PROMOTING QUALITY USE OF MEDICINE IN CHRONIC RESPIRATORY DISEASES IN VIETNAM: THE ROLE OF PHARMACISTS

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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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GLOSSARY OF ABBREVIATIONS AND ACRONYMS

ADR	Adverse drug reactions
COPD	Chronic Obstructive Pulmonary Disease
DALY	Disability Adjusted Life Years
DPI	Dry powder inhalers
DUE	Drug use evaluation
EQ-5D-5L	EuroQol - 5 Dimensions – 5 Levels
FIP	International Pharmaceutical Federation
GDP	Gross Domestic Product
GOLD	Global Initiative for Chronic Obstructive Lung Disease
GPP	Good Pharmacy Practice
HRQL	Health Related Quality of Life
MDI	Metered dose inhalers
MMAS	Morisky Medication Adherence Scale
MoH	Ministry of Health
NCD	Non-communicable Diseases
QALY	Quality Adjusted Life Year
QoL	Quality of Life
TDM	Therapeutic drug monitoring
VAS	Visual Analog Scale
WHO	World Health Organization

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ABSTRACT

Nowadays, the role of pharmacists has evolved to become health care providers of pharmaceutical care services that incorporates patient-orientated and product-orientated services. They not only work together with other health care providers, but also with patients in order to achieve positive outcomes for their therapeutic management. However, in Vietnam and other developing countries, both community and hospital pharmacists are still substantially under-utilised for patient care compared against the pharmaceutical care model of practice**.** How to improve the contribution of pharmacists in health care is still a tough question that need to be answered, especially in Vietnam with a rising number of better-qualified pharmacists as well as a shortage in other health care human resources, such as doctors and nurses.

At the same time, non-communicable diseases are becoming a major public health issue putting a heavy burden on society and the economy of Vietnam. Of these diseases, prevention and treatment of COPD and asthma is contributing to several problems including increasing number of patients, high rate of non-adherence to therapy in patients, and a low proportion of patients using inhalers correctly. Therefore, in exploring how to increase the role of hospital pharmacists in Vietnam, our study has chosen inhaler technique and medication adherence to demonstrate the role of hospital pharmacists' interventions in the management of COPD and asthma. Our findings showed that hospital pharmacists can teach COPD patients to improve their inhaler technique and counsel patients to improve adherence in a very efficient manner. The pharmacist-led programs also showed positive impact on patients' quality of life.

How to improve pharmacists' contribution to management of asthma in the community setting is another issue that needs to be addressed. Literature showed that a continuing education program is a key strategy for the community pharmacy sector to assist in improving the management of asthma in developing countries like Vietnam. Our present study developed and

evaluated an educational program for community pharmacists and evaluated its effectiveness with the simulated patient method. The study demonstrated that our training program was highly effective in equipping community pharmacists with the necessary knowledge and practical skills to counsel asthmatic patients about the management of their condition and medications. It is suggested that such education programs should be promptly implemented and made compulsory for community pharmacists in Vietnam to improve the quality of counselling for patients with asthma and other non-communicable diseases.

Overall, our studies demonstrated that with proper encouragement and simple continued professional education, both hospital and community pharmacists can expand their role to contribute to better management of asthma and COPD in Vietnam. This model may produce the same positive outcomes in other chronic diseases and should be considered by the relevant authorities in Vietnam and other developing countries.

CHAPTER 1. INTRODUCTION

Pharmacists have numerous roles in the health care system across a wide variety of settings, including community pharmacy, hospital pharmacy, the pharmaceutical industry and academia. They are also involved in health service administration and regulation in government and non-government organisations (NGOs) [1]. When taking a retrospective look at the pharmacy profession, the role of pharmacists has changed dramatically in recent years. Fifty years ago, pharmacists' responsibilities generally focused primarily on dispensing and compounding drugs (product-oriented services), and they rarely communicated with patients about their medications or disease management. Pharmacists have evolved to become health care providers of pharmaceutical care services, which also incorporates patient-oriented services. They not only work together with other health care providers (e.g. doctors and nurses), but also with patients to achieve positive outcomes for their medication therapy [1, 2]. The value of the expanded role of pharmacists has been well demonstrated in the literature [3-5]. For example, pharmacy services have been shown to significantly improve health and economic outcomes, decrease medication-related adverse events, increase quality of life, and reduce morbidity and mortality [1, 5, 6]. This also includes improving patients' adherence to their medications, especially for chronic diseases, in both low and middle-income countries [3-5].

In developed countries, the full range of pharmacy services are often available and pharmacists are recognised as an integral part of the health care team. However, both community and hospital pharmacists are significantly underutilised for patient care in developing countries [7, 8], whereby the majority of their time is devoted to dispensing medicines [9, 10] and their clinical role is generally not well recognised by physicians and patients [11]. There are a number of reasons that contribute to the underutilisation of pharmacists, especially in developing countries [5, 8, 9, 12]. One of the main barriers is the

quality and quantity of pharmacists that are available and capable of undertaking the clinical roles [2, 9, 11]. In addition, lack of finance is another major barrier that prevents pharmacists from expanding their professional roles. For example, investing money in technology to help pharmacists save time from dispensing is costly [2]. Other barriers and challenges include lack of professional regulation, lack of access to databases of evidence, and lack of standard guidelines for prevention and treatment of diseases. These issues are unique to low and middle-income countries [8, 9, 11, 12].

This PhD thesis is focused on improving the quality use of medicines in Vietnam through enhancing the contribution of hospital and community pharmacists. In order to improve and expand the role of pharmacists in the health care system of developing countries, it is important to firstly understand their health care system, the current roles and capabilities of pharmacists, and their achievements and challenges to date.

1. The health care system in Vietnam

General information on Vietnam

Vietnam is among the group of low- and middle-income countries in the South East Asian region. Since gaining independence 70 years ago, the country has witnessed a great change in socioeconomic and health status. Currently, Vietnam has a population of over 90 million people with a fairly high population density (259 people per km^2) [13]. The population structure has changed dramatically, with the proportion below 15 years of age decreasing from 33% in 1999 to 25% in 2009. In the same period, the percentage of working age (16-59 years) and elderly (aged over 60) increased gradually in the past two decades. For example, the proportion of elderly people increased from 8% in 1999 to 9% in 2009 (9.4% in 2010). Population age index increased by 11% from 24.5 (1999) to 35.7 (2009) (Figure 1) [14].

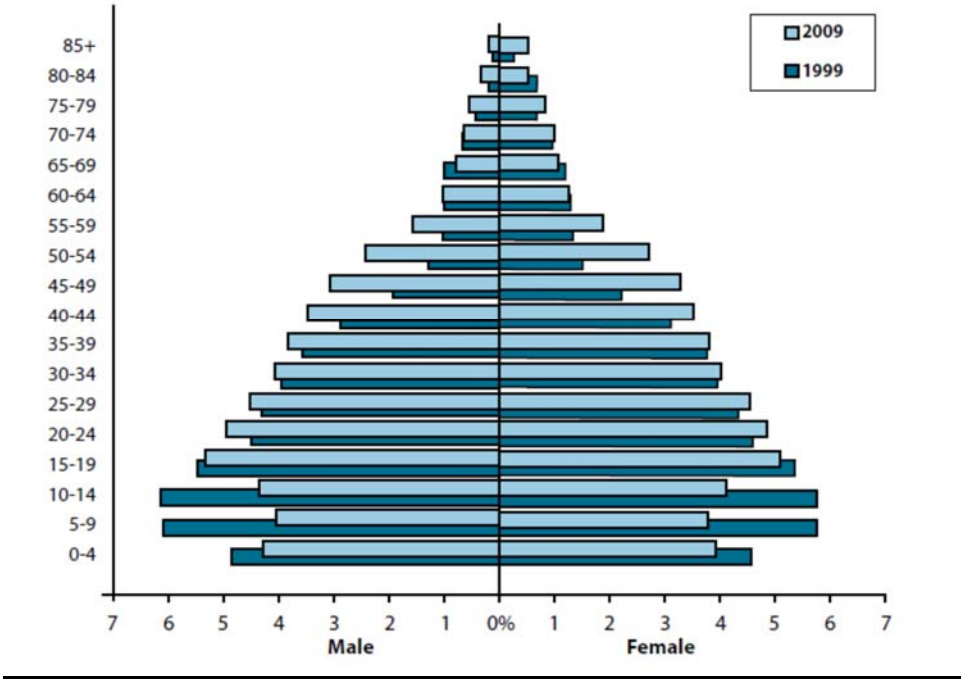


Figure 1: Comparison of population pyramids of Vietnam, 1999 vs. 2009

Changes in population demography can have large impacts on the health status of the population of the country (Table 1). For example, changes in the population structure will lead to increased health care requirements for the elderly in coming years. At the same time, there is a gradual increase in women entering reproductive years, which will affect the need for reproductive health services and paediatric care [13, 15].

Table 1: Selected health indicators in Vietnam over a 5-year period (2009-2013) [16]

Indicators	Year 2009	Year 2010	Year 2011	Year 2012	Year 2013
Average life expectancy (years)	73.0	72.9	73.0	73.0	73.1
Maternal mortality ratio (per 100,000 live births)	69	68	67	49	49
Infant mortality rate (per 1000 live births)	16.0	15.8	15.5	15.4	15.3
Under-five mortality rate (per 1000 live births)	25.0	23.8	23.3	23.2	23.1
Under-five child malnutrition rate (underweight) (%)	18.9	18.0	16.8	16.2	15.3

In terms of morbidity and burden of disease, there is a clear change in morbidity patterns (Figure 2), with non-communicable diseases (NCDs) increasing significantly over the period of 30 years. NCDs were the major cause for all hospital visits since the later part of the 1990s and accounted for nearly 72% in 2010. In contrast, communicable diseases have declined from about 60% in 1986 to under 20% in 2010 [13]. According to the Global Burden of Disease Study, burden from NCDs increased significantly from 42% to 66% of total disability-adjusted life years (DALYs) (Figure 3) [16].

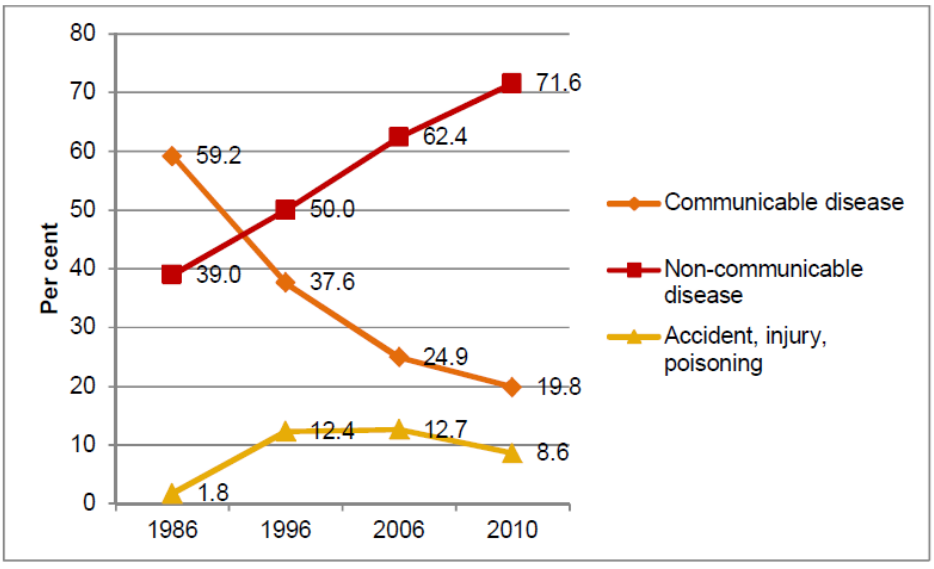
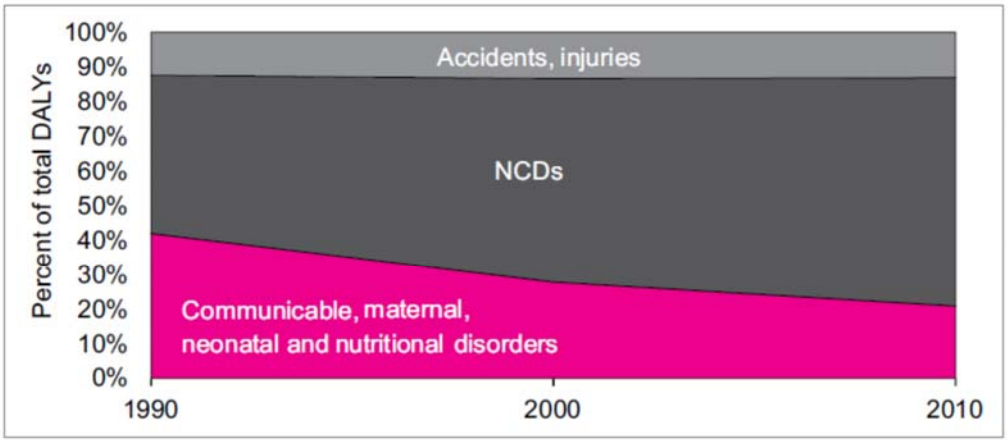


Figure 2: Trend in morbidity based on health care visits at state facilities, 1986-2010 [13]



Source: Calculated using data from the Global Burden of Disease Study 2010. Global Burden of Disease Study 2010 (GBD 2010) Results by Cause 1990-2010 - Vietnam Country Level. Seattle, United States: Institute for Health Metrics and Evaluation (IHME), 2013 .

Figure 3: Trends in morbidity patterns measured in DALYs, 1990-2010 [16]

Vietnamese health care system

The Vietnamese health care system is controlled and managed by the Ministry of Health. The system is organised into four main levels – central, provincial, district and commune. The Ministry of Health is responsible for planning and formulating national health policies, as well as guiding and monitoring the implementation of strategies, plans and national health programs [17].

Human resources for health care

The number of health workers has increased substantially in the past decade, especially the number of doctors, pharmacists and nurses. In 2003, the ratio of the health workforce (per 10,000 population) was 5.9, 0.8, 6.0 for doctors, pharmacists and nurses, respectively. After a decade, these ratios (per 10,000 population) have increased to 7.5 doctors (2013), 2.1 pharmacists (2013) and 10.02 nurses (2011) [16, 17]. However, there are still three major issues

related to the human resources for health care in Vietnam. The first issue is a shortage in the number of staff in the system. For example, according to the Global Pharmacy Workforce report from the International Pharmaceutical Federation (FIP), the number of pharmacists (per 10,000 population) in Vietnam ranked 51st in 82 countries. In comparison to other countries in South East Asia, the number of pharmacists in Vietnam (per 10,000 population) is just higher than Cambodia, but lower than Malaysia, Thailand and Singapore [18].

The second issue is a regional imbalanced distribution of the human resource. Health workers with higher qualifications, such as doctors and pharmacists, are primarily concentrated at central and provincial level facilities in urban areas and large centres. At the central level, 45 percent of human resources in the health sector have university or higher training, compared to only 23 percent in the provinces. Nearly 50% of all pharmacists (48%) are working in Hanoi and Ho Chi Minh City – the two biggest cities in Vietnam [16].

The final issue is the quality of the health care personnel. According to self-assessments by recent medical graduates, only 45% knew how to make an early diagnosis and provide appropriate initial treatment for communicable diseases, 50.9% knew how to implement some simple procedures, and only 37.6% had the ability to implement monitoring and management of chronic diseases in the community [17]. According to a national survey of 76 central and provincial hospitals in 2010, approximately 40% of pharmacists working in the clinical pharmacy units had no training in clinical pharmacy during their undergraduate university programs [19]. The main reason contributing to this problem is the slow change in the training and education programs for both doctors and pharmacists [17].

Health care financing

There are two major public financial funding sources for health care in Vietnam: (i) the state budget that is allocated directly to service providers through the Ministry of Health and

Provincial Health and Finance Departments, and (ii) the social health insurance fund (with 66.8% of the population having health insurance in 2012) [17]. Apart from these two public funding sources, households also contribute significant direct out-of-pocket payments to service providers or to pharmacies to buy medications when ill. After a decrease, out-of-pocket expenditure on health increased from 44.8% in 2010 to 48.8% in 2012 (Table 2) [16]. According to the World Health Organization (WHO), total health spending needs to reach at least 4-5% of Gross Domestic Product (GDP) in order to achieve goals of health care for all [20]. In this respect, Vietnam spent 6% of GDP for health in 2012. Compared to many other countries in the region, for example Malaysia (4.0% in 2012), Thailand (4.5% in 2012), Indonesia (3.0% in 2012) and China (5.4% in 2012), Vietnam spends a relatively high share of GDP on health [21]. In addition, Vietnam is striving to maintain the total state budget spending for health at 10%, which will gradually decrease the out-of-pocket expenditure on health [17]. However, in recent years, total expenditure on health has reduced due to a downturn in the economic situation. For example, the state budget funding for non-communicable disease programs (including cancer, hypertension, diabetes, mental health protection, and COPD/asthma) stood at a rather low 12.7% of total funds in 2013, which declined from 15.6% in 2012. In fact, budget allocations for NCD projects for 2014 was have been cut up by 68% compared to the 2013 allocation [16]. This would ultimately lead to an increase in out-of-pocket expenditure for patients.

Table 2: Indicators of health financing in Vietnam (2008-2012) [16]

Indicators	2008	2009	2010	2011	2012
Total expenditure on health as a percentage of the GDP (%)	6.0	6.5	6.9	6.8	6.6
General government expenditure on health as a percentage of total government expenditure (%)	8.0	8.5	10.1	10.2	9.5

Out-of-pocket expenditure on health as a percentage of private expenditure on health (%)	88.1	87.4	83.9	83.2	85.0
Per capita total expenditure on health at average exchange rate (US$)	62.5	71.8	82.8	93.5	102.5
External resources for health as a percentage of total expenditure on health (%)	2.9	3.4	3.0	2.6	2.4
Out-of–pocket expenditure as a percentage of total expenditure on health (%)	54.3	50.8	44.8	45.6	48.8

Health service delivery

Health care services in Vietnam are provided by both the public and private sectors, which are under the control of the Ministry of Health. A variety of health care services are provided, including primary health care services, preventive medicine, family planning services, and medical examination and treatment. In addition, the Government has established and implemented national target programs and projects as a guarantee of effective and equal provision of services [17]. The medical services network has continued to expand in both the public and private sectors. However, the public sector has a dominating role in health care provision with 1030 public hospitals [17]. By the end of 2013, there were 24.2 inpatient beds per 10,000 population in public hospitals. In contrast, according to data from the Medical Services Administration (MSA), there are currently 170 private hospitals nationwide with a total of 8627 hospital beds, which account for 11% of total hospitals and 4.2% of total hospital beds nationally. In addition, there are more than 30,000 private clinics and other medical service facilities [16]. The private hospitals are generally concentrated in large cities and urban areas where people with high income with purchasing power reside.

