CPS in Vietnamese hospitals – hospital boards (Opportunity); other healthcare professionals (Motivation); lack of clinical experience, knowledge, and skills (Capability); and lack of workforce (Opportunity). These barriers have also been reported in similar studies conducted in

other countries (23, 24), with lack of human resources, lack of capacity, and difficulty communicating with other healthcare professionals being common factors.

This study highlighted that most clinical pharmacists felt that they lacked capability in specialized clinical and medical knowledge to practice alongside doctors, especially in optimizing therapy for patients. The clinical pharmacists interviewed were dissatisfied with their current capability and said that the content of university-level training was insufficient to work as a competent and professional clinical pharmacist. Previous research on clinical pharmacy activities in Vietnam also identified limitations in the competency of clinical pharmacists (14). For example, our 2015 study on CPS in Vietnamese hospitals revealed that the majority of pharmacists felt that their pharmacy school education lacked sufficient medical subjects and clinical experience to allow them to effectively and competently practice as clinical pharmacists in hospitals (14). This may explain the lack of clinical experience among pharmacy graduates and the necessity for Vietnamese pharmacy schools to revise their curricula accordingly.

Furthermore, this study also showed that the lack of CPS being present in clinical wards was one of the reasons why clinical pharmacy activities are so limited. Our previous study (Chapter 2) in 2018 across 560 hospitals in Vietnam showed that there was an average of only 0.4 full-time equivalent clinical pharmacists per hospital. Previous studies conducted in Ethiopia produced comparable results (25, 26). In fact, several countries around the world have reported shortages in the number of pharmacists, caused not just by insufficient resources but also by the increased demand of pharmacists to be more evolved in providing pharmaceutical care (27). A potential recommendation from the results of this study is for the Ministry of Health to review the number of pharmacists assigned to each level of healthcare facilities in Vietnam.

To improve the practice capacity of clinical pharmacists, it was stated that the curriculum of pharmacy programs at the universities should be updated. Options such as decreasing non-clinical courses to make more space in the curriculum for clinical courses must be examined. In addition, pharmacy trainees should be required to receive clinical training early on to appropriately develop their skills.

According to the interviewees, there was a high percentage of other healthcare staff that did not understand the activities of clinical pharmacists, especially in hospitals during the early stages of implementing CPS. This is another barrier to the motivation of clinical pharmacists. In many developing countries, pharmacists do not have a prominent role in monitoring the use of medications, as neither community nor other healthcare professionals acknowledge pharmacists as an integral part of the healthcare team (24). Nevertheless, the results of this study also indicate a positive shift in the perspectives of other healthcare professionals to the role of clinical pharmacists. This is an optimistic sign for clinical pharmacist collaboration in multidisciplinary teams in the near future.

With regard to the study limitations, it should be noted that a single investigator transcribed all of the interviews and performed most of the coding, which may have affected the rigour of our findings, as other investigators might have coded responses slightly differently and might have identified different themes from the same data. In addition, the sample size of the study was insufficient to differentiate the barriers and benefits by subgroup (e.g., hospital class, duration of clinical pharmacy adoption, or clinical pharmacist experience). However, as a preliminary exploratory investigation, the study results would assist to establishing baseline information for factors affecting the implementation of CPS for future studies to confirm. As clinical pharmacy activities rely on multidisciplinary collaborations, future research should concentrate on the

attitudes and perceptions of other healthcare professionals and patients towards clinical pharmacy practice. In conjunction with the barriers and facilitators identified in this study, further studies are required to inform the development and deployment of more effective and meaningful CPS for developing countries such as Vietnam.

## 5 Conclusion

Facilitators and barriers to the implementation of pharmaceutical care services were identified by pharmacy managers and clinical pharmacists who directly conduct pharmacy care activities in hospitals in Vietnam. Lack of manpower, absence of professional guidelines and specific instructions for performing services, and confusion among other healthcare staff regarding the role of clinical pharmacists could impede the extent of pharmaceutical care services for patients. In contrast, the support of hospital management and pharmacy leaders, as well as the positive motivation and perspectives of pharmacists are advantageous to the implementation of this activity. Potential solutions for Vietnamese hospitals to implement and increase CPS include enhancing the human resources capacity, increasing government funding, developing implementation guidelines, and promoting these activities to professional organisations.

## Declarations

**Ethics approval:** This study was granted ethics approvals by the Human Research Ethics Committee (HREC) at the University of Newcastle, Australia (Approval Number H-2020-0248).

**Consent to participate:** All participants have provided written consents to participate.

**Consent for publication:** Not applicable

**Availability of data and material:** All data generated and analysed during the current study are available from the corresponding author on reasonable request.

**Competing interests:** The authors declare that they have no competing interests.

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**Author contributions**

- Phuong Thi Xuan Dong: Conceptualization, Methodology, Data collection, Formal analysis, Writing – Original Draft, Writing – Review & Editing.
- Huong Thi Lien Nguyen: Conceptualization, Methodology, Writing – Review & Editing, Project administration
- Linh Khanh Duong: Methodology, Data collection, Writing – Review & Editing
- Van Thi Thuy Pham: Conceptualization, Methodology, Writing – Review & Editing.
- Susan Hua: Conceptualization, Methodology, Writing – Review & Editing, Supervision.
- Shu Chuen Li: Conceptualization, Methodology, Writing – Review & Editing, Supervision,
- All authors read and approved the final manuscript.

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**Appendix**

## Appendix 1. Interview Guide for participant

### Part 1. Interview guide for interviewing Head of Pharmacy Department/ Head of Clinical Pharmacy Division

**Researcher's script:**

- Thank you for joining the interview. Interview time will last about …… minutes.
- Today, we will discuss the barriers and facilitators you encountered during implementing pharmaceutical care services.
- For any question, if you do not want to answer or want more time to think and answer later, please let me know.
- Interview will be audio-recorded. All personal information will be removed from the reports to protect your privacy.
- Do you have any questions you before we start?

***Demographic information:***

1. Gender:
2. Age:
3. In what year did you graduate from pharmacy school?
4. In what year did you start working in this hospital?
5. What is your highest education qualification?

***Pharmaceutical care activities in your hospital***

1. Please describe pharmaceutical activities that you are currently involved in your hospitals
2. In your opinion, what area of **knowledge/skills** does a clinical pharmacist need to provide quality pharmaceutical care for patients?
3. Do you **believe** that the clinical pharmacists in your hospital have the required skills/knowledge to providing CPS for patients? Please explain your answers. What skills/knowledge that you need them to learn more?
4. How would the current pharmaceutical care activities of clinical pharmacist **fit into the professional roles of a pharmacist**?
5. What do you think about a clinical pharmacist can take **main role** in a multidisciplinary team to provide healthcare services for patients?

6. What **direct feedbacks** have you received from healthcare professionals (HCPs) about your pharmaceutical care activities? Beyond the direct responses received from other HCPs, do you **feel/think** other HCPS about the quality and the satisfaction of about your activities?
7. What would you need and what would **facilitate** setting up pharmaceutical care activities for patients?
8. What would be the **barriers** that need to be overcome in your CPS for patients?
9. How do you think that CPS that your pharmacy department is providing is **influenced by HCPs**?
10. In your opinion, what are the **benefits/cost** of pharmaceutical care activities for patients?
11. Please suggest solutions for the discussed barriers.
12. Please give your opinion about how to improve the quality of current pharmaceutical care activities in your hospital?

**Part 2. Interview guide for interviewing Clinical pharmacists**

**Researcher's script:**

- Thank you for joining the interview. Interview time will last about …… minutes.
- Today we will discuss the barriers and facilitators you encountered during implementing pharmaceutical care services.
- For any question, if you do not want to answer or want more time to think and answer later, please let me know.
- The interview will be audio-recorded. All personal information will be removed from the reports to protect your privacy.
- Do you have any questions you before we start?

***Demographic information***

1. Name:
2. Gender:
3. Age:
4. In what year did you graduate from pharmacy school?
5. In what year did you start working in this hospital?
6. What is your highest education qualification?
6. How long have you been doing pharmaceutical care activities?
7. What is the specific ward where you are performing pharmaceutical care activities?
8. How often do you provide pharmaceutical care activities?

***Provision of pharmaceutical care activities***

| Domain | Interview questions |
|---|---|
| Knowledge | In your opinion, what area of **knowledge/skills** does a clinical pharmacist need to provide quality CPS for patients? |
| Skill | Do you know how to deliver CPS for patients?<br>Have you attended any training course about how to provide CPS? |
| Social/professional role | What do you think about the opinion that pharmaceutical care activities is not **compatible** with your professional role? |
| Beliefs about capabilities | How easy or difficult do you find delivering CPS?<br>What problems have you encountered when delivering CPS for patients?<br>How **confident** are you that you can do CPS? |
| Beliefs and consequences | what are the **benefits/cost** of CPS for patients?<br>these services have advantages compared with the standard care? |
| Motivation and goals | How **motivated** are you to deliver CPS?<br>Are there incentives to provide these services? |
| Environmental context and resources | To what extent do **physical factors or resources** facilitate or hinder delivering pharmaceutical care activities?<br>Are the **necessary resources available** to undertake these activities?<br>Do government and local authorities provide **sufficient support** for these activities?<br>Do you have any support from the hospitals or from other HCPs in the hospital? |
| Social influences | What **direct feedbacks** have you received from healthcare professionals (HCP) about your pharmaceutical care activities?<br>What do you **feel/think** about the quality and the satisfaction of other HCPS about your activities? |
| Emotion | What do you feel when providing CPS? |
| Behavioural regulation | Do government and local authorities provide SOP for these activities?<br>Is there any guideline/SOP from the hospital or pharmacy department? |
| Natural of behaviours | NA |

Please suggest solutions for discussed difficulties.

Please give your opinion about how to improve the quality of current pharmaceutical care activities in your hospital?

# PART B. CURRENT SITUATION OF DRUG USE IN GERIATRIC INPATIENTS IN VIETNAMESE HOSPITALS

# Chapter 4. Unintentional Medication Discrepancies at Admission Among Elderly Inpatients with Chronic Medical Conditions in Vietnam: A single-centre observational study

This chapter has been published in the following peer-reviewed journal:

Dong PTX, Pham VTT, Nguyen TT, Nguyen HTL, Hua S, Li SC. Unintentional Medication Discrepancies at Admission Among Elderly Inpatients with Chronic Medical Conditions in Vietnam: A Single-Centre Observational Study. Drugs Real World Outcomes. 2022;9(1):141-512.

**Abstract**

**Background** Elderly patients are at high risk of unintentional medication discrepancies during transition care as they are more likely to have multiple comorbidities and chronic diseases that require multiple medications.

**Objective** of the study was to assess the frequency of unintentional medication discrepancies and identify the associated risk factors and potential clinical impact of them in elderly inpatients during hospital admission.

**Patients and Methods** A prospective observational study was conducted from July to December 2018 in a 800-bed geriatric hospital in Hanoi, North Vietnam. Patients over 60 years of age, admitted to one of selected internal medicine wards, taking at least one chronic medication before admission, and staying at least 48 hours were eligible for enrolment. Medication discrepancies of chronic medications before and after admission of each participant were identified by a pharmacist using a step-by-step protocol for the medication reconciliation process. The identified discrepancies were then classified as intentional or unintentional by an assessment group comprised of a pharmacist and a physician. A logistic regression model was used to identify risk factors of medication discrepancies.

**Results** Among 192 enrolled patients, 328 medication discrepancies were identified, with 87 (26.5%) identified as unintentional. Nearly 1/3 of enrolled patients (32.3%) had at least one unintentional medication discrepancy. The most common unintentional medication discrepancy was omission of drugs (75.9% of 87 medication discrepancies). The logistic regression analysis revealed a positive association between the number of discrepancies at admission and the type of treatment wards.

**Conclusions** Medication discrepancies are common at admission among Vietnamese elderly inpatients. This study highlights the importance of obtaining a comprehensive medication history at hospital admission and supports implementing a medication reconciliation program to reduce the negative impact of medication discrepancy, especially for the elderly population.

**Key points**

- This is the first study that assessed the frequency of unintentional medication discrepancies and the associated risk factors in elderly patients at hospital admission in Vietnam.
- Unintentional medication discrepancy was common in elderly inpatients at admission and persisted throughout the patients' hospital stay until discharge.
- The study highlights the importance of implementing standard operating procedures to attain a complete preadmission medication history for patients as well as implementing a medication reconciliation program in Vietnam

# 1 Introduction

Medication discrepancies are defined as inconsistencies between two or more medication lists of patients and can occur during the transition between healthcare facilities, including on admission, transfer, and discharge [1]. The discrepancies (e.g. medication omission, addition of a new medication, change in medication dose, or change in the route of administration) can be either intentional or unintentional, but not documented in any of the patients' medical records [1]. These discrepancies, especially those that are unintentional, can often lead to preventable medication errors and potentially be harmful to patients [2, 3]. In practice, medication errors due to unintended discrepancies have been reported to occur in up to 50–70% of patients during transitions in care [3] .

The majority of these medication discrepancies can be intercepted through medication reconciliation at all transitions in care [1]. Many organizations have demonstrated that implementing medication reconciliation at all interface of care is an effective and necessary strategy for identifying medication discrepancies and thus ensuring patient safety [1, 4, 5]. According to the World Health Organization (WHO), "medication reconciliation is the formal process in which health care professionals partner with patients to ensure accurate and complete medication information transfer at interfaces of care" [1]. The Institute for Healthcare Improvement (IHI) defines medication reconciliation as the process of creating the most accurate list possible of all medications a patient is taking and comparing that list against the physician's order at all transition of care [5]. The medication reconciliation service has shown to be successful in identifying most discrepancies and preventing harm to patients [3, 6], thus resulting in significant financial saving [7, 8]. Currently, medication reconciliation has become a standard healthcare practice recommended by the WHO [9] and many countries [5, 10, 11].

Often suffering multiple morbidities requiring multiple medications, elderly patients theoretically have a high risk of many medication issues, including inappropriate prescribings [12], drug–drug interactions, drug–disease interactions, adverse drug events (ADEs) [13], and medication errors, especially medication discrepancies[14]. Actually, regarding medication discrepancies, prevalences of 49.5 to 81.9% during transitions in care had been reported in this population [15-18]. Furthermore, elderly patients can also suffer from psychological (e.g. anxiety, depression, and dementia) and physiological factors (e.g. impaired hearing and vision function) that may impair their ability to communicate effectively with medical and healthcare staff, thus further contributing to potential medication discrepancies in this population. Elderly patients are, therefore, more vulnerable to medication discrepancies and should be a priority target population for medication reconciliation.

In Vietnam, obtaining the medication history from patients is the responsibility of doctors, nurses, and clinical pharmacists during ward rounds. However, the concept of medication reconciliation is still very new and has not been mandated in any government regulations or standard professional practice guidelines. As such, there is no standard operating procedure for medication reconciliation in Vietnam. This is further attested by a literature search performed by our research team that found no studies on this topic performed in Vietnam to date. Hence, the frequency and clinical impact of medication discrepancies remain unknown as a potential clinical problem in Vietnam. Without this information, it is difficult to request the healthcare administrators to allocate appropriate resources to rectify this clinically important but amendable problem.

Therefore, the main objective of the present study was to assess the frequency of medication discrepancies and identify the associated risk factors and potential clinical impact of

them in elderly patients at hospital admission in Vietnam. The results are expected to support the importance of obtaining a comprehensive medication history at hospital admission and implementing a medication reconciliation program to reduce the negative impact of medication discrepancy, especially for the elderly population. This would also provide evidence to persuade the healthcare administrators in Vietnam to allocate additional resources to rectify this problem.

## 2 Methods

### 2.1 Study setting and patient recruitment

This prospective observational study was conducted at Friendship Hospital, an 800-bed public geriatric hospital in Hanoi, which has 23 clinical units in total with 22,700 admissions in 2018. Patients over 60 years of age, admitted to 7 selected internal medicine units of the hospital, taking at least one chronic medication before admission, and staying at least 48 hours were eligible for enrolment. The selected internal medicine units were endocrine and metabolism, orthopedics, cardiovascular, respiratory, gastroenterology, psychiatry and neurology, and general internal medicine (coded from 01 to 07 respectively in the present study). These selected units practically covered all the internal medical specialties at the hospital. Patients were excluded if they were unable to give consent due to their clinical conditions or refused to participate in the study. The patient recruitment process took place over 14 non-consecutive weeks from July 2018 to December 2018, with two weeks of recruitment for each unit. During this period, all patients admitted to the units and met the selection criteria were eligible to be included in the study.

## 2.2 Data collection

For each enrolled participant, the following information was collected age, gender, comorbidity, current admission diagnosis, treatment unit, outpatient management status (i.e. whether the patient was managed as an outpatient by the study hospital), patient's existing chronic medical conditions, and the available sources for patients' medication information (e.g. electronic medical records, paper-based outpatient medical records, and paper-based inpatient medical records). Patients were followed to collect information from admission to discharge.

## 2.3 Process of identifying medication discrepancies

At the time of the study, there was no standard operating procedure (SOP) available for healthcare staff to obtain the medication history from patients and to reconcile the information with the admission medication prescriptions. The physician or nurse would normally collect the information regarding patients' preadmission medications during the medical examination and record this in the patients' medical record (paper-based medical record) without a SOP to perform any reconciliation for discrepancy. To identify any medication discrepancies at admission, the research group conducted a process of medication reconciliation that was independent of the normal practice of other healthcare professional staff (i.e. physicians and nurses). The activities of the study researchers did not interfere with the healthcare process for the patients.

Using the information from the WHO High 5s programme, a step-by-step protocol for the medication reconciliation process was developed and training was provided for a group of study data collectors. Overall, the process of medication reconciliation for each participant consisted of the following key steps.

- *Step 1: Obtain the Best Possible Medication History (BPMH) list for patients*: The BPMH form suggested by the WHO High 5s programme was employed to obtain preadmission medication information of patients [1]. The BPMH was obtained from multiple available sources, including patient interviews, computer–based medical record systems, and paper-based medical records. Patient interviews were conducted at the patients' bedside, using a structured form to guide the interview and record the data (**Supplementary file 1. Interview guide).**
- *Step 2: Identify medication discrepancies in chronic medications*: The list of admission medication prescriptions (i.e. the first 24 hours after patient's admission to the hospital) was collected from paper-based medical records for each patient. The list was then compared to the BPMH obtained by a study researcher as described above. Any differences between the chronic medications on the BPMH and admission medication prescription list was considered a potential medication discrepancy. Herbal products, traditional herbal medicine, dietary supplements, and other nonprescription medications were excluded from assesment as these products were usually stopped by the physicians at patient's admission.

To examine the extent of the medication discrepancy resolution by physicians during the patients' hospital stay, the medication discrepancy was also assessed at 48 hours after admission and at the time of discharge using the same approach described above. After this time, each potential medication discrepancy was discussed with the physician to determine if it was intentional or unintentional. To ensure the accuracy of the process for determining the reason of each medication discrepancy, several potential reasons were considered such as diagnosis of a new clinical condition, occurrence of adverse drug events, or a specific medication was unavailable in the Department of Pharmacy at the hospital **(Supplementary file 2. Process of**

**Medication Discrepancies Classification).** Medication discrepancies that were accepted by the physician as being unreasonable were classified as unintentional medication discrepancies. Each unintentional medication discrepancy was then classified by drug class (according to the Anatomical Therapeutic Chemical Classification System – ATC) [19] and type of unintentional medication discrepancy (e.g. omission of medication, change of medication, extra medication, or difference in dose or dosing frequency).

The potential clinical impact of UMD were assessed and rated jointly by a panel of clinical experts (TXP Dong, TT Nguyen and TTV Pham) using both an explicit tool and clinical judgment. A consensus was reached by the expert panel for potential clinical impact of all discrepancies after group discussion. Particularly, for omission discrepancies, the panel used "Reducing Harm from omitted and delayed medicines in hospital" tool developed by Specialist Pharmacy Service, United Kingdom, which is a list of drug groups evaluated according to the degree of impact on the clinical condition if delayed in treatment [20]. Finally, each discrepancy was classified into 3 categories based on the classification used by several studies [2, 21-23]: *Risk 1*. discrepancies with the potential to cause mild discomfort or clinical deterioration*; Risk 2.* discrepancies with the potential to cause moderate discomfort or clinical deterioration, and *Risk 3.* discrepancies with the potential to result in severe discomfort or clinical deterioration.

**Other assessment**

The data collector calculated the CCI score for each patient based on information gathered from medical records and patient interviews. In the meantime, ADL was obtained through patient interviews. The patients' medication history and the current treatment during the hospital admission were collected as part of the medication reconciliation process described below**.**

Description and scoring interpretation of the CCI and ADL are rather lengthy and details can be found in these previous publications.

### 2.4 Ethics approval

This study was granted ethics approvals by The Hospital Science and Technology Committee at Friendship Hospital (Vietnam) and the Human Research Ethics Committee (HREC) at the University of Newcastle (Australia).

### 2.5 Data analysis

The collected data were analyzed by using the Statistical Package for Social Sciences (SPSS), version 20.0 (IBM statistics, Armonk, NY, United States). Percent and frequency were used to describe medication discrepancy.

Multivariate logistics regression was used to identify risk factors associated with unintentional medication discrepancies in our study population. The Backward Stepwise (Wald) method was employed to identify appropriate multivariate logistic regression, with p values at 0.10 as the threshold for entering or removing variables. Based on previous researches and our experience, we selected the independent variables that could have a significant impact on the likelihood of unintentional medication discrepancies, including: age, gender, treatment, number of comorbidities, number of chronic medications, CCI, and ADL group. The independent variables then were examined to include in the logistic regression model by the univariate analysis. The regression analysis results were expressed as odds ratio with 95% confidence intervals. The influence of factors was considered to be statistically significant with $p<0.05$.

## 3 Results

## 3.1 Demographics and baseline characteristics of the participants

During the study period, a total of 395 patients were admitted to the study units. Of these, 203 patients were excluded from the study – 14 were admitted for less than 48 hours, 127 were not taking any chronic medications or had no chronic disease, 30 refused to participate, and 32 were unable to give consent. There was a total of 192 eligible patients included in the study (Figure 4.1).

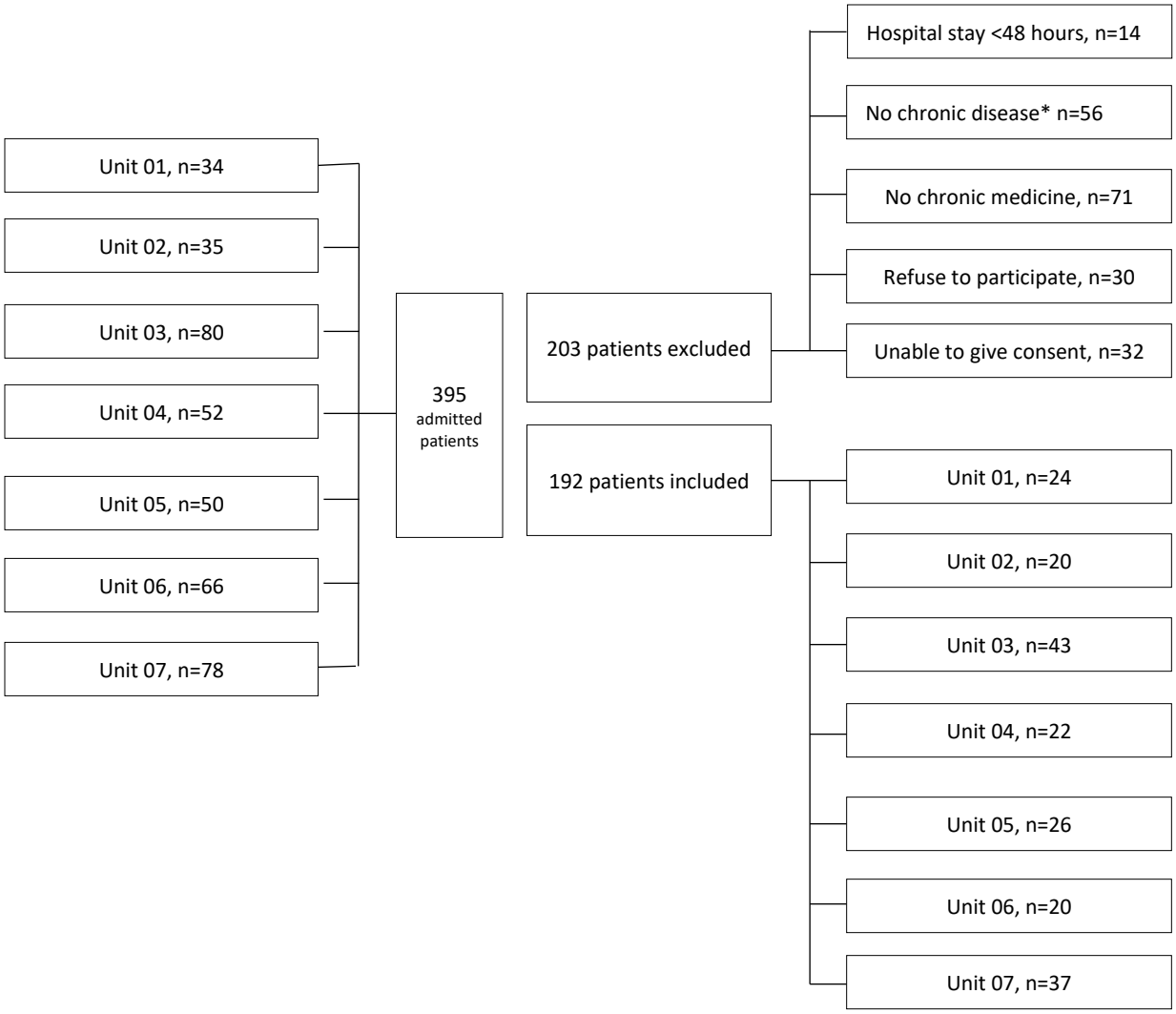


***Figure 4.1.*** *Flowchart of the patient recruitment process*

The demographics and baseline characteristics of the 192 patients included in the study are shown in Table 4.1. The average age of the study participants was 75.6 (± 7.0) years and 77.1% were males. Polypharmacy (at least 5 medications) before admission was seen in almost half of the patients (44.8%). The most common chronic diseases in the study participants were hypertension (86.5%), hyperlipidemia (61.5%), type 2 diabetes (45.3%), chronic coronary syndrome (37.0%), and osteoarthritis (25.5%). The average number of co-morbidities was 5.1 ± 1.8.

***Table 4.1.*** *Demographics and baseline characteristics of the study participants*

| Characteristics | Number of participants (%) (N=192) |
|---|---|
| **Gender** | |
| Male | 148 (77.1) |
| Female | 44 (22.9) |
| **Age (years)** | |
| Mean ± SD | 75.6 ± 7.0 |
| Age group: | |
| 60 - 65 | 13 (6.8) |
| 66 - 85 | 165 (85.9) |
| >85 | 14 (7.3) |
| **Activities of Daily Living (ADL)** | |
| Independent | 88 (45.8) |
| Dependent (≥1ADL) | 104 (54.2) |
| **Charlson Co-morbidity Index (CCI)** | |
| 0 | 43 (22.4) |
| 1 - 2 | 115 (59.9) |
| ≥3 | 34 (17.7) |
| **Number of comorbidities per patient** | |
| Mean ± SD | 5.1 ± 1.8 |
| **Top 5 common diseases** | |
| Hypertension | 166 (86.5) |
| Hyperlipidemia | 118 (61.5) |
| Type 2 diabetes | 87 (45.3) |
| Chronic coronary syndrome | 71 (37.0) |
| Osteoarthritis | 49 (25.5) |
| **Number of preadmission medications per patient** | |
| Mean ± SD | 4.5 ± 2.2 |
| 1-2 | 38 (19.8) |
| 3-4 | 68 (35.4) |
| ≥5 | 86 (44.8) |
| **Number of preadmission chronic medications per patient** | |
| Mean ± SD | 3.1 ± 1.5 |
| 1-2 | 75 (39.1) |
| 3-4 | 81 (42.2) |
| ≥5 | 36 (18.8) |

### 3.2 Frequency and type of medication discrepancy

Among the 192 patients recruited, there were 328 chronic medication discrepancies identified between the BPMH list and the 24-hour medication prescription (intentional and unintentional), with a mean ± SD of 1.7 ± 1.4 discrepancies per patient. All of the identified discrepancies had no documented reason in either the paper-based medical records or electronic medical records of the patients. After discussion with the physicians in charge, 87 discrepancies were classified as unintentional in 32.3% of patients (n=62). The frequency of medication discrepancies among the study population is presented in Table 4.2. Among the types of unintentional medication discrepancies, medication omission accounted for the highest proportion (75.9%), followed by medication change (21.8%). After the first 48 hours of admission, the number of unintentional medication discrepancies remained high (90.8%) and persisted until the time of discharge (77.0%).

***Table 4.2.*** *Medication discrepancies (MD) at 24 hours after admission in all 192 study participants*

| Characteristics of MD[a] | Number (percentage) |
|---|---|
| **Number of MD** | 328 |
| Intentional MD | 241 (73.5%) |
| Unintentional MD | 87 (26.5%) |
| **Number of MD per patient (**Mean ± SD) | 1.7 ± 1.4 |
| 0 | 40 (20.8%) |
| 1 | 55 (28.6%) |
| 2 | 48 (25.0%) |
| 3 | 29 (15.1%) |
| ≥ 4 | 20 (10.4%) |
| **Number of patients with no UMD** | **130 (67.7%)** |
| **Number of patients with at least 1 UMD** | **62 (32.3%) (95%CI: 25.7% - 38.9%)** |
| 1 UMD | 42 (21.9%) |
| 2 UMDs | 15 (7.8%) |
| 3 UMDs | 5 (2.6%) |
| **Number of different types of UMD[b] (N=87)** | |
| Medication omission | 66 (75.9%) |
| Medication change | 19 (21.8%) |
| Incorrect dose | 2 (2.3%) |
| **Numbers of UMD[b] unresolved (N=87)** | |
| At 48 hours | 79 (90.8%) |
| At discharge | 67 (77.0%) |

*Note: [a]MD = medication discrepancy; [b]UMD = unintentional medication discrepancy*

Cardiovascular agents were the most common drug therapies involved in medication discrepancies among the study participants. This included lipid-modifying drugs (39 cases, 44.8%), antihypertension drugs (18 cases, 20.7%), and antithrombotic drugs (11 cases, 12.7%) (Table 4.3).

***Table 4.3.*** *Unintentional medication discrepancies (UMD) according to drug class*

| Drug class | ATC[a] code | Number (n) | Percentage (%) |
|---|---|---|---|
| Lipid modifying agents | C10A | 39 | 44.8 |
| Antihypertensive agents | C02 | 18 | 20.7 |
| Antithrombotic agents | B01A | 11 | 12.7 |
| Blood glucose lowering drugs | A10B | 9 | 10.3 |
| Beta-blocking agents | C07A | 5 | 5.7 |
| Dopaminergic agents | N04B | 2 | 2.3 |
| Calcium | A12A | 1 | 1.1 |
| Thyroid preparations | H03A | 1 | 1.1 |
| Antinematodal agents | PP02C | 1 | 1.1 |
| **Total** | | **87** | **100.0** |

[a] *ATC: Anatomical Therapeutic Chemical Classification System*

### 3.3 Risk factors associated with unintentional medication discrepancies

The study used multivariate logistics regression with the Backward Stepwise (Wald) method to eliminate variables and selected suitable multivariate models to identify factors associated with the likelihood of unintentional medication discrepancies. Accordingly, the frequency of unintentional medication discrepancies was significantly higher among patients admitted to the orthopedics, respiratory, and gastroenterology units in comparison to those admitted to the endocrine and metabolism unit (odds ratio 10.03, 5.44 and 6.98, respectively; $p<0.05$). In addition, the risk of medication discrepancy significantly increased among patients using a least 5 chronic medications (polypharmacy) before admission compared to patients who were taking only 1 or 2 chronic medications at preadmission (odds ratio 4.65, $p < 0.05$) (Table 4.4).

***Table 4.4.*** *Risk factors associated with unintentional medication discrepancies*

| Factors | Number (%) | Odds ratio (95% CI) | p-value |
|---|---|---|---|
| **Treatment Units** | | | |
| Unit 01 (n=24) | 4 (16.7) | 1 (control) | - |
| Unit 02 (n=20) | 11 (55.0) | 10.03 (2.32 – 43.37) | 0.002 |
| Unit 03 (n=43) | 13 (30.2) | 3.00 (0.81 – 11.05) | 0.100 |
| Unit 04 (n=22) | 9 (40.9) | 5.44 (1.30 – 22.83) | 0.021 |
| Unit 05 (n=26) | 13 (50.0) | 6.98 (1.73 – 28.12) | 0.006 |
| Unit 06 (n=20) | 7 (35.0) | 3.79 (0.87 – 16.44) | 0.075 |
| Unit 07 (n=37) | 5 (13.5) | 1.04 (0.24 – 4.55) | 0.956 |
| **Number of chronic medicines using before admission** | | | |
| 1-2 (n=75) | 18 (24.0) | 1 (control) | - |
| 3-4 (n=81) | 26 (32.1) | 1.78 (0.83 – 3.81) | 0.137 |
| ≥5 (n=36) | 18 (50.0) | 4.65 (1.82 – 11.87) | 0.001 |

### 3.4 Clinical importance of UMD

Most of unintentional medication discrepancies (n = 69, 79.3%) were classified into risk 1 group (i.e., associated to a mild potential harm or deterioration to patients). There were 3 discrepancies belonging to risk 3 group, including the omission of dabigatran in a patient with atrial fibrillation and the omission of levodopa+benserazid in a patient with Parkinsonism (Table 4.5).

***Table 4.5.*** *Potential clinical impact of Unintentional medication discrepancies*

| Type of UMD[a] | Risk 1 | | Risk 2 | | Risk 3 | | Total | |
|---|---|---|---|---|---|---|---|---|
| | n | % | n | % | n | % | N | % |
| Medication omission | 52 | 59.8 | 11 | 12.6 | 3 | 3.5 | 66 | 75.9 |
| Medication change | 16 | 18.4 | 3 | 3.5 | 0 | 0.0 | 19 | 21.8 |
| Incorrect dose | 1 | 1.1 | 1 | 1.1 | 0 | 0.0 | 2 | 2.3 |
| **Total** | **69** | **79.3** | **15** | **17.2** | **3** | **3.5** | **87** | **100.0** |

[a]*: Unintentional Medication Descrepancies*

## 4 Discussion

To the best of our knowledge, this is the first study to examine the frequency of medication discrepancies among hospital inpatients in Vietnam. The study was focused on elderly patients, as they are a particularly vulnerable population to medication discrepancies and other drug-related problems (e.g. inappropriate indication, dose, or adverse effects). While the discrepancies can come from all kinds of patients' preadmission medications, including chronic and non-chronic medical conditions, we also focused only on chronic medications, due to their importance in managing long-term elderly's conditions. The results showed an average of 1.7 (SD 1.4) medication discrepancies per patient at the time of admission and 32.3% of the study participants had at least one unintentional medication discrepancy regarding their chronic medications.

To interpret the results meaningfully, we compared our findings with similar studies conducted in other countries, which also focused on identify UMD in elderly patients during admission from 2010 onwards. As shown in Table 4.6, the prevalence of unintentional

medication discrepancies varied widely between the published studies from other countries. The studies that showed a much higher rate include those conducted by Belda-Rustarazo et al in 2015 (64.5%) [24], Vargas et al in 2016 (49.5%) [15], and Magalhães et al in 2014 (48.0%) [25]. Similar and lower prevalence rates were reported in the study by Cornu et al in 2012 (40.9%) [16], Quélennec et al in 2013 (33.2%) [21], and Climente-Martí et al in 2010 (9.1%) [22]. Reasons for the marked variation in results include differences in the study population, the definition of unintentional medication discrepancy used, and the protocol applied to conduct medication reconciliation. For example, the studies by Belda-Rustarazo et al [24], Vargas et al [15], and Magalhães et al [25] selected patients with at least 3 or 5 preadmission medications, whereas our study only required at least one preadmission medication. This may explain why the frequency of unintentional medication discrepancy is lower in our current study when compared to some other published studies. Furthermore, we only classified medication discrepancies as being 'unintentional' after clarification and approval from the managing physicians, which could have reduced the proportion of unintentional medication discrepancies identified. Despite this, our study still indicates a relatively high frequency of unintentional medication discrepancies, and the current practice of obtaining the medication history from patients and reconciliating this with the medications prescribed at hospital admission is not adequate in Vietnam.

This study also demonstrates that the number of unintentional medication discrepancies remained very high at 48 hours after admission (90.8%) and even persisted until the patient was discharged (77.0%). Discrepancies in medication records can occur during transition between various healthcare facilities. If they are not identified and effectively communicated to the patient or the patient's general practitioner (GP) following hospital discharge, the unresolved

medication discrepancies may continue indefinitely and can lead to adverse consequences for the patient (e.g. omission of a vital medication).

***Table 4.6.*** *Summary of similar studies related to unintentional medication discrepancy (UMD) in elderly inpatients on hospital admission*

| Authors and country | Year | Study population | Justification of UMD | Number of UMD | Prevalence of UMD | Common types of UMD (%) | Risk factors |
|---|---|---|---|---|---|---|---|
| Dong et al (present study), Vietnam | 2018 | 192 patients aged over 60 using at least 1 chronic preadmission medication | Identified by researcher and confirmed by physician | 87 | 32.2% | Medication omission (75.9%) | Treatment units; Using at least 5 chronic preadmission medications |
| Vargas et al, Spain [15] | 2016 | 206 patients aged over 65 and using at least 5 preadmission medications | Identified by clinical pharmacist and confirmed by physician | 359 | 49.5% | Medication omissions (65.1%) | Physician experience; Number of preadmission prescribed medications; Previous surgeries |
| Belda-Rustarazo et al, Spain [24] | 2015 | 814 patients aged over 65 and using at least 5 preadmission medications | Identified by pharmacist and confirmed by physician | 1175 | 64.5% | Medication omissions (73.6%) | Number of preadmission prescribed medications; Number of comorbidities |
| Magalhães et al, Brazil [25] | 2014 | 58 patients (mean age 65) using at least 3 preadmission medications | Identified by researcher and confirmed by physician | 32 | 48.0% | Different medication dose | Not reported |
| Quelennec et al, France [21] | 2013 | 256 elderly patients | Identified by researcher and confirmed by physician | 173 | 33.2% | Medication omissions (87.9%) | Not reported |
| Cornu et al, Belgium [16] | 2012 | 199 patients aged over 65 and using at least 1 preadmission medication | Identified by pharmacist and confirmed by physician | 681 | 40.9% | Medication omissions | Not reported |
| Climente-Martí et al, Spain [22] | 2010 | 120 patients (mean age 76) using at least 1 chronic preadmission medication | Identified by pharmacist and confirmed by physician | 14 | 9.1% | Medication omissions (92.7%) | Age |

The most frequent type of unintentional medication discrepancy was medication omissions (75.9%), followed by medication change (21.8%). This result is in line with previous studies that have reported medication omission as the most common type of discrepancy [15, 22, 24, 26]. Potential reasons for the unintentional omission of medications when patients are admitted to hospital or leave hospital include incomplete information regarding the patients' preadmission medication lists, issues surrounding the amnesia of patients during interviews, and the complexity of patients' medication regimens. These findings suggest the need for strategies to identify and improve barriers in the transition of care pathways to ensure continuity and integration of care for the patient.

In term of medication class, unintentional medication discrepancy was identified mostly for cardiovascular drugs (e.g. lipid-modifying agents, antihypertensive agents, and antithrombotic agents), followed by blood glucose lowering drugs. Other medication reconciliation studies had also identified cardiovascular drugs as being one of the most frequent drug classes associated with medication discrepancies [15, 24, 25]. Other frequently reported medication classes include drugs affecting the blood and hematopoietic system [22, 24], the nervous system [15, 24], and the gastrointestinal system [15, 22]. This may suggest that some medication classes require special attention when implementing medication reconciliation procedures.

The assessment of the potential clinical impact of the unintentional discrepancies detected in the current study showed that 20.7% of UMD were judged to be of risk 2 and risk 3 groups, indicating that they had the potential to cause moderate discomfort or clinical deterioration (17.2%%) or severe discomfort or clinical deterioration (3.5%). In comparison, several previous studies showed a wide variation of proportions of UMD (from 1.5% to 65.0%) at hospital admission that were able to cause moderate to severe discomfort or clinical deterioration [2, 21-23, 27, 28]. The lack of an appropriate

explicit assessment tool can be the main reason leading to these differences. Nevertheless, our findings highlighted the necessity to detect and resolve these discrepancies in a timely manner.

Associations between the number of unintentional medication discrepancies and the type of internal medicine unit as well as the number of medications at admission were found in the present study. The unintentional medication discrepancies were 10.03, 5.44 and 6.98 times more likely to occur among patients admitted to the orthopedics, respiratory, and gastroenterology units, respectively, in comparison to patients admitted to the endocrine and metabolism unit. Similar variations in the prevalence of unintentional medication discrepancy among hospital wards were also reported by other studies [22, 29]. For example, Tamiru et al [22, 29] found that the frequency of medication discrepancy was significantly reduced among patients admitted to the surgery ward compared to patients admitted to the medical ward (adjusted odds ratio 0.27 [0.10-0.74]). These variations may be due to not having a standard operating procedure for medication reconciliation in the different units of the study hospital. The different charactersitics of patients admitted to these units and the different specialties of the physicians in these units may also be contributing factors. In resource-limited settings such as Vietnamese hospitals, this information could help the hospital administrators to strategically assign resources.

Furthermore, the likelihood of medication discrepancy was also significantly increased among patients taking a least 5 chronic medications prior to hospital admission compared to patients who had 1 or 2 preadmission chronic medications. This finding was consistent with other studies regarding the risk factors of unintentional medication discrepancies [15, 29]. For example, Vargas et al reported that the risk of suffering unintentional medication discrepancies increased by 20% for each additional drug [15]. In addition, this study also found patients with unintentional medication discrepancies took significantly more medications than those without

unintentional medication discrepancies (9.2 vs. 7.6; $p<0.01$). Similarly, Cornu et al showed that for every additional drug in the medication history, the likelihood of experiencing one or more drug discrepancies increased by 47% (adjusted OR =1.47; 95% CI: 1.24 to 1.74; $p<0.001$)[16]. These findings suggest that medication reconciliation by clinical pharmacists can be prioritized to elderly inpatients with polypharmacy at hospital admission if resources are limited. It should be noted that, in contrast to several previous studies [15, 22, 24], multivariate logistic regression analysis did not show any associations between number of unintentional medication discrepancies and age, gender or number of comorbidities in our present study. The absence of these associations may be due to the small sample size of our study, the different patient population, or the different study setting. In addition, the lack of association between the number of comorbidities and the number of unintentional medication discrepancies (while the number of medications was a risk factor in the study) might be explained by the commonly observed phenomenon of under-treatment for elderly patients in Vietnamese hospitals.

There are a few limitations that should be considered when interpreting the findings of the present study. First, the study period was over 14 non-consecutive weeks during six months which may potentially affect discrepancy rate due to variation in types of patients being admitted during the study period. Nevertheless, the study only identified discrepancies related to medications in patients with chronic diseases, where their admissions were much less affected by season. In addition, the study took place within the same year with no change in the hospital formulary nor any SOP affecting our study. Therefore, we considered that the effect of prolonged sampling time in the study to be minimal. Second, the results may not represent the current practice of the whole country, as the study was only conducted at a single hospital in Vietnam. However, as mentioned above, the concept of ‘medication reconciliation’ is still very new in

Vietnam and has not been mentioned in any official documents or professional practice standards. Hence, there is a lack of standard operating procedures in Vietnamese hospitals for this practice. In addition, the study hospital is one of the biggest geriatric hospitals in Vietnam with a large number of elderly patients admitted each year. Therefore, the current results are likely to be applicable to other Vietnamese hospitals. The third limitation is that the review of the medications prescribed was limited to only chronic medical conditions, which may have led to an underestimation of the frequency of unintentional medication discrepancies. We only focused on this group of medications due to their importance in managing elderly's conditions. Lastly, the potential clinical impact of some of the unintentional medication discrepancies identified was assessed by an expert panel due to a lack of appropriate assessment instrument. Therefore, the results of UMD clinical significance may depend on the subjective opinion of the experts in the study, however, this would at least somewhat minimised by the requirement of consensus for each assessment.

## 5 Conclusion

This study highlights that the frequency of medication discrepancies among elderly patients admitted to hospital in Vietnam is similar to the study results reported in other jurisdictions. The most frequent type of unintentional medication discrepancy was medication omission, which commonly occurred for drugs of the cardiovascular system. Another important observation from our study was that unintentional medication discrepancy persisted throughout the patients' hospital stay until discharge. Overall, our results support the importance of implementing standard operating procedures to obtain a complete preadmission medication history for patients as well as implementing a medication reconciliation program in Vietnam to facilitate better

healthcare management for the patients. Besides filling the information gap of UMD among Vietnamese patients with chronic disease at hospital admission, our results may provide some reference values for countries in similar position as Vietnam for healthcare planning or conducting similar studies.