According to the WHO, the number of beds per 10,000 people in Vietnam was considered high among Southeast Asian countries [17]. However, overcrowding in public hospitals is still the most serious problem in Vietnam. Despite the number of beds increasing annually, overall bed occupancy ratio remains at a high level. For example, the bed occupancy ratio was 119.2% in 2011 and 105.5% in 2015 at the central level, [22] particularly in tertiary hospitals of some specialty departments (e.g. oncology, paediatrics, cardiology, gynaecology and endocrinology). Some central hospitals had consistently very high bed occupancy rates, including Vietnam National Cancer Hospital (172%), Bach Mai Hospital (168%) and Cho Ray Hospital (139%) [16]. The ratio in provincial and district levels were over 110% from 2011 to 2015 [22]. The main reasons for overcrowding in hospitals are inadequacy in physical facilities, equipment, staff numbers, and quality of the staff at the commune and district levels. This leads to patients lacking trust in the quality of treatment at lower level facilities and, therefore, bypass health care facilities at lower levels [16]. In addition, overcrowding in hospitals is also caused by incentives of the financial mechanism and undesired effect of some policies (e.g. mechanism for state budget allocation to hospitals, hospital autonomy, user fee policy) [13] [17].

Pharmaceutical products

Pharmaceutical products including drugs, vaccines and other biological products are considered as special goods that require specific regulations to avoid poor quality and inappropriate use. This also ensures appropriate prices so that people are able to access them without having to pay out-of-pocket expenses or go through their health insurance [14]. To control the quality of pharmaceutical products, the Government of Vietnam has developed and implemented a series of good practice standards such as the good practice standards in manufacturing (GMP), storing (GSP), laboratory testing (GLP), distribution (GDP), and pharmacy (GPP). The National Drug Policy (1996) and The Pharmaceutical Law (2005) in Vietnam were established to ensure

adequate supply of quality drugs at affordable prices and to ensure rational, safe and effective use of drugs. These documents also regulated every activity in the pharmaceutical field, including business, registration and circulation of drugs, use of drugs, drug supply, management of drug information, advertising of drugs, and clinical testing of drugs. With regards to the management of the price of medicines, the Ministry of Health implemented the drug price stabilisation policy, guidelines for price declaration, and drug competitive bidding [23].

Pharmaceutical products in Vietnam are supplied by both domestic companies (conventional and traditional medicines) and imported from international enterprises, with nearly 50% of the value of drugs consumed in the market being imported primarily from France, India, Korea, Sweden, Germany and the United States [14]. There has been a significant increase in the percentage of domestic pharmaceutical production following the Government setting it as a priority. While the percentage was under 50% in 2010 and 2011, the value of domestically produced drugs in 2012 was estimated at USD 1.2 billion and accounted for 52.3% of the value of drugs consumed in the market. Currently, domestic production covers 234 out of 314 active pharmaceutical substances in the Vietnam Essential Medicine List [17] [13]. Taking advantage of an abundant resource of herbal medicine, Vietnam also promotes the development of traditional medicine and medicinal materials. By the end of 2012, there were more than 80 herbal medicine manufacturers and more than 300 traditional medicine manufacturers. Turnover from local herbal medicines has also increased significantly, with increases of 25% in 2010 and 33% in 2011 in comparison to previous years [17].

Regarding the distribution system, Vietnam has gradually expanded the pharmaceutical supply network throughout the country. Distribution of drugs is currently undertaken by enterprises, pharmacies and medical facilities in the public and private sectors. According to a report from Ministry of Health in 2010, there were 1350 domestic enterprises, 91 direct importers/exporters, 438 foreign drug suppliers, and 38,916 drug outlets in Vietnam [17]. In

particular, there was a huge increase in the number of private pharmacies in Vietnam. The number of private pharmacies per 10,000 population was 4.5 according to the updated Ministry of Health report in 2014 [16].

Despite improvements in the pharmaceutical manufacturing, regulation, distribution and supply chain, there are still some significant challenges in the management of pharmaceutical products in Vietnam. The first challenge is that drug prices remain high in comparison to the International Reference Prices [24] [17]. Many physicians and patients believe imported drugs to be better, therefore resulting in frequent prescribing of the more expensive imported brand-name drugs. In addition, representatives from drug companies often offer larger incentives to doctors for prescribing imported rather than domestically produced drugs. Drug manufacturers themselves are highly dependent on the price of pharmaceutical ingredients which are mostly imported (90%), thus contributing to the difficulty in controlling drug prices [14] [17].

The second major challenge is that misuse and irrational use of drugs is quite common in Vietnam. Among the numerous reasons, the most important one is non-compliance with prescription drug regulations in pharmacies. In particular, the sale of prescription drugs to patients without prescriptions is widespread throughout Vietnam [22]. Furthermore, the lack of up-to-date standard treatment guidelines has also led to the irrational use of drugs. Treatment practices can be significantly different between hospitals and doctors for the same disease. Economic factors can also influence unsafe and irrational use of drugs. For example, when the drugs are too expensive, especially for chronic diseases, many patients will simply not purchase a full dose due to a lack of funds. Consequently, the treatment is ineffective and the disease may become more severe [14].

2. Activities of pharmacists for improving quality use of medicines in Vietnam

Providing drug information

The provision of drug information is important to the quality use of medicines. In Vietnam, there are many sources of information that can influence the prescribing behaviour of doctors, especially in hospitals. As a result, monitoring and supplying reliable drug information is an important role for hospital pharmacists that has been defined and regulated in guidelines by the Ministry of Health [25]. The most common methods applied by hospital pharmacists to provide drug information are "active provision" and "directly answer". The first method focuses on actively providing updated information about new guidelines, new treatments, new approved medicines or drug safety. This method is generally applied across all levels of Vietnamese hospitals due to a lesser requirement in monetary and manpower resources. For the "directly answer" or "ask-answer" method, the phone numbers of Drug Information Units and/or hospital pharmacists are provided to other health care professionals. During working hours, hospital pharmacists are assigned to collect enquires and answer questions directly. This method is particularly useful for emergency situations and is also preferred by doctors, as they can discuss specific information related to their patients with the pharmacists [26, 27].

Monitoring adverse drug reactions (ADR) and other pharmacovigilance activities

Monitoring for ADRs is another important and routine task for hospital pharmacists, due to the fact that ADRs are one of the main causes of hospital admissions [28]. This intervention has been shown to decrease the number of adverse events and improve the quality of ADR reporting [29]. Therefore, the Vietnamese Ministry of Health issued a national ADR report form and a guideline for ADR monitoring in hospitals, which include explicit duties and procedures for hospitals pharmacists [30]. Presently, hospital pharmacists in Vietnam are involved in all aspects of ADR monitoring. They are responsible for detecting adverse events happening in

patients when checking medical records, and they work together with doctors and nurses to manage the adverse events. Hospital pharmacists are also responsible for assessing causality between drugs and adverse events, as well as complete ADR report forms to send to the National Center of Drug Information and ADR [27, 30]. Furthermore, hospital pharmacists are also involved in other pharmacovigilance activities such as quality drug guarantee and monitoring for medication errors. Research has shown that the proportion of medication errors in Vietnam is relatively high and clinical pharmacists can potentially contribute to decreasing the number of errors [31, 32]. For example, a recent study conducted in two Vietnamese hospitals demonstrated that a clinical pharmacist-led training program significantly decreased the prevalence of clinically relevant erroneous doses from 64% to 48.9% ($p<0.001$) [33].

Drug use evaluation

Drug use evaluation (DUE) is a useful tool to enhance the appropriate use of drugs. The goal of DUE is to encourage optimal drug use and the provision of high-quality drug therapy that is cost-effective. By undertaking these activities, hospital pharmacists can have a significant impact on the prescribing habits of physicians and/or provide evidence-based information for establishing guidelines [34, 35]. Hence, the Vietnamese Ministry of Health has stated that DUE is a priority task for hospital pharmacists [25]. Outcomes from these activities not only examine the status of drug use, but also help physicians in their diagnosis and to determine appropriate actions to improve the quality use of drugs in hospitals.

Evaluation of drug use is mainly performed in Vietnamese hospitals through co-operation between hospital pharmacists and researchers in universities. Generally, hospital pharmacists determine DUE-based research questions from their practice and then work with university researchers to determine the significance of the problem, collect and analyse data, and establish new or update existing guidelines. Through collaboration with universities, hospital

pharmacists are able to evaluate drug-related problems in a wide range of diseases (e.g. endocrine diseases [36], stroke, hypertension [37] and infectious conditions [38, 39]) or in specific groups of patients [40]. These findings are highly beneficial to improving the quality use of medicines in Vietnam.

A key example supporting the positive contribution of pharmacists in the quality use of medicines in Vietnam is in the area of antibiotic prescribing and use. Antibiotic use in Vietnam has rapidly increased in the last decade, which has resulted in a significant rise in antibiotic resistance [17]. For example, a recent study on antibiotic therapy for community-acquired pneumonia was conducted in 10 hospitals in Vietnam with the involvement of pharmacists [38]. The study revealed concerning findings about how the condition was treated across all participating hospitals. In particular, 93.4% of antibiotics were administrated intravenously regardless of the severity of pneumonia and nearly 80% of cases were prescribed a 3rd-generation cephalosporin mono- or combination therapy for initial empirical management regardless of disease severity. These inappropriate practices were considered partly due to a lack of national guidelines for the management of the disease, including standard criteria for diagnosis, assessment of severity and treatment [38]. To address this issue, the Ministry of Health released new national guidelines for antibiotic use as requested from hospital pharmacists in Vietnam [41].

Therapeutic drug monitoring

While therapeutic drug monitoring (TDM) is commonly practiced in many countries, this procedure is not performed routinely in Vietnam. TDM is generally limited to research studies conducted between hospital pharmacists and researchers. Nevertheless, findings from TDM studies have provided evidence of its benefit to improve the quality use of medicines in Vietnamese hospitals, especially in central cities. To date, TDM studies have focused

predominantly on a wide range of antibiotic groups that are commonly used in Vietnamese hospitals, including aminoglycosides [42, 43], vancomycin [44, 45] and carbapenem [46]. Findings from the studies have identified the current status of antibiotic use in Vietnam and have provided suggestions for physicians to improve the pharmaceutical management of the conditions. Pharmacists' recommendations have included the choice of dose and dosing intervals, administration route, and treatment regimens [44, 45] [46], and have led to the development of guidelines by hospitals to improve the safety and efficacy of antibiotic prescribing [47].

Patient counselling

Patient counselling is a very important role of pharmacists both in community and hospital pharmacy settings. However, in Vietnamese hospitals, physicians and nurses are still the primary source for counselling patients. Patient counselling by pharmacists is often integrated with dispensing, which still takes priority over any counselling activities by hospital pharmacists [27]. In the community setting, quantity and quality of medication counselling are still major limitations [48].

3. Difficulties and Challenges

Despite the enormous potential for the positive contribution of pharmacists in the Vietnamese health care system, there are some challenges for them to be fully recognised as a key member of the health care team. Similar to pharmacists in other low and middle-income countries, the factors causing these challenges can prevent Vietnamese pharmacists from performing a wide range of roles in the pharmaceutical management of patients.

Shortage of pharmacists

The first challenge is the insufficient number of qualified pharmacists available in developing countries like Vietnam [2, 9, 11]. The number of pharmacists in Vietnam is 1.92 pharmacists per 10,000 population (2011) [17]. Although this figure has increased substantially in the past decade (2.4 pharmacists per 10,000 population in 2015 [22]), it is still far lower than the average in the world (6.02 pharmacists per 10,000 population [18]). Furthermore, the shortage of hospital pharmacists occurs in all levels of hospitals and is especially serious in rural areas. The average number of hospital pharmacists per hospital ranges from 3.6 to 8.8 depending on the region in Vietnam [16]. However, many pharmacy departments in rural hospitals are unable to recruit a pharmacist [13]. In a recent 2017 survey, the number of full-time clinical pharmacists per 100 beds was only 0.36 in Vietnam. This figure is far below what is needed to adequately provide clinical pharmacy services (3.2 pharmacists per 100 beds), including general professional duties (e.g. procurement, dispensing and quality assurance of medicines) and to implement clinical pharmacy activities [27].

Insufficient quality of pharmacists

Another major challenge for pharmacists in Vietnam is insufficient training and qualification to undertake professional duties in the quality use of medicines for the community. This includes clinical skills in drug knowledge, communication, evaluation of information, and disease and medication management [2, 11]. According to a national survey in 76 central and provincial hospitals in 2010, approximately 40% of pharmacists working in clinical pharmacy units had no training in clinical pharmacy in their undergraduate programs [49]. Only 58.3% of pharmacists in these hospitals attended continuing professional training programs that focused primarily on drug information and ADR monitoring. The majority of the pharmacists read common textbooks to improve their clinical knowledge, however many textbooks are not

updated in Vietnam [49]. In a recent qualitative study [27], hospital pharmacists also admitted that they did not feel confident in their knowledge and skills to perform clinical pharmacy activities, with the majority rated as having "fair" or "not good" clinical knowledge and skills. Their level of specialty and up-to-date knowledge was also inadequate [27]. In term of community pharmacists, the quality of interactions with patients was very limited because of a lack of qualified pharmacists [48].

Lack of recognition of pharmacists as medication counsellors

There is a lack of recognition of clinical pharmacy and clinical pharmacists in Vietnam. Trinh HT et al pointed out that physicians and other health care professionals were not fully aware of the role of clinical pharmacists [27]. This has also been reported in China where doctors and patients often did not understand the role of clinical pharmacists in hospitals and, therefore, were unwilling to listen to the advice from pharmacists [11]. Interestingly, Olsson E et al described the role of community pharmacists in Vietnam as medication counsellors, the doctor's assistant or the businessman [50]. While pharmacists described themselves as medication counsellors, most of the doctors and patients considered community pharmacists as the doctor's assistant or businessman [50]. Clearly, the isolation and lack of recognition of pharmacists as a health care professional are obstacles to their role in the health system [9, 51].

Limited role of pharmacists in community pharmacy

In Vietnam, there are a large number of public and private pharmacies. The majority are private and owned by pharmacists who have pharmacy practice's certificate from the Health Department. In addition, majority of pharmacies are mainly located in big cities like Hanoi and Ho Chi Minh City. The main activity of pharmacists in community pharmacies is dispensing medicines, with very little role in counselling patients on medication use. This is in contrast to

the role of community pharmacists in developed countries. For example, in the UK, community pharmacists can visit patients at their home to conduct medication reviews, discuss medication management plans with general practitioners (GPs), establish pharmaceutical care plans, and continue monitoring progress [52]. In Germany, community pharmacists will be trained in pharmaceutical care programmes for management of diabetes, asthma and hypertension. Participating in these programmes, pharmacists' services will be remunerated by health insurance companies [53]. Almost all community pharmacies in Vietnam have no procedure for giving advice or developing pharmaceutical care plans for patients with chronic diseases. In addition, there is no official training program for community pharmacists and no requirement for them to undergo continuing professional training to run a private pharmacy. Furthermore, presently, there is a variety of qualification levels of pharmacists (pharmacist and pharmacist's assistants) working in community pharmacies. Despite this, the majority of patients, including those with chronic diseases, will often approach community pharmacies first when they are sick or have worsening disease [54, 55]. Community pharmacists have already been shown to improve the quality use of medicines for patients with chronic condition (e.g. asthma, arthritis management, cardiovascular diseases and mental illness) in developed countries [56]. This highlights the urgent need to identify the knowledge and skills of community pharmacists, particularly in the management of chronic diseases, to allow the Ministry of Health to establish proper training programs to improve the quality use of medicines in community pharmacies in Vietnam.

4. Strategies for enhancing the role of pharmacists in Vietnam

Several strategies have been applied in Vietnam to improve the role and contribution of pharmacists in the health care system, especially as medication counsellors. These strategies include administrative strategies, educational strategies, investment in technology, and

international co-operation with other universities in pharmacy. Of these strategies, managerial methods (e.g. setting up new policies and guidelines) and educational methods (e.g. changes in the curriculum of university pharmacy programs) are the more effective approaches.

Administrative strategies

The initial and most important step for this strategy is to establish the rational use of drugs as a priority target for the health care system in Vietnam. This was achieved with the National Drug Policy in 1996 and the Pharmaceutical Law in 2005 [57]. It was only in 2016, in which the Pharmaceutical Law defined the concept of "clinical pharmacy" and set the law for clinical pharmacy activities [58]. Recently, the Vietnamese Government has approved the national master plan for the development of Vietnamese pharmaceuticals towards 2020 and the extended vision for 2030 [59]. According to these documents, clinical pharmacy units need to be strengthened and established in 50% of provincial and central hospitals by 2020. In addition, the plan has set a target of 2.5 pharmacists per 10,000 population by 2020, including 30% as clinical pharmacists [59]. These documents support and encourage the expanded roles of pharmacists in the health care system.

The next step is the establishment of legal regulations to allow hospital pharmacists to perform clinical activities. Similar to other countries, the Vietnamese Ministry of Health issued legal documents stipulating these conditions to the Drug and Therapeutic Committee in 1997 (updated in 2013) and the Pharmacy Department of Hospitals in 2011. The Drug and Therapeutic Committee is responsible for building and providing tools for hospital pharmacists, including the list of drugs used in hospitals, clinical guidelines, methods for analysing drug-related problems, and ADR monitoring. Together, these legal regulations have provided hospital pharmacists with both government and hospital administrative support that are crucial for the implementation of non-dispensing clinical services [11, 27]. This has also led to the

Head of Hospital Pharmacy Departments to be able to reduce the dispensing workload for some pharmacists and assign more time for other clinical pharmacy activities [27].

Another essential step is the establishment of official guidelines that encompass the specific functions and duties of clinical pharmacists. This was achieved in 2012 by the Ministry of Health for activities of clinical pharmacists in hospitals and included the concept of "clinical pharmacists" [25]. Along with the updated Pharmaceutical Law [58], this guideline not only defined qualification requirements for clinical pharmacists, but also imposed requirements on the facilities for practising these activities. Moreover, the guideline also clearly stated the duties that needed to be fulfilled by clinical pharmacists to improve the quality use of drugs in hospitals [25]. With regards to the community setting, the Ministry of Health established legal documents for the regulation of pharmacists activities in community pharmacies following the Good Pharmacy Practice standards (GPP) [60]. According to the legal documents, besides dispensing and selling medications to customers, pharmacists also need to spend more time counselling patients to ensure the rational use of medicines. This further supports the expanded role of pharmacists as medication counsellors in Vietnam and makes them responsible for the information they provide to patients.

Educational strategies

According to the regulations of Ministry of Health, hospital pharmacists must be trained in clinical pharmacy and have sufficient qualifications to conduct clinical pharmacy services [25]. In order to achieve this, there has been a significant change in clinical pharmacy education in Vietnam. The two biggest pharmacy universities, Hanoi University of Pharmacy and the University of Medicine and Pharmacy at Ho Chi Minh city, have designed new curriculum that are focused on strengthening knowledge and maximising clinical skills and experiences. For strengthening knowledge, new subjects have been incorporated into the program that reinforce

and strengthen foundation knowledge of pharmacy and therapeutics. Students are provided with updated knowledge and equipped with skills to solve clinical problems. In order to improve clinical skills, students are placed in simulated situations before working with patients and doctors. Patient counselling and training on clinical cases are two main subjects that allow students to apply knowledge from previous subjects (e.g. pharmacotherapy) to explain and evaluate doctors' treatment choices using evidence-based guidelines. This is the basis for drug evaluation, which is one of key duties of clinical pharmacists [25].

The new curriculum also integrates an internship program in hospitals for students. All students have a compulsory requirement to work in a hospital pharmacy for 3 months, which include visiting patients with doctors and other clinical pharmacists, discussing the management plan for patients, and presenting clinical cases to supervisors. The internship not only strengthens clinical knowledge and skills, but also helps pharmacy students establish contact with other health professionals. This is important for improving the recognition of the role of pharmacists by physicians, nurses and other health care professionals [19, 27].

Other educational strategies that have been applied in Vietnam include developing and promoting continuing professional training in clinical pharmacy [27]. This is particularly important for the existing workforce because nearly 40% of pharmacists working in a clinical setting were not trained in any clinical aspects of pharmacy at university [49]. According to the Ministry of Health, currently, it is compulsory for pharmacists to attend continuing professional training to become a clinical pharmacist in hospitals [25]. Therefore, Hanoi University of Pharmacy, one of biggest pharmacy universities in Vietnam, has organised continuing professional training programs for pharmacists already working in hospitals based on the guidelines from the Ministry of Health [25, 61]. These pharmacists will be awarded additional qualifications after successfully completing each course. In addition, Hanoi University of Pharmacy offers a flexible timetable in the school year for pharmacists and appoints lecturers

to provincial colleges based on demand to maximise the number of pharmacists attending continuing professional training courses [61].

5. Conclusion

The role of pharmacists has significantly evolved over time to one that incorporates both product-oriented services and patient-oriented services. This is an international trend for developed countries and is gradually being established in more developing countries, including Vietnam. In recent years, the health care system in Vietnam had been reformed to adapt to increasing non-communicable diseases and demand for higher quality in medical services. Therefore, it is necessary for pharmacists to involve themselves more and more in new clinical services that focus on improving the quality use of medicines for patients with chronic diseases. Although pharmacists in Vietnam currently face a number of difficulties to performing their jobs, several recommendations have been considered and/or implemented to support their value in the health care system. However, there is limited available evidence specific to the contribution of pharmacists in Vietnam to the management of patients with chronic diseases. Therefore, there is an urgent need to design studies that address this issue to determine the impact of pharmacists in patient care in both the hospital and community settings. This includes developing strategies to improve the knowledge and skills of pharmacists, particularly in community pharmacies. Therefore, the rationale for my project is to promote the role of pharmacists in the management of chronic diseases in Vietnam. The reason for choosing chronic obstructive pulmonary disease (COPD) and asthma will be discussed in the following chapter (Chapter 2).

This PhD thesis includes 6 chapters:

- **Chapter 1.** Introduction
- **Chapter 2.** Improving contribution of pharmacists in the management of COPD and asthma in Vietnam
- **Chapter 3.** Hospital pharmacists' interventions to improve inhaler technique for COPD patients in the national program
- **Chapter 4.** Pharmacist-led pharmaceutical care program to improve medication adherence, quality of life and clinical outcomes for COPD patients in the national program
- **Chapter 5.** Educational training to improve knowledge and practice for pharmacists in counselling asthmatic patients in community pharmacy
- **Chapter 6.** Conclusions

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CHAPTER 2. IMPROVING CONTRIBUTION OF PHARMACISTS IN MANAGEMENT OF ASTHMA AND COPD IN VIETNAM

1. Prevalence and burden of asthma and COPD in the world and Vietnam

Chronic obstructive respiratory disease (COPD) and asthma are two of leading causes of mortality, morbidity, economic and social burden internationally [1, 2]. According to the new updated report of Global Asthma Network, there are 334 million people suffering from asthma worldwide, with 14% of children and 8.6% of young adults experiencing asthma symptoms globally. The burden of disability is very high, particularly in low- and middle-income countries with the fastest increasing prevalence of asthma [1]. Similarly, the prevalence and mortality of COPD have risen significantly over the past 2 decades [3]. COPD prevalence in the Asia Pacific region was 6.3%, the highest number in comparison to the world [4]. It is estimated that 3 million people died of COPD every year. About 90% of these deaths occur in low- and middle-income countries [4]. The Global Burden of Disease Study projected that COPD will become the third leading cause of death globally in 2020 [2]. More importantly, COPD is placing a heavy financial burden on the healthcare system and on the society of many countries. Total cost for COPD is greater than for other respiratory diseases such as asthma, pneumonia and tuberculosis [5]. In European countries, COPD accounted for 56% (€38.6 billion) of the total direct costs of respiratory diseases. In United State, it is estimated that the direct and indirect costs of COPD are $32.0 billion and $20.4 billion, respectively [2].

In Vietnam, the prevalence of chronic respiratory diseases (COPD and asthma) is also increasing substantially (about 10% of population) [6, 7]. Especially, the prevalence of these diseases in the elderly population is relatively high at nearly 20% [8]. According to the Global Asthma Network, the prevalence of asthma symptoms (i.e., with current wheeze) and severe

symptom (i.e. with severe wheeze) among Vietnamese children of 13-14 year old is higher than the global data and of other countries in the same region (Table 1) [1].

Table 1. Comparison of prevalence of asthma symptoms among some countries (2014)

Country	Asthma ever (%)	Current wheeze (%)	Symptom of severe wheeze (%)
Vietnam	5.0	29.5	9.3
Malaysia	12.0	8.9	3.3
Philippines	20.9	8.4	3.7
Singapore	26.5	11.4	4.7
Thailand	12.0	10.3	5.9
Indonesia	10.8	5.1	2.1
Global Total	12.6	14.1	6.8

The National Program for Management of COPD and Asthma operating for more than 7 years in Vietnam reported that the prevalence of asthma in Vietnam as 3.9% (2011) [9]. For COPD, the prevalence of COPD in Vietnamese patients is the highest in the Asia-Pacific region (6.7%) in comparison with Thailand (5.0%), Singapore (6.3%), Philippines (3.5%), Malaysia (4.7%) and Indonesia (5.6%) [10]. In Vietnam, COPD patients often occupy up to 25% of beds in respiratory departments in hospitals and pose a severe burden to the health care system [11]. In term of the burden of COPD and asthma, it is estimated that these disease account for 5.5% of total DALYs of people aged 60-64 and even higher in older groups. Specifically, COPD and asthma were responsible for 68% and 24% of the total DALYs of lung diseases in Vietnam respectively (2015) [8]. Presently, management of COPD and asthma are among the top healthcare priorities in Vietnam where the smoking rate is high and the number of older persons is on the rise [8, 12].

2. National program for management of asthma and COPD

To prevent and control COPD and asthma in Vietnam, the Ministry of Health (MoH) had set up and implemented a national project since 2010 that included a series of projects focusing on non-communicable diseases [12]. Beside hypertension, diabetes and cancer, the management of COPD and asthma was the latest project. In 2015, Prime Minster of Vietnam had approved the national strategies for prevention and control of non-communicable diseases, 2015-2025 [13]. The latest official document illustrated the efforts and determination of Vietnam in the combating the outbreak of non-communicable diseases including COPD and asthma in the community. The COPD and asthma project's general objectives were to (i) improve people's knowledge about COPD and asthma and their risk factors; (ii) improve the quality of diagnosis, treatment, prevention and management of COPD and asthma at all levels of health facilities; and (iii) reduce the rate of morbidity and mortality from these diseases [12].

The specific objectives of the project are providing training programs for doctors, disease screening for the general population, organizing a scientific conference and developing professional guidance. After 3 years of implementation, there were thousands of doctors, respiratory specialists and technicians trained through the project [11]. They became the new core trainers to delivery further training to health professionals at provincial, district and commune levels. The project also organised scientific conferences on World Asthma Day and World COPD day. More importantly, the project setup and maintained patient clubs for sharing experience among COPD and asthma patients in Bach Mai Hospital, one of the biggest hospitals in Vietnam [12]. Another achievement of the COPD and asthma project is developing and publishing practice guidelines for diagnosis and treatment of COPD [14] and asthma [15]. Following the recommendations in international guidelines, the Vietnamese guidelines included detailed guides for management of both acute episodes and stable periods of the diseases [2, 16].

However, the implementation of COPD and asthma projects faced some challenges. Firstly, there was a shortage of trained human resources with specialized training in COPD and asthma at all level of hospitals including central, provincial and commune levels. This problem was similar to the issues distressing the entire health care system that mentioned previously in Chapter 1. The second issue is the limited and unstable budget allocated for the COPD and asthma projects. Some essential activities depend on the availability of a small fund. There was a long delay for approval of budget plan in many provinces participating in the projects. Other difficulties pointed out in the recent report comprised limitation in access to medications and lack of equipment especially at the commune levels [12].

From the perspective of the pharmacists, the role and the involvement of pharmacists in the projects as experts of using medications need to be explored. Although the national strategies mentioned health care professionals in general, doctors and nurses were subjects who are primarily targeted and have more opportunities to attend training [12, 13]. There is no clearly defined duty of pharmacists in the project except the traditional dispensing with limited patient counselling. Furthermore, there is no specific training program for pharmacists about COPD and asthma in hospitals in order to participate in the project in the future. That means pharmacists are left "outside" the project at all levels. In fact, in the latest report from the MoH about difficulties in running the project, shortage of trained health care human resource is one of the main shortcomings [6, 12]. Considering the increasing rate of COPD and asthma, it is necessary for integrating pharmacists into the project to overcome this skilled work force shortage. It will be a solution to reduce physicians' stress and burden in view of overcrowding hospital situation in Vietnam nowadays.

The involvement of pharmacists should be considered an effective and long-term solution for the revealed difficulties that national projects are facing, particularly the shortage of trained human resources. The question is what are the areas that pharmacists can take part in and how

to demonstrate the value of pharmacists' contribution to COPD and asthma patients. The potential involvement of pharmacists will be discussed in the following sections.

3. The importance of inhaler therapies and inhaler technique for COPD and Asthma management

The importance of inhaler therapy

The inhaler therapy plays a crucial role in management of COPD and asthma. In emergency situations, rapid acting inhaler therapy such as short acting beta agonist can be used for patients with acute bronchospasm which can occur suddenly in asthma patients exposed to triggers. For long term control, preventer or controller inhaler therapy containing long acting substances or corticosteroids is useful for persistent symptoms, improvement of lung function and reduction of severe exacerbations. Besides providing more rapid bronchodilation than both parenteral and oral administration [3], inhaler devices also possess the advantages of delivering medicine directly to the bronchial surface, thus minimising the systemic effects and enhancing the therapeutic ratio.

Among the inhaler devices, pressurised metered dose inhalers (MDI) and dry powder inhalers (DPI) are the most commonly used in clinical practice because of portability and convenience of administration [3]. However, the amount of drug delivered to the lung fluctuates widely and depends highly on inhalation technique of patients [17]. Often, MDIs can only deliver 15% to 60% of actual dose, while DPIs even lower, at just 10% to 30% of labelled dose because of the impacts on oropharynx [3, 18]. Each type of device has its own instructions including the steps that users should correctly follow. If poorly handled or incorrectly used, it will lead to diminished therapeutic effect, resulting in poor control of symptoms and disease management [19, 20].

Incorrect inhaler technique is very common

Unfortunately, a high percentage of patients incorrectly use inhaler devices even in developed countries. The rate of errors reported varies from under 5% to over 90% of patients depending on the devices and study method [19]. More importantly, about one-third of patients committed critical errors that could significantly affect drug disposition to the lung [18, 21]. According to a cross-sectional study of 3811 patients by Molimard et al, 76% of patients made at least one error when handling MDI compared to 49-55% with breath-actuated inhalers [21]. Another observation of 100 hospitalized patients in an US hospital reported that misuse was very common (86% with MDI and 71% with DPI), and the rates of inhaler misuse were similar in COPD and asthma patients [22]. A recent study conducted in 300 patients with COPD and asthma in India, a developing country indicated poor use of inhaler devices with 247 patients (82.3%) making at least one error. Of those, 94.3% used MDI incorrectly and 82.3% misused DPI. Not surprisingly, without instruction from health professionals, all self-trained patients performed poorly in inhaler technique [17].

Although the rate of errors in handling inhaler devices is high, it can be improved by effective interventions, especially pharmacist-led interventions [23-26]. These interventions could also help to improve asthma outcomes, increase the number of patients with controlled asthma and better medication adherence [24, 26]. By using teach-to-goal method in a hospital-based education, Press et al showed that MDI inhaler misuse decreased significantly in comparison with verbal instruction and provision of a copy of written instructions [23]. According to a 6 month-cluster randomized trial conducted in Spain, a pharmacists-led intervention helped patients to improve their inhaler technique. The percentage of patients with correct inhaler technique significantly increased between baseline (19.5%) and intermediate visit (57.0%, $p<0.001$), and between intermediate visit and final visit (75.7%, $P<0.001$) [24]. All patients in another study did benefit from pharmacists' intervention regardless of their

former training experiences. The number of patients that made at least one mistake dropped from 597 to 214 ($p<0.001$) after 4-6 weeks. The average number of errors also declined dramatically from 2.5 to 0.5 per patient ($p<0.001$) [25].

In this respect, there were very few studies on inhaler technique for COPD and asthma conducted in Vietnam [27, 28]. The first study showed the rate of incorrect technique among Vietnamese patients was similar to the rate published in the literature [18, 27]. In a study on MDI, 60 out of 84 (74.6%) COPD and asthmatic patients performed incorrect inhaler technique categorised as unacceptable. Only 6% of patients had perfect technique [27]. However, the study included a relatively small number of COPD and asthmatic patients (n=80). With the increase in the number of patients with these conditions and the importance of inhaler devices in managing COPD and asthma, there is an urgent need to ascertain the rate of errors in inhaler technique, the type of critical errors and factors associated the incorrect use in Vietnamese patients. The data will be invaluable for designing interventions to improve inhaler technique and disease outcomes.

4. The role of medication adherence in COPD and asthma

Concept of adherence

According to WHO, adherence is defined as "the extent to which a person's behaviour – taking medication, following a diet, and/or executing lifestyle changes, corresponds with agreed recommendations from a health care provider" [29]. This definition places emphasis on the difference between adherence and compliance because adherence requires the patient's agreement to the recommendation. It emphasises the patients should be active partners with health professionals in their own care. However, poor adherence is a real challenge in treatment of long-term diseases such as chronic heart diseases or respiratory diseases. In fact, nowadays, poor adherence is an international problem and its consequences include poor health outcomes

and increased health care costs. Due to its impacts, poor adherence of patients requires every health system to develop strategies to meet this challenge. However, to improve patients' adherence, it is necessary to identify contributing factors in order to establish proper interventions [29].

Medication adherence status in COPD and asthma treatment

Being chronic diseases requiring long term treatment, good medication adherence is an essential requirement in the management of COPD and asthma [2, 16]. Good therapeutic adherence not only helps to maximize the effect of therapy, but also enhances the quality of life for patients. Furthermore, direct and indirect cost of treatment will be reduced if patients adhere to their treatment [30, 31]. However, currently, improvement of medication adherence for these diseases is a real challenge in clinical practice. In comparison with other chronic diseases (such as hypertension, diabetes, hyperlipidemia, and depression), the rate of adherence to COPD and asthma treatment is substantial lower [30, 32].

Substantial fluctuation in the reported adherent rate of COPD and asthmatic patients exists depending on assessment and monitoring methods [31-33]. Medication adherence rate in asthmatic patients was reported as only 30-40% in practice, but about 70% in well monitored clinical trials [34]. According to the recent review of medication adherence in asthmatic children in developed countries (USA, Australia, and Netherlands), the adherence rate of inhaler corticosteroids varied widely from 28% to 92%. Among these studies, there were 11 out of 15 studies recording adherence rates under 60%, and 6 under 50% [33].

In term of adherence to COPD treatment, according to a recent review, the adherence rate to therapy in real-life conditions was much lower (10-40%) than the rate reported in the literature (40-60%) and those recorded in clinical trials (70-90%). The review also cited a national survey in Italy where medication adherence was a major issue. There were 7 million

patients with COPD and asthma in Italy, with 1 million patients who had never used spray inhalers, 1.3 million stopped using them and 2.7 million used these drugs intermittently [31]. There are a variety of factors associated with medication non-adherence in patients with COPD and asthma including patient factors, therapeutic factors and social factors**.** For patients with asthma, the fear of adverse events, belief that medication is not working, worrying about addiction were patient-related factors contributing to poor adherence [30]. Whereas, the main factors in COPD patients included older age, educational level, and co-morbidities [30, 32, 35]. Therapeutic regimes also play an important role in patient adherence. Particularly, taking multiple doses of a medication daily reduces adherence in comparison with once daily dosing regimens (from 43% to 23%)[34]. Moreover, medication adherence is significantly hampered by complex technique, time of action, adverse effects and cost of drugs [31, 35]. Additionally, social factors also exert a great influence on adherence to therapy of COPD and asthmatic patients. For example, stigmatization is one of the barriers for asthmatic children. Other researchers also pointed out lack of social support and poor relationship with health care professionals as obstacles to COPD patients' adherence [30, 32, 35].