## Declarations

**Funding** This research received no specific grant from any funding agency in the public, commercial or not-for-profit sectors.

**Competing interests** The authors declare that they have no competing interests

**Availability of data and material** All data generated and analysed during the current study are available from the corresponding author on reasonable request.

**Code availability** Not applicable

**Ethics approval** This study was granted ethics approvals by The Hospital Science and Technology Committee at Friendship Hospital, Vietnam (approved on 28th March, 2018) and the Human Research Ethics Committee (HREC) at the University of Newcastle, Australia (Approval Number H-2018-0130). The study was performed in accordance with the Declaration of Helsinki. The participants were informed of the objectives of the study and the risks and benefits of the explorations to be carried out (Informed Consent).

**Consent to participate** All participants have provided written consents to participate

**Consent to publication** Not applicable

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**Asuthor contributions**

- Phuong Thi Xuan Dong: Conceptualization, Methodology, Data collection, Formal analysis, Writing – Original Draft, Writing – Review & Editing.
- Van Thi Thuy Pham: Conceptualization, Methodology, Writing – Review & Editing.
- Thao Thi Nguyen: Data collection, Writing – Review & Editing.

- Huong Thi Lien Nguyen: Conceptualization, Methodology, Writing – Review & Editing.
- Susan Hua: Conceptualization, Methodology, Writing – Review & Editing, Supervision.
- Shu Chuen Li: Conceptualization, Methodology, Writing – Review & Editing, Supervision, Project administration.
- All authors read and approved the final manuscript

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**Appendix**

## Supplementary file 1. INTERVIEW GUIDE

## Interviewing patients abour their medications

### Introduction

My name is……. and I am one of  the pharmacists in the hospital.

I would like to have a chat with you about your medicines. One of my jobs is to make sure we have a full list of all the medications you were taking at home. So I'd like to know what medications you take, how much you take and how often you take them.

1. Do you normally take medicines at home?

2. Do you know how many different medicines you are taking?

For each medication (question 3 – 5):

3. What is the name of the medication?

4. How strong is the medication? How much of that medication do you take at a time?

5. How many times a day do you take it?

6. Do you have any medicines at home that you only take when you need them (not everyday)?

7. Do you take any medicines not prescribed for you by your doctor?

8. What is the name of the medication ?

9. How strong is the medication? How much of that medication do you take at a time?

10. How many times a day do you take it?

11. Have you ever had an allergic reaction to any medication? What happened?

12. Have you ever had a side effect from any medicine? What happened?

**Supplementary file 2. Process of Medication Discrepancies Classification**

Each identified medication discrepancy was assessed all aspects below to determine whether it was intentional or unintentional. The assessment was conducted by a physician and a research pharmacist for each medication discrepancy retrospectively.

| Checklist Items | Reasons | How to do |
|---|---|---|
| The rationale of the participants' preadmission medication | To identify cases of medication discrepancies due to correct the inappropriateness of preadmission medication | Reviewing the appropriateness of the indications and dosages of the preadmisison medication by using the product characteristics and the patient's current and existing medical conditions. |
| The availability of medication in Department of Pharmacy. | To identify cases of medication discrepancies due to the absence of similar active ingredients, strengths and dosage forms in the hospital formulary. | Talking to pharmacists working in supply section at the Department of Pharmacy. |
| Contraindications, warnings on preadmisison medication. | To identify cases of medication obmission due to the preadmission medication being contraindicated or not recommended for the patient's acute condition at admission. | Using the summary product characteristics, check the "contraindications" and "precautions" sections against the patient's clinical and laboratory conditions to determine if the patient has a contraindication to the preadmission medication or not |
| The ability to manage chronic disease of preadmission | To identify cases of medication discrepancies due to preadmisison medications no longer adequately manage the patient's chronic | Considering the patient's causes of admission, clinical and laboratory symptoms (new diagnoses, new laboratory values) to determine the |

| | | |
|---|---|---|
| medication | conditions. | likelihood of adequate chronic disease control with preadmission medication. |
| The patient's tolerance to the preadmission medication | To identify cases of medication discrepancies due to the adverse drug reaction caused in the patient by preadmission medication. | Interviewing patients to explore possible drug-related ADEs with preadmission medication.<br>Reviewing the medical history to determine the tolerability-related reason noted by the physician in the medical record. |

# Chapter 5. Prevalence and Risk Factors of Potentially Inappropriate Prescribing in Elderly Inpatients in Geriatric Hospitals in Vietnam according to STOPP/START version 2

*(Will be submitted to the Journal of Clinical Pharmacy and Therapeutics)*

**Abstract**

**Background:** Potentially inappropriate prescribing (PIP) is common among geriatric patients admitted to hospitals in many countries. It is a significant risk factor for morbidity and mortality among the elderly, resulting in an increase in the cost of health care. However, there is a scarcity of research on the prescribing patterns in geriatric patients hospitalised in Vietnam. Therefore, to assess PIP in elderly inpatients, STOPP/START version 2 was utilized in this study.

**Aim:** To measure the frequency and risk factors of PIP in geriatric inpatients in Vietnamese hospitals.

**Method**: An observational, prospective study in two public general geriatric hospitals in Hanoi, Vietnam, which included patients $\geq 60$ years. The second versions of the Screening Tool of Older Person's Prescriptions (STOPP) and the Screening Tool to Alert doctors to Right Treatment (START) were applied to detect potentially inappropriate medications (PIM) and potential prescribing omissions (PPO), respectively. Data were collected from patients' medical records and interviews. Main outcome measures were prevalence of PIM and PPO during hospital stay. A logistic regression model was used to identify risk factors of PIP.

**Results**: The frequency of PIM and PPO were 22.4% and 33.5% of patients according to the STOPP and START version 2 criteria, respectively. The most common types of PIM were long-acting benzodiazepines and first-generation antihistamines, while the most common PPO were statins and beta-blockers. The length of stay, the risk of falls, and the number of comorbidities were identified as risk factors for PIP in the study population.

**Conclusion**: The study findings indicate that the prevalence of PIP according to the STOPP/START version 2 was relatively high in geriatric inpatient in Vietnamese hospitals,

which is consistent with studies conducted in other countries. The findings suggest that there is a need for interventions aimed at reducing PIP among elderly inpatients in Vietnam.

**Keywords**: Potentially Inappropriate Prescribing, elderly, STOPP/START version 2 criteria

# 1 Introduction

Population aging is a global phenomenon affecting the healthcare system of many countries (1). Age-related physiological changes and multimorbidity are two of the elderly population's most concerning health characteristics (2, 3). As a result of multi-morbidity, there is also a high prevalence of polypharmacy (concurrent use of more than five medications) (4) in this population. Elderly patients are more likely to experience a variety of drug-related problems due to age-associated physiological changes as well as the high prevalence of multiple comorbidities and polypharmacy. These may include inappropriate prescribing, drug-drug interactions, drug-disease interactions, and medication errors (3, 5, 6) – which frequently lead to adverse drug reactions (ADR) and other negative clinical outcomes. Therefore, appropriate prescribing, selection and review of medications for geriatric patients are clearly important and challenging tasks (7).

Among the various drug-related problems, potentially inappropriate prescribing (PIP) is a term used to describe a number of suboptimal prescribing practices. For example, the use of medications where the risk of treatment potentially outweighs the benefit, especially when a safer or more effective alternative therapy is available for the same condition (8). There are several patterns of PIP such as inappropriate dose or duration of therapy, prescribing drugs having significant drug–disease or drug–drug interactions, and the omission of potentially beneficial medications (7).

Over the last two decades, there has been an increase in research to develop instruments to identify PIP in the elderly, as well as studies on the prevalence of PIP using these instruments. Initially, there were implicit tools for determining prescribing appropriateness such as the

Medication Appropriateness Index (9). These were followed by the introduction of explicit tools to assist in screening of the elderly for PIP such as Beers' criteria (10), Screening Tool of Older Person's Prescriptions (STOPP), Screening Tool to Alert doctors to Right Treatment (START) (11), EU(7)-PIM (12), and Fit fOR The Aged (FORTA) list (13). Using these explicit screening tools for PIP, many studies have also shown a high prevalence of inappropriate prescriptions in the elderly in primary settings (14), secondary settings (15), and nursing homes with negative clinical outcomes (15).

By the beginning of 2018, the population in Vietnam aged over 65 years was estimated as 10% of the total population and this was predicted to rapidly increase (16). As a result of the older population consuming more healthcare resources, there would likely be an increase in demand for health services. However, doctors in Vietnam already have high clinical workloads, with a current ratio of 7.8 doctors per 10,000 population in 2016 (16). Based on the lack of studies available (17, 18), inappropriate prescribing in geriatric patients in Vietnam is thought to be a severe concern under such intense clinical pressure. Therefore, further research is urgently needed to assess the amount of inappropriate prescribing in the elderly. This information would assist health administrators and clinicians to find ways and allocate resources to address this rising problem to deliver better healthcare in Vietnam.

The study aimed to evaluate the prevalence of potentially inappropriate prescribing (PIP) by using STOPP-START version 2 criteria among elderly inpatients in two Vietnamese geriatric hospitals and to evaluate the risk factors associated with potentially inappropriate prescribing in this population.

## 2 Methods

## 2.1 Study design and setting

A prospective observational study was conducted on a group of geriatric patients admitted to the 310-bed National Geriatric Hospital and 800-bed Friendship Hospital, which are located in Hanoi, Vietnam. These are the two largest public general geriatric hospitals administered by the Vietnamese Ministry of Health in Hanoi and the north of Vietnam. In the two hospitals, patient safety practices and prescribing policies are applied uniformly.

## 2.2 Study population and data collection

Individuals aged over 60 years admitted to 7 selected internal medicine units of the two hospitals, staying in the hospital at least one day, and prescribed at least one medicine during the hospital stay were selected to participate in the study. We excluded patients who were unable to participate due to their clinical conditions (e.g., in a coma or could not give the consent). The selected internal medicine units were endocrine and metabolism, orthopedics, cardiovascular, respiratory, gastroenterology, mental and neurology, and general internal medicine. The patient recruitment process took place over 14 non-consecutive weeks from July 2018 to December 2018, with two weeks of recruitment for each unit. During this period, all patients that were admitted to the units, met the selection criteria, and gave informed consent were included in the study. Patients were followed to collect information from admission to discharge. Researchers gathered data on each recruited participant by analyzing their medical records and conducting interviews with them. The medical record contained information about patients' sociodemographic characteristics (age, gender), clinical information (primary and secondary diagnoses, length of hospital stay), and medical chart (complete data on the name, dosage, and

duration of drug treatment). Complementing the interview data were a history of diseases, a medication history, a history of falls, and other functional data.

### 2.3 Sample size

The proportion of patients with at least 1 PIP at hospital admission (prevalence of PIP) was chosen as the main outcome of this study. To calculate the sample size, the equation of sample size for single proportion was used:

$$n=(Z\alpha\Delta)2p(1-p)$$

According to previous studies in other countries, the prevalence (p) of PIP in secondary setting was between 37 to 77%. In our study, the value of p was set at 50% to achieve the maximum sample size. After rounding up and compensating for loss due to various reasons by 20%, a total of 465 patients were required for the study.

### 2.4 Assessment of Potentially Inappropriate Prescribing

To screen for potential inappropriate medications (PIM), STOPP version 2 criteria were used, while START was used to detect potential prescribing omissions (PPO) in patients. Two researchers (DTXP and VTT) familiar with the STOPP/START criteria independently and thoroughly assessed each participant's medication records. Their findings for each subject were then compared and examined to reconcile any discrepancies. The admission prescriptions of patients were compared to the toolkit's criteria for PIM and PPO screening. PIM was also considered for medications provided during a hospital stay of more than three days. Meanwhile, a PPO was recorded if the medicine was not prescribed at any moment during patients' hospital stay, after excluding contraindication cases.

### 2.5 Primary outcomes

The prevalence of PIP was defined as the proportion of patients prescribed at least one PIM medication according to STOPP, or at least one PPO according to START during the hospital stay.

### 2.6 Other assessments

To determine the patient health status and comorbidities, the Charlson Comorbidity Index (CCI) was employed (19). The independence level in Activities of Daily Living (ADL) was assessed for each patient and categorized patients into two functional groups: dependent and independent (20). To assess the risk of falls and the risk of bleeding, the Morse Fall Scale and HAS-BLED score were used, respectively. These assessments were conducted by the researcher for each patient using information from their medical records and patient interviews. Description and scoring interpretation of these assessments are rather lengthy and details can be found in these previous publications (19,20).

### 2.7 Data analysis

SPSS Version 22.0 was used to analyze the data collected. The factors relating to PIP were investigated using multivariable logistic regression. For nonparametric data, descriptive statistics including median and interquartile range (IQR) were used; for normally distributed data, mean and standard deviation were calculated. Percentage and frequency were used to describe characteristics and distribution of PIP. To find appropriate multivariate logistic regression models and risk factors related with PIM/PPO, the Backward Stepwise (Wald) method was used, which would be adjusted for age and gender. The dependent variable was the occurrence of at least one PIM or PPO during hospital stay; the input independent variables were age, gender,

number of comorbidities per patient, number of medications per patient, CCI, ADL, length of hospital stay, and risk of falls, history of fall, history of fracture. The results of the regression analysis were reported as odds ratios with 95% confidence intervals. The influence of factors was statistically significant with $p < 0.05$.

### 2.8 Ethics approval

This study was granted ethics approvals by The Hospital Science and Technology Committee at Friendship Hospital, Vietnam (approved on March 2018), the Human Research Ethics Committee (HREC) at the National Geriatric Hospital (approved on June 2018) and the Human Research Ethics Committee (HREC) at the University of Newcastle, Australia (Approval Number H-2018-0130).

## 3 Results

### 3.1 Characteristics of the study population

A total of 469 geriatric patients (64.7% male, mean age 76.9 ± 7.1 years) met the selection criteria. Table 5.1 summarizes the major characteristics of the study population. The most frequently admitted wards were Cardiovascular (18.6%) and Respiratory (17.7%). The average length of stay was 13.0 ± 6.4 days. The average number of medications given to each patient was 9.2 ± 3.8. Polypharmacy was administered to 82.5% of patients (5 or more medications), while 32.8% of patients had more than ten medications during their hospital stay. In addition, 62.9% of patients had a CCI score of one to two, and 11.9% had a history of falls.

***Table 5.1.*** *Baseline characteristics of the study population (n=469)*

| **Demographic parameters** | | **Number of patients (%)** |
|---|---|---|
| Age (years) | 60 – 74 | 177 (37.7) |
| | 75 – 84 | 221 (47.1) |
| | ≥ 85 | 71 (15.1) |
| | Mean ± SD* | 76.9 ± 7.1 |
| Gender | Male | 316 (64.7) |
| | Female | 153 (32.6) |
| Admission wards | Cardiovascular | 87 (18.6) |
| | General internal | 64 (13.6) |
| | Respiratory | 83 (17.7) |
| | Gastroenterology | 49 (10.4) |
| | Orthopedics | 61 (13.0) |
| | Mental & Nervous System | 70 (14.9) |
| | Endocrine & Metabolism | 55 (11.7) |
| Number of comorbidities per patient | Mean ± SD * | 4.6 ± 1.6 |
| | Min - Max | 1 - 9 |
| Length of stay (days) | | 13.0 ± 6.4 |
| Charlson Co-morbidity Index (CCI) | 0 | 105 (22.4) |
| | 1 – 2 | 295 (62.9) |
| | ≥ 3 | 69 (14.7) |
| Number of medications per patient | ≤ 5 | 82 (17.5) |
| | 6 – 10 | 233 (49.7) |
| | >10 | 154 (32.8) |
| | Mean ± SD* | 9.2 ± 3.8 |
| Activities of Daily Living (ADL) | Independent | 171 (36.5) |
| | Dependent ≥ 1 ADL | 298 (63.5) |
| History of fall during 3 months | Yes | 56 (11.9) |
| | No | 413 (88.1) |
| Risk of fall | High | 190 (40.5) |
| | Moderate | 197 (42.0) |
| | Low | 82 (17.5) |

**SD: Standard Deviation*

### 3.2 Prevalence of Potentially Inappropriate Prescribing

We identified 126 PIM and 228 PPO in the study population during their hospitalization period using STOPP and START version 2 criteria, respectively. According to STOPP, 22.4% of geriatric patients had at least one PIM, whereas 33.5% of patients had at least one PPO according to START version 2 (Table 5.2). Overall, nearly half of the patients had at least one PIP (46.5%).

***Table 5.2.*** *Frequency of PIP in patients according STOPP/START criteria*

| Number | PIM[a] according to STOPP | | PPO[b] according to START | | PIP[c] (total PIM and PPO) | |
|---|---|---|---|---|---|---|
| | n | (%) | n | (%) | n | % |
| 0 | 364 | 77.6 | 312 | 66.5 | 251 | 53.5 |
| 1 | 86 | 18.3 | 103 | 22.0 | 127 | 27.1 |
| 2 | 17 | 3.6 | 36 | 7.7 | 57 | 12.2 |
| 3 | 2 | 0.4 | 18 | 3.8 | 23 | 4.9 |
| 4 | - | - | - | - | 10 | 2.1 |
| **5** | **-** | **-** | **-** | **-** | **1** | **0.2** |
| **Total** | **469** | **100.0** | **469** | **100.0** | **469** | **100.0** |

[a:] *PIM = Potentially Inappropriate Medication*

[b] *PPO: Potentially Prescribing Omission*

[c] *PIP: Potentially Inappropriate Prescribing*

### 3.3 Characteristics of Potentially Inappropriate Medications and Potential Prescribing Omissions

Table 5.3 lists 16 different types of PIM based on the STOPP criteria, with a total of 126 PIM in the study population. The use of long-acting benzodiazepines (46.8%) was the most common PIM, followed by first generation antihistamines (15.1%) and NSAIDs if eGFR was less than 50 ml/min/1.73m$^2$ (11.9%). START version 2 criteria revealed 228 PPO, with 74 PPO (32.4%)

being statin therapy with a documented history of coronary, cerebral, or peripheral vascular disease; a quarter of PPO (25.8%) being beta-blocker therapy with ischaemic heart disease; and 12.7% of PPO being antiplatelet therapy with a documented history of coronary, cerebral, or peripheral vascular disease (Table 5.4).

***Table 5.3.*** *Distribution of PIM[a] according to STOPP criteria*

| Code | Criteria | Frequency | % |
|---|---|---|---|
| A3 | Any duplicate drug class prescription | 6 | 4.8 |
| B10 | Centrally-acting antihypertensives (e.g. methyldopa, clonidine, moxonidine, rilmenidine, guanfacine) | 5 | 4.0 |
| C3 | Aspirin, clopidogrel, dipyridamole, vitamin K antagonists, direct thrombin inhibitors or factor Xa inhibitors with concurrent significant bleeding risk | 3 | 2.4 |
| C4 | Aspirin plus clopidogrel as secondary stroke prevention, unless the patient has a coronary stent(s) inserted in the previous 12 months or concurrent acute coronary syndrome or has a high grade symptomatic carotid arterial stenosis | 3 | 2.4 |
| D14 | First-generation antihistamines | 19 | 15.1 |
| D2 | Initiation of Tricyclic Antidepressants (TCAs) as first-line antidepressant treatment | 1 | 0.8 |
| D5 | Benzodiazepines for ≥ 4 weeks | 1 | 0.8 |
| D6 | Antipsychotics (i.e. other than quetiapine or clozapine) in those with parkinsonism or Lewy Body Disease | 1 | 0.8 |
| D7 | Anticholinergics/antimuscarinics to treat extra-pyramidal side-effects of neuroleptic | 1 | 0.8 |
| E4 | NSAIDs if eGFR < 50 ml/min/1.73m$^2$ | 15 | 11.9 |
| E6 | Metformin if eGFR < 30 ml/min/1.73m$^2$ | 1 | 0.8 |
| F1 | Prochlorperazine or metoclopramide with Parkinsonism | 1 | 0.8 |
| H7 | COX-2 selective NSAIDs with concurrent cardiovascular disease | 1 | 0.8 |
| K1 | Benzodiazepines in patients with high risk of fall | 59 | 46.8 |
| K4 | Hypnotic Z-drugs (e.g. zopiclone, zolpidem, zaleplon) | 7 | 5.6 |

| | | | |
|---|---|---|---|
| N1 | Concomitant use of two or more drugs with antimuscarinic/anticholinergic properties | 2 | 1.6 |
| **Total** | | **126** | **100.0** |

[a:] *PIM = Potentially Inappropriate Medication*

***Table 5.4.*** *Distribution of PPO[a] according to START criteria*

| Code | Criteria | Frequency | % |
|---|---|---|---|
| A1 | Vitamin K antagonists or direct thrombin inhibitors or factor Xa inhibitors in the presence of chronic atrial fibrillation. | 3 | 1.3 |
| A3 | Antiplatelet therapy with a documented history of coronary, cerebral or peripheral vascular disease. | 29 | 12.7 |
| A4 | Antihypertensive therapy where systolic blood pressure consistently > 160 mmHg and/or diastolic blood pressure consistently >90 mmHg; if systolic blood pressure > 140 mmHg and /or diastolic blood pressure > 90 mmHg, if diabetic. | 1 | 0.4 |
| A5 | Statin therapy with a documented history of coronary, cerebral or peripheral vascular disease, unless the patient's status is end-of-life or age is > 85 years. | 74 | 32.4 |
| A6 | Angiotensin Converting Enzyme (ACE) inhibitor with systolic heart failure and/or documented coronary artery disease | 2 | 0.9 |
| A7 | Beta-blocker with ischaemic heart disease. | 59 | 25.8 |
| A8 | Appropriate beta-blocker (bisoprolol, nebivolol, metoprolol or carvedilol) with stable systolic heart failure | 1 | 0.4 |
| B1 | Regular inhaled β2 agonist or antimuscarinic bronchodilator for mild to moderate asthma or COPD. | 1 | 0.4 |
| B2 | Regular inhaled corticosteroid for moderate-severe asthma or COPD | 4 | 1.8 |
| C1 | L-DOPA or a dopamine agonist in idiopathic Parkinson's disease with functional impairment and resultant disability | 2 | 0.9 |
| E1 | Disease-modifying anti-rheumatic drug (DMARD) with active, disabling rheumatoid disease | 1 | 0.4 |
| E2 | Bisphosphonates and vitamin D and calcium in patients taking long-term systemic corticosteroid therapy | 3 | 1.3 |
| E3 | Vitamin D and calcium supplement in patients with known osteoporosis and/or previous fragility fracture(s) and/or (Bone Mineral Density T-scores more than -2.5 in multiple sites). | 25 | 10.9 |

| | | | |
|---|---|---|---|
| E4 | Bone anti-resorptive or anabolic therapy in patients with documented osteoporosis, where no pharmacological or clinical status contraindication exists and/or previous history of fragility fracture(s). | 10 | 4.4 |
| E6 | Xanthine-oxidase inhibitors with a history of recurrent episodes of gout. | 5 | 2.2 |
| E7 | Folic acid supplement in patients taking methotrexate. | 1 | 0.4 |
| F1 | ACE inhibitor or Angiotensin Receptor Blocker in diabetes with evidence of renal disease i.e. dipstick proteinuria or microalbuminuria (>30mg/24 hours) with or without serum biochemical renal impairment. | 4 | 1.8 |
| G1 | Alpha-1 receptor blocker with symptomatic prostatism, where prostatectomy is not considered necessary | 3 | 1.3 |
| **Total** | | **228** | **100.0** |

[a]*PPO: Potentially Prescribing Omission*

### 3.4 Risk Factors for Potentially Inappropriate Prescribing

The study employed multivariate logistic regression with the Backward Stepwise (Wald) approach to exclude variables and selected appropriate multivariate models to discover variables linked with the probability of PIM and PPO. Table 5.5 and 5.6 show the risk factors associated with the occurrence of PIM and PPO in study participants.