Assessment of medication adherence is a difficult task in a clinical setting. To date, there is no standardized method for these evaluation for COPD and asthma [34]. Measuring adherence in asthma and COPD is categorized into objective and subjective assessments. The objective measurements include direct observed therapy, dose counting on controller medications (manually or electronically), rate of prescription refills, measurement of drugs or biomarkers in serum**.** These methods are probably more accurate than subjective methods [29]. Normally, these methods are time-consuming, expensive, so not applied commonly in clinical conditions [30, 34]. However, along with development of electronic medical records and prescription, assessment of adherence by prescribed refill record is used frequently in studies and clinical settings. This objective method can be done by pharmacy staff working in the

Pharmacy Department or pharmacies [34]. In practice, subjective methods such as self-report by patients, treatment diary etc., although less accurate than objective measures, are most commonly performed in studies because of less resource requirement in time, man power and money. Additionally, self-report methods may be able to distinguish between intentional and unintentional non-adherence. It also has moderate correlation with electronic monitoring methods [36]. To assess medication adherence, self-report by answering a questionnaire was the most commonly used (37.8%), followed by prescription refill data (32.8%)[32]. Some popular questionnaires used include Morisky Medication Adherence Scale (MMAS), Medication Adherence Rating Scale (MARS for COPD and Asthma), and ASK-20 [30-32]. It is recommended that combining both subjective and objective measures would describe more correctly the status of medication adherence [32].

Medication adherence of COPD and asthmatic patients in Vietnam

In Vietnam, studies on medication adherence have been focused on HIV/AIDS patients using antiretroviral drugs [37] and hypertensive patients [38]. There is a paucity of information about therapeutic adherence status of chronic respiratory diseases such as COPD and asthma. Specifically, there is no publication of these data in the national program. However, a study conducted in 106 children with acute asthma not attending a national program showed worrying results, with 52.2% of patients withdrawing preventing therapy intentionally. Nearly 80% of patients did not follow-up their appointment with doctors [39]. Therefore, the data on adherence status of COPD and asthmatic patients is needed for health care professionals as well as authorities for making policies and a national program. In addition, a thorough analysis of causes and factors contributing to non-adherence should be performed to inform effective intervention in the future.

5. Pharmacists' interventions to improve inhaler technique and medication adherence for COPD and asthmatic patients in Vietnam

After reviewing the literature, inhaler technique and medication adherence play a vital role in the management of COPD and asthma. These are also domains that pharmacists can play an active role and make significant contributions in improvement of quality of life, clinical states and saving costs on the treatments [25, 40, 41]. In Vietnam, interventions in improving inhalation technique and rate of good adherence will be two areas where pharmacists can involve themselves actively to improve quality use of medicine for COPD and asthmatic patients in hospitals and the community.

Improving pharmacists' role in management of COPD and asthma in hospitals

In Vietnamese hospitals, pharmacists rarely take part in counselling for patients with chronic diseases including asthmatic and COPD patients. Besides playing the role as dispensers, hospital pharmacists who spent part of their time as clinical pharmacists focus on providing advice to nurses and physicians. In addition, pharmacists often concentrate on acute diseases such as infectious conditions or patients in ICU departments [42-44]. The counselling role for patients with chronic diseases commonly are being assumed by the physicians or the nurses. Hence, the role of pharmacists in providing cognitive care to patients with chronic diseases is still a missing part in the management of these patients in Vietnam. Particularly, there is a scarcity in evidence of Vietnamese pharmacists' contributions to management of patients with COPD and asthma. Therefore, there is a need to conduct a study to explore the role of Vietnamese pharmacists in counselling for these patients. Examining and improving inhaler technique and medication adherence in patients with COPD and asthma would be potential starting platforms for pharmacists' interventions in Vietnam.

Improving contribution of community pharmacists in management of asthma in pharmacies

As previously mentioned, there is a shortage of studies on community pharmacists' involvement in management of chronic diseases in Vietnam. Previous publications mainly focused on common diseases such as childhood diarrhoea, community respiratory infections [45, 46]; and common medications sold in pharmacies such as contraceptive pills [46], corticosteroids [47], and antibiotics [48, 49]. Medications for chronic diseases are commonly sold in community pharmacies (mainly without prescription). However, there is no information on how these medications (including asthma and COPD medications) are sold to patients and what information is provided to patients by the community pharmacists for using these medications.

Because of diversity in pharmacy education and qualification levels in Vietnam [50], another concern is the capability of community pharmacists in playing the role as a counsellor for patients with chronic diseases such as asthmatic patients. Meanwhile, the Vietnamese Ministry of Health has not yet imposed a formal requirement on continuous professional education for practicing pharmacists. Therefore, it is a pertinent to investigate the current level of knowledge and counselling skills of community pharmacists in asthma and COPD. Then, an educational program to improve capability of community pharmacists in counselling COPD and asthmatic patients can be designed and implemented. Outcomes of the program may potentially show the positive impact of pharmacists' involvement in the management of COPD and asthma in community pharmacy.

Therefore, in the subsequent chapters of this thesis, I will be presenting the findings of studies that were performed in both the hospital and community pharmacies among COPD and asthmatic patients in Vietnam to show the potential contribution of pharmacists to the health care system in Vietnam.

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CHAPTER 3. PHARMACISTS' TRAINING TO IMPROVE INHALER TECHNIQUE OF PATIENTS WITH CHRONIC OBSTRUCTIVE PULMONARY DISEASE IN VIETNAM

Introduction

Chronic Obstructive Pulmonary Disease (COPD), the fourth leading cause of death worldwide, is also major cause of chronic morbidity all over the world, particularly in developing countries. As such, COPD places health care systems under high pressure because of its social and economic burden which are projected to increase in coming decades.[1, 2] In Vietnam, nearly 10% of the population suffer from respiratory diseases;[3] with 4.2% of people over 40 years old affected by COPD due to the high smoking rate and continued exposure to other risk factors. COPD patients occupy approximately 25% of beds in the respiratory wards of the hospitals.[4]

In the management of COPD, inhaler devices play a pivotal role in optimizing the delivery of medicines to the lungs. However, incorrect use of inhalers is very common and subsequently leads to poor control of respiratory diseases, including COPD and asthma.[5, 6] The high prevalence of suboptimal inhaler technique is supported by a recent systematic review. The review found that despite many teaching and training programs available for COPD patients, poor inhaler technique remains common and has not improved over 40 years from 1975 to 2014.[7]

For COPD, the literature supports the vital role of pharmacists in educating and counselling patients.[8, 9] With knowledge of both diseases and medicines, pharmacists can help patients to better understand their condition(s) and the importance of each medication. COPD patients tend to have better medication adherence with pharmacist counselling, subsequently improving their quality of life as well as clinical outcomes.[9] More specifically, previous studies have demonstrated the positive impact of pharmacists on improving inhaler

device technique with COPD and asthma patients. Direct education by pharmacists has been shown to be more effective than other teaching methods, including watching videos and providing inhaler pamphlets.[8]

Although the role of pharmacists in the management of COPD has expanded recently,[8, 10, 11] there are only a few studies that specifically focus on the role of pharmacists in counselling and educating COPD patients in developing countries. Vietnam is a typical example of a developing country where health care resources are heavily constrained and the role of pharmacists limited mainly to dispensing in pharmacies and hospitals. However, in Vietnam there is a national program for the management of asthma and COPD in operation for about 7 years with very limited involvement of pharmacists.[12] With increasing number of COPD patients, individualized counselling for patients is a challenge for the limited number of physicians. The potential contribution of pharmacists to the COPD management program to produce better patient outcome is yet to be explored. Since correct inhaler technique is crucial to delivering positive outcomes in COPD and asthma, the most logical approach would be to assess the role of pharmacists' intervention to improving inhaler technique among patients. Therefore, the objective of our study was to evaluate the impact of pharmacists' training in the improvement of inhaler technique for COPD patients enrolled in the national program for management of asthma and COPD in Vietnam. Besides Vietnam, the results of this current study may be applicable in other countries/jurisdictions in informing clinical pharmacy practice.

Material and Methods

Study participants

The study was conducted in Bach Mai Hospital in Hanoi where a national program for management of COPD has been running for 7 years. All patients recorded in the list of COPD

outpatients attending the COPD program from January to December in 2016 were invited to participate in the study during their monthly medical consultation. To be eligible, the patient needed to satisfy the study inclusion criteria that include: had a diagnosis of COPD by the physician, attended the COPD program at least once per month, and had at least one inhaler medication including a metered dose inhaler (MDI) and/or Turbuhaler (AstraZeneca, Cambridge, England) prescribed for COPD. The exclusion criteria included patients with serious visual, hearing and communication problems; deficit of mental function; at end stage of serious diseases such as cancer; attending other programs related to pulmonary diseases; and unable or unwilling to provide written informed consent. All eligible patients provided their signed consent forms before enrolling in the study.

Study design

The study was designed as a pre- and post-intervention study. The study was approved by the Scientific and Ethics Committee at Bach Mai Hospital and Human Research Ethics Committee at the University of Newcastle, Australia (No: H-2015-0333).

Develop checklist and scoring of inhaler technique

The checklist step of each inhaler device (MDI, and dry powder inhaler Turbuhaler) (Tables 2 and 3) was derived from COPD guidelines,[1, 13] and published literature.[14-16]. In order to assess the use of the inhaler devices quantitatively, we assigned a score to each correct step. As all the steps are considered important to achieving optimal medication delivery, they were, therefore, allocated equal weighting and assigned a score of 1 point each. Hence, the maximum score that patients could attain was 8 points when they used the inhaler devices correctly in every step.

Setting and training description

Participating patients were invited to meet the pharmacists in a counselling room in the hospital after their medical consultation and obtaining their medicines from the hospital pharmacy. During the pharmacist's counselling, relevant personal data, such as age, gender, education level, and history of smoking were first collected from the patient. Other information including years suffering from COPD, years enrolled in the national program, and the level of COPD by GOLD classification, [1] was obtained from patient's medical records.

Training description: Face-to-face training was then conducted, with one patient to one pharmacist. Patients were asked to demonstrate their inhaler technique on placebo inhaler devices (the same devices as prescribed by their physician) in front of the pharmacist. If the patient made any mistakes, the pharmacist would correct and explain why the missing step(s) were important. The pharmacist then demonstrated to the patient every inhaler step, both verbally and physically, by using the placebo inhalers. Patients were requested to perform the technique again until they could demonstrate all steps correctly ("teach back"). The training was applied every month in the first 3 months, then repeated at the 6th month and 12th month.

Sticking reminder label: If the patients made any mistake, one additional reminder label (Box 1) that included a summary of the steps was stuck onto their inhaler device(s). Pharmacists made sure that patients were able to read the label.

Box 1. Reminder label of inhaler technique

MDI	Turbuhaler
1. REMOVE CAP **2. SHAKE WELL** **3. BREATHE OUT** **4. BREATHE IN + PRESS CANISTER AND CONTINUE BREATHE IN SLOWLY AND DEEPLY** **5. HOLD BREATH 5 SECONDS**	**1. REMOVE CAP** **2. ROTATE GRIP UNTIL HEAR "CLICK"** **3. BREATHE OUT** **4. BREATHE IN STRONGLY AND DEEPLY** **5. HOLD BREATH 5 SECONDS**

Assess patients' technique: Pharmacists would assess inhaler technique by recording and scoring the correct step(s) before the training (T0), then re-assessing the patients' inhaler technique after 1 month (T1), 3 months (T2), 6 months (T3) and 12 months (T4) from baseline evaluation.

Outcomes: The three outcomes used to assess the impact of training were: (1) percentage of patients having "correct technique" that was achieved when patients performing all the steps correctly, (2) number of patients having improvement in each step, and (3) score technique improvement.

Statistical Analysis

The relevant patient information as well as the inhaler technique scores were analysed by using description statistics and expressed as percentages where appropriate. One-way ANOVA (with post-hoc test) and t-test were applied to identify the difference among mean of scores at the different time points. McNemar test was used for determining the difference of dichotomous dependent variables between 2 groups in pre-post intervention study. Statistical significance was set at p value ≤ 0.05 (two- tailed). All data were analysed with SPSS version 22.0 (IBM Corporation©).

Results

Sociodemographic and disease-related characteristics of study patients

Most of the participating COPD patients were elderly subjects with a mean age of 66.6 (±8.2) years (Table 1). As expected, there were more male patients due to the high rate of smoking in Vietnamese males (84.4%). Nearly 70% of patients had an education level of high school or below. In addition, the majority of participants had COPD for more than 3 years. Over 90% of patients were at Gold C and D classifications, the most severe levels of the disease. [1] Nearly

80% of patients had attended the program for more than 1 year. The number of participants at the various time points is detailed in Figure 1.

Table 1. Sociodemographic and disease-related characteristics of patients participating the study

Age in years	Mean (±SD)	66.6 (±8.2)
Gender	Male	178 (84.4%)
	Female	33 (15.6%)
Comorbidity	Yes[(a)]	134 (63.5%)
	No	77 (36.5%)
Education level	Below high school	69 (32.7%)
	High school	75 (35.5%)
	Above high school	67 (31.8%)
Ever a smoker	Yes	171 (81.0%)
	No	40 (19.0%)
Years suffering of COPD	≤ 3 yrs	50 (23.7%)
	>3-5 yrs	42 (19.9%)
	> 5 yrs	119 (56.4%)
GOLD classification	Gold B	12 (5.7%)
	Gold C	49 (23.2%)
	Gold D	150 (71.1%)
Years attending the COPD program	< 1 yr	51 (24.2%)
	1-3 yrs	92 (43.6%)
	>3-5 yrs	56 (26.5%)
	> 5 yrs	12 (5.7%)

Note: [(a)]: Hypertension (25.6%), osteo-related conditions (20.2%), gastrointestinal disorders (10.7%), hyperlipidemia (8.3%), diabetes type 2 (6.0%), other cardiovascular diseases/conditions (13.7%), other minor ailments (15.5%).

Abbreviations: GOLD classification from Global Initiative for Chronic Obstructive Lung Disease guideline, COPD: Chronic Obstructive Pulmonary Disease; SD: standard deviation, yr: year

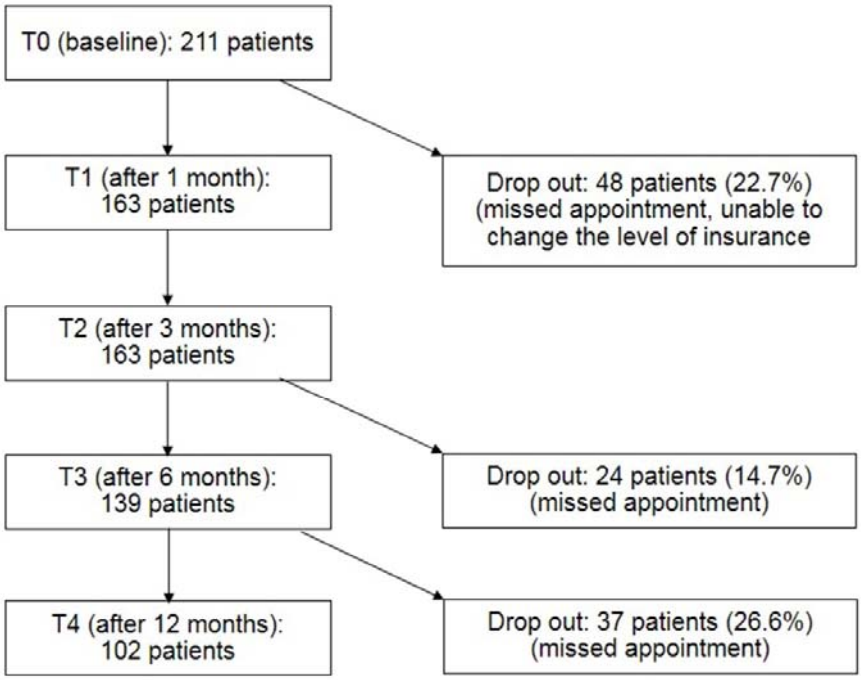

Figure 1 Flow diagram for the time of assessing technique and drop out rates

Improvement of inhaler technique at each step

Before training (T0), the percentages of patients demonstrating correct inhaler technique were 13.9% and 20.5% for MDI and Turbuhaler, respectively (Figure 2). The training took 6 minutes on average for the first counselling session and 3 minutes after the first time. After training with pharmacists (Figure 2), the percentage of patients performing the technique correctly increased from 13.9% and 20.5% (T0) to 56.8% and 61.9% (T3) for MDI and Turbuhaler respectively. When the period between the training was longer (6 months from T3 to T4), the percentage of patients having correct technique decreased from over 61.9% to 48.7% with Turbuhaler (p=0.302). For MDI, after 6-month period, the percentage of patients having correct technique decrease significantly from 58.6% to 33.3% (p=0.002).

Regarding the specific steps, as shown in Table 2 and Table 3 (T0), no mistakes were observed for Step 1, however mistakes were recorded for every other step thereafter. The most

common mistake for both inhaler devices was Step 4 (breathe out), with <30% of patients remembering to perform this step. The second common mistake was Step 6 for both MDI and Turbuhaler. After training, the number of patients that performed each step correctly increased significantly.

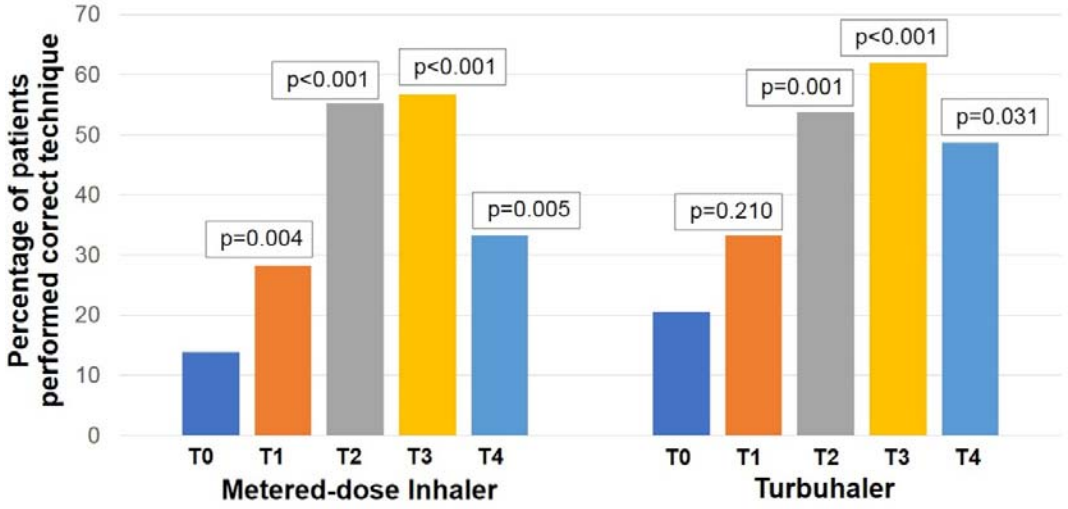

Figure 2. Comparison of the percentage of patients performing the "correct inhaler technique" over the study period

Note: T0 (baseline), T1 (after 1 month), T2 (after 3 months), T3 (after 6 months), T4 (after 12 months). p: p value of McNemar test determined the difference of the percentage of patients that performed the correct technique (all the correct steps) between time point T1, T2, T3, T4 and T0.

Table 2. Number of patients that showed technique improvement in each step with MDI

Steps of usage MDI	**T0 (n=208)**	**T1 (n=163)**	**T2 (n=163)**	**T3 (n=139)**	**T4 (n=102)**
Step 1. Remove the cap	208 (100)	163 (100)	163 (100)	139 (100)	102 (100)
Step 2. Shake inhaler well	157 (75.5)	157 (96.3) p<0.001	155 (95.1) p<0.001	131 (94.2) p<0.001	96 (94.1) p=0.001
Step 3. Hold inhaler upright	192 (92.3)	159 (97.5) p=0.057	159 (97.5) p=0.057	138 (99.3) p=0.012	101 (99.0) p=0.008
Step 4. Breathe out all the way	50 (24.0)	71 (43.6) p<0.001	104 (63.8) p<0.001	88 (63.3) p<0.001	48 (47.1) p=0.002

Step 5. Place the inhaler mouthpiece between your lips (and teeth)	195 (93.8)	158 (96.9)	162 (99.4)	139 (100)	102 (100)
Step 6. Prime the inhaler just after starting a very slow and very deep breath in (until the lung is full)	102 (49.0)	109 (66.9) p=0.003	141 (86.5) p<0.001	130 (93.5) p<0.001	75 (73.5) p<0.001
Step 7. Remove the inhaler from your mouth and hold your breath 5 seconds (or as long as possible)	156 (75.0)	159 (97.5) p<0.001	161 (98.8) p<0.001	134 (96.4) p<0.001	80 (78.4) p=0.864
Step 8. Breathe out slowly	206 (99.0)	162 (99.4)	162 (99.4)	139 (100)	102 (100)

Note: T0 (baseline), T1 (after 1 month), T2 (after 3 months), T3 (after 6 months), T4 (after 12 months), p: p value of McNemar test for comparison of percentage between time point T1, T2, T3, T4 and T0 (analysed when appropriate)

Abbreviation: MDI: metered-dose inhaler

Table 3. Number of patients that showed technique improvement in each step with Turbuhaler

Steps of usage Turbuhaler	**T0 (n=83)**	**T1 (n=63)**	**T2 (n=52)**	**T3 (n=42)**	**T4 (n=39)**
Step 1. Remove mouthpiece cover	83 (100)	63 (100)	52 (100)	42 (100)	39 (100)
Step 2. Keep the inhaler upright	81 (97.6)	63 (100)	52 (100)	42 (100)	39 (100)
Step 3. Rotate the grip counter clockwise and then back until a “click” is heard	79 (95.2)	63 (100)	52 (100)	42 (100)	39 (100)
Step 4. Breathe out normally and away from mouthpiece	23 (27.7)	31 (49.2) p=0.078	33 (63.5) p<0.001	30 (71.4) p<0.001	20 (51.3) p=0.167

Step 5. Place the inhaler mouthpiece between your lips (and teeth)	81 (97.6)	63 (100)	52 (100)	42 (100)	39 (100)
Step 6. Inhale forcefully and deeply	66 (79.5)	50 (79.4) p=0.629	45 (86.5) p=0.549	36 (85.7) p=0.998	36 (92.3) p=0.016
Step 7. Hold breath for at least 5 seconds	67 (80.7)	60 (95.2) p=0.006	52 (100) p<0.001	42 (100) p=0.002	35 (89.7) p=0.344
Step 8. Exhale normally but not through inhaler	80 (96.4)	63 (100)	52 (100)	42 (100)	39 (100)

Note: T0 (baseline), T1 (after 1 month), T2 (after 3 months), T3 (after 6 months), T4 (after 12 months), p: p value of McNemar test for comparison of percentage between time point T1, T2, T3, T4 and T0 (analysed when appropriate)

Improvement of mean inhaler technique scores

Evaluation of the mean inhaler technique scores with MDI across the five assessment time points showed mean scores of 6.09, 6.97, 7.49, 7.49 and 6.93 for T0 (baseline), T1 (after 1 month), T2 (after 3 months), T3 (after 6 months) and T4 (after 12 months), respectively (Figure 3). Overall, there was a significant difference in patients' inhaler technique scores after training ($p < 0.001$). In particular, significant increases were observed at 1, 3, 6 and 12 months after training in comparison to baseline values (T0). Results for the Turbuhaler technique (Figure 4) were similar to those of the MDI technique. However, significant increases in scores were only observed at 3 months ($p=0.001$) and 6 months ($p<0.001$) after training when compared to baseline values (T0). For both inhaler devices, there was a decrease in the mean technique score from the 6^{th} month (T3) to the 12^{th} month (T4).

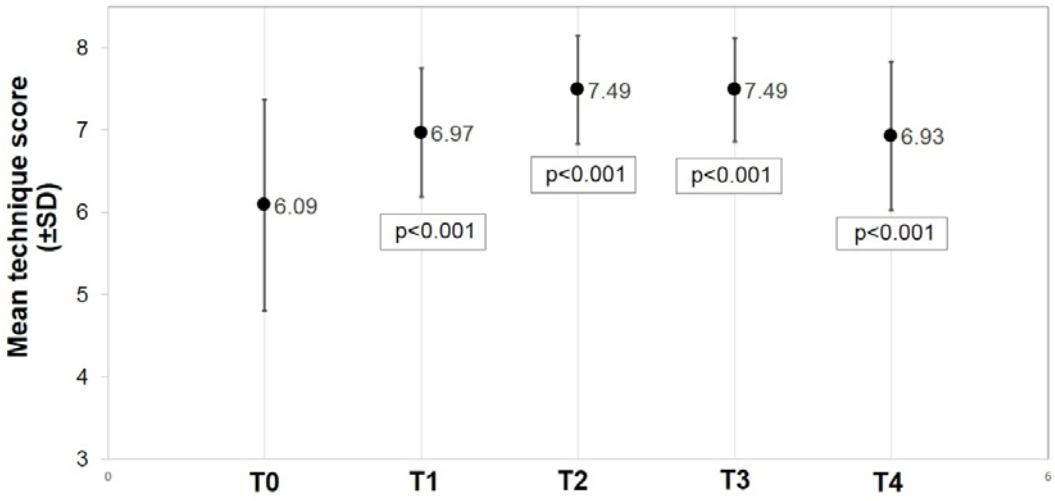

Figure 3 Comparison of the mean technique score for MDI across the study period.

Note: T0 (baseline), T1 (after 1 month), T2 (after 3 months), T3 (after 6 months), T4 (after 12 months), p: p value of ANOVA and post-hoc test in comparison of the score between after the training (T1, T2, T3, T4) and before training (T0)

Abbreviation: SD: standard deviation

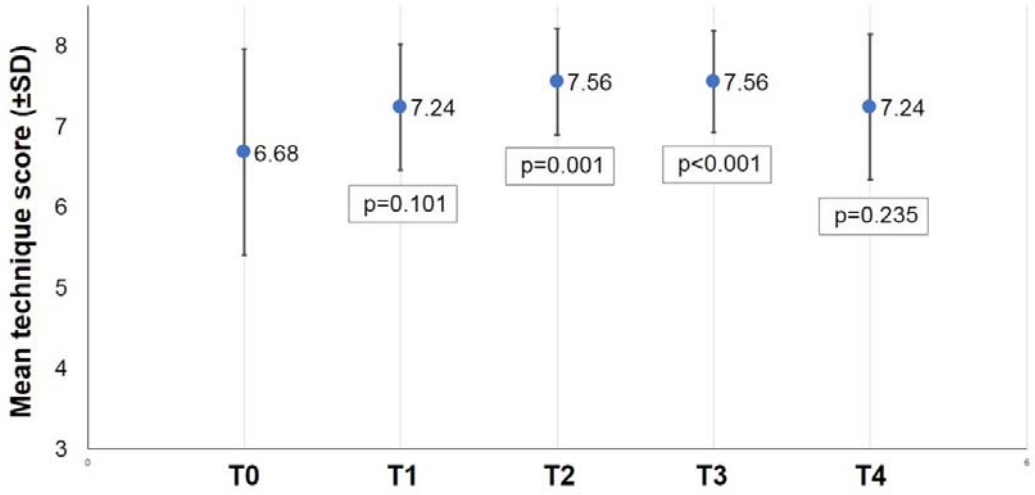

Figure 4 Comparison of the mean technique score for Turbuhaler across the study period.

Note: T0 (baseline), T1 (after 1 month), T2 (after 3 months), T3 (after 6 months), T4 (after 12 months), p: p value of ANOVA and post-hoc test in comparison of the score between T1, T2, T3, T4 and T0

Abbreviation: SD: standard deviation

Technique scores based on patient demographics

Baseline values (T0, Table 4) showed a significant difference in technique scores among different age groups of participants (p=0.01), with younger patients having higher overall scores. However, the scores of all patients increased significantly after attending the training program and no significant differences were observed after the T2 assessment time point. Before the training, years of suffering COPD and attendance in the national program were two factors that influenced the inhaler technique score (T0, Tables 5 and 6). More specifically, patients that participated in the program for longer or those that have suffered COPD for a longer duration had higher baseline scores ($p<0.05$). However, the technique scores improved in all patient sub-groups after the training, with no significant difference between the scores in these groups ($p>0.05$) (T1-4, Tables 5 and 6).

Table 4. Patients' age and improvement of technique score with MDI

Time	< 60 years (mean (±SD))	60-75 years (mean (±SD))	> 75 years (mean (±SD))	p
T0	6.77 (0.94)	6.00 (1.25)	6.10 (1.96)	0.01
T1	7.19 (0.75)	6.96 (0.81)	6.85 (1.07)	0.32
T2	7.50 (0.65)	7.45 (0.71)	7.05 (1.11)	0.04
T3	7.78 (0.42)	7.41 (0.74)	7.39 (0.79)	0.07
T4	6.81 (0.91)	6.93 (0.90)	7.00 (0.91)	0.84

Note: T0 (baseline), T1 (after 1 month), T2 (after 3 months), T3 (after 6 months), T4 (after 12 months), p: p value of ANOVA test for comparison of mean score between age groups

Abbreviation: SD: standard deviation

Table 5. Years of suffering COPD and improvement of technique score with MDI

Time	≤ 3 years (mean (±SD))	>3-5 years (mean (±SD))	> 5 years (mean (±SD))	p
T0	5.69 (1.50)	5.90 (1.16)	6.31 (1.22)	0.01
T1	6.97 (0.80)	6.97 (0.91)	6.99 (0.83)	0.98
T2	7.44 (0.56)	7.29 (0.86)	7.44 (0.80)	0.63
T3	7.35 (0.84)	7.26 (0.66)	7.58 (0.67)	0.08
T4	6.95 (1.02)	7.00 (0.98)	6.88 (0.83)	0.85

Note: T0 (baseline), T1 (after 1 month), T2 (after 3 months), T3 (after 6 months), T4 (after 12 months), p: p value of ANOVA test for comparison of mean score between groups with different period of suffering COPD.

Abbreviation: SD: standard deviation

Table 6. Years of attending the program and improvement of technique score with MDI

Time	< 1 year (mean (±SD))	1-3 years (mean (±SD))	>3-5 years (mean (±SD))	> 5 years (mean (±SD))	p
T0	5.65 (1.64)	6.14 (1.08)	6.30 (1.22)	6.42 (1.38)	0.04
T1	7.14 (0.83)	6.91 (0.87)	6.93 (0.77)	7.38 (0.74)	0.33
T2	7.45 (0.67)	7.30 (0.82)	7.48 (0.75)	8.00 (0.00)	0.08
T3	7.62 (0.57)	7.36 (0.78)	7.49 (0.68)	7.83 (0.41)	0.25
T4	7.10 (0.85)	6.96 (0.95)	6.78 (0.85)	6.60 (0.89)	0.54

Note: T0 (baseline), T1 (after 1 month), T2 (after 3 months), T3 (after 6 months), T4 (after 12 months), p: p value of ANOVA test for comparison of mean score between groups with different period of attending the program.

Abbreviation: SD: standard deviation

Discussion

To the best of our knowledge, the present study is the first to evaluate the role of pharmacists in educating COPD patients to correctly use their inhaler devices in a developing country. Our results showed that COPD patients' inhaler technique improved significantly after receiving training from pharmacists. In our study, over 85% of MDI users and 80% of DPI-Turbuhaler users in the national COPD program used inhaler devices incorrectly prior to training (T0). This is consistent with other published findings in COPD patients including those in developed countries.[7, 15, 17] Thus, our results have highlighted that mishandlings of inhaler medications are common among COPD patients, and as shown in previous studies, is likely to negatively impact on COPD management.[15, 18-20]

Participants made the most errors in Steps 4, 6 and 7 for both inhaler devices. Step 4 (breathe out all the way) is important for helping to deposit drug molecules deeper into the airways, but recorded the highest error rate in our study (>70% of patients). Likewise, Lavorini et al showed that "No exhalation before inhalation" was the most frequent error made by asthma and COPD patients using all common DPIs (including Turbuhaler);[21] and 50% of users not exhaling before actuation when using MDI in another study of 1664 patients conducted by Melani et al.[5] Step 6 focusses on the method of inhalation. Whilst all MDI require users to breathe in slowly at the same time as pressing down on the inhaler, DPIs need forceful and deep inspiration.[14, 16] Over 50% of our study patients had problems with this coordination. In fact, the lack of hand-lung synchronization is the main error reported for using MDI; and is considered as the most difficult step for patients, especially the elderly.[6, 14, 17, 19] More patients performed Step 6 correctly using DPI Turbuhaler devices (70.1%) compared to MDI (47.1%) in our study. This again is consistent with other studies,[14, 15, 22, 23] where significantly more patients made more critical errors using MDI than patients using other devices, including Turbuhaler.[15] Unlike MDI, there is no need to coordinate the delivery of

aerosol drug with an inspiration with DPIs. Therefore, correctly using DPIs is relatively easier than using MDI.[14, 22, 23]

After training with pharmacists, our results showed significant improvement in inhaler technique of COPD patients in both steps and scores. Patients that correctly performed the step checklists increased after each visit with the pharmacist. More importantly, patients made less mistakes in Steps 4, 6 and 7, the most error-prone steps before training. Furthermore, there was a dramatic increase in patients' overall technique scores when using both MDI and DPI Turbuhaler. The results of subgroups analysis also illustrated that the pharmacists training made equal impact upon inhaler technique in different patient subgroups (Tables 4, 5, and 6). These findings are consistent with other published literature.[9, 16, 24-27]

Quantitative scoring of the inhaler technique was used in this study to facilitate simpler and more consistent evaluation. Health workers and caregivers just need to check the steps by scoring 1 point for each correct step and 0 for each incorrect step. Even family members of patients can use the checklist to score and report to health professionals. Scoring inhaler technique has also been utilized in previous studies.[9, 16, 24, 25] These studies allocated points to each inhaler technique step based on its level of significance in the overall process.[15, 28] Hence, it is critical to define which step (classified as critical step) would lead to little or no medication reaching the lungs if performed incorrectly.[15, 17] However, there is no clear agreement on the importance of each step as shown by the many checklists used in the assessment of inhaler technique in published studies and clinical practice. A review by Basheti et al compared 24 checklists for the appropriate use of DPI-Turbuhaler, and found substantial variation in the number of steps listed (ranging from 3 to 14 steps), as well as different critical steps identified in 10 of the checklists.[28] Besides likely to create inconsistency between evaluators, focusing on critical steps may also lead assessors to ignore "less important" steps that may significantly affect drug delivery.[17] Therefore, equal scoring of the inhalation steps

used in our study appears to be a more suitable method for its simplicity and consistency when applied in clinical practice.

Pharmacists are important health educators and are in the best strategic position in counselling patients during the patient's clinical consultation process. Medication counselling by pharmacists has been demonstrated to be more effective than other methods such as watching videos or reading pamphlets.[8] However, in developing countries like Vietnam, pharmacists are widely under-utilized in the health care team with their role mainly limited as a dispenser of medicines. Therefore, our findings provide evidence of their valuable contribution to improving inhaler technique in COPD patients. With the increasing prevalence of COPD in Vietnam and the low doctor-to-patients ratio, involvement of pharmacists would be a solution for the lack of health professionals and a strategy to better employment of an under-utilized resource in the overcrowded hospitals.[12, 29]

The training applied in our present study was specially chosen to cater for COPD patients who are generally older and have additional comorbidities. The first method was face-to-face training of COPD patients by the pharmacists. "One pharmacist-to-one patient" training has been described as the best method to teach patients how to use inhalers properly.[16, 30] Secondly, "Teach-back" has also been shown to be an effective method for COPD patients by evaluating their understanding of the inhalation technique as they practiced using the inhaler in front of pharmacists.[30] Thirdly, our study is the first to apply the use of "inhaler reminder labels" for COPD patients. This method has previously been applied successfully in other studies for asthma patients using DPI Turbuhaler and Diskus.[16] The label helped patients to better remember the correct technique.[27] This was considered a better method than providing patients with other take-home materials such as video instructions or medication leaflets containing excessive information.[16, 27] However, unlike previous studies, we used labels with larger font size and patients were asked to confirm that they could read the label clearly.