After adjusting for age and gender, a much higher risk for PIM was recognized in patients who had high risk of falls [OR = 6.016, 95% CI: 2.435 – 14.862] compared to patients with low risk. In addition, the occurrence of PIM also significantly increased in patients with > 10 medications [OR: 2.936, 95% CI: 1.326-6.502]

In terms of PPO, while the number of medications and co-morbidities both significantly increase the risk of developing PPO in a patient, increasing age slightly reduces this risk [OR:0.968; 95% CI: 0.940-0.996]

***Table 5.5.*** *Multivariate logistic regression for PIM[a] according to STOPP version 2 criteria*

| Independent factor | No. of patients in each subgroup | OR[b] (95% CI[c]) | p-value |
|---|---|---|---|
| **Gender** | | | |
| Male | 316 (67.4) | reference | |
| Female | 153 (32.6) | 1.292 (0.790-2.113) | 0.306 |
| **Risk of fall** | | | |
| Low | 82 (17.5) | reference | |
| Medium | 197 (42.0) | 1.303 (0.499 – 3.399) | 0.598 |
| High | 190 (40.5) | 6.016 (2.435 – 14.862) | <0.001 |
| **Number of medications** | | | |
| ≤ 5 | 82 (17.5) | reference | |
| 6 – 10 | 233 (49.7) | 1.291 (0.591-2.823) | 0.522 |
| >10 | 154 (32.8) | 2.936 (1.326-6.502) | 0.008 |

*[a:]PIM: Potentially Inappropriate Medication; [b]OR: Odd Ratio; [c]CI Confidence Interval*

***Table 5.6.*** *Multivariate logistic regression for having at least one PPO[a] according to START version 2 criteria*

| Independent factor | No. of patients in each subgroup n (%) | OR[b] (95% CI[c]) | p-value |
|---|---|---|---|
| **Age** | - | 0.968 (0.940-0.996) | 0.028 |
| **Number of co-morbidities** | - | 1.440 (1.250 – 1.660) | <0.0001 |
| **Number of medications** | | | |
| ≤ 5 | 82 (17.5) | reference | |
| 6 – 10 | 233 (49.7) | 2.111 (1.093 – 4.077) | 0.026 |
| >10 | 154 (32.8) | 2.117 (1.047 – 4.281) | 0.037 |
| **History of fracture** | | | |
| No | 448 (95.5) | reference | |
| yes | 21 (4.5) | 2.344 (0.921-5.966) | 0.074 |

*[a:]PPO: Potentially Prescribing Omissions; [b]OR: Odd Ratio; [c]CI Confidence Interval*

## 4 Discussion

To the best of our knowledge, this is the most recent of the limited studies available (17, 18) investigating prescribing appropriateness among geriatric inpatients in Vietnam. It is also one of the few studies available in the field of prescription to the elderly in Southeast Asia (21). To effectively identify PIP, the most important characteristics of a prescribing screening tool are its formulary relevance and sensitivity for screening PIP in the population. As a result, many countries have developed their own set of PIP criteria that are tailored to their country's drug list and prescribing practices (11-13, 22-25). Vietnam currently lacks an explicit screening tool for

PIP, and developing one would take considerable time and expert manpower. Therefore, STOPP/START version 2 were chosen in this study as they have shown to be applicable and transferable to Asia, and have been used in many Asian countries, including Malaysia (21), Taiwan (26) and India (27). More importantly, it is a validated tool, with studies demonstrating a link between the identified PIP and preventable adverse drug events (ADE) as well as indicators of hospitalizations and quality of life.

According to the STOPP/START criteria, our study's overall PIP prevalence (at least one STOPP PIM or at least one START PPO) was reported as 46.5%. The prevalence of PIM detected in our study (22.4%) is comparable with the prevalence reported in the literature, which ranges from 20 to 88% in patients aged 65 and up (21, 26, 28-34). Similarly, our study also identified a prevalence of PPO (33.5%) that was comparable to values reported in the literature of 34 to 65% (21, 26, 29-31, 34). There are many factors that contribute to the variance in the study results. For example, studies differed in their design and population sampled, such as patients from community-dwellings, hospitals, geriatric clinics, and long-term care facilities. In addition, some studies (32, 35) only used a portion of the STOPP/START criteria, which can lead to lower prevalence and complicate direct comparisons. Our present study also excluded implicit criteria A1-A3 from the STOPP list, as these criteria are difficult to evaluate precisely without consulting the treating physician. For instance, A1 is the circumstances that are not specified, while A2 refers to cases that require a longer treatment term than necessary and also require unanimity with the treating physician. This exclusion may be one reason accounting for the lower rate of PIP in this study in comparison to several other studies where these criteria were employed (36, 37) [REF].

In the study, PIM were associated with drugs from the central nervous system, with frequently observed over-utilization of benzodiazepines, which have been linked to clinically significant adverse effects in older persons, such as impaired cognition and falls (38). The finding of the benzodiazepines being the most prevalent PIM is comparable with previous published reports (37, 39, 40). The most prevalent drug classes with omissions were statins, beta-blockers, and calcium-vitamin D supplements. Again, this analysis of drugs commonly associated with PPO is comparable to a number of other studies that have reported vitamin D, vitamin D and calcium (29, 31), and beta-blockers and statins (31).

In the present study, PIMs were found to be related with the risk of fall and the patients using more than 10 medications. The PIP were 6.016 times more likely to occur among patients with high risk of fall, in comparison to patients who had low risk. Similar variations in the prevalence of PIP among different risks of fall were also reported by other studies (29). Similarly, polypharmacy is also often highlighted as a PIM risk factor, with some studies indicating that the use of 10 medicines doubles the likelihood of PIM incidence (41, 42), comparable with our study. Regarding PPOs, they were associated with the number of co-morbidity and the number of medications, which was accordance with literature (29, 42) Fractures have also been cited as predictors (31). In our analysis, however, the link between fracture and PPO was not statistically significant (p=0.076). Furthermore, the findings of the study revealed that older age tended to reduce the risk of PPO occurrence in the study population. This appears to contradict other risk factor analyses in which increasing age is frequently identified as a risk factor for PPO. This could be an artifact of the sample size, as the risk reduction is minor and nearly reaches 1 in the 95% CI of the OR [OR 0.968 95%CI: 0.940-

0.996] .Another possible cause would be the contribution of other confounding factors that were not tested in the analysis.

**Strengths and Limitations**

Accurately assessing PIM and PPO requires extensive collection of clinical, laboratory, and patient history information and is time-consuming. Therefore, the prospective design of this study allows for sufficient information to be collected for the most accurate PIP screening. This is the strength of the study compared to studies that retrospectively screened PIP on databases. In comparison to other prospective studies, this study enrolled a relatively large number of patients at two of Vietnam's largest geriatric hospitals. As a result, the study's findings would more accurately reflect the current state of PIP prescribing in the geriatric population in general.

However, the study results should be considered with the following limitations. Due to time constraints, the study only detected PIP without examining possible important outcome factors to establish the clinical importance of the PIP. However, several studies and systematic reviews have demonstrated these significant links (43-45), emphasizing the need for PIP detection and reduction methods. Further PIP studies in Vietnam are still required to assess the outcomes in order to allow an assessment of cost-effectiveness of any intervention strategies.

Second, the study took place over 14 non-consecutive weeks over six months, which could alter the PIP prevalence due to the variety of patients admitted throughout that time. Nonetheless, almost of PIP criteria were indicated in chronic conditions, which means the prescriptions of them were less affected by the season. Furthermore, the study was conducted within the same year, with no changes in the hospital formulary altering our findings. Therefore, we concluded that the effect of the study's extended sampling duration was minor.

As previously stated, the study did not use the entire set of STOPP/START criteria, with the judgement-based criteria (A1-A3) excluded. As a result, the prevalence of PIP in our study was underdetemined. In addition, the use of STOPP/START has its own set of limitations. There may be a distinction between evidence-based suggestions and what is best for the individual patient [27]. Despite the fact that STOPP/START screening methods are easy to use and can detect potentially inappropriate prescribing, they are limited in their ability to take into consideration the holistic needs of each patient. This demonstrates that, in addition to using STOPP/START criteria, comprehensively detecting inappropriate prescription requires an individual patient analysis for each prescribed medication. Therefore, educating physicians and pharmacists participating in medication reviews, as well as developing electronic prescription assistance with PIP alerts are recommended for successful interventions (46, 47).

## 5 Conclusion

According to the study findings, the prevalence of PIP according to the STOPP/START version 2 was relatively high in geriatric inpatients in Vietnamese hospitals, which is consistent with the data reported in other countries. The medications most frequently recognized as PIMs belonged to the central nervous system, whereas PPOs were connected with musculoskeletal and cardiovascular system medications. Patients with increased risk of having PIP were also identified. The findings indicate that interventions aimed at reducing PIP among elderly inpatients are necessary to improve both medication safety and the quality use of medicines in this vulnerable population group in Vietnam.

**Abbreviation:**

PIM: Potentially Inappropriate Medication

PIP: Potentially Inappropriate Prescribing

PPO: Potentially Prescribing Omission

START: Screening Tool to Alert doctors to Right Treatment

STOPP: Screening Tool of Older Person's Prescriptions

**Declarations**

**Ethics approval:** This study was granted ethics approvals by The Hospital Science and Technology Committee at Friendship Hospital, Vietnam (approved in March, 2018), the Human Research Ethics Committee at National Geriatric Hospital (approved in June 2018) and the Human Research Ethics Committee (HREC) at the University of Newcastle, Australia (Approval Number H-2018-0130).

**Consent to participate:** All participants have provided written consents to participate.

**Consent to publication:** All listed authors have approved the manuscript before submission, including the names and order of authors.

**Availability of data and material:** All data generated and analysed during the current study are available from the corresponding author on reasonable request.

**Competing interest:** The authors declare that they have no competing interests.

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**Author contributions**

- Phuong Thi Xuan Dong: Conceptualization, Methodology, Data collection, Formal analysis, Writing – Original Draft, Writing – Review & Editing.
- Van Thi Thuy Pham: Conceptualization, Methodology, Writing – Review & Editing.
- Trinh Thi Vu: Methodology, Datacollection, Writing – Review & Editing.
- Huong Thi Lien Nguyen: Conceptualization, Methodology, Writing – Review & Editing.
- Susan Hua: Conceptualization, Methodology, Writing – Review & Editing, Supervision.
- Shu Chuen Li: Conceptualization, Methodology, Writing – Review & Editing, Supervision, Project administration.
- All authors read and approved the final manuscript.

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## Appendix

**Screening Tool of Older Persons' Prescriptions (STOPP) version 2.**

The following prescriptions are potentially inappropriate to use in patients aged 65 years and older.

**Section A: Indication of medication**

1. Any drug prescribed without an evidence-based clinical indication.

2. Any drug prescribed beyond the recommended duration, where treatment duration is well defined.

3. Any duplicate drug class prescription e.g. two concurrent NSAIDs, SSRIs, loop diuretics, ACE inhibitors, anticoagulants (optimisation of monotherapy within a single drug class should be observed prior to considering a new agent).

**Section B: Cardiovascular System**

1. Digoxin for heart failure with normal systolic ventricular function (no clear evidence of benefit).

2. Verapamil or diltiazem with NYHA Class III or IV heart failure (may worsen heart failure).

3. Beta-blocker in combination with verapamil or diltiazem (risk of heart block).

4. Beta blocker with bradycardia (< 50/min), type II heart block or complete heart block (risk of complete heart block, asystole).

5. Amiodarone as first-line antiarrhythmic therapy in supraventricular tachyarrhythmias (higher risk of side-effects than beta-blockers, digoxin, verapamil or diltiazem).

6. Loop diuretic as first-line treatment for hypertension (safer, more effective alternatives available).

7. Loop diuretic for dependent ankle oedema without clinical, biochemical evidence or radiological evidence of heart failure, liver failure, nephrotic syndrome or renal failure (leg elevation and /or compression hosiery usually more appropriate).

8. Thiazide diuretic with current significant hypokalaemia (i.e. serum K+ < 3.0 mmol/l), hyponatraemia (i.e. serum Na+ < 130 mmol/l) hypercalcaemia (i.e. corrected serum calcium > 2.65 mmol/l) or with a history of gout (hypokalaemia, hyponatraemia, hypercalcaemia and gout can be precipitated by thiazide diuretic).

9. Loop diuretic for treatment of hypertension with concurrent urinary incontinence (may exacerbate incontinence).

10. Centrally-acting antihypertensives (e.g. methyldopa, clonidine, moxonidine, rilmenidine, guanfacine), unless clear intolerance of, or lack of efficacy with, other classes of 2 antihypertensives (centrally-active antihypertensives are generally less well tolerated by older people than younger people).

11. ACE inhibitors or Angiotensin Receptor Blockers in patients with hyperkalaemia.

12. Aldosterone antagonists (e.g. spironolactone, eplerenone) with concurrent potassium conserving drugs (e.g. ACEI's, ARB's, amiloride, triamterene) without monitoring of serum potassium (risk of dangerous hyperkalaemia i.e. > 6.0 mmol/l – serum K should be monitored regularly, i.e. at least every 6 months).

13. Phosphodiesterase type-5 inhibitors (e.g. sildenafil, tadalafil, vardenafil) in severe heart failure characterised by hypotension i.e. systolic BP < 90 mmHg, or concurrent nitrate therapy for angina (risk of cardiovascular collapse).

**Section C: Antiplatelet/Anticoagulant Drugs**

1. Long-term aspirin at doses greater than 160mg per day (increased risk of bleeding, no evidence for increased efficacy).

2. Aspirin with a past history of peptic ulcer disease without concomitant PPI (risk of recurrent peptic ulcer ).

3. Aspirin, clopidogrel, dipyridamole, vitamin K antagonists, direct thrombin inhibitors or factor Xa inhibitors with concurrent significant bleeding risk, i.e. uncontrolled severe hypertension, bleeding diathesis, recent non-trivial spontaneous bleeding) (high risk of bleeding).

4. Aspirin plus clopidogrel as secondary stroke prevention, unless the patient has a coronary stent(s) inserted in the previous 12 months or concurrent acute coronary syndrome or has a high grade symptomatic carotid arterial stenosis (no evidence of added benefit over clopidogrel monotherapy).

5. Aspirin in combination with vitamin K antagonist, direct thrombin inhibitor or factor Xa inhibitors in patients with chronic atrial fibrillation (no added benefit from aspirin)

6. Antiplatelet agents with vitamin K antagonist, direct thrombin inhibitor or factor Xa inhibitors in patients with stable coronary, cerebrovascular or peripheral arterial disease (No added benefit from dual therapy).

7. Ticlopidine in any circumstances (clopidogrel and prasugrel have similar efficacy, stronger evidence and fewer side-effects).

8. Vitamin K antagonist, direct thrombin inhibitor or factor Xa inhibitors for first deep venous thrombosis without continuing provoking risk factors (e.g. thrombophilia) for > 6 months, (no proven added benefit).

9. Vitamin K antagonist, direct thrombin inhibitor or factor Xa inhibitors for first pulmonary embolus without continuing provoking risk factors (e.g. thrombophilia) for > 12 months (no proven added benefit).

10. NSAID and vitamin K antagonist, direct thrombin inhibitor or factor Xa inhibitors in combination (risk of major gastrointestinal bleeding).

11. NSAID with concurrent antiplatelet agent(s) without PPI prophylaxis (increased risk of peptic ulcer disease).

**Section D: Central Nervous System and Psychotropic Drugs**

1. TriCyclic Antidepressants (TCAs) with dementia, narrow angle glaucoma, cardiac conduction abnormalities, prostatism, or prior history of urinary retention (risk of worsening these conditions).

2. Initiation of TriCyclic Antidepressants (TCAs) as first-line antidepressant treatment (higher risk of adverse drug reactions with TCAs than with SSRIs or SNRIs).

3. Neuroleptics with moderate-marked antimuscarinic/anticholinergic effects (chlorpromazine, clozapine, flupenthixol, fluphenzine, pipothiazine, promazine, zuclopenthixol) with a history of prostatism or previous urinary retention (high risk of urinary retention).

4. Selective serotonin re-uptake inhibitors (SSRI's) with current or recent significant hyponatraemia i.e. serum Na+ < 130 mmol/l (risk of exacerbating or precipitating hyponatraemia).

5. Benzodiazepines for ≥ 4 weeks (no indication for longer treatment; risk of prolonged sedation, confusion, impaired balance, falls, road traffic accidents; all benzodiazepines should be withdrawn gradually if taken for more than 4 weeks as there is a risk of causing a benzodiazepine withdrawal syndrome if stopped abruptly).

6. Antipsychotics (i.e. other than quetiapine or clozapine) in those with parkinsonism or Lewy Body Disease (risk of severe extra-pyramidal symptoms).

7. Anticholinergics/antimuscarinics to treat extra-pyramidal side-effects of neuroleptic medications (risk of anticholinergic toxicity),

8. Anticholinergics/antimuscarinics in patients with delirium or dementia (risk of exacerbation of cognitive impairment).

9. Neuroleptic antipsychotic in patients with behavioural and psychological symptoms of dementia (BPSD) unless symptoms are severe and other non-pharmacological treatments have failed (increased risk of stroke).

10. Neuroleptics as hypnotics, unless sleep disorder is due to psychosis or dementia (risk of confusion, hypotension, extra-pyramidal side effects, falls).

11. Acetylcholinesterase inhibitors with a known history of persistent bradycardia (< 60 beats/min.), heart block or recurrent unexplained syncope or concurrent treatment with drugs that reduce heart rate such as beta-blockers, digoxin, diltiazem, verapamil (risk of cardiac conduction failure, syncope and injury).

12. Phenothiazines as first-line treatment, since safer and more efficacious alternatives exist (phenothiazines are sedative, have significant anti-muscarinic toxicity in older people, with the exception of prochlorperazine for nausea/vomiting/vertigo, chlorpromazine for relief of persistent hiccoughs and levomepromazine as an anti-emetic in palliative care).

13. Levodopa or dopamine agonists for benign essential tremor (no evidence of efficacy)

14. First-generation antihistamines (safer, less toxic antihistamines now widely available).

**Section E: Renal System.**

The following drugs are potentially inappropriate in older people with acute or chronic kidney disease with renal function below particular levels of eGFR (refer to summary of product characteristics datasheets and local formulary guidelines)

1. Digoxin at a long-term dose greater than 125µg/day if eGFR < 30 ml/min/1.73m2 (risk of digoxin toxicity if plasma levels not measured).

2. Direct thrombin inhibitors (e.g. dabigatran) if eGFR < 30 ml/min/1.73m2 (risk of bleeding).

3. Factor Xa inhibitors (e.g. rivaroxaban, apixaban) if eGFR < 15 ml/min/1.73m2 (risk of bleeding).

4. NSAID's if eGFR < 50 ml/min/1.73m2 (risk of deterioration in renal function).

5. Colchicine if eGFR < 10 ml/min/1.73m2 (risk of colchicine toxicity).

6. Metformin if eGFR < 30 ml/min/1.73m2 (risk of lactic acidosis).

Section F: Gastrointestinal System

1. Prochlorperazine or metoclopramide with Parkinsonism (risk of exacerbating Parkinsonian symptoms).

2. PPI for uncomplicated peptic ulcer disease or erosive peptic oesophagitis at full therapeutic dosage for > 8 weeks (dose reduction or earlier discontinuation indicated).

3. Drugs likely to cause constipation (e.g. antimuscarinic/anticholinergic drugs, oral iron, opioids, verapamil, aluminium antacids) in patients with chronic constipation where nonconstipating alternatives are available (risk of exacerbation of constipation).

4. Oral elemental iron doses greater than 200 mg daily (e.g. ferrous fumarate> 600 mg/day, ferrous sulphate > 600 mg/day, ferrous gluconate> 1800 mg/day; no evidence of enhanced iron absorption above these doses).

**Section G: Respiratory System**

1. Theophylline as monotherapy for COPD (safer, more effective alternative; risk of adverse effects due to narrow therapeutic index).

2. Systemic corticosteroids instead of inhaled corticosteroids for maintenance therapy in moderate-severe COPD (unnecessary exposure to long-term side-effects of systemic corticosteroids and effective inhaled therapies are available).

3. Anti-muscarinic bronchodilators (e.g. ipratropium, tiotropium) with a history of narrow angle glaucoma (may exacerbate glaucoma) or bladder outflow obstruction (may cause urinary retention)

4. Non-selective beta-blocker (whether oral or topical for glaucoma) with a history of asthma requiring treatment (risk of increased bronchospasm).

5. Benzodiazepines with acute or chronic respiratory failure i.e. $pO2 < 8.0$ kPa ± $pCO2 > 6.5$kPa (risk of exacerbation of respiratory failure).

**Section H: Musculoskeletal System**

1. Non-steroidal anti-inflammatory drug (NSAID) other than COX-2 selective agents with history of peptic ulcer disease or gastrointestinal bleeding, unless with concurrent PPI or H2 antagonist (risk of peptic ulcer relapse).

2. NSAID with severe hypertension (risk of exacerbation of hypertension) or severe heart failure (risk of exacerbation of heart failure).

3. Long-term use of NSAID (>3 months) for symptom relief of osteoarthritis pain where paracetamol has not been tried (simple analgesics preferable and usually as effective for pain relief).

4. Long-term corticosteroids (>3 months) as monotherapy for rheumatoid arthrtitis (risk of systemic corticosteroid side-effects).

5. Corticosteroids (other than periodic intra-articular injections for mono-articular pain) for osteoarthritis (risk of systemic corticosteroid side-effects).