Lager font size would increase noticeability and readability, and has been shown to be effective in improving compliance. [31, 32] Hence, our reminder label with larger font size may also contribute positively to better inhaler technique in combination with direct training.

Repeated training is crucial to maintaining proper inhaler technique and is recommended by respiratory experts and guidelines.[1] However, there is no consensus of exact period of time for regular checks and training for assuring proper maintenance. It has been suggested that checks should be performed every 1 to 3 months or every time patients visit their doctor or pharmacy.[24] In our study, we initially reviewed the patients' technique intensively every month for the first 3 months, and then at 6 months and 12 months thereafter. Intensive training at the beginning of inhaler use is very important, as it is difficult for COPD patients to remember all of the steps at the first meeting. [33] Furthermore, forgetfulness commonly occurs especially in older patients. [34] Thus, it is necessary to repeat the checking and training process for inhaler technique along with other outcomes of COPD. Our findings suggest that complete training should be repeated every 3 months after the first intensive period, as our study showed an increased number of patients making mistakes and a decrease in technique scores for both inhaler devices 6 months after intensive training (i.e., T3 to T4 of our study time points). Therefore, this suggested that a 3-month period would be the optimal time for re-training after the initial intensive training.

Our study also showed the application of these pharmacists' interventions for COPD patients are feasible as part of pharmacists' everyday duties. The average time for the first meeting was approximately 6 minutes, which included time for checking inhaler technique, pointing out incorrect steps, asking the patient to demonstrate inhaler use again, and sticking a technique label to the device if necessary. The duration of the second and third visit gradually decreased to approximately 3 minutes. The time taken in our study is similar to the time of intervention recorded in other studies.[16] For example, Basheti et al. reported a median time

taken for inhaler technique intervention of 5 minutes (± 2min) for the first meeting, and 2 minutes and 1 minute for the second and third visit, respectively.[16]

This is the first study that has evaluated the impact of pharmacist-led training to improving the proper use of inhaler devices for COPD patients in a developing country. We have developed a comprehensive method that is suitable for training a diversity of population groups, including older patients, in order to optimize effectiveness of inhaler devices. We have also applied an unbiased and simple scoring method for assessing outcomes, as well as identified an appropriate period of time for re-training patients to maintain correct inhaler technique. There are several limitations in our study. Firstly, the study only included patients enrolled in the national program, which may over-estimate the ability of the general COPD patients who would have less support than those in the program. Secondly, the study has not yet correlated the improvement in inhaler technique with clinical outcomes. Clinical improvement depends on many factors such as drug selection, patient compliance, control of other risk factors such as the environment and nutrition. Nevertheless, proper inhaler use has been shown to be closely related to improving clinical outcomes of COPD patients [5] Thirdly, the relative high drop-out rate (~ 50%) may also affect the robustness of our study results. However, we had also analysed the data only for the patients who were assessed at every assessment point and the results did not differ. Furthermore, we also compared the demographic and other characteristics between drop-out and non-dropout groups, and again found no significant difference except in age. Although the drop-out group was slightly younger, the mean ages of both groups were similar to the total group. An inference from these additional analyses would be the high drop-out rate did not affect our final results.

Conclusion

Our study showed that a pharmacist-led comprehensive inhaler technique intervention program using an unbiased and simple scoring system can significantly improve the inhaler techniques in COPD patients. We also identified an optimal time period between training and re-training for maintaining correct inhaler technique. Our model of pharmacist-led training should be considered as an effective solution for managing COPD patients, and better utilization of human resources in healthcare especially in a developing country like Vietnam.

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Author contributions

All authors contributed to tool development and study design, data analysis, drafting and revising the manuscripts. All authors also agree to be responsible for all aspects of the study.

Disclosure

The authors report no conflicts of interest in this work.

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CHAPTER 4. IMPACT OF PHARMACEUTICAL CARE IN THE IMPROVEMENT OF MEDICATION ADHERENCE AND QUALITY OF LIFE FOR COPD PATIENTS IN VIETNAM

Introduction

Chronic Obstructive Pulmonary Disease (COPD) is the fourth leading cause of mortality worldwide and is also a major cause of chronic morbidity all over the world, particularly in developing countries [1]. Hence, COPD places health care systems under high pressure as its social and economic burden are projected to increase in coming decades [1, 2]. In Vietnam, 4.2% of the population over 40 years old is affected by COPD due to the high smoking rate and continued exposure to other risk factors [3]. In non-smoking individuals, the prevalence of COPD in rural and urban areas of Vietnam is 6.9%, which is higher than other countries in the same region [4]. Consequently, COPD patients occupy approximately 25% of beds in the respiratory wards of the hospitals [3], indicating patients' health related quality of life is severely affected by COPD [4].

In the management of COPD, good inhaler technique and medication adherence play a pivotal role, including significantly reducing the risk of death and hospital admissions [5]. However, the rate of adherence to COPD medications is substantial lower in comparison to other chronic diseases, such as hypertension, diabetes, hyperlipidemia and depression [6, 7]. Furthermore, the adherence rate to COPD therapy in "real-life" conditions is considered to be much lower (10-40%) than the rate reported in the literature (40-60%) and those recorded in clinical trials (70-90%) [8]. The adverse consequences of non-adherence to medications for COPD patients have clearly been demonstrated in literature. Poor adherence to COPD medications was strongly associated with increased respiratory symptoms, mortality, hospitalization, medical costs and decreased patients' quality of life [5, 9, 10]. Therefore,

improving the rate of patients adhering to their treatment is the top priority in all COPD intervention programs [10].

The literature supports the role of pharmacists in educating and counselling patients with COPD [11, 12]. With a knowledge of both diseases and medications, pharmacists are ideally positioned to help patients better understand their condition(s) and the importance of each medication. Pharmacists' counselling and intervention have been shown to improve medication adherence, quality of life and clinical outcomes for COPD patients [12]. In particular, pharmaceutical care programs designed and led by pharmacists have demonstrated the positive impact on medication adherence for this cohort of patients [13].

Although the role of pharmacists in the management of COPD has expanded recently [11, 14, 15], there are only a few studies that specifically focus on the role of pharmacists in counselling and educating COPD patients in developing countries. Vietnam is a typical example of a developing country where health care resources are heavily constrained, and the role of pharmacists is limited mainly to dispensing in community pharmacies and hospitals. Although there is a national program for the management of asthma and COPD in Vietnam in operation for approximately 7 years, currently there is very limited involvement of pharmacists in this national program [16]. Proper management of COPD is a constant challenge in Vietnam owing partly to the limited number of physicians, and this is only going to get more difficult with the rapidly increasing number of COPD patients. In this respect, the potential contribution of pharmacists to the national COPD management program in Vietnam to produce better patient outcomes is yet to be explored. Therefore, the objective of our study was to evaluate the impact of a pharmaceutical care program in the improvement of medication adherence, quality of life and clinical outcomes for COPD patients enrolled in the national COPD management program in Vietnam.

Methods

Study design

A pre- and post-intervention study design was used. This was approved by the Scientific and Ethics Committee at Bach Mai Hospital and the Human Research Ethics Committee at the University of Newcastle, Australia (No: H-2015-0333).

Study participants

The study was conducted in Bach Mai Hospital in Hanoi where the national COPD management program has been running for approximately 7 years. All patients that were recorded on the list of COPD outpatients participating in the national COPD management program from January to December in 2016 were invited to participate in the study during their monthly medical consultation. To be eligible, patients needed to satisfy the study inclusion criteria that included the following: had a diagnosis of COPD by the physician and attended the COPD program at least once per month. The exclusion criteria included patients with serious visual, hearing and communication problems; deficit of mental function; at end stage of serious diseases such as cancer; attending other programs related to pulmonary diseases; and unable or unwilling to provide written informed consent. All eligible patients provided their signed consent forms before enrolling in the study. From these participants, socio-demographic information including age, gender, comorbidity, education level, smoking history, and COPD severity were collected. Participants of this study were the same as those participating in the inhaler technique training program reported in our recent published study [17].

Pharmaceutical care program

Medication intervention and counselling by the hospital pharmacists were conducted after COPD patients were examined by the physicians. The applied pharmaceutical care program was composed of inhaler technique training as well as individual counselling about COPD and the associated medications. Inhaler technique training focused on correct inhalation technique and the effective use and storage of inhaler devices. The effectiveness of the inhaler technique training was reported in our recent publication [17]. During the individual counselling, patients were provided information about the pathophysiology of COPD and the rationale of the medications. The pharmacists would also emphasize the importance of adhering to the medications used for long-term maintenance therapy. In addition, pharmacists would answer questions and provide information related to any potential side effects. The inhaler technique training took an average of 3 minutes for each patient [17]. Counselling time per patient was approximately 5-10 minutes depending on the number of questions raised by the patients.

Measures and instruments

Morisky Medication Adherence Scale

The level of medication adherence was assessed using the Morisky Medication Adherence Scale (MMAS) in Vietnamese (Table 1). The questionnaire and scoring method were used under a signed contract with the author of the scale. The medication adherence scale has 3 levels: “good adherence” (score = 8); “intermediate adherence” (6 ≥ score < 8); and “poor adherence” (score < 6) [18-20].

Table 1. Morisky Medication Adherence Scale (MMAS)

	Questions	Yes	No
1	Do you sometimes forget to take your COPD medication(s)?		
2	People sometimes miss taking their medications for reasons other than forgetting. Thinking over the past two weeks, were there any days when you did not take your COPD medication(s)?		
3	Have you ever cut back or stopped taking your medication(s) without telling your doctor, because you felt worse when you took it?		
4	When you travel or leave home, do you sometimes forget to bring along your COPD medication(s)?		
5	Did you take your COPD medication(s) yesterday?		
6	When you feel like your COPD is under control, do you sometimes stop taking your medication(s)?		
7	Taking medication(s) every day is a real inconvenience for some people. Do you ever feel hassled about sticking to your COPD treatment plan?		
8	How often do you have difficulty remembering to take all your medication(s)? (Please circle your answer below) Never/Rarely……....4 Once in a while……3 Sometimes……....2 Usually…….1 All the time……..0		

EuroQol-5 dimensions-5 levels (EQ-5D-5L)

Health-related quality of life (HRQOL) was measured using EuroQol-5 dimensions-5 levels (EQ-5D-5L). The Vietnamese version was provided by the developers. The five dimensions of EQ-5D-5L with five levels of response can be combined to 3125 possible health states. Patients were also asked to self-rate their health on a 20 cm vertical, visual analogue scale called EQ-VAS with endpoints labelled ‘the best health you can imagine’ and ‘the worst health you can imagine’ [21]. Each health state can be transformed to one “utility score” by using the interim

scoring for EQ-5D-5L. Because of the unavailability of a Vietnamese crosswalk value set, the current study used the Thailand value set with the score ranging from -0.451 to 1 [21, 22]. Patients' adherence and HRQOL were evaluated at baseline, 3 months, 6 months and 12 months after pharmacists' intervention.

Clinical score

The scores of 5 main symptoms (cough, sputum, wheezing, dyspnea, and chest tightness) were assessed by respiratory physicians when examining patients at their monthly appointments (Table 2). The overall clinical score was calculated by adding together the individual scores for each of the symptoms.

Table 2. Scoring method for calculating symptom score of patients

SCORE	0	+1	+2
Cough	No cough	Yes, but not much	Yes, a lot
Sputum	No sputum	Yes, but not much	Yes, a lot
Wheezing	No wheezing	Yes, but not much	Yes, a lot
Dyspnea	No dyspnea	Yes, but not much	Yes, a lot
Chest tightness	No chest tightness	Yes, but not much	Yes, a lot

Statistical Analysis

The socio-demographic information and disease-related characteristics of patients were analyzed using descriptive statistics and expressed as percentages where appropriate. One-way analysis of variance with post-hoc test and paired-sample t-test were applied to identify the difference among mean of adherence, quality of life and clinical scores at different time points. The McNemar's test was used to determine the difference between percentages of adherence levels before and after intervention. Statistical significance was set at p-value ≤ 0.05. All data were analysed using SPSS version 22.0 (IBM Corp, USA).

Results

Socio-demographic and disease-related characteristics of study participants

The majority of the study participants were elderly patients with a mean age of 66.6 (±8.2) years (Table 3). As expected, there were more male patients due to the high rate of smoking in Vietnamese males (84.4%). Nearly 70% of patients had an education level of high school or lower. In addition, the majority of participants had COPD for more than 3 years. Over 90% of patients were at Gold C and D classifications, which are the most severe levels of the disease. Nearly 80% of patients had attended the national COPD management program for more than 1 year.

Table 3. Socio-demographic and disease-related characteristics of study participants

Age in years	Mean (±SD)	66.6 (±8.2)
Gender	Male	178 (84.4%)
	Female	33 (15.6%)
Comorbidity	Yes	134 (63.5%)
	No	77 (36.5%)
Education level	Below high school	69 (32.7%)
	High school	75 (35.5%)
	Above high school	67 (31.8%)
Ever a smoker	Yes	171 (81.0%)
	No	40 (19.0%)
Years suffering of COPD	≤ 3 yrs	50 (23.7%)
	>3-5 yrs	42 (19.9%)
	> 5 yrs	119 (56.4%)
GOLD classification	Gold B	12 (5.7%)
	Gold C	49 (23.2%)
	Gold D	150 (71.1%)
Years attending the COPD program	< 1 yr	51 (24.2%)

	1-3 yrs	92 (43.6%)
	>3-5 yrs	56 (26.5%)
	> 5 yrs	12 (5.7%)

Abbreviations: GOLD classification from Global Initiative for Chronic Obstructive Lung Disease guideline; COPD, Chronic Obstructive Pulmonary Disease; SD, standard deviation; yr, year

Improvement in medication adherence

Results showed a significant improvement in the medication adherence scores and levels for COPD patients following participation in the pharmaceutical care program (Tables 4 and 5). At baseline (T0), the mean adherence score was 6.7 out of a maximum of 8.0 using the MMAS. The mean score increased to 6.9 (T1) and 7.4 (T2 and T3) after each following 3-month period ($p<0.001$, Table 4 and Figure 1). Table 5 and Figure 2 show the level of medication adherence based on the MMAS classification. The percentage of study participants with good adherence increased from 37.4% (T0) to 55% (T2) and 53.2% (T3) after 6 and 12 months, respectively. Correspondingly, there was a decrease in the percentage of study participants with poor adherence, with 20.4% at baseline (T0) to less than 1.0% after 12 months. The percentage of study participants with medium adherence fluctuated between 40% and 50% throughout the study period (Table 5).

Table 4. Means of medication adherence score

	T0 (n=211)	**T1 (n=156)**	**T2 (n=140)**	**T3 (n=109)**	**p**
Mean medication adherence score (SD)	6.7 (1.4)	6.9 (1.0)	7.4 (0.8)	7.4 (0.8)	< 0.001
Minimum – Maximum scores	1.5-8.0	4.0-8.0	4.0-8.0	5.0-8.0	

Note: T0, baseline; T1, after 3 months; T2, after 6 months; T3, after 12 months

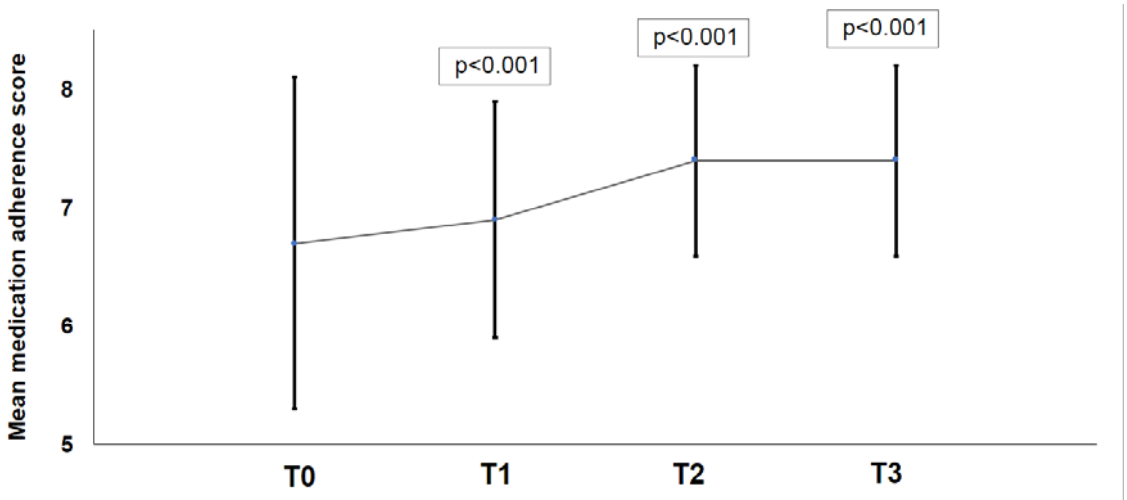

Figure 1 Comparison of the mean medication adherence scores across the study period.

Note: T0 (baseline), T1 (after 3 month), T2 (after 6 months), T3 (after 12 months), p: p value of ANOVA and post-hoc test in comparison of the score between after the training (T1, T2, T3) and before training (T0)

Abbreviation: SD: standard deviation

Table 5. Level of medication adherence as classified by MMAS

Medication adherence level	T0 (n=211)	T1 (n=156)	T2 (n=140)	T3 (n=109)
Good adherence	79 (37.4%)	49 (31.4%)	77 (55.0%)	58 (53.2%)
Medium adherence	89 (42.2%)	89 (57.1%)	58 (41.4%)	50 (45.9%)
Low adherence	43 (20.4%)	18 (11.5%)	5 (3.6%)	1 (0.9%)

Note: T0, baseline; T1, after 3 months; T2, after 6 months; T3, after 12 months

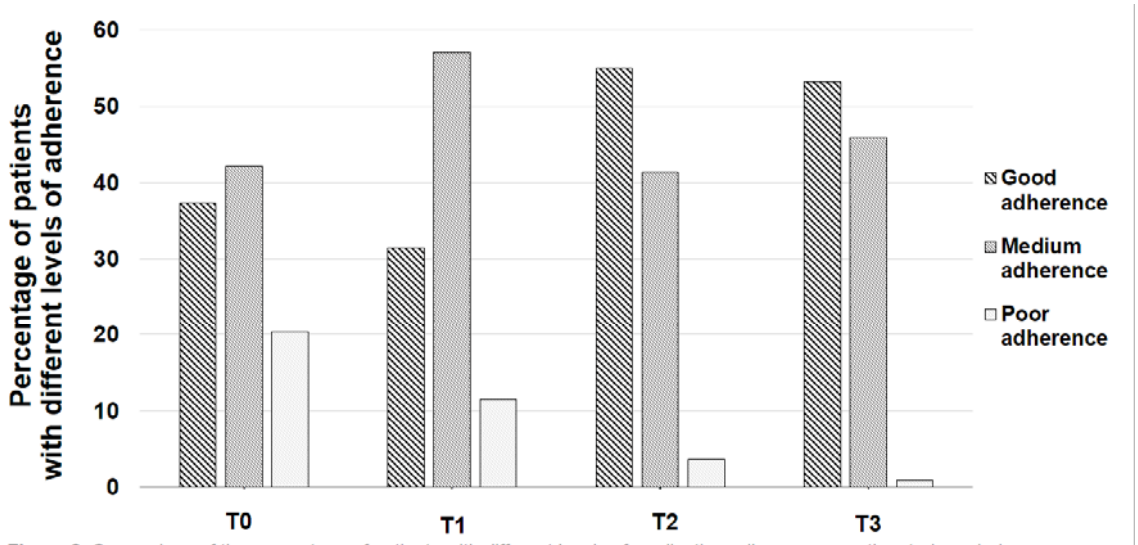

Figure 2. Comparison of the percentage of patients with different levels of medication adherence over the study period

Note: T0 (baseline), T1 (after 3 month), T2 (after 6 months), T3 (after 12 months). p: p value of McNemar test determined the difference of the percentage between time point T1, T2, T3 and T0.

Improvement in health-related quality of life (HRQOL)

The health profiles of study participants based on their response to the EQ-5D-5L questionnaire are depicted in Table 6. In general, the percentage of patients that stated having "no problems" or "slight problems" in all dimensions increased over the duration of the study. For example, the levels for "no pain" and "not anxious or depressed" improved from 33.3% and 66.2% at baseline (T0) to 64.2% and 92.7% after 12 months (T3), respectively. The only EQ-5D dimensions that fluctuated across the duration of the study were mobility and self-care. In particular, there was an increase in the percentage of patients that stated having "no problems" after 3 months (T1) and 6 months (T2), followed by a decrease after 12 months (T3) to nearly the same level as baseline (T0). The percentage of study participants that stated having severe or extreme levels in any EQ-5D dimension was always under 3.5% at T2 and T3, with the exception being the mobility dimension which had levels of 8.5% (T2) and 7.3% (T3).

The health state profiles were then converted into index values and the mean EQ-5D-5L index values were calculated for each assessment time point (Table 7). The mean EQ-5D-5L index value increased significantly from 0.47 at baseline (T0) to 0.62, 0.63 and 0.59 at T1, T2

and T3, respectively ($p<0.001$). However, there was no significant change in the average EQ VAS score that was self-rated by patients ($p=0.313$). In fact, the EQ VAS scores were approximately 50 out of a maximum of 100 at every assessment time point (Table 7).

Table 6. Health state profiles according to the EQ-5D-5L dimensions

EQ-5D-5L dimension		T0 (n=211)	T1 (n=156)	T2 (n=140)	T3 (n=109)
Mobility	No problems	11.9%	32.2%	24.8%	11.9%
	Slight problems	27.2%	43.7%	47.5%	45.0%
	Moderate problems	33.3%	20.3%	17.7%	35.8%
	Severe problems	27.6%	3.8%	8.5%	7.3%
	Unable to walk	0.0%	0.0%	1.4%	0.0%
Self-care	No problems	35.7%	59.5%	46.8%	37.0%
	Slight problems	26.2%	25.3%	39.7%	47.2%
	Moderate problems	22.9%	8.9%	10.6%	13.0%
	Severe problems	13.8%	3.2%	1.4%	1.9%
	Unable to do	1.4%	3.2%	1.4%	0.9%
Usual activity	No problems	22.4%	44.3%	44.0%	38.5%
	Slight problems	29.0%	26.6%	35.5%	40.4%
	Moderate problems	22.9%	15.8%	14.2%	17.4%
	Severe problems	18.1%	5.7%	3.5%	2.8%
	Unable to do	7.6%	7.6%	2.8%	0.9%
Pain/ discomfort	No pain	33.3%	43.7%	66.7%	64.2%
	Slight pain	29.5%	39.9%	24.8%	25.7%
	Moderate pain	23.8%	12.7%	7.1%	9.2%
	Severe pain	12.9%	3.8%	1.4%	0.9%
	Extreme pain	0.5%	0.0%	0.0%	0.0%
Anxiety/ depression	Not anxious or depressed	66.2%	84.8%	89.4%	92.7%
	Slightly anxious or depressed	9.5%	7.6%	7.1%	5.5%
	Moderately anxious or depressed	12.4%	5.7%	1.4%	1.8%

	Severely anxious or depressed	10.5%	1.9%	2.1%	0.0%
	Extremely anxious or depressed	1.4%	0.0%	0.0%	0.0%

Note: T0, baseline; T1, after 3 months; T2, after 6 months; T3, after 12 months

Table 7. EQ VAS and EQ-5D-5L index value

	T0 (n=211)	**T1 (n=156)**	**T2 (n=140)**	**T3 (n=109)**	**P value**
EQ-5D-5L index value (SD)	0.47 (0.20)	0.62 (0.22)	0.63 (0.22)	0.59 (0.16)	<0.001
EQ VAS (SD)	50.7 (18.1)	48.6 (17.6)	51.4 (16.4)	49.9 (16.7)	0.313

Note: T0, baseline; T1, after 3 months; T2, after 6 months; T3, after 12 months. Maximum of EQ-5D-5L is 1.0, maximum score of EQ-VAS is 100.0. P value of ANOVA test to compare the mean values between time points.

Evaluation of clinical scores

Table 8 depicts the mean clinical scores calculated from clinical symptoms by the physicians. The higher scores indicate worsening of COPD. As shown in the table, there was a slight fluctuation in the mean clinical scores across the duration of the study. After increasing in the first 6 months from 6.5 to 7.1, the mean clinical score decreased to 6.6 and 6.5 over the next 6 months. However, there was no statistical difference in the average clinical scores recorded over the 12 months (Table 8).

Table 8. Mean clinical scores over the study period

Time of assessment	Baseline	3 months	6 months	9 months	12 months	P value
Mean clinical score (SD)	6.5 (2.0)	7.1 (1.6)	7.1 (1.9)	6.6 (2.0)	6.5 (2.0)	>0.05
Score range	4.0-10.0	3.0-10.0	1.0-10.0	2.0-10.0	2.0-10.0	

Note: T0, baseline; T1, after 3 months; T2, after 6 months; T3, after 12 months. Maximum score of 10.0. P value of ANOVA test to determine the difference of mean between time points.

Discussion

Pharmaceutical care in Vietnam is at the beginning of the development process. Pharmacists are gradually moving from a dispensing-only role to incorporate education and counselling in the management of medications for patients. This study is the first to show the importance of the role of pharmacists in Vietnam to improving medication adherence and quality of life for COPD patients, through the implementation of a simple pharmaceutical care program.

Medication adherence in COPD is a pivotal factor in controlling disease progression. Poor adherence to COPD medications is strongly associated with an increase in mortality and hospital admission rates due to exacerbation of the disease [9]. Furthermore, good adherence is correlated with reductions in health care utilization by patients with COPD [6]. However, the proportion of COPD patients that adhere to therapy is considerably lower compared to those with other chronic diseases [6, 7]. As expected, our study also demonstrated a significant issue with patient adherence to COPD medications using the MMAS – a self-reported questionnaire which is recommended by the American Medical Association for the routine evaluation of patient compliance with medications [23, 24]. Prior to the intervention, our results showed a

low rate of medication adherence among COPD patients which is consistent with other published findings [25, 26].

Interventions that improve medication adherence in COPD patients are warranted to improve the overall management of this chronic condition. Our study incorporated brief counselling focusing on the role of COPD medications and the importance of adherence for optimal therapy as well as inhaler technique at regular time points throughout the study (1 month, 2 months, 3 months, 6 months and 12 months). This was achieved within 5 to 10 minutes depending on the number of questions raised by the patients. Pharmacist-led patient education, which was applied in our study and other publications [27, 28], is considered one of the most effective strategies to improving medication adherence [29]. Inhaler technique improved significantly after training with pharmacists [17]. Patients' adherence to medications also improved after the brief counselling (Tables 4 and 5). Brief counselling by pharmacists has also been successfully performed by De Tullio et al in COPD patients taking theophylline [30]. An intervention that involves important information delivered over a short duration is preferable, especially for countries which have a large and increasing number of COPD patients and limited health care resources such as Vietnam [16].

Quality of life is one of the most important outcomes in the management of chronic diseases through pharmaceutical care interventions. Our study applied a well-validated generic questionnaire EQ-5D-5L for pre- and post-assessment of quality of life after implementation of a pharmaceutical care program. This instrument has been successfully utilized for evaluating health-related quality of life of COPD patients [31, 32] and is capable of differentiating between the various stages of COPD severity [32]. The EQ-5D-5L questionnaire has also been previously used to evaluate the quality of life profile of the general Vietnamese population [22]. The results from our study showed an improvement in the 5 dimensions of health profiles according to the EQ-5D questionnaire after implementation of a pharmaceutical care program.

There was a significant increase in the percentage of patients having “no problems” and “little problems” as well as a decrease in the percentage of patients having “severe problems”. This supports the improvement in the quality of life of COPD patients after participation in the pharmacist-led pharmaceutical care program. These results are consistent with those of previous studies that are focused on pharmaceutical care of COPD patients in other countries [13, 33]. The positive outcome in the quality of life of COPD patients in our study may be due to improvement in inhaler technique and medication adherence, which together are important in reducing the risk of exacerbations of the disease. Our patients achieved better inhalation technique after being trained by pharmacists as a part of the pharmaceutical care program [17]. At the same time, patients in our study also showed better adherence to their medications. The significant correlation between inhaler technique, medication adherence and quality of life has also been demonstrated in previous publications [27, 28, 33, 34].

In contrast, our study did not show significant improvement in clinical outcomes for COPD patients after participation in the pharmaceutical care program. Clinical scores were based on symptom severity in the patients’ medical records after they had met with the respiratory physicians. The results indicated that the clinical state of the study participants was stable and did not worsen during the study period. Considering the nature of a progressive and non-reversible disease like COPD, keeping the disease stable over time is always an important objective in COPD management and has been recommended in clinical guidelines [1]. Although no improvement in clinical outcomes based on clinical scores of symptoms were observed in the study, the significant improvement in inhaler technique and medication adherence are important targets of our pharmaceutical care program for COPD patients. Patients with better inhaler technique and good medication adherence have been previously shown to have improved clinical outcomes [6, 35].

There were some strengths and limitations in our study. Presently, there was a need for studies focusing on pharmaceutical care programs led by pharmacists to improve COPD medication adherence [36]. Our study is the first to demonstrate the important role of pharmacists in the management of COPD in Vietnam, through implementation of brief counselling in the national program. Results showed improvement in medication adherence and quality of life for COPD patients in a country with limited health care resources and high patient loads [37]. With regards to limitations, the study was conducted only in one hospital which may limit the generalization of our findings to all COPD patients in the national program. However, our results may be a motivation for other hospitals to apply the same strategies with pharmacists' involvement. In addition, the clinical outcomes in our study were only assessed by symptom score instead of other potential indicators such as respiratory function tests, days of hospitalization, and number of exacerbation periods – which were commonly used in other published studies [10, 27]. However, these indicators are only collected correctly and easily in a health care system which have effective connections between hospitals. This is not feasible in a developing country like Vietnam where the storing and sharing of patients' information among hospitals are limited. For example, COPD patients may stay in a hospital with no information being recorded of the hospital stay in other hospitals. Therefore, at this stage, scoring important clinical symptoms of disease may be an appropriate and feasible method for evaluating disease severity and progression of COPD.

Conclusion

Our study showed that a pharmaceutical care program led by pharmacists can significantly improve medication adherence and quality of life for COPD patients. The intervention also helped to stabilize the condition, which is important for progressive and non-reversible diseases such as COPD. Our model of a pharmacist-led intervention should be considered as an effective

solution for managing COPD patients and a better utilization of human resources in health care, especially in a developing country like Vietnam.

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Author contributions

All authors contributed to the tool development and study design, data analysis, drafting and revising the manuscript. All authors also agree to be responsible for all aspects of the study.

Disclosure

The authors report no conflicts of interest in this work.

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CHAPTER 5. EFFECTIVENESS OF A SHORT TRAINING PROGRAM FOR COMMUNITY PHARMACISTS TO IMPROVE KNOWLEDGE AND PRACTICE OF ASTHMA COUNSELLING

Introduction

Asthma is a major health problem affecting 334 million people worldwide, with a high prevalence in low- and middle-income countries [1]. Despite being a global health problem, the clinical management of asthma is not always optimal, with many patients still suffering from poorly controlled symptoms [2]. Poor asthma control is common, with studies suggesting up to 46% and 58% in paediatric and adult patients, respectively [3]. In addition, over 80% of patients from community asthma specialty clinics in the US were reported to have poor asthma control [4]. The main reasons for this include medication non-adherence, poor inhaler technique, and exposure to triggers. Evidence from randomized controlled trials confirm that supported self-management for asthma can improve asthma control and requires a partnership between patients and different health care providers, including pharmacists [1, 5, 6].

Community pharmacists are valuable contributors in the primary healthcare team, and have shown to be an effective resource for improving asthma management in the community. They have the advantage of being strategically placed for identifying patients with poorly controlled asthma, as they are far more accessible and have the opportunity to see patients more frequently when they pick up repeat medications [7, 8]. In particular, management interventions by community pharmacists have had a positive effect on asthma control by improving medication adherence, inhaler technique, asthma knowledge, and changes in patients' perception of their disease and their behavior [8, 9]. Therefore, community pharmacists are able to have a significant role in improving the management of asthma in patients.

In order to effectively contribute to improving asthma management, pharmacists need to have the necessary foundation knowledge to appropriately counsel and educate patients in both a hospital and community setting. This includes understanding the basic pathophysiology of asthma, asthma severity, level of control, and choice of therapy. Pharmacotherapy knowledge helps pharmacists to teach patients on how to correctly use asthma medications so they actually benefit from them, including the different roles of controller and reliever medications, dosage, dose administration techniques (e.g. inhaler devices), route of administration, and potential side effects. Furthermore, pharmacists may be involved in writing asthma action plans to help patients monitor their daily symptoms, assess their level of control, and determine what actions and medications should be taken based on that information [10].

One of the main barriers reported by pharmacists to providing appropriate interventions for asthma patients is their lack of sufficient knowledge, skills and confidence in the management of asthma [11-13]. For example, Bilun et al [11] reported that the mean number of correct steps performed by a cohort of community pharmacists for all the inhaler devices was below 5 out of a total of 10. In addition, less than 50% of the pharmacists correctly answered questions related to the acute and chronic treatment of asthma. This lack of knowledge about asthma and inhaler devices is not adequate to effectively counsel patients and improve asthma management outcomes [14]. Therefore, there is an urgent need for the development of training programs to help pharmacists provide counselling and management services more confidently and proficiently, particularly in developing countries.

In Vietnam, asthma was included in the 'National Strategy on Prevention and Control of Non-communicable Diseases 2015-2025' that aims to halt the increase of morbidity and mortality due to these diseases [15]. Despite the evidence supporting the positive role of pharmacists in improving asthma management in the community, this government initiative has not incorporated any pharmacist-led strategies. In order for any changes to occur with the policy

makers in Vietnam, the pharmacy profession will need to provide evidence that pharmacists are a valuable resource in community asthma management [15]. However, it is still uncertain whether community pharmacists in Vietnam have enough knowledge and skills to support their role in educating and managing common diseases, including asthma. This is due to the rather complicated pharmacy education system in Vietnam and the lack of recognition of the role of pharmacists in the primary healthcare team. Therefore, this study was conducted to assess the level of knowledge and skill of community pharmacists in asthma management in Vietnam, and the impact of a short training program to improving knowledge and practice in asthma counselling. The results of this study will also be significant for other countries where pharmacy practice is not yet well developed.

Material and methods

Study design

The study was conducted from December 2016 to August 2017 in Hanoi, Vietnam, and was approved by the Department of Health in Hanoi, Hanoi Pharmaceutical Association, and the Human Research Ethics Committee at the University of Newcastle, Australia (No: H-2015-0333). The study comprised of 3 parts:

- Part 1 (Baseline Study). Assessment of asthma knowledge and inhaler technique among community pharmacists (conducted from December 2016 to February 2017).
- Part 2 (Training). Development and implementation of a training program to assess asthma knowledge and inhaler technique after training (conducted from March 2017 to June 2017). This was the first study evaluating the impact of the training program.
- Part 3 (Simulated patient study). Assessment of pharmacists counselling simulated asthmatic patients using a standardized scenario in community pharmacy (conducted from

July 2017 to August 2017). This was the second study evaluating the impact of the training program in a real-life situation.