6. Long-term NSAID or colchicine (>3 months) for chronic treatment of gout where there is no contraindication to a xanthine-oxidase inhibitor (e.g. allopurinol, febuxostat) (xanthineoxidase inhibitors are first choice prophylactic drugs in gout).

7. COX-2 selective NSAIDs with concurrent cardiovascular disease (increased risk of myocardial infarction and stroke).

8. NSAID with concurrent corticosteroids without PPI prophylaxis (increased risk of peptic ulcer disease).

9. Oral bisphosphonates in patients with a current or recent history of upper gastrointestinal disease i.e. dysphagia, oesophagitis, gastritis, duodenitis, or peptic ulcer disease, or upper gastrointestinal bleeding (risk of relapse/exacerbation of oesophagitis, oesophageal ulcer, oesophageal stricture).

**Section I: Urogenital System**

1. Antimuscarinic drugs with dementia, or chronic cognitive impairment (risk of increased confusion, agitation) or narrow-angle glaucoma (risk of acute exacerbation of glaucoma), or chronic prostatism (risk of urinary retention).

2. Selective alpha-1 selective alpha blockers in those with symptomatic orthostatic hypotension or micturition syncope (risk of precipitating recurrent syncope).

**Section J. Endocrine System**

1. Sulphonylureas with a long duration of action (e.g. glibenclamide, chlorpropamide, glimepiride) with type 2 diabetes mellitus (risk of prolonged hypoglycaemia).

2. Thiazolidenediones (e.g. rosiglitazone, pioglitazone) in patients with heart failure (risk of exacerbation of heart failure).

3. Beta-blockers in diabetes mellitus with frequent hypoglycaemic episodes (risk of suppressing hypoglycaemic symptoms).

4. Oestrogens with a history of breast cancer or venous thromboembolism (increased risk of recurrence).

5. Oral oestrogens without progestogen in patients with intact uterus (risk of endometrial cancer).

6. Androgens (male sex hormones) in the absence of primary or secondary hypogonadism (risk of androgen toxicity; no proven benefit outside of the hypogonadism indication).

**Section K: Drugs that predictably increase the risk of falls in older people**

1. Benzodiazepines (sedative, may cause reduced sensorium, impair balance).

2. Neuroleptic drugs (may cause gait dyspraxia, Parkinsonism).

3. Vasodilator drugs (e.g. alpha-1 receptor blockers, calcium channel blockers, long-acting nitrates, ACE inhibitors, angiotensin I receptor blockers, ) with persistent postural hypotension i.e. recurrent drop in systolic blood pressure ≥ 20mmHg (risk of syncope, falls).

4. Hypnotic Z-drugs e.g. zopiclone, zolpidem, zaleplon (may cause protracted daytime sedation, ataxia).

**Section L: Analgesic Drugs**

1. Use of oral or transdermal strong opioids (morphine, oxycodone, fentanyl, buprenorphine, diamorphine, methadone, tramadol, pethidine, pentazocine) as first line therapy for mild pain (WHO analgesic ladder not observed).

2. Use of regular (as distinct from PRN) opioids without concomitant laxative (risk of severe constipation).

3. Long-acting opioids without short-acting opioids for break-through pain (risk of persistence of severe pain).

**Section N: Antimuscarinic/Anticholinergic Drug Burden**

Concomitant use of two or more drugs with antimuscarinic/anticholinergic properties (e.g. bladder antispasmodics, intestinal antispasmodics, tricyclic antidepressants, first generation antihistamines) (risk of increased antimuscarinic/anticholinergic toxicity).

**Screening Tool to Alert to Right Treatment (START), version 2.**

Unless an elderly patient's clinical status is end-of-life and therefore requiring a more palliative focus of pharmacotherapy, the following drug therapies should be considered where omitted for no valid clinical reason(s). It is assumed that the prescriber observes all the specific contraindications to these drug therapies prior to recommending them to older patients.

**Section A: Cardiovascular System**

1. Vitamin K antagonists or direct thrombin inhibitors or factor Xa inhibitors in the presence of chronic atrial fibrillation.
2. Aspirin (75 mg – 160 mg once daily) in the presence of chronic atrial fibrillation, whereVitamin K antagonists or direct thrombin inhibitors or factor Xa inhibitors are contraindicated.
3. Antiplatelet therapy (aspirin or clopidogrel or prasugrel or ticagrelor) with a documented history of coronary, cerebral or peripheral vascular disease.
4. Antihypertensive therapy where systolic blood pressure consistently > 160 mmHg and/or diastolic blood pressure consistently >90 mmHg; if systolic blood pressure > 140 mmHg and /or diastolic blood pressure > 90 mmHg, if diabetic.
5. Statin therapy with a documented history of coronary, cerebral or peripheral vascular disease, unless the patient's status is end-of-life or age is > 85 years.
6. Angiotensin Converting Enzyme (ACE) inhibitor with systolic heart failure and/or documented coronary artery disease.
7. Beta-blocker with ischaemic heart disease.
8. Appropriate beta-blocker (bisoprolol, nebivolol, metoprolol or carvedilol) with stable systolic heart failure.

**Section B: Respiratory System**

1. Regular inhaled □2 agonist or antimuscarinic bronchodilator (e.g. ipratropium, tiotropium) for mild to moderate asthma or COPD.
2. Regular inhaled corticosteroid for moderate-severe asthma or COPD, where FEV1 <50% of predicted value and repeated exacerbations requiring treatment with oral corticosteroids.
3. Home continuous oxygen with documented chronic hypoxaemia (i.e. pO2 < 8.0 kPa or 60 mmHg or SaO2 < 89%).

**Section C: Central Nervous System& Eyes**

1. L-DOPA or a dopamine agonist in idiopathic Parkinson's disease with functional impairment and resultant disability.
2. Non-TCA antidepressant drug in the presence of persistent major depressive symptoms.
3. Acetylcholinesterase inhibitor (e.g. donepezil, rivastigmine, galantamine) for mildmoderate Alzheimer's dementia or Lewy Body dementia (rivastigmine).
4. Topical prostaglandin, prostamide or beta-blocker for primary open-angle glaucoma.
5. Selective serotonin reuptake inhibitor (or SNRI or pregabalin if SSRI contraindicated) for persistent severe anxiety that interferes with independent functioning.
6. Dopamine agonist (ropinirole or pramipexole or rotigotine) for Restless Legs Syndrome, once iron deficiency and severe renal failure have been excluded.

**Section D: Gastrointestinal System**

1. Proton Pump Inhibitor with severe gastro-oesophageal reflux disease or peptic stricture requiring dilatation.
2. Fibre supplements (e.g. bran, ispaghula, methylcellulose, sterculia) for diverticulosis with a history of constipation.

**Section E: Musculoskeletal System**

1. Disease-modifying anti-rheumatic drug (DMARD) with active, disabling rheumatoid disease.
2. Bisphosphonates and vitamin D and calcium in patients taking long-term systemic corticosteroid therapy.
3. Vitamin D and calcium supplement in patients with known osteoporosis and/or previous fragility fracture(s) and/or (Bone Mineral Density T-scores more than -2.5 in multiple sites).
4. Bone anti-resorptive or anabolic therapy (e.g. bisphosphonate, strontium ranelate, teriparatide, denosumab) in patients with documented osteoporosis, where no pharmacological or clinical status contraindication exists (Bone Mineral Density T-scores -> 2.5 in multiple sites) and/or previous history of fragility fracture(s).
5. Vitamin D supplement in older people who are housebound or experiencing falls or with osteopenia (Bone Mineral Density T-score is > -1.0 but < -2.5 in multiple sites).
6. Xanthine-oxidase inhibitors (e.g. allopurinol, febuxostat) with a history of recurrent episodes of gout.
7. Folic acid supplement in patients taking methotexate.

**Section F: Endocrine System**

1. ACE inhibitor or Angiotensin Receptor Blocker (if intolerant of ACE inhibitor) in diabetes with evidence of renal disease i.e. dipstick proteinuria or microalbuminuria (>30mg/24 hours) with or without serum biochemical renal impairment.

Section G: Urogenital System

1. Alpha-1 receptor blocker with symptomatic prostatism, where prostatectomy is not considered necessary.
2. 5-alpha reductase inhibitor with symptomatic prostatism, where prostatectomy is not considered necessary.
3. Topical vaginal oestrogen or vaginal oestrogen pessary for symptomatic atrophic vaginitis.

**Section H: Analgesics**

1. High-potency opioids in moderate-severe pain, where paracetamol, NSAIDs or low-potency opioids are not appropriate to the pain severity or have been ineffective.
2. Laxatives in patients receiving opioids regularly.

**Section I: Vaccines**

1. Seasonal trivalent influenza vaccine annually
2. Pneumococcal vaccine at least once after age 65 according to national guidelines

# PART C. POTENTIAL CONTRIBUTION OF

# CLINICAL PHARMACISTS

# Chapter 6. Impact and Cost-effectiveness of Pharmacist-initiated Educational Interventions on Improving Medication Reconciliation Practice in Geriatric Inpatients during Hospital Admission in Vietnam

This chapter has been published in the following peer-reviewed journal:

Dong, PTX, Pham, VTT, Nguyen, LT, et al. Impact of pharmacist-initiated educational interventions on improving medication reconciliation practice in geriatric inpatients during hospital admission in Vietnam. *J Clin Pharm Ther*. 2022; 1- 8. doi:10.1111/jcpt.13758

**Abstract**

**Background:** Unintentional medication discrepancies (UMDs) is common in geriatric patients during care transitions, especially during hospital admission, resulting in frequent undesirable consequences affecting the patients. Medication reconciliation when properly conducted could be a useful practice to prevent or ameliorate such discrepancies. However, this practice in Vietnamese hospitals has not been well established nor standardized. Therefore, the aim of this study was to determine the effect of pharmacist-initiated educational interventions on improving the quality of medication reconciliation practice.

**Methods:** This prospective 6-month pre- and post- study was carried out in two internal medicine wards in an 800-bed public hospital in Vietnam. Patients aged over 60 years, using ≥1 chronic medicine, and with hospital admission exceeding 48 hours were recruited. The interventions consisted of a training session and short-term support by pharmacists to physicians about medication reconciliation practice. Unintentional medication discrepancies (UMDs) in pre- and post-interventions phases were identified and the potential clinical significance of these UMDs was assessed based on a potential adverse drug event score. Primary outcome measures were the proportions of patients with at least one UMD at admission. Secondary outcome measures were the proportions of patients with a preventable Adverse Drug Events (pADE ) score ≥ 0.1 due to these UMDs. Odds ratio and 95% confidence intervals were assessed based on a multivariate logistic regression model.

**Results:** 152 patients were recruited in the pre-intervention phase, and 146 in the post-intervention phase. Following the intervention, the proportion of geriatric patients with ≥1 UMD at admission significantly decreased from 55.3 to 25.3% (ORadj 0.255, 95% CI: 0.151 – 0.431).

Similarly, the proportion of patients with a pADE ≥0.1 at admission reduced from 44.1 to 11.6% (ORadj 0.188, 95% CI: 0.105-0.340] post-intervention.

**Conclusions:** Our pharmacist-initiated educational interventions have demonstrated substantial improvement in medication reconciliation practice, leading to a significant decrease in the frequency of UMDs and overall reduction in potential harm. A nationwide standardized implementation of the practice would facilitate better healthcare delivery in reducing medication errors with resultant cost savings in Vietnam. Our model may be a viable and cost-effective option for consideration, especially for jurisdictions with limited pharmacy workforce.

# 1 Introduction

Unintentional medication discrepancies (UMDs) defined as unexplained differences in medication regimens, commonly occur during transfer between sites of care (1-4). These discrepancies can be medication errors causing adverse drug events that are potentially harmful to patients and reduce effective treatment (5, 6). As a countermeasure, medication reconciliation (MedRec) has been widely accepted as one of the most important initiatives to prevent or reduce medication discrepancies and improve patient safety (7-9). According to the World Health Organization (WHO), "MedRec is the formal process in which health care professionals partner with patients to ensure accurate and complete medication information transfer at interfaces of care" (7). The medication reconciliation service has proven to be successful in identifying most discrepancies and preventing harm to patients (6). For example, a systematic review in 2016 showed that medication reconciliation services led to significant reduction in adverse drug event-related hospital revisits, emergency department presentations, and hospital readmissions by 67%, 28% and 19%, respectively (8). Correspondingly, medication reconciliation is also associated with significant financial savings. Financial savings per 100 patients that received medication reconciliation was estimated to be between $35,000 and $42,300 according to several studies (10, 11). Currently, medication reconciliation has become a standard healthcare practice recommended by the WHO (12) and many countries (7, 13-17).

In many low- and middle-income countries like Vietnam, standardized medication reconciliation has not been fully defined or implemented. In practice, taking the patients' medication history during hospital admission is still performed routinely by physicians without any formal Standard Operating Procedure (SOP) or quality assurance requirements. Although local research data has been limited, our recent study found a relatively high rate of medication

discrepancies at hospital admission among geriatric patients in Vietnam (18). This suggests a need for interventions to improve this practice in Vietnam, especially for the older population.

Effective implementation of medication reconciliation is challenging. It requires successful efforts in human resources allocation, workflow redesign, and inter-professional collaboration. In many low- and middle-income countries like Vietnam, there are a number of additional barriers to standardize the implementation of medication reconciliation, including the lack of clear assignment of roles, the shortage of human resources, limited time devoted to this clinical activity, and insufficient knowledge of healthcare staff (19-22). In order to effectively implement medication reconciliation, many studies worldwide have reported pharmacists to be the most suitable to carry out this activity (23, 24). However, implementing comprehensive large-scale pharmacist-led medication reconciliation programs is not feasible in Vietnamese hospitals due to limited human resources of pharmacists available (25-27).

Based on the current workforce situation and that of the foreseeable future, it is unlikely for hospitals in Vietnam to have sufficient numbers of pharmacists to conduct medication reconciliation on a routine basis. Hence, it would be prudent to find the most cost-efficient approach to utilizing pharmacists for this activity, with minimal disruption to their current clinical practice. We propose that the provision of a short educational program tailored for physicians may be the most appropriate approach to increase their awareness of the problem as well as to provide some standard training in medication reconciliation (28). In particular, the main aim of the study was to determine the effect of pharmacist-initiated educational interventions (training interventions and short-term support) on the proportion of geriatric patients with UMDs during hospital admission. At the same time, we assessed the potential clinical impact of the educational intervention on UMDs pre- and post-interventions. A cost-

effectiveness analysis of the educational intervention was also performed. This study is important to identifying effective approaches to improving medication reconciliation in jurisdictions with limited pharmacy and other healthcare workforce, which would lead to better health outcomes with minimum input and system reorganization.

## 2 Methods

### 2.1 Study design

This was a 6-month prospective before and after study carried out in an 800-bed general public hospital located in Hanoi, Vietnam from October 2020 to April 2021. The study consisted of three phases conducted in two internal medicine wards with 60 and 80 beds, respectively. The first phase (pre-intervention phase) was a cross-sectional study aimed to assess the frequency and characteristics of UMDs among elderly inpatients during hospital admission, as a reflection of the current quality of medication reconciliation practice in the study hospital. The second phase was the intervention phase, in which a clinical pharmacist provided medication reconciliation interventions for physicians working in the study wards. The final phase (post-intervention phase) was similar to the first phase, in which the frequency of UMDs was assessed to evaluate the impact of pharmacist-initiated interventions on the quality of physician-led medication reconciliation practice. The study procedure with the time and duration of each phase is presented in Figure 6.1.

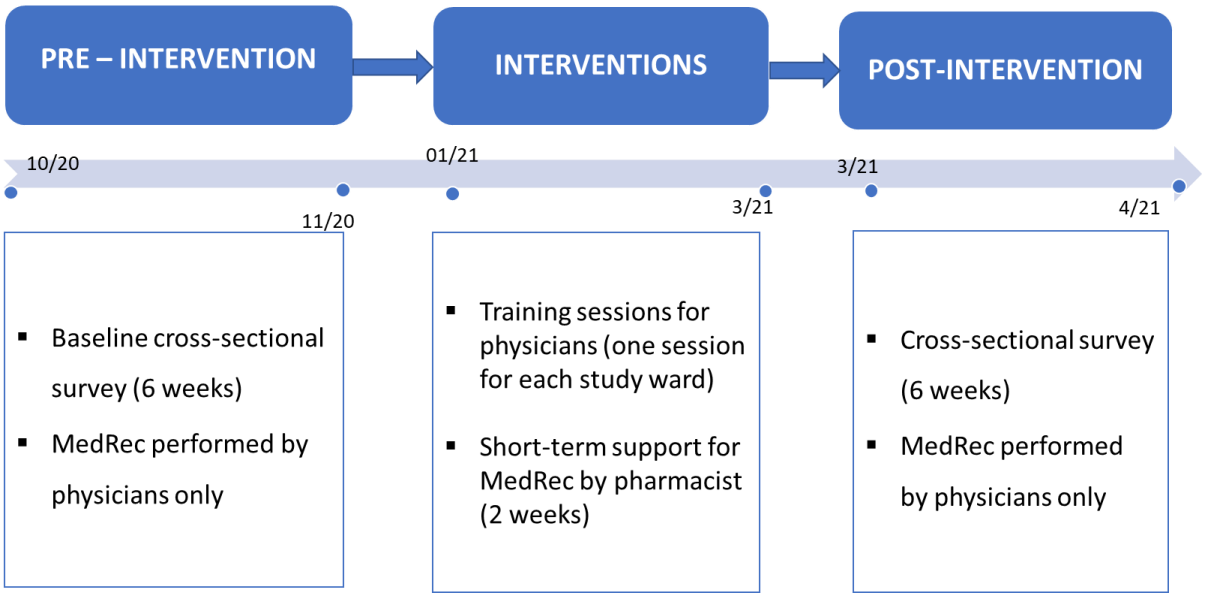


***Figure 6.1.*** *Study procedure*

## 2.2 Ethics approval

This study was granted ethics approvals by The Hospital Science and Technology Committee at Friendship Hospital (Vietnam) and the Human Research Ethics Committee (HREC) at the University of Newcastle (Australia). All participants provided written consent to participate in the study.

## 2.3 Usual care at admission

In Vietnam, medication reconciliation has not been well standardized. Currently, there is no mandatory regulatory requirements or standard professional practice guidelines. In practice, healthcare staff (i.e., physicians or nurses) would normally take the medication history of patients during clinical examination and record this in the patients' medical record (paper-based medical record) without a SOP. Hospital pharmacists have not been involved in this process routinely.

## 2.4 Interventions

Pharmacist-initiated interventions to improve the quality of medication reconciliation practice were conducted in two study wards. The first intervention involved an audit of the feedback intervention and training interventions for physicians. A 2-hour training session with learning materials was conducted in each study ward in January 2021. Training topics included:

- Report of the current pattern of medication reconciliation practice in the two study wards according to the results of the pre-intervention phase (audit-feedback activitiy);
- Discussion of the importance of medication reconciliation practice, especially for geriatric inpatients;
- Discussion of how the medication reconciliation process should be performed;
- Introduction and consensus on a pilot SOP for medication reconciliation in the post-intervention phase.

Based on the WHO High 5s programme (7), a step-by-step SOP for pro-active MedRec process was developed for physicians, in which the physician completed the Best Possible Medication History (BPMH) for each patient before prescribing the admission order. According to the SOP, the BPMH should be obtained from multiple available sources, including patient interviews and computer–based medical record systems. Patient interviews should be conducted at the patients' bedside, using a structured form to guide the interview and documented medication history in paper-based medical records. During the prescription process, the physician should document the reason for any difference between the BPMH and admission medication prescription list, especially for chronic medications.

The second intervention involved short-term support by a clinical pharmacist for medication reconciliation practice. During the period from 1/03/2021 to 15/3/2021, a clinical

pharmacist was assigned to support medication reconciliation process at the two study wards through a retro-active MedRec model (i.e., the pharmacist performed MedRec during 24 hours admission but after the physician had prescribed the admission order). More specifically, within 24 hours of the patient's admission, the pharmacist completed taking the patient's medication history and documented it on the BPMH introduced in the consensus SOP. The latter was done using at least two of the following sources: electronic medical records, paper-based medical records, or patient interviews. The pharmacist then compared the BPMH and 24-hour prescriptions to identify any medication discrepancies, detect UMDs, and assist the physicians to correct the UMDs as necessary. The purpose of this intervention was to provide an opportunity for the clinical pharmacist and the physicians in charge of individual patients to discuss medication reconciliation. From there, the pharmacist was able to inform the physicians about the steps of the newly applied medication reconciliation process, and situations that should be noticed during collecting BPMH (e.g., patients may use medications prescribed from other hospitals, situations where patients may not adhere to medications because of side effects, etc.).

### 2.5 Target population

Patients over 60 years of age, admitted to one of the two internal medicine wards (study wards A and B) of the hospital, taking at least one chronic medication before admission, staying at least 48 hours, and willing to participate (by providing a written consent form) were eligible for enrolment.

## 2.6 Data collection

In the pre- and post-intervention phases, for the data collection purpose, the research team performed independent medication reconciliation process during patient hospital stay to identify UMDs at admission. Particularly, a pharmacy Master student uninvolved in the intervention was trained to collect BPMH and identify medication discrepancies under the supervision of the one of the investigators (DTXP). Two clinical pharmacists of the hospital then accessed whether each discrepancy was intended or unintended. To ensure the accuracy of the reason of each medication discrepancy, the clinical pharmacists scrutinized patients' medical records for several potential reasons, such as diagnosis of a new clinical condition, contraindication, occurrence of adverse drug events, or a specific medication was unavailable in the Department of Pharmacy at the hospital *(Supplementary file 2. Process of Medication Discrepancies Classification).* Medication discrepancies without valid reason were considered as UMDs. Each UMD was then classified by drug class (according to the Anatomical Therapeutic Chemical Classification System – ATC) (29) and type of UMD (e.g., omission of medication, substitution of medication, added medication, different dose or dosing frequency). Other patient information that was collected during the study period included age, gender, comorbidity, current admission diagnosis, treatment unit, and the available sources for patients' medication information (e.g., electronic medical records, paper-based outpatient medical records, and paper-based inpatient medical records).

## 2.7 Outcome measures

**Assessing potential clinical significance of UMDs**

Determination of the potential and severity of harm that a patient would experience due to an UMD was based on the methodology described by Nesbit et al (30-32) to produce a pADE score. The pADE score is a potential and severity score for discomfort, harm and/or clinical deterioration caused by an UMD. The assessment uses the following categories for probability and severity of harm: 0 (zero; no harm expected by the UMD); 0.01 (very low: some harm is expected, but not clinically relevant); 0.1 (low: some harm is expected but poorly clinically relevant); 0.4 (medium; harm is expected, clinically relevant); or 0.6 (high; harm is expected, life threatening). After random presentation and blinding, UMDs identified in the pre- and post-intervention phases were sent to two external clinical experts (one pharmacist with advanced training in pharmacotherapy and one internal medicine specialist) to assess their potential clinical significance. Each expert independently assigned a pADE score to each UMD, and any difference in assessment was discussed and resolved through consensus in a meeting between the two aforementioned experts.

The effects on medication reconciliation practice pre- and post-interventions were evaluated by the following outcomes. The primary outcome was the proportion of patients with at least one UMD at 24 hours after admission. The secondary outcome was the proportion of patients with at least a pADE score ≥ 0.1 due to an UMD.

### 2.8 Sample size

The sample size was calculated based on the primary outcome of this study, using the following equation:

$$n = \left( \frac{Pc\ (1 - Pc)}{k} + Pi\ (1 - Pi) \right) \left( \frac{Z_{1-\alpha} - Z_{1-\beta}}{Pc - Pi} \right)^2$$

The proportion of patients with at least one UMD at admission was estimated to be 50% based on our pilot study. With an estimated 30% reduction of errors due to the intervention, an alpha of 0.05 and a power of 0.80, the calculated sample size was 130. Based on the number of admissions to the study wards within a month and an estimated loss of 50% of the patients not meeting the selection critertia, we estimated a study period of six weeks. Therefore, a pre- and post-intervention period of 6 weeks was chosen.

### 2.9 Assessing the Cost-effectiveness of the Intervention

The initial calculation of cost-effectiveness of the intervention in the study was restricted on the study period. In assessing the cost-effectiveness of the intervention, we estimated the cost of avoiding an adverse drug event (ADE) with pADE score ≥0.1 for the study period by dividing the total cost of implementing the study by the difference in the number of UMDs with pADE score ≥0.1 pre- and post-intervention. The costs involved in the implementation of the educational interventions included the time in preparing the educational material by the pharmacists, the time spent by the pharmacists in conducting the workshop for the physicians, short-term support for physicians in each wards, and the costs of printing learning materials. To calculate the labor cost, the average salary of pharmacists in the study hospital was employed (9.000.000 VND for 22 working days per month and 8 hours per day, equaling €1.94/hour). We then conducted a linear project assuming that the same reduction would occur in the next one year by providing a repeated training session after 6 months (without 2 week support by pharmacists). In this assumption, the cost of the intervention was calculated based on the time spent by the clinical pharmacist on the training session and the cost associated with the learning materials.

### 2.10 Data analysis

The collected data were analyzed by using the Statistical Package for Social Sciences (SPSS), version 27.0 (IBM statistics, Armonk, NY, USA). Independent two sample t-test (for continuous normally distributed variables), Mann-Whitney U test (for continuous non-normally distributed variables), and Chi-square test (for categorical variables) were employed to compare patients' characteristics in pre-intervention and post-intervention phases. Characteristics of UMDs were described by percentage and frequency. For the primary (the proportions of patients with at least 1 UMD at admission) and secondary outcomes (the proportions of patients with a pADE score of ≥0.1 at admission), adjusted odds ratios and 95% confidence intervals (95% CI) were calculated by using a multivariate logistic regression. Potential variables were selected using a univariate analysis ($p < 0.20$). The independent variables assessed included: research phase, age, gender, study ward, number of comorbidities, number of chronic medications.

## 3 Results

### 3.1 Characteristics of participants

A total of 298 patients were included in the study, with 152 patients in the pre-intervention phase and 146 patients in the post-intervention phase. There was no statistically significant difference in baseline clinical and demographic characteristics between the two groups of patients (Table 6.1).

***Table 6.1.*** *Characteristics of participants*

| Characteristics | Pre-intervention (n=152) | Post-intervention (n=146) | p-value |
|---|---|---|---|
| **Age** (years), mean (SD) | 75.7 (6.5) | 76.8 (7.1) | 0.188[a] |
| **Gender**, n (%) | | | 0.267[b] |
| Female | 69 (45.4) | 57 (39.0) | |
| Male | 83 (54.6) | 89 (61.0) | |
| **Ward**, n (%) | | | 0.827[b] |
| A | 80 (52.6) | 75 (51.4) | |
| B | 72 (47.4) | 71 (48.4) | |
| **Comorbidities** | | | |
| Mean (SD) | 4.3 (1.1) | 4.2 (1.2) | 0.593[a] |
| **Top 5 common diseases, n (%)** | | | |
| Hypertension | 125 (82.2) | 103 (70.5) | |
| Type 2 diabetes | 47 | 39 | |
| Gerd | 46 | 40 | |
| Hyperlipidemia | 43 | 35 | |
| Chronic coronary syndrome | 26 | 19 | |
| **Medication on BPMH** | | | |
| Mean (SD) | 3.6 (2.1) | 3.2 (1.6) | 0.054[a] |
| Polypharmacy[c], n (%) | 50 (32.9) | 33 (22.6) | 0.067[b] |
| Chronic medication, mean (SD) | 3.0 (1.7) | 2.6 (1.6) | 0.079 |
| Total medication | 449 | 382 | |
| **Medication on admission order** | | | |
| Mean (SD) | 6.6 (1.9) | 6.3 (2.4) | 0.165[a] |
| Polypharmacy[c], n (%) | 129 (84.9) | 108 (74.0) | 0.022[b] |
| Chronic medication, mean (SD) | 2.24 (1.4) | 2.14 (1.5) | 0.561[a] |
| Total medication | 1007 | 916 | |

*Footnote: SD: Standard Deviation; BPMH: Best possible Medication History; [a] Independent t-test; [b] Chi-square test, [c] ≥ 5 medications*

### 3.2 Characteristics of Identified UMDs

A total of 195 UMDs were identified in both phases, with 151 UMDs in the pre-intervention phase and 44 UMDs in the post-intervention phase. There was no difference in the distribution of the types of UMDs identified between the two phases ($p = 0.076$, Chi Square test), with the majority of UMDs being omissions (73.5% versus 59.1% respectively), incorrect substitution (22.5% versus 38.6%), and changes in dose (4.0% versus 2.3%). In terms of drug class, the majority of UMDs in the two phases were related to antihypertensive drugs (30.3%), lipid-lowering drugs (26.2%), antiplatelet drugs (10.3%), and beta-blockers (10.3%) (Table 6.2).

***Table 6.2.*** *Characteristics of Identified Unintentional Medication Discrepancies*

| Characteristics | Pre-intervention (UMD = 151) | Post-intervention (UMD = 44) | p-value |
|---|---|---|---|
| **Total UMD** | 151 | 44 | |
| **Medication with UMD** (% of all medication) | 34.1 | 11.5 | $p < 0.001$ |
| **UMD types** | | | 0.076 |
| Omission | 111 (73.5) | 26 (59.1) | |
| Substitution | 34 (22.5) | 17 (38.6) | |
| Different dose | 6 (4.0) | 1 (2.3) | |
| **UMD significance – pADE score** | | | |
| 0 | 0 (0.0) | 0 (0.0) | 0.006 |
| 0.01 | 40 (25.2) | 24 (59.1) | |
| 0.1 | 96 (63.6) | 17 (38.6) | |
| 0.4 | 15 (9.9) | 3 (6.8) | |
| 0.6 | 0 (0.0) | 0 (0.0) | |
| **UMD by Classes, n (%)** | | | |
| Antihypertensive agents | 40 (26.1) | 20 (45.5) | |
| Lipid modifying agents | 44 (28.8) | 8 (18.2) | |
| Antithrombotic agents | 19 (12.4) | 1 (2.3) | |
| Beta-blocking agents | 16 (10.5) | 4 (9.1) | |
| Mineral supplement | 5 (3.3) | 7 (15.9) | |
| Blood glucose lowering drugs | 7 (4.6) | 2 (4.5) | |
| Other cardiac preparation | 7 (4.6) | 0 (0.0) | |
| Proton pump inhibitor | 6 (3.9) | 0 (0.0) | |
| Other* | 9 (5.9) | 2 (4.6) | |

** Other includes: Vaso-protectives, Immunosuppressant, Anti-gout preparation, Calcium channel blocker, Direct acting antiviral, Corticosteroids, Thyroid preparation, Adrenergic inhalant/corticosteroid*

### 3.3 Primary outcome

Table 6.3 shows the results related to univariate and multivariate logistic regression for the risk factors associated with UMDs (i.e. primary outcome). There was a significant improvement after the interventions. In the pre-intervention phase, 55.3% of patients had at least one UMD during admission compared to 25.3% in the post-intervention phase (ORadj 0.255 95% CI: 0.151 – 0.431, p<0.001).

### 3.4 Secondary outcome

The proportion of patients with a pADE score ≥ 0.1 at admission was reduced from 44.1% in pre-intervention phase to 11.6% in the post-intervention phase (OR 0.188, 95% CI: 0.105-0.340, p<0.001). The mean number of UMDs per patient was 1 (min–max: 0–5) in the pre-intervention phase compared to 0 (min–max: 0–2; p < 0.001) in the post-intervention phase (Table 6.4).

***Table 6.3.*** *Univariate and Multivariate Logistic Regression of Factors Associated with UMDs*

| Covariate | Categories | Crude OR (95% CI) | Adjusted OR (95%CI) | Multivariate P-value |
|---|---|---|---|---|
| Phase | Pre-intervention phase (152) | 1 | | |
| | Post-intervention (146) | 0.251 (0.153-0.412) | **0.255[a] (0.151-0.431)** | <0.001 |
| Gender | Female (126) | 1 | | |
| | Male (172) | 1.708 (1.069-2.729) | 1.704 (0.983– 2.955) | 0.058 |
| Ward | A (155) | 1 | | |
| | B (143) | 1.708 (1.070-2.726) | 1.483 (0.865- 2.544) | 0.152 |
| Age | 60 – 69 | 1 | | - |
| | 70-79 | 0.942 (0.451-1.968) | | |
| | ≥80 | 1.224 (0.734-2.042) | | |
| Number of chronic medications in BPMH | | 1.438 (1.236-1.673) | 1.462 (0.865- 2.544) | 0.152 |
| Number of chronic medications in admission order | | 1.013 (0.867-1.185) | | |

[a]*Adjusted for gender, ward and number of chronic medication*

***Table 6.4.*** *Other Unintentional Medication Discrepancy Outcomes*

| UMD outcomes | Pre-intervention phase (n = 152) | Post-intervention phase (n = 146) | OR [95%CI] | p_value |
|---|---|---|---|---|
| Patient with at least 0.1 pADE score, n (%) | 67 (44.1) | 17 (11.6) | 0.188[b] (0.105-0.340) | < 0.001 |
| Patients with the following, n (%) | | | | < 0.001 |
| 0 UMD | 68 (44.7) | 109 (74.7) | | |
| 0.01 pADE[a] | 17 (11.2) | 20 (13.7) | | |
| 0.1 pADE[a] | 54 (35.5) | 14 (9.6) | | |
| 0.4 pADE[a] | 13 (8.6) | 3 (2.1) | | |
| UMD per patient, median (min–max) | 1 (0–5) | 0 (0–2) | | < 0.001[c] |

Footnote:
[a] *The higher risk level was applied if more than one UMD were observed on a patient.*
[b] *Adjusted for gender, ward and number of chronic medication*
[c] *Mann –Whitney U test*

### 3.5 Preliminary cost analysis of pharmacist-initiated interventions

The total cost of the interventions and the cost for avoiding one UMD during the study are presented in Table 6.5. The cost of the interventions was €489.6 during the study period, and this was estimated to be up to €512.6 for the whole year if the educational interventions were repeated after 6 months to maintain the same impact on the reduction of UMDs. The cost for avoiding one clinically significant UMD was €5.4 during the study period and this would decrease to €0.65 after one year.

***Table 6.5.*** *Preliminary Cost Analysis of Pharmacist-initiated Interventions*

| | Activities | Resource | Estimated time | Estimated cost (euro) |
|---|---|---|---|---|
| **Cost of implementing interventions (2 wards)** | | | | |
| (1) | Preparing the learning material (including analyse results of pre-intervention phase) | Labor | 160 hours | 311.1 |
| (2) | Training | Labor | 4 hours | 7.78 |
| (3) | Short-term support | Labor | 80 hours | 155.5 |
| (4) | Other cost for learning materials (i.e., printing) | Money | - | 15.2 |
| (5) | Total cost = (1)+(2)+(3)+(4) | | | **489.6** |
| (6) | Cost of implementing intervention in the project | | | |
| (7) | Cost of implementing repeated intervention after 6 month (training+ printing materials) = (2) + (4) | | | 23.0 |
| (8) | Total cost of intervention in one year = (6)+(7) | | | **512.6** |
| **Number of UMD avoidance** | | | | |
| (9) | Number of UMD with pADE score ≥1 avoidance during study period (6 weeks) | | | 91 |
| (10) | Estimated number of UMD with pADE score ≥1 avoidance in 1 year (52 weeks) = (9)x52/6 | | | 788.6 |
| **Cost of UMD avoidance** | | | | |
| (12) | Cost for avoiding 1 UMD with pADE score ≥0.1 during study period = (5)/(9) | | | 5.4 |
| (13) | Cost for avoiding 1 UMD with pADE score ≥0.1 during one year = (8)/(11) | | | 0.65 |

## 4 Discussion

To our knowledge, this is the first published study in a hospital setting in Vietnam to assess the potential contribution of hospital pharmacists to improving medication reconciliation practice on admission for geriatric patients through the implementation of educational interventions. This study is also one of the few studies available that have been conducted in Southeast Asian countries (33-35) as well as in developing countries related to this issue.

Medication reconciliation is critical to assuring medication safety for patients, particularly geriatric patients. Pharmacist-led MedRec (whereby pharmacists perform this practice alongside physicians or nurses) or using information technology to enhance MedRec are two common strategies for improving the quality of this practice – both strategies have been examined extensively around the world. All of these strategies have been shown to improve patient safety by lowering the rate of medication errors (i.e., UMDs) (8, 9, 36). However, these interventions are difficult to apply in countries with limited resources such as Vietnam. The low ratio of pharmacists per physician and capita as well as the low level of utilization of information technology in healthcare institutions are the main barriers to the implementation of these strategies (25-27). In addition, the role of pharmacists to deliver patient-centered care in Vietnam is under-developed, with clinical pharmacy services not implemented as routine practice in many hospitals. Medication reconciliation provided by hospital pharmacists would also cause major disruption to their current clinical practice in Vietnam. Therefore, it is not feasible to assign a pharmacist permanently to the clinical department to participate in medication reconciliation practice.

With all the aforementioned constraints, the medication reconciliation interventions applied in this study were chosen to ensure the long-term feasibility of implementation and effectiveness of the interventions in the context of Vietnam (37). As a result, providing physicians with brief education to raise their knowledge of the problem as well as a short conventional training session may be the most appropriate method (28). Our study showed that pharmacist-led educational interventions are clinically significant by reducing the number of UMDs (including major UMDs), and are a low-cost approach that does not require significant modifications to the current healthcare system in nations with low human resources, such as Vietnam.

The results in the pre-interventions phase demonstrated a high prevalence of UMDs among geriatric inpatients at admission, with at least one UMD identified in 56.6% of the study participants. These results are consistent with our previous study in 2018 (18) as well as published studies conducted in other countries with similar populations (1, 2, 38, 39). The majority of UMDs (75.5%) in the pre-intervention phase were classified as having potential harms, thereby confirming the importance of medication reconciliation practice. Importantly, the baseline characteristics of the two groups of patients (i.e., pre-intervention and post-intervention) were similar in our study, particularly in terms of the number of comorbidities, the number of drugs prescribed in the medication history, and the 24-hour prescription – this increases the reliability of comparisons regarding the efficacy of the interventions.

In terms of lowering the frequency of UMDs, the main results of the current study showed that there were significant outcome improvements in the post-intervention phase compared with the pre-intervention phase. The proportion of elderly patients with at least one UMD during admission was reduced from 56.6% to 24.7% (OR 0.255;

95%CI: 0.151 – 0.431). Regarding the clinical significance of UMDs, the proportion of patients with at least one pADE >0.1 also decreased significantly, from 42.8% to 12.3% (OR 0.188; 95% CI: 0.105-0.340). Although a quarter of the patients (24.7%) after intervention still had unexplained medication discrepancies, most of these UMDs were considered as being of low clinical significance. This suggests that physicians have paid more attention to the continuity of prescribing of important medications to patients.

Furthermore, we also conducted a cost analysis to find the economic impact of the pharmacist-initiated educational interventions. The results showed that the cost of intervention during the study period was €489.6 and the cost for avoiding one clinical significant UMD was €5.4 during the study period. Due to differences in the healthcare system and costs, it is not meaningful to compare the costs of our interventions with studies conducted in other countries. Even so, the cost of our educational interventions are still considered generally reasonable. For example, in a pharmacist-led medication reconciliation study conducted by Bosma et al. in the Netherlands (30) involving a fulltime pharmacist, the cost of the intervention was substantial (€7475 during the 14-week intervention).

There have been few studies on the effect of education and feedback on physicians' medication reconciliation practice. A study by Lea et al in 2016 showed that the introduction of a non-mandatory training course for physicians did not improve the recording accuracy of the patients' medication history and required more intensive interventions to achieve improvements (40). In contrast, Chan et al (41) reported a succesful educational intervention to improve the recording of medicines on admisison. This difference in impact may be due to the difference in the composition of the two educational interventions. When compared with our study, in addition to the mandatory

training sessions, we included 2 weeks of pharmacist-support to the MedRec activity. This allowed the medication reconciliation practice to be conducted directly with individual physicians on specific patient situations, which may be the cause of our better results.

When comparing the results of this study with other intervention strategies, the improvement in the rate of significant difference may be lower. For example, systematic reviews conducted by Mekonnen et al in 2016 (8, 9) of pharmacist-led medication reconciliation at transitions in care (either admission or discharge) showed a significant reduction of 66% in patients with medication discrepancies (RR 0.34; 95% CI: 0.23-0.50) compared with usual care. Despite this, our results are consistent with the trend presented in published studies that having pharmacists directly involved in the MedRec process produces a greater improvement compared to when MedRec is performed by physicians alone. It should be noted that a strength of our interventions was that it did not require long-term manpower commitment for the practice, nor significant changes to the physicians' workflow. Therefore, our current study demonstrates that hospital pharmacists can still be involved in patient-centered care to improve the quality of clinical activities such as medication reconciliation in resource-restricted setting like Vietnam. This model can serve as an example for countries with similar healthcare systems and pharmacy practice as Vietnam when implementing interventions to improve the quality of MedRec for patients.

The current study has some limitations. Firstly, the assessment of UMDs was conducted independently by two clinical pharmacists without discussion with a physician. The study used this approach to avoid the reluctance of admitting medication errors by the physicians. This mentality has been shown in a number of studies, but this

approach may result in bias in some situations due to the lack of physician's opinions. Secondly, as the evaluation of medications prescribed was limited to chronic medical conditions, the frequency of UMDs may have been underestimated. We concentrated exclusively on this class of medications due to their critical role in managing the conditions associated with geriatric patients. Thirdly, the study only calculated the cost of avoiding one UMD but not the associated cost benefit. Additional studies on the average treatment cost per pADE are required to calculate this parameter, which are not currently available in Vietnam. Lastly, the study did not evaluate the long-term effect of the intervention, whether improvements in physicians' practice could be maintained over time. Therefore, other strategies may be needed to maintain the long-term effectiveness of these medication reconciliation interventions. Nevertheless, this intervention strategy can be viewed as an effective and feasible way to expand to other hospital departments or hospitals in Vietnam.

## 5 Conclusion

Pharmacist-initiated educational interventions was effective in improving the quality of medication reconciliation practice, leading to a significant decrease in the frequency of UMDs and reduction in potential harm. The findings of the study demonstrate that an effective strategy can help maximize pharmacists' contribution to improving the quality use of medicines in the geriatric population in countries with limited human resources, such as Vietnam, without changing the work structure of the health practitioners. A nationwide standardized implementation of our medication reconciliation interventions would facilitate better healthcare delivery in reducing medication errors and promoting a patient safety culture, with resultant cost savings to the healthcare system in Vietnam.

## List of abbreviations

BPMH: Best Possible Medication History

CI: Confidence Intervals

MD: Medication Discrepancy

MedRec: Medication Reconciliation

OR: Odds Ratio

SD: Standard Deviation

SOP: standard Operating Procedure

UMD: Unintentional Medication History

WHO: World Health Organization

## Declarations

**Ethics approval** This study was granted ethics approvals by The Hospital Science and Technology Committee at Friendship Hospital, Vietnam and the Human Research Ethics Committee (HREC) at the University of Newcastle, Australia (Approval Number H-2020-0187).

**Consent to participate** All participants have provided written consents to participate

**Consent to publication** All listed authors have approved the manuscript before submission, including the names and order of authors

**Availability of data and material** All data generated and analysed during the current study are available from the corresponding author on reasonable request.

**Competing interests** The authors declare that they have no competing interests

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- Shu Chuen Li: Conceptualization, Methodology, Writing – Review & Editing, Supervision, Project administration.
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# Chapter 7. Implementation and Evaluation of Clinical Pharmacy Services on Improving Quality of Prescribing in Geriatric Inpatients in Vietnam: an Example in a Low–Resources Setting

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**Abstract**

**Purpose:** Geriatric inpatients generally have a high risk of Drug-Related Problems (DRP) in prescribing following hospital admission, which are likely to cause negative clinical consequences. This is particularly evident in developing countries such as Vietnam. Therefore, clinical pharmacy service (CPS) aims to identify and resolve these DRPs to improve the quality use of medicines in the older population following hospital admission.

**Patients and methods:** The study was conducted as a prospective, single-center study implemented at a general public hospital in Hanoi. Patients aged ≥60 years with at least three chronic diseases admitted to an Internal Medicine Department between August 2020 and December 2020 were eligible to be enrolled. A well-trained clinical pharmacist provided a structured CPS to identify any DRP in prescribing for each patient in the study. Clinical pharmacist interventions were then proposed to the attending physicians and documented in the DRP reporting system.

**Results**: A total of 255 DRP were identified in 185 patients during the study period. The most frequent types of DRP were underuse (21.2%), dose too high (12.2%), and contraindication (11.8%). There was a very high rate of approval and uptake by the physicians regarding the interventions proposed by the clinical pharmacist (82.4% fully accepted and 12.5% partially accepted). Of the interventions, 73.4% were clinically relevant (pADE score ≥ 0.1). In general, 9 out of 10 physicians agreed that CPS has significant benefit for both patients and physicians.

**Conclusions:** Improving clinical pharmacy services can potentially have a positive impact on the quality of prescribing in elderly inpatients. These services should

officially be implemented to optimize the quality use of medicines in this population group in Vietnam.

**Keywords: pharmacy practice, quality use of medicine, geriatrics**

# 1 Introduction

Optimizing prescribing for the geriatric population is a challenge, especially in the hospital setting, due to a number of factors such as multi-morbidity associated polypharmacy, age-related physiological changes, and pharmacokinetic and pharmacodynamics alterations (1, 2). Studies in elderly inpatients worldwide have highlighted that Drug-Related Problems (DRP) in prescribing following hospital admission are frequent in this vulnerable population, including unintentional medication discrepancies (3-7) and potentially inappropriate prescribing (PIP) (8-10). These DRPs have been associated with adverse consequences such as prolonged hospital stay, worsening clinical conditions, and increasing healthcare costs (11). Therefore, prescribing in elderly inpatients requires special consideration and attention to optimize quality use of medicines and minimize or avoid drug-related issues.

Implementation of clinical pharmacy services (CPS) is aimed at improving patient outcomes and minimizing medication harm through the provision of patient-centered pharmaceutical care (12). In the hospital setting, clinical pharmacists work with physicians in a multidisciplinary team to optimize medication prescribing by identifying, correcting and preventing DRPs. Clinical pharmacist interventions (CPI) are defined as ‘‘any actions initiated by a pharmacist that directly result in a change to patient management or drug therapy’’ (13). Clinical pharmacists have played essential roles in improving the quality use of medicines in many settings. The positive clinical and economic outcomes of their interventions have been well-established for many decades in North America, Australia, and European countries (12, 14-18).

In Vietnam, the proportion of the population aged 60 and over is increasing dramatically and will constitute 10% of the total population by 2025 (19). There will be a resultant increase in demand for health services as the older population is known to consume more healthcare resources (20). However, Vietnamese physicians currently face a heavy workload in their routine practice – with a reported ratio of 7.8 doctors per 10,000 population in 2016. The situation is unlikely to improve in the short to medium term. Our recent findings suggest that prescribing issues particularly in geriatric inpatients in Vietnam will continue to be serious concern stemming from heavy clinical workloads (7). Similar to other health care services, optimal prescribing in geriatric inpatients requires inter-professional teamwork, with the involvement of clinical pharmacists. However, the contribution of clinical pharmacists as an integrated part of a multi-disciplinary team in improving the quality use of medicines has not been widely evaluated in Vietnam up to now. Currently, the extent of implementation of CPS in Vietnamese hospitals varies widely due to differences in pharmacy human resources and the level of acceptance of CPS by medical staff at the hospital (21-23). Identified barriers to the implementation of CPS include limited research on the effectiveness of the activity and the lack of institutional implementation strategy.

In order to provide support for the implementation of CPS in Vietnamese hospitals, the impact of these services needs to be assessed. Therefore, this study aimed to evaluate bedside CPS for geriatric inpatients as an example of a model of pharmacist-led pharmaceutical care engaged in clinical practice in a low-resources setting. Outcome measures of the study were the number of DRPs in prescribing identified by the clinical pharmacist, the number of clinical pharmacy interventions (CPI), and the physicians'

acceptance of the clinical pharmacy interventions. The perceptions and opinions of physicians regarding CPS were also evaluated.

## 2 Methods

### 2.1 Study settings and population

This study was conducted at Friendship Hospital, an 800-bed public general hospital that provides healthcare services for retired geriatric patients in Hanoi. CPS were implemented in a pilot program at the 80-bed Internal Medicine Department over five months from August 2020 to December 2020. This was the first model of ward-based pharmacy services implemented in the study hospital. Due to staffing limitations in clinical pharmacy, the CPS was provided to patients at high risk of experiencing DRP during hospital stay. In particular, the patients targeted for CPS were those aged over 60 years, currently taking at least three drugs regularly to manage chronic diseases, and with at least three chronic conditions. Patients were expected to stay in the ward for a minimum of 48 hours.

### 2.2 Usual care before implementing CPS

Before the implementation of CPS, the attending physician was solely responsible for prescribing medications to the patients throughout the duration of their hospital admission. Under some special clinical situations, the attending physician may request a consultation for additional prescribing advice from senior physicians or other specialties. Clinical pharmacists were not involved in the physician's prescribing process for the patients.

## 2.3 Clinical Pharmacy Services (CPS)

A clinical pharmacist was assigned to work for 4 hours per day (0.5 Full-time Equivalent) at the study department from Monday to Friday every week during the study period. The assigned pharmacist was trained with a clinical pharmacy–orientated curriculum at the undergraduate level, eligible to practice clinical pharmacy according to the standards of Decree No. 131 about Clinical Pharmacy Practice in Vietnam, and had a 6-month internship at the study department before officially implementing CPS. The clinical pharmacist provided bedside activities for each enrolled patient according to a structured process, focusing on improving the quality of prescribing with the primary goal of detecting, evaluating and resolving DRPs in their prescribed medications. The CPS process followed by the pharmacist is summarized in Figure 7.1.

Briefly, the pharmacist conducted medication reconciliation for each eligible patient and recorded the patient's medication history on the pharmacist's medication reconciliation form. After that, the pharmacist collected information related to diagnosis, clinical and laboratory test results, and patient's symptoms – these were recorded in the pharmacist's Patient Monitoring Form. The pharmacist then reviewed each medication in the admission order for all aspects of appropriate prescribing, including indication, dose, dosage form, dosing regimen, timing of administration, lack of treatment, and lack of clinical/laboratory test monitoring to identify any potential DRPs. The clinical judgment was made using evidence-based materials, including current/official Vietnamese or hospital therapeutic guidelines, Summary of Product Characteristic (SmPC) and potentially inappropriate prescribing screening tools for the elderly such as STOPP/START version 2 (24).

In addition, patients were also reviewed to determine whether follow-up was needed based on defined criteria (e.g., patients prescribed antibiotics, patients with a severe acute condition, and patients prescribed with narrow therapeutic index medications). The DRPs detected during this process were recorded in the DRP summary sheet as a basis for discussion with the attending physicians. The clinical pharmacist actively communicated with the physicians the identified DRPs and the proposed CPI through face-to-face communication during ward-rounds, text messages, or phone calls. As part of the CPS, the clinical pharmacist also provided medication information on the selection, dosage, and adverse drug reactions (ADR) of drugs if requested by the physicians at the study ward.

The physicians' acceptance rate for CPIs and their response at three levels were recorded. The following shows the definition of the three levels. 'Completely accepted' – the physician agreed with the DRP and the clinical pharmacist's intervention, and the prescribing order was changed according to the recommendation of the clinical pharmacist. 'Partially accepted' – the physician agreed with the DRP but the change of prescribing order may not be the same as the clinical pharmacist's intervention (e.g., change to a drug that was not the same as suggested or the changed dose was not the same as recommended). 'Not accepted' – the physician disagreed with the DRP and the clinical pharmacist's intervention, and no changes to the medical order were made. For medication information related to prescribing (i.e., the physicians asked the clinical pharmacist to calculate the drug dose or select a drug for an indication), the intervention was counted as being 'completely accepted' if the physician agrees with the drug/active ingredient corresponding to the pharmacist's advice.

## 2.4 Data collection

Information about the patients, characteristics of DRPs, and approval status of CPIs by physicians were collected through (i) Pharmacist's Medication reconciliation form, (ii) Pharmacist's Patient Monitoring sheet, (iii) DRP summary sheet for each patient, and (iv) Weekly Pharmacist's Summary Report. The Weekly Pharmacist's Summary Report was sent to the Head of Pharmacy Department and the head of the study department. The demographic information collected for each patient included age, gender, weight, primary diagnosis, comorbidities, list of medication history, medications prescribed for 48 hours, duration of hospital admission, and Charlson Comorbidity Index (25). The Pharmaceutical Care Network Europe (PCNE) DRP classification system was used to classify and document DRPs (26).

## 2.5 Outcome measure

The impact of CPS was assessed through the number of DRPs identified, the number of clinical pharmacist interventions, and the physician's acceptance rate of clinical pharmacist interventions. In addition, the clinical significance of accepted DRPs and the physicians' assessment of CPS were also evaluated.

***Assessment of clinical significance of DRPs***

Determination of the potential and severity of harm that a patient would experience due to a DRP was based on the methodology described by Nesbit et al. (27-29) to produce a potential Adverse Drug Event (pADE) score. The pADE score is a potential and severity score for discomfort, harm and/or clinical deterioration caused by a DRP. The assessment uses the following categories for probability and severity of harm: 0 (no harm expected by the DRP, 0.01 (very low: some harm is expected, but not clinically

relevant), 0.1 (low: some harm is expected but poorly clinically relevant), 0.4 (medium; harm is expected, clinically relevant), or 0.6 (high; damage is expected, life-threatening). After being randomly presented and blinded, DRPs identified were sent to two external clinical experts (one pharmacist with advanced training in pharmacotherapy and one internist – both had 10-year experience in practice) to assess the potential clinical significance. Each expert independently assigned a pADE score to each DRP and resolved any difference in assessment through consensus in a meeting of the two aforementioned experts.

***Evaluation of physicians' opinions on clinical pharmacy services***

All physicians who worked in the study department were sent an anonymous questionnaire about their views on CPS during the implementation period. The research team designed the questionnaire to determine the level of agreement of the physicians across four themes: (i) the pharmacist's competence, (ii) the contribution of each CPS, (iii) the overall benefit of the CPS, and (iv) the expectation in the future. The questionnaire used a 5-point Likert scale to determine the physicians' perspectives, whereby level 1 corresponded to 'strongly disagree' and level 5 corresponded to 'strongly agree'. The questionnaire was delivered to and collected from the physicians by a research member that was independent of the CPS implemented in the study department. The survey took place in January 2021.

### 2.6 Data analysis

Data related to participants, medication prescriptions, and clinical pharmacist interventions were recorded into an Excel database (version 2020 Microsoft Corporation, Redmond, WA, USA). Statistical analysis was performed using SPSS version 27 (SPSS, Inc, Chicago, IL, USA). Descriptive statistics included median and

interquartile range (IQR) for nonparametric data; mean and standard deviation were calculated for normally distributed data. Characteristics and DRPs were described by percentage and frequency.

## 3 Results

### 3.1 Participant characteristics

A total of 185 geriatric inpatients was included in the study during the implementation period. The demographics and baseline characteristics of these patients are shown in Table 7.1. The average age of the study participants was relatively high at 78.9 (± 8.0) years, and 68.6% were males. The most common chronic diseases in the study participants were hypertension (83.2%), chronic coronary syndrome (73.0%), heart failure (37.8%), type 2 diabetes (35.1%), and hyperlipidemia (23.2%). The average number of co-morbidities was 4.4 ± 1.9. Each patient was prescribed an average of 7.7 (± 2.3) medications on their admission prescription order and stayed 14.0 (± 7.6) days at the study department.

### 3.2 Characteristics of drug-related problems identified by a clinical pharmacist

The clinical pharmacist detected a total of 255 DRPs, involving 285 drugs (Table 7.2). The number of DRPs related to inappropriate prescribing accounted for a very high rate, with the most frequent types of DRP being underuse (21.2%), dose too high (12.2%), and contraindication (11.8%). Drug-related problems were found in many different classes of drugs. The most commonly involved drug groups were cardiovascular drugs (anti-ischemic agents, antihypertension agents, antithrombotic agents, anti-hyperlipidemic agents), proton pump inhibitors, and antidiabetic drugs (Table 7.3).

### 3.3 Type, acceptance rate and clinical significance of clinical pharmacist interventions

The type, acceptance rate and clinical significance of CPIs are summarized in Table 7.4. Corresponding to the types of DRP detected, the most common clinical pharmacist interventions were initiation of a new drug (21.2%), discontinuation of a drug (17.6%), and change of drug (17.3%). The overall rate of physicians' approval with the interventions proposed by the clinical pharmacist was very high (82.4% fully accepted and 12.5% partially accepted). Although there was variation in acceptability for different types of interventions, high acceptance rate was observed in all types of interventions. Among these, 100% of cases of counselling of drug or dose selection were accepted, followed by discontinuation (91.1%), dose reduction (84.4%), and clinical/subclinical monitoring (85.8%). In term of clinical significance of clinical pharmacist interventions, 73.4% of interventions were considered as clinically relevant (pADE score ≥ 0.1). One-fifth of them had at least moderate clinical significance according to the experts' assessment.

### 3.4 Physicians' perspectives about clinical pharmacy services

All physicians (n=10) that worked in the study department of Friendship Hospital during the CPS implementation period answered the questionnaire with generally positive opinions (Table 7.5). The level of satisfaction of the physicians with the clinical pharmacist's knowledge and skills was very high. For example, 6/10 physicians strongly agreed and 3/10 physicians agreed that the clinical pharmacist had sufficient knowledge regarding medications and therapeutics, and 9/10 physicians strongly agreed

that the clinical pharmacist demonstrated effective communication skills. Related to each CPS activity, all physicians agreed that the clinical pharmacist provided an accurate medication history and in a timely manner (9/10 strongly agreed and 1 agreed) as well as provided appropriate medication information when requested (9/10 strongly agreed and 1 agreed). In general, 9/10 physicians agreed that CPS have significant benefit for both patients and physicians.

## 4 Discussion

To the best of our knowledge, this is the first study in Vietnam to investigate the role of CPS in improving the quality of prescribing in the geriatric population in a hospital setting. As confirmed in several studies, pharmaceutical care activities on individualized patients have not been standardized in Vietnamese hospitals (21-23). The participation of pharmacists in optimizing prescribing for inpatients has been limited and varied depending on the available human resources, the hospital policies, as well as the approach of each pharmacist. This study is expected to provide meaningful evidence of how to implement novel CPS in Vietnamese hospital settings as well as demonstrate their impact.

The shortage of human resources is one of the most significant barriers to implementing CPS in hospitals (21-23). With this lack of human resources, it is essential to identify priority patients and prioritize clinical pharmacy activities. In this study, with 0.5 FTE clinical pharmacist per 80 bed, we developed a structured process of CPS for geriatric inpatients to make this process sustainable, time-efficient, and effective. Geriatric patients were selected as the target population for CPS because they are highly vulnerable to DRPs and suboptimal prescribing due to multiple risk factors.

Our study results provide supporting evidence for the positive contribution of clinical pharmacists in the multidisciplinary team to improving the quality of prescribing in geriatric patients in a developing country. This was demonstrated through several important outcomes: (i) a large number of DRPs in prescribing were identified, (ii) the high rates of physicians acceptance of CPI, (iii) the high proportion of clinically significant CPIs, and (iv) the physicians' positive assessment of the overall effectiveness of CPS. Therefore, there is significant opportunity for clinical pharmacists in Vietnamese hospitals to contribute to enhancing the quality use of medicines, especially in geriatric inpatients.

***Numbers and types of DRPs***

The amount of DRPs and the characteristics of the DRP detected by CPS varies widely in the literature. This is likely attributed to the different study settings, the capacity of clinical pharmacists, number of the pharmacist/number of bed ratio, and the type of DRP that was the focus of each study (30-32). For this current study, only the CPIs that improved the quality of prescriptions was described and only the DRPs that were communicated to the physicians were calculated. Some other groups of DRPs such as those related to patients' medication adherence and medication administration were not included in the study. Therefore, the average number of DRPs for each patient in this study may be lower compared to those reported by other studies. Despite this, our study has unequivocally shown that DRPs in geriatric inpatients are relatively common in Vietnam, thereby confirming the necessity of CPS in improving the quality of prescribing in this population group. Furthermore, DRPs were detected across many different drug groups, with the most common (e.g., cardiovascular drugs and diabetes

drugs) related to long-term medications for managing chronic diseases in geriatric patients. Therefore, the detection and resolution of these DRPs during the hospital stay could be expected to provide long-term benefits to the patient post-discharge into the community.

***Clinical pharmacist interventions and physicians' acceptance rate***

In this study, the physicians' approval rate for the clinical pharmacist's interventions was relatively high (82.4% of CPI). This rate is congruent with a number of other published studies (30-37) that were in the range of 76 to 93%. However, it is in contrast to some other studies in the geriatric population such as the study by Somer et al. which reported a 54% acceptance rate (38). There are several reasons for the difference in acceptance rates. Factors that are associated with higher acceptance include the class of medications, types of CPI, types of diseases, physicians' specialties, and experiential background of clinical pharmacists (39, 40). The latter could partly explain the high acceptance rate in this current study through a high degree of physicians' appreciation of the pharmacist's knowledge and expertise. This shows that pharmacist competence is the core to providing effective CPS. The high acceptance rates also indicate that the physicians in the study department of the hospital are open to collaboration with pharmacists, although CPS is still a new concept in Vietnam. This study included an assessment of the clinical significance of the approved interventions. Of the DRPs and corresponding CPIs, 69.8% were assessed as clinically significant with a pADE score $\geq$0.1 and one-fifth of the interventions were classified as having moderate to high clinical significance. The results also emphasize the contribution of CPI to the prescribing practice of physicians in this study.

***Physicians' opinion about CPS***

All physicians working in the department during the study period participated in answering the questions. Physicians generally agreed that the benefits of CPS to physicians and patients are substantial, thereby indicating that the introduction of CPS activities to support prescribing was successful. In this study, the positive reviews could be explained by a number of factors: (i) the pharmacist had 6 months of familiarity with the study department before implementing CPS; (ii) Standard Operating Procedures were developed and introduced to the physicians; and (iii) CPIs were made based on evidence and communicated appropriately. Studies across the world on the implementation of new clinical pharmacy activities have shown similar results in terms of physicians' perspectives on cooperation with CPS. This reinforces the attitude of physicians to working in collaboration with pharmacists and shows an open view of physicians when there is one more support person to improve the quality of prescriptions for patients (41-45)

***Limitations***

There are several limitations to our study. The study was conducted in only one internal medicine department at a large hospital in Hanoi, with one clinical pharmacist involved in the provision of services. Therefore, the amount of DRPs detected as well as the physicians' approval were significantly dependent on the pharmacist's expertise and communication skills as well as the perception of the physicians with regards to CPS. The study did not evaluate the impact of CPS using solid clinical endpoints (i.e., mortality, morbidity) nor calculate the costs related to the service (healthcare utilization)

or quality of life of patients. The process parameters, including the number of identified DRPs, the acceptance rate of physicians, and the clinical significance of DRPs were employed to demonstrate the benefits of CPS in this initial study. Despite these limitations, the results represent a very important finding that CPS is likely to deliver benefits for patients in Vietnam. Lastly, during the study period, all physicians were aware of the purpose of the study. Hence, the occurrence of the Hawthorne effect (46) could not be ruled out, meaning the physician may have taken the prescription/action differently from usual because they perceived that they were a part of the study and, therefore, caused a reduction in DRPs observed during the study period.

## 5 Conclusion

This study clearly demonstrates that the prevalence of DRPs in prescribing was high among geriatric inpatients in Vietnam. A well-developed CPS can contribute to the detection and resolution of these DRPs with good acceptance by physicians. The results suggest a positive benefit of ward-based pharmacy services to improving the quality use of medicines in geriatric inpatients. These results can also form a basis for developing a standard operating model of clinical pharmacy activities aimed at utilizing the limited human resources in the Vietnamese healthcare system in a more effective way.

**List of abbreviations**

CCI: Charlson Co-morbidity Index (CCI)

CI: Confidence Intervals

CPS: Clinical Pharmacy Services

CPI: Clinical Pharmacist Intervention

DRPs: Drug-Related Problems

pADE: potential Adverse Drug Event

QUM: Quality Use of Medicine

SD: Standard Deviation

SOP: Standard Operating Procedure

WHO: World Health Organization

**Disclosure**

**Ethics approval** This study was granted ethics approvals by The Hospital Science and Technology Committee at Friendship Hospital, Vietnam and the Human Research Ethics Committee (HREC) at the University of Newcastle, Australia (Approval Number H-2020-0187). The study was performed in accordance with the Declaration of Helsinki.

**Consent to participate** All participants have provided written consents to participate

**Consent to publication** All listed authors have approved the manuscript before submission, including the names and order of authors

**Availability of data and material** All data generated and analysed during the current study are available from the corresponding author on reasonable request.

**Competing interests** The authors declare that they have no competing interests

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**Author contributions**

- Phuong Thi Xuan Dong: Conceptualization, Methodology, Data collection, Formal analysis, Writing – Original Draft, Writing – Review & Editing.
- Van Thi Thuy Pham: Conceptualization, Methodology, Writing – Review & Editing.
- Chi Thi Dinh: Methodology, Data collection, Writing – Review & Editing.
- Ha Thi Hai Tran: Conceptualization, Methodology, Writing – Review & Editing
- Van Anh Le: Coneptualization, Methodology, Writing – Review & Editing
- Huong Thi Lien Nguyen: Conceptualization, Methodology, Writing – Review & Editing.
- Susan Hua: Conceptualization, Methodology, Writing – Review & Editing, Supervision.
- Shu Chuen Li: Conceptualization, Methodology, Writing – Review & Editing, Supervision, Project administration.
- All authors read and approved the final manuscript

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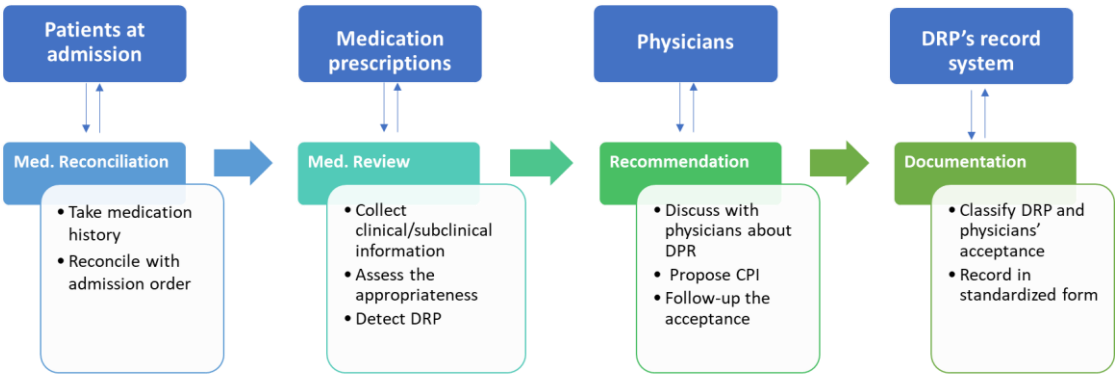


***Figure 7.1.*** *Process of clinical pharmacy services in the study. Abbreviations: DRP: Drug-Related Problem, CPI: Clinical Pharmacist Interventions*

***Table 7.1.*** *Demographics and characteristics of the study participant*

| **Characteristics** | **Number of participants (%) (n=185)** |
|---|---|
| **Gender** | |
| Male | 127 (68.6) |
| Female | 58 (31.4) |
| **Age (years)** (Mean ± SD) | 78.9 ± 8.0 |
| **Charlson Co-morbidity Index (CCI)** | |
| 0 | 42 (22.7) |
| 1 - 2 | 82 (44.3) |
| ≥3 | 61 (33.0) |
| **Number of comorbidities per patient** (Mean ± SD) | 4.4 ± 1.9 |
| **Top 5 common diseases** | |
| Hypertension | 154 (83.2) |
| Chronic coronary syndrome | 135 (73.0) |
| Heart failure | 70 (37.8) |
| Type 2 diabetes | 65 (35.1) |
| Hyperlipidemia | 43 (23.2) |
| **Length of ward stay (days)** (Mean ± SD) | 14.0 ± 7.6 |
| **Number of presciptions order at 48h** (Mean ± SD) | 7.7 ± 2.3 |
| **Number of identified DRP in prescribing** (Mean ± SD) | 1.4 ± 1.0 |
| **0** | 32 (17.2) |
| **1-2** | 135 (73.0) |
| **3-4** | 14 (7.6) |
| **>4** | 4 (2.2) |

*Note: SD: Standard Deviation. DRP: Drug-Related Problem*

***Table 7.2.*** *Types of identified drug-related problems (n=255)*

| PCNE code | Type of DRPs | Number (n) | Percentage (%) |
|---|---|---|---|
| **C1** | **Drug selection** | | |
| C1.1 | Inappropriate drug | 18 | 7.1 |
| C1.2 | Contraindication | 30 | 11.8 |
| C21.3 | No indication for drug | 13 | 5.1 |
| C1.4 | Inappropriate combination of drugs (drug-drug interactions) | 18 | 7.1 |
| C1.5 | Inappropriate duplication of drugs | 8 | 3.1 |
| C1.6 | No or incomplete drug treatment (underuse) | 54 | 21.2 |
| C2 | Drug form | | |
| C2.1 | Inappropriate drug dosage form | 8 | 3.1 |
| **C3** | **Dose selection** | | |
| C3.1 | Drug dose too low | 4 | 1.6 |
| C3.2 | Drug dose too high | 31 | 12.2 |
| C3.5 | Incorrect dose administering instruction | 23 | 9.0 |
| C3.3 | Incorrect frequency of dosing | 12 | 4.7 |
| **C9** | **Others** | | |
| C9.1 | No or inappropriate outcome monitoring | 7 | 2.7 |
| C9.2 | (Others) Request of drug information | 27 | 10.6 |
| C9.3 | (Others) ADR | 2 | 0.8 |
| | **Total** | 255 | 100.0 |

*PCNE:* Pharmaceutical Care Network Europe
*DRP: Drug-Related Problem*
*ADR: Adverse Drug Reaction*

***Table 7.3.*** *Categories of medications related to DRPs (n=285)*

| **Drug class** | **Frequency** | **Percentage (%)** |
|---|---|---|
| Anti-ischemic agents | 41 | 14.4 |
| Antibiotics | 33 | 11.6 |
| Antihypertensive agents | 30 | 10.5 |
| Antithrombotic agents | 27 | 9.5 |
| Anti-hyperlipidemia agents | 25 | 8.8 |
| Proton pump inhibitors | 22 | 7.7 |
| Antiarrhythmics | 16 | 5.6 |
| Blood glucose lowering agents | 15 | 5.3 |
| Diuretics | 15 | 5.3 |
| Parenteral nutrition | 9 | 3.2 |
| Nervous system agents | 8 | 2.8 |
| Mineral supplement | 7 | 2.5 |
| Analgesic agents | 6 | 2.1 |
| Antigout | 5 | 1.8 |
| Antihistamine H1 | 5 | 1.8 |
| Others* | 21 | 7.4 |
| **Total** | 285 | 100.0 |

**Others include: prostatic hypertrophy, antiemetic agents, constipation treatment, heart failure with reduced ejection fraction treatment, antiemetics, blood preparation, corticosteroid, antispasmodics, diosmin, and hesperidin.*

***Table 7.4.*** *Type, acceptance rate and clinical significance of clinical pharmacist interventions*

| Type of intervention Drug level | Number (%) | Acceptance rate | | | Clinical significance | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | | Accepted n (%) | Partially accepted n (%) | Not accepted n (%) | 0.01 | 0.1 | 0.4 | 0.6 | NA[a] |
| **Stop drug** | 45 (17.6) | 41 (91.1) | 3 (6.7) | 1 (2.2) | 7 (15.6) | 13 (28.9) | 24 (53.3) | 0 | 1 (2.2) |
| **Start drug** | 54 (21.2) | 38 (70.4) | 10 (18.5) | 6. (11.1) | 2 (50.0) | 33 (61.1) | 13 (24.0) | 1 (1.9) | 6 (11.1) |
| **Dose decrease** | 33 (12.9) | 28 (84.8) | 3 (9.1) | 2 (6.1) | 0 (0.0) | 30 (90.9) | 1 (3.0) | 0 | 2 (6.1) |
| **Dosage increase** | 4 (1.6) | 3 (75.0) | 0 (0.0) | 1 (2.2) | 2 (50.0) | 1 (25.5) | 0 | 0 | 1 (25.5) |
| **Switch drug** | 44 (17.3) | 33 (75.0) | 9 (20.5) | 2 (4.5) | 10 (22.7) | 19 (43.2) | 13 (29.5) | 0 | 2 (4.5) |
| **Regimen change** | 34 (13.3) | 28 (82.4) | 6 (17.6) | 0 (0.0) | 17 (50.0) | 17 (50.0) | 0 | 0 | 0 |
| **Clinical/subclinical monitoring** | 14 (5.5) | 12 (85.8) | 1 (7.1) | 1 (7.1) | 0 | 13 (92.9) | 0 | 0 | 1 (7.1) |
| **Information** | 27 (10.6) | 27 (100.0) | 0 (0.0) | 0 (0.0) | 0 | 0 | 0 | 0 | 27 (100.0) |
| **Total** | 255 (100.0) | 210 (82.4) | 32 (12.5) | 13 (5.1) | 37 (14.5) | 126 (49.4) | 51 (20.0) | 1 (0.4) | 40 (15.7) |

[a]*NA: Not applicable*

***Table 7.5.*** *Physicians' perspectives about clinical pharmacy services (CPS) (n=10)*

| Opinions of physicians | Strongly disagree | Disagree | Neutral | Agree | Strongly agree |
|---|---|---|---|---|---|
| **Knowledge and skills of the clinical pharmacist (CP)** | | | | | |
| CP had broad and deep knowledge about medications and therapeutics | 0 | 0 | 1/10 | 3/10 | 6/10 |
| CP communicated effectively with physicians | 0 | 0 | 0 | 1/10 | 9/10 |
| **Contribution of CPS** | | | | | |
| CPS provided an accuracy medication history and in timely manner. | 0 | 0 | 0 | 2/10 | 8/10 |
| CPS improved the optimal prescribing for patients | 0 | 0 | 1/10 | 1/10 | 8/10 |
| CPS provided appropriate medication information when requested | 0 | 0 | 0 | 1/10 | 9/10 |
| **Overall benefit of CPS** | | | | | |
| CPS have significant benefits for patients | 0 | 0 | 1/10 | 1/10 | 8/10 |
| CPS have significant benefits physicians | 0 | 0 | 1/10 | 1/10 | 8/10 |
| **Future perspectives in collaboration** | | | | | |
| Willing to collaborate in future | 0 | 0 | 0 | 1/10 | 9/10 |

# PART D. DISCUSSION AND CONCLUSION

# Chapter 8. Discussion and Conclusion

## 1 Major findings

While clinical pharmacy services in North America and Europe have a long history of implementation, and the role of pharmacists in promoting safe and effective medication use in both hospital and community settings are well recognised, clinical pharmacy services in developing countries such as Vietnam have only recently begun. Clinical pharmacy concepts were introduced in Vietnam in the 1990s. Since 1997, the Vietnamese Ministry of Health has released official documents governing Pharmacy and Therapeutics Committees, medicines information centres in hospitals, medicines information in marketing and communication, and clinical pharmacy. Clinical pharmacy and medications information concepts became increasingly accepted in Vietnamese hospitals as a result of these official regulations and the actions of clinical pharmacists. In December 2012, the Vietnam Ministry of Health issued the first regulation of clinical pharmacy – "Circular 31 for Clinical Pharmacy" (Regulation 31) (1) – that outlined the clinical pharmacist's duties in hospitals. Clinical departments in hospital setting are encouraged to collaborate with their departments of pharmacy to provide clinical pharmacy services under this regulation. Clinical pharmacists are to be recruited by hospital directors to provide clinical pharmacy services. For the first time, the new Pharmaceutical Law (2) included an official definition of "clinical pharmacists" and the legislative framework for clinical pharmacy to be practiced in Vietnamese hospitals. However, implementing clinical pharmacy activities routinely in practice still presents numerous problems and challenges.

To provide supporting evidence for the future implementation of effective clinical pharmacy activities in Vietnam, this thesis evaluated the impact of a variety of clinical pharmacy interventions implemented in a hospital setting to improve the quality of

prescribing in geriatric inpatients. Due to the high risk of drug-related problems and possible adverse outcomes, this population group was chosen as a priority target for evaluating the impact of clinical pharmacy activities. Six studies were conducted to address three distinct questions: (i) What is the current state of clinical pharmacy services (i.e., pharmaceutical care activities) in Vietnamese hospitals? (ii) How widespread are drug-related problems in prescribing to geriatric inpatients in Vietnamese healthcare settings? and (iii) Can pharmacist-initiated interventions improve the quality of prescribing for geriatric inpatients? The following sections summarise the main findings from the conducted research studies and discuss their implications for clinical practice.

**Part A. Clinical Pharmacy in Vietnam: Current Practice, Barriers, and Facilitators**

Part A of this thesis (Chapters 2 and 3) investigated the existing practice of clinical pharmacy in Vietnamese hospitals as well as the barriers and facilitators to implementing this practice. In this section, the overall purpose is to provide background information regarding the existing clinical pharmacy practice in Vietnam, and to prepare for future effective and efficient clinical pharmacy service models.

***Chapter 2***

Chapter 2 presents findings on the current practice of clinical pharmacy services from our national study of 560 hospitals in Vietnam on the workforce and the extent of clinical pharmacy services provided. To the best of our knowledge, this was the first study that surveyed clinical pharmacy services in hospitals on the national scale in Vietnam. According to the findings of the study, the human resource available for clinical pharmacy services was limited and did not correlate to the size and level of the hospitals studied. When compared to developed countries, Vietnam implements these activities at a significantly lower level.

Regarding trained pharmacy personnel, there were only 0.4 clinical pharmacist full-time equivalents (FTE) per 100 beds. This figure is much lower compared to clinical pharmacy practice in developed countries (such as in USA (3)), but it is comparable to some other countries such as 0.4 FTE in China (4). More importantly, the human resource shortage in Vietnamese hospitals for clinical pharmacy activities has barely improved over time. The lack of improvement in pharmacy human resource is evident when compared with earlier surveys in Hanoi in 2015 (5) and Ho Chi Minh City in 2019 (6) that revealed 0.36 and 0.67 FTE clinical pharmacists per 100 beds, respectively. In general, clinical pharmacy activities were implemented to varying degrees depending on the type of activity and classification of the hospitals in Vietnam. More established clinical pharmacy activities were conducted in higher-class institutions with a greater number of clinical pharmacists. Despite this, the current implementation status is focused primarily on non-patient-specific activities, with patient-specific activities still being in the early stages of development in Vietnam.

***Chapter 3***

Chapter 3 examines the facilitators and challenges to the adoption of clinical pharmacy services from the perspective of stakeholders, with the goal of providing some suggestions for providing better clinical practice. The following section focuses on the barriers related to human resources, barriers related to environments, and facilitators.

*Barriers related to human resources*

Along with the quantitative research in Chapter 2, the qualitative research in Chapter 3 highlighted that the primary barrier to implementing clinical pharmacy activities is, yet again, a shortage of human resources. This could be partially explained by the fact that the majority of Vietnamese pharmacy departments still require pharmacists to spend the majority of their

time on supply and dispensing of medication, thus leaving little time for clinical pharmacy activities. In addition, while Vietnamese hospitals can charge patients for clinical services provided by doctors and nurses, currently, they cannot charge for clinical pharmacy services. Consequently, under the current funding model, recruiting more human resources and securing dedicated financing for clinical pharmacy and drug information services are difficult.

In terms of the competency of pharmacists to provide clinical pharmacy services, especially hospital clinical pharmacy, the research study in Chapter 3 revealed that the majority of clinical pharmacists thought they lacked the specialised medical expertise necessary to provide clinical pharmacy activities. The majority of pharmacists also indicated that their pharmacy school curriculum did not equip them with sufficient clinical courses and practical experience to practice as clinical pharmacists in hospitals. The current five-year Bachelor of Pharmacy curriculum in Vietnam includes approximately two months of hospital practice placements during which the pharmacy student can witness everyday pharmacy department activities. However, this observation placement is strongly weighted toward dispensing chores as opposed to therapeutic services. This could account for the lack of clinical experience of pharmacy graduates, thereby highlighting the importance of revising and changing the pharmacy curriculum in Vietnamese pharmacy schools. Additionally, all pharmacists thought that communication skills were critical to their capacity to effectively communicate information to other healthcare personnel.

*Barriers related to environments*

Clinical pharmacy activities were viewed as novel in several of the surveyed hospitals. Other healthcare workers' perceptions and acceptance to new clinical pharmacy functions and tasks varied significantly among hospitals. Similar to other countries, the primary and traditional

role of doctors and nurses is patient care, which may include prescribing, advising on medication use, and administering medications. As a result, incorporating additional pharmacist interventions into this process may present challenges associated with the acceptance by other healthcare workers – an important issue of fostering inter-professional collaboration.

*Facilitators*

In light of these challenges, the primary facilitator of implementing clinical pharmacy activities in Vietnam are the government's efforts to provide a legal foundation for implementing clinical pharmacy activities, and the agreement of directors of health care facilities to implement clinical pharmacy activities at their respective facilities. The qualitative study in Chapters 3 indicated that official requirements and the backing of the Hospital Board of Directors were the most important enablers for clinical pharmacy services in Vietnamese hospitals. All interviewees agreed that these legislative frameworks facilitated the increased roles for pharmacists in medication usage and encouraged pharmacy departments to train pharmacists to meet the new demands. However, further studies, including longitudinal ones, are needed to evaluate the impact of the legislation on the provision of clinical pharmacy services and the workforce that provides these services.

**Part B. Prescribing in Geriatric Inpatients: Some Common Drug-related Problems**

In the context of limited human resources and non-standardised clinical pharmacy activities, it is critical to identify priority patients and priority activities in order to maximise efficiency and effectiveness. As discussed in the 'Introduction' chapter, elderly hospitalised patients are at high risk for drug-related problems, particularly related to prescribing. Therefore, they should be the focus of clinical pharmacy activities. A large number of studies around the world have revealed that drug-related problems in the elderly are extremely widespread (7-

14). However, the prevalence, scope, and severity of prescription problems among the elderly in Vietnam have largely remained unexplored until recently. The concepts of medication reconciliation, drug-related problems, potentially inappropriate prescribing, and other DRPs were not explicitly defined in Vietnam's professional or practice documents. Therefore, the second part of this thesis, Part B, (Chapters 4 and 5), determined the prevalence and extent of drug-related problems in prescribing for geriatric inpatients, particularly unintentional medication discrepancies (UMD) and potentially inappropriate prescribing (PIP) – two of the most common and serious problems among the elderly.

***Chapter 4 Unintentional Medication Discrepancies (UMD)***

The focus of Chapter 4 is on concerns related to prescribing in geriatric patients during the hospitalisation period, which is a vulnerable period for the occurrence of UMDs producing adverse effects in the patients. An observational study was conducted in one of Vietnam's leading geriatric hospitals in seven clinical departments in 2018. The study found that the proportion of older patients with at least one UMD at the time of admission was rather high, consistent with the findings across the world (7-11). The most common type of UMD was medication omission, which occurred more frequently in medications used to treat cardiovascular diseases. Another significant finding was that UMDs remained throughout the patients' hospitalisation and until they were discharged from the facility. Our findings support the implementation of a medication reconciliation program with officially approved standard operating procedures to ensure patients in Vietnam have a complete pre-admission medication history. This would contribute to reducing UMDs among geriatric inpatients.

***Chapter 5 Potentially Inappropriate Prescribing (PIP)***

Through a prospective observational study conducted from July to December 2018 at two major geriatric hospitals in Vietnam, the frequency of PIPs in elderly inpatients was examined in Chapter 5. The STOPP/START version 2 toolkit was used to screen for Potentially Inappropriate Medications (PIMs) and Potentially Prescribing Omissions (PPOs) in the study population. A high percentage of the criteria in this toolkit, developed by European experts using the Delphi consensus process, are relevant in Vietnam, making it a suitable choice for our study. Aside from that, the toolkit has been shown to be related to clinical outcomes and is frequently used to identify PIPs in elderly people around the world. According to our study, the prevalence of PIPs according to the STOPP/START version 2 was relatively high in geriatric inpatients in Vietnamese hospitals, consistent with data from other countries (12-14). Our study is one of the first to examine this topic in Vietnam. In light of the findings, initiatives aimed at reducing PIPs among geriatric inpatients are required urgently in Vietnam.

**Part C. The role of clinical pharmacists in improving the quality of prescribing in elderly inpatients**

In Part C, we evaluated the impact of clinical pharmacy interventions on improving prescribing quality in geriatric patients to reduce drug-related problems on prescriptions. This section will summarise the educational interventions and ward-based clinical pharmacy services.

***Chapter 6 Educational Interventions***

A pharmacist-initiated educational intervention designed as a before-and-after study to improve the quality of medication reconciliation practice in geriatric inpatients was reported in Chapter 6. The primary findings of the study revealed that there were statistically

significant improvements in outcomes in the post-intervention phase as compared to the pre-intervention phase. At the time of admission, the proportion of geriatric patients that suffered from at least one UMD dropped from 56.6% to 24.7% ($p<0.05$). In terms of the clinical relevance of UMDs, the proportion of patients with at least one pADE>0.1 reduced significantly from 42.8% to 12.3% ($p<0.05$). Hence, educational interventions initiated by pharmacists were found to be helpful in enhancing the quality of medication reconciliation practice, resulting in a significant decrease in the incidence of UMDs and a reduction in the risk of potential harm.

***Chapter 7 Ward-Based Clinical Pharmacy Services***

As part of our effort to optimise the prescribing process for older patients, we assessed a clinical pharmacist model at an internal medicine department in Chapter 7. Treatment concerns such as under-treatment, over-treatment, drug interactions, and other issues related to prescribing to patients were identified and resolved with the treating physicians. According to the study findings, pharmacists were able to identify a large number of clinically significant prescribing problems, and the acceptance rate of physician interventions was extremely high. Furthermore, the consensus among clinicians regarding the importance and benefits of clinical pharmacy activities were extremely good. These results demonstrate the potential contribution of pharmacists to the improvement of the quality use of medicines for the elderly.

**Contribution to pharmacy practice**

The purpose of this thesis was to evaluate the impact of clinical pharmacists on improving the quality of prescribing in geriatric inpatients. In addition to the evidence of contributions in

terms of the effectiveness of clinical pharmacy interventions discussed above, this research project's contributions to practice are reflected in the following points.

The thesis approach exemplifies how, in the context of clinical pharmacist shortages, it is critical to identify the priority patient population and the type of priority intervention so that it can be implemented in a feasible and sustainable manner. For effective medication reconciliation practice, instead of using the strategy of pharmacists directly participating in activities (as is common in developed countries today), an educational intervention by pharmacists was chosen because it takes less time and human resources while still achieving significant efficiency. Meanwhile, the ward-based clinical pharmacy services (CPS) only targeted geriatric patients who had high-risk factors for DRPs. Therefore, the interventional approach used in the study may be useful in settings where the number of clinical pharmacy personnel is limited but expansion of their role in direct patient care is still warranted to contribute to better health outcomes.

Furthermore, the interventions carried out within the framework of the thesis are two-way interactions between the treating physician and the pharmacist. One of the barriers to CPS identified in Chapter 3 is the lack of recognition and cooperation by treating physicians, who were previously solely responsible for prescribing medications to patients. The physician-pharmacist relationship can be improved as a result of the aforementioned direct interaction interventions, and pharmacists can partially demonstrate their roles and abilities in the fields of optimizing drug use for patients. Once this relationship is established, it can serve as a foundation for deeper coordination activities in patient health care between physicians and pharmacists. This highlights the importance of inter-professional collaboration, especially when starting on any type of clinical pharmacy activity.

In conclusion, the findings of this thesis demonstrate that pharmacists can have a significant impact on the quality of prescribing for geriatric inpatients in Vietnamese

hospitals. When it comes to better healthcare for aging populations and better utilisation of human resources in developing healthcare systems such as Vietnam, our approach should be considered as an effective option. We believe that our findings will assist healthcare facilities in justifying the investment of additional resources to establish an expanded model of care in which a pharmacist is present and engages directly in the healthcare team for patients.

## 2 Limitations and Future perspectives

This research contributes to our understanding of the impact of clinical pharmacists on the process of prescribing in geriatric inpatients. However, there are still some limitations to the studies in the thesis in terms of time and research scope. Hence, the significance of our overall study has to be interpreted appropriately in relation to the limitations. Furthermore, future research is required to elucidate the difficulties raised.

1. With the ongoing Covid-19 pandemic in Vietnam during the study period, research on the prevalence of DRPs in geriatric inpatients could only be conducted in one (Chapter 4) or two health care facilities (Chapter 5). Therefore, for the purpose of confirming prescribing concerns among geriatric inpatients in Vietnam, further research with larger sample sizes and conducted in more centers around the country is required.
2. Due to time constraints, the impact of intervention studies (Chapters 6 and 7) could only be examined through process indicators (i.e., the rate of UMDs and DRPs), without assessing other clinical and humanistic outcomes. It is necessary to conduct additional studies with better and more comprehensive outcomes, such as rehospitalisation, ADEs

exposed and overall quality of life, to further confirm the potential important contributions of the clinical pharmacy activities.

3. There is a lack of comprehensive economic evaluations of the clinical pharmacy services in Vietnam published in the scientific literature. It is recommended that future studies into the impact of ward-based clinical pharmacy services include an economic evaluation to assess the cost-effectiveness of the practice. The financial and economic implication of the interventions will provide more comprehensive evidence to allow the healthcare administrators to decide on funding clinical pharmacy activities.

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