Pharmacist recruitment

Pharmacists were selected randomly from the list of pharmacies provided by the Department of Health in Hanoi, Vietnam. After excluding pharmacies that were wholesalers or located in hospitals, there were 1475 pharmacies across 6 central districts of Hanoi that were included in the final selection. Of these pharmacies, a sample size of 305 were randomly selected from the list by quota method to ensure selection of a similar number of pharmacies from each district in Hanoi. The sample size was calculated using online software for a survey study (https://www.surveysystem.com/sscalc.htm). The sample size was estimated from the total pharmacies (1475) with 95% confidence interval and 5% error. From each pharmacy, one pharmacist was randomly selected and invited to participate in the study (for pharmacies having more than one pharmacist). After providing informed consent and other demographic information (e.g. age, gender, experience of working in pharmacy, level of pharmacy education, history of asthma and use of inhaler devices), participating pharmacists were requested to complete the questionnaire during the appointment with the researchers. The pharmacists were then asked to demonstrate how to use the inhaler devices in front of the researchers – pressurised metered dose inhalers (MDI) and dry powder inhalers (DPI-Turbuhaler). This formed Part 1 of the study (baseline). These same pharmacists were also invited to participate in the training program.

Asthma knowledge questionnaire and inhaler checklist

An asthma knowledge questionnaire with 20 closed-ended questions was developed based on the necessary knowledge required of pharmacists [10], published questionnaires [11, 16], and

current guidelines [5, 17]. A draft questionnaire was reviewed thoroughly by 4 lecturers from Hanoi University of Pharmacy, 2 experienced researchers at the University of Newcastle, 2 respiratory specialists in Hanoi, and 3 experienced community pharmacists working in Hanoi. The questionnaire was then pilot tested on 10 community pharmacists and 50 pharmacy final year students before being finalized (Appendix A). For evaluating and comparing the knowledge of community pharmacists in the study, each correct answer was assigned a score and the maximum score attainable was 20 points. The overall score was calculated by giving (+1) for each correct answer, (0) for each "not sure" answer, and (-1) for each incorrect answer.

Two inhaler devices (MDI and DPI-Turbuhaler) were selected from a survey of the most common devices used by asthmatic patients available in community pharmacies in Hanoi. These two devices are prescribed by almost all physicians in Vietnam according to two respiratory specialists who were our study advisers. The 8-step-checklists of these inhalers were developed from published articles and current guidelines [5, 17]. Pharmacists were asked to demonstrate how to use the inhaler devices using placebo inhalers. These demonstrations were recorded and evaluated by researchers using the checklists. Each correct step was assigned a score to allow quantitative assessment. As all the steps were deemed important to achieving optimal medication delivery, they were considered to be of equal weighting and assigned a score of 1 point each [18]. Therefore, the maximum score attainable was 8 points for each inhaler device when used correctly in every step.

Training program and the trainers

A 4-hour training program was designed to focus on basic asthma knowledge and the management of asthma. Basic asthma knowledge included the pathophysiology of asthma and signs of poorly controlled asthma (1 hour). For asthma management, the training focused on differentiating between relievers and preventers, the role of inhaled corticosteroids in asthma

management, the importance of adherence, common side effects, and the role of spacers (2 hours). Pharmacists were also taught the differences between a MDI and DPI, and were given the opportunity to practice using the inhaler devices correctly (1 hour). The training materials were prepared from official guidelines, standard textbooks for continuous training, and guidance from 2 respiratory specialists and 3 experienced community pharmacists. The training materials and lectures were also pilot tested on a small group of pharmacy final year students before being finalized. Four lecturers (teaching experience >8 years) in the Clinical Pharmacy Department in Hanoi University of Pharmacy volunteered to be the trainers for the pharmacists. All pharmacists who accepted the invitation were organized to participate in a 4-hour training session. After completing the training, the pharmacists were asked to attempt the post-test questionnaire, which was the same questionnaire completed at pre-training (Part 1 of the study).

Simulated patient study and case study

An asthma case study was developed after discussion with the 2 respiratory experts and 3 community pharmacists who have extensive experience in counselling patients with asthma. The scenario described an asthmatic patient approaching the community pharmacist to buy a reliever and to seek advice on their current prescribed medications (Appendix B). This case study was chosen as it commonly happens in community pharmacies in Vietnam. The main objectives were to assess whether the pharmacist: (i) can distinguish a preventer from a reliever, (ii) is able to identify and discuss the importance of medication adherence, (iii) knows how to counsel patients about the potential side effects of asthma medications, and (iv) is competent when instructing patients on the correct use of the inhaler devices. Ten final-year pharmacy students volunteered to be the simulated patients for the study, and were trained to role play the scenario in a 3-week period with lecturers and experienced pharmacists in the pharmacy lab at Hanoi University of Pharmacy. Six to eight weeks after the training, the 10 simulated patients

visited two groups of pharmacies to seek advice for the prescription as described in the case study. The first group included all pharmacists who had attended the training program, whereas the second group were pharmacists that had not attended the training program (control) and were selected based on their similar demographic background as those in the first group. Simulated patients were also trained to use the checklist and record the responses from the pharmacists after completing the case scenario (Appendix C).

Assessment of pharmacists' response to the simulated patient study

To assess the responses from the pharmacists to the simulated patient study and allow comparison between the pharmacists that had and had not attended the training program, a scoring method was developed as shown in Table 1.

Table 1. Scoring tool for assessing pharmacist's response in the simulated patient study

Items for assessment	Answer	Score
Distinguish between a reliever and a preventer	Distinguish correctly	+ 1
	No answer/advise patient to ask doctor	0
	Distinguish incorrectly	- 1
Counsel about adherence	Advise patient not to stop preventers and explain correctly	+ 2
	Advise patient not to stop preventers with no explanation/advise patients to follow the prescription	+ 1
	No answer/advise patient to ask doctor	0
	Agree to stop a preventer	- 1
Counsel about side effect – habit forming or dependence	Counsel correctly (not habit forming)	+ 1
	No answer/ advise patient to ask doctor	0
	Counsel incorrectly	- 1
	Mention oral candidiasis and remind to rinse the mouth	+ 3

Counsel about side effect – oral candidiasis and prevention	NOT mention oral candidiasis but remind to rinse the mouth	+ 2
	Mention oral candidiasis but NOT remind to rinse the mouth	+ 1
	NOT mention oral candidiasis and NOT remind to rinse the mouth	0

Statistical analysis

Results were expressed as mean ± standard deviation (SD) and percentage (%) where appropriate. One-way ANOVA test and post-hoc test were applied for checking the difference of the means between groups. Chi-square test and t-test were used for determining the difference in the percentage and mean between groups, respectively. The value of $p \leq 0.05$ was considered statistically significant. All data were analysed using the SPSS 23.0 (IBM Corp©).

Results

Demographics of the participants

The demographics of the community pharmacists participating in Part 1 (baseline) of the study (n=300) are summarized in Table 2. The average age of the pharmacists was 32.6 years, with nearly 90% being female. With regards to qualifications, the majority of the pharmacists (85.4%) had either a secondary diploma (SDPharm) or college diploma (CDPharm) in pharmacy. Nearly half of the participants (46.0%) had worked in community pharmacy for more than 5 years. The majority (83.6%) of the pharmacists indicated that they had met at least one asthma patient every week. Approximately 10% of them had met at least one asthma patient a day.

Table 2. Demographics of the study participants

Age (years)	Mean (±SD)	32.6 (±10.2)
	Min/Max	20-68
Gender	Female	268 (89.3%)
	Male	32 (10.7%)
Years since graduating from pharmacy school	> 10	47 (15.7%)
	6-10	83 (27.7%)
	3-5	89 (29.6%)
	< 3	81 (27.0%)
Pharmacy qualification[a]	BPharm or higher	34 (11.3%)
	CDPharm	86 (28.7%)
	SDPharm	170 (56.7%)
	EDPharm	10 (3.3%)
Work experience in community pharmacy (years)	> 10	70 (23.3%)
	6-10	68 (22.7%)
	3-5	78 (26.0%)
	< 3	84 (28.0%)
Frequency of meeting an asthmatic patient in the pharmacy	≥ 1 patient/day	31 (10.3%)
	1 patient/2-3 days	109 (36.3%)
	1 patient/week	111 (37.0%)
	<1 patient/week	49 (16.4%)
Being an asthmatic or having asthmatic family member(s)		16 (5.3%)

Note: [a] EDPharm: elementary diploma in pharmacy (1.5-year program), SDPharm: secondary diploma in pharmacy (2-year program), CDPharm: college diploma in pharmacy (3-year program), BPharm: bachelor of pharmacy (5-year program).

The flowchart in Figure 1 illustrates the number of participating pharmacists in the different parts of the study. Among the 300 community pharmacists that consented to participate in Part 1 of the study and had completed the pre-training questionnaire, 103 pharmacists accepted the invitation to attend the training program (34.3% response rate). The remaining pharmacists (n=197) who did not accept the invitation mainly stated the reason of having no free time to attend the training program (nearly 90%). In Part 3, the simulated patient study was conducted on 87 pharmacists who attended the training program and 99 pharmacists who did not attend the training (control). It should be noted that 16 pharmacists who had attended the initial training program and 19 pharmacists who did not attend the training program were unable to participate in the patient simulated study, due to having no time (~10%) or they were not physically present in the pharmacy when the simulated patient entered to conduct the study (~90%).

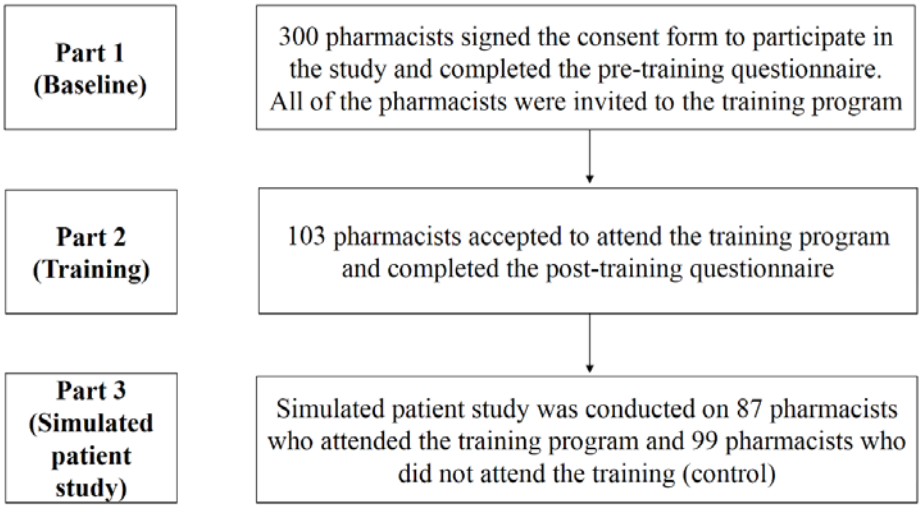

Figure 1. Flowchart of the number of participating pharmacists in the different parts of the study

Baseline knowledge of asthma and asthma management of the study participants

Prior to the initiation of the training program, baseline asthma knowledge results (Table 3) showed that the majority of the respondents correctly answered questions related to asthma pathophysiology (77.7%) and the signs of asthma (87.7%). In addition, over 70% of the study participants were able to correctly recognize that cigarette smoking was not the main factor associated with the disease. However, nearly half of the pharmacists incorrectly thought that asthma was an infectious disease. Only one respondent was able to give the correct answers to the questions relating to signs of uncontrolled asthma. Although 70.7% of respondents answered correctly to the "night waking" sign, approximately 60% of these pharmacists were not aware or not sure that using relievers more than 2 times a week is a sign of uncontrolled asthma.

Table 3. Summary of the basic asthma knowledge component of the questionnaire

	Statement/question	Number of participants (n=300)		
		Correct answer	Incorrect answer	Not sure
1	Asthma is an infectious disease of the airways (W[a])	151 (50.3%)	121(40.3%)	28 (9.3%)
2	Asthma is a chronic, inflammatory disease of the airways (R[b])	233 (77.7%)	43 (14.3%)	24 (8.0%)
3	Frequent wheezing or coughing (especially at night or in the early morning) are signs of asthma (R)	263 (87.7%)	22 (7.3%)	15 (5.0%)
4	The majority of patients with asthma are cigarette smokers (W)	212 (70.7%)	45 (15.0%)	43 (14.3%)
5	If a patient requires reliever medications more than twice/week, his/her asthma is considered well-controlled (W)	127 (42.3%)	133(44.3%)	40 (13.3%)
6	Night waking due to asthma is one of the signs of uncontrolled asthma (R)	212 (70.7%)	36 (12.0%)	52 (17.3%)

Note: [a] W = Wrong, [b] R = Right

Regarding knowledge of the management of asthma (Table 4), most of the study participants (98%) correctly identified the role of inhaled salbutamol as a rescue medication and approximately 60% were correct that inhaled corticosteroids are the most appropriate medication for the long-term maintenance of asthma. However, over 50% of the pharmacists were incorrect about the role of inhaled salmeterol, which is a slow acting medication, and nearly 60% did not know that corticosteroids cannot be used as a reliever for asthmatic patients. In addition, half of the participating community pharmacists were incorrect to claim that patients can stop using inhaled corticosteroids whenever they feel better and that long-term use of inhalers can be habit-forming.

Regarding side effects, only 23.7% of the respondents knew that inhaled salbutamol does not cause oral candidiasis and nearly 60% were overly concerned about side effects of inhaled corticosteroids. Consequently, they incorrectly believed that inhaled corticosteroids should only be used for severe asthma (Q12) and can be stopped whenever the patient felt better to reduce side effects (Q13).

Similarly, for the questions focused on OTC medicines and supportive devices provided by pharmacists without the need of a prescription, nearly half of the study participants incorrectly thought that a cough caused by asthma can be treated using cough suppressants (which is contraindicated) (Q7). In addition, one fifth of the pharmacists did not know that herbal medicines could not be used alone for asthma (Q15) and nearly 70% did not correctly know the role of spacers in facilitating the use of inhalers (Q19 and Q20).

Baseline knowledge of inhaler technique of study participants

When dispensing inhalers, only 30% of the study participants indicated that they would proactively ask whether the patients know how to use the inhaler device(s). Of the 300 community pharmacists that participated in Part 1 of the study, 225 (75%) and 60 (20%) believed that they could correctly use the MDI and DPI-Turbuhaler, respectively. However, when these pharmacists were asked to demonstrate how to use the placebo inhalers, only one and two pharmacists (0.3% and 0.6%) could perfectly perform the 8 steps of using the MDI and DPI-Turbuhaler, respectively. The study participants made mistakes practically in every step for both the MDI and DPI- Turbuhaler. In particular, the steps "breathe out" and "hold breath" were correctly performed by under 10% of participants with both the MDI and DPI. For the MDI, under 30% of pharmacists remembered to shake the inhaler to ensure receiving the correct dose and over 70% did not know how to correctly coordinate "pressing inhaler" with "slow breathing in" when using the MDI. Regarding the use of the DPI-Turbuhaler, nearly 50% of pharmacists did not load the medicine, which meant no medication was available for inhalation in the next steps.

Table 4. Summary of the asthma medication component of the questionnaire

	Statement/Question	Number of participants (%)		
		Correct answer	**Incorrect answer**	**Not sure**
7	It is appropriate to use cough suppressants to treat coughing caused by asthma (W[a])	169 (56.3%)	118 (39.3%)	13 (4.3%)
8	Inhaler medications containing salbutamol can be used as a rescue at home for patients with acute asthma attack (R[b])	294 (98.0%)	5 (1.7%)	1 (0.3%)
9	Inhaler medications containing salbutamol can cause oral candidiasis (W)	71 (23.7%)	141 (47.0%)	88 (29.3%)

10	Medications containing salmeterol can be used as a rescue at home for patients with acute asthma attack (W)	96 (32.0%)	162 (54.0%)	42 (14.0%)
11	Inhaler medications containing corticosteroid can be used as a reliever for patients (W)	123 (41.0%)	134 (44.7%)	43 (14.3%)
12	Inhaled corticosteroids are associated with many side effects, therefore they should only be used in patients with severe asthma (W)	135 (45.0%)	123 (41.0%)	42 (14.0%)
13	Patients with asthma can stop using inhaled corticosteroids whenever they feel better to reduce side effects (W)	128 (42.7%)	151 (50.3%)	21 (7.0%)
14	Long-term use of inhalers can be habit-forming (W)	110 (36.7%)	152 (50.7%)	38 (12.6%)
15	Herbal medications such as Hen P/H[c] can be used alone for asthma treatment (W)	223 (74.3%)	58 (19.4%)	19 (6.3%)
16	Inhaled medicines generally cause more side effects than oral medicines (W)	165 (55.0%)	68 (22.7%)	67 (22.3%)
17	The most appropriate medication for the long-term maintenance of asthma is inhaled corticosteroids (R)	178 (59.3%)	87 (29.0%)	35 (11.7%)
18	Patients need to rinse their mouth with water and spit out after using inhaled corticosteroids (R)	149 (49.7%)	102 (34.0%)	49 (16.3%)
19	Spacers reduce the risk of oral candidiasis from inhaled corticosteroids (R)	99 (33.0%)	40 (13.3%)	161 (53.7%)
20	Spacers are only suitable for children (W)	82 (27.3%)	64 (21.3%)	154 (51.4%)

Note: [a] W = Wrong, [b] R = Right, [c] Hen PH is a herbal cough medication in Vietnam

Improvement of asthma knowledge and inhaler technique after the training program

Comparison of the results of the questionnaire on asthma management knowledge and inhaler techniques for the pharmacists who completed Part 2 of the study (n=103) is shown in Figure 2 and Table 5. There was a significant improvement in the scores for asthma management knowledge after the pharmacists participated in the training program, with an increase in the

number of correct answers from 11.1 to 18.4 ($p<0.001$). Mean knowledge scores, based on a negative scoring matrix, increased significantly from 5.3 to 17.2 (an increase of 229.8%) out of a maximum of 20 ($p<0.001$). With regards to inhaler technique at baseline, nearly no pharmacists were able to correctly perform all of the steps for the MDI and DPI-Turbuhaler. However, after completing the training program, 48.5% and 53.4% of the pharmacists demonstrated correct MDI and DPI-Turbuhaler technique, respectively. Correspondingly, the mean technique scores for both the MDI and DPI-Turbuhaler also improved from 3.0 to 7.4 and 0.1 to 7.4 out of a maximum score of 8.0, respectively ($p<0.001$). In comparison with pharmacists who did not attend the training (Table 5), the pharmacists that had attended the training program achieved four times higher in knowledge scores (17.2 vs 4.4, $p<0.001$) and 2.6 times higher in MDI technique scores (7.4 vs 2.8, $p<0.001$).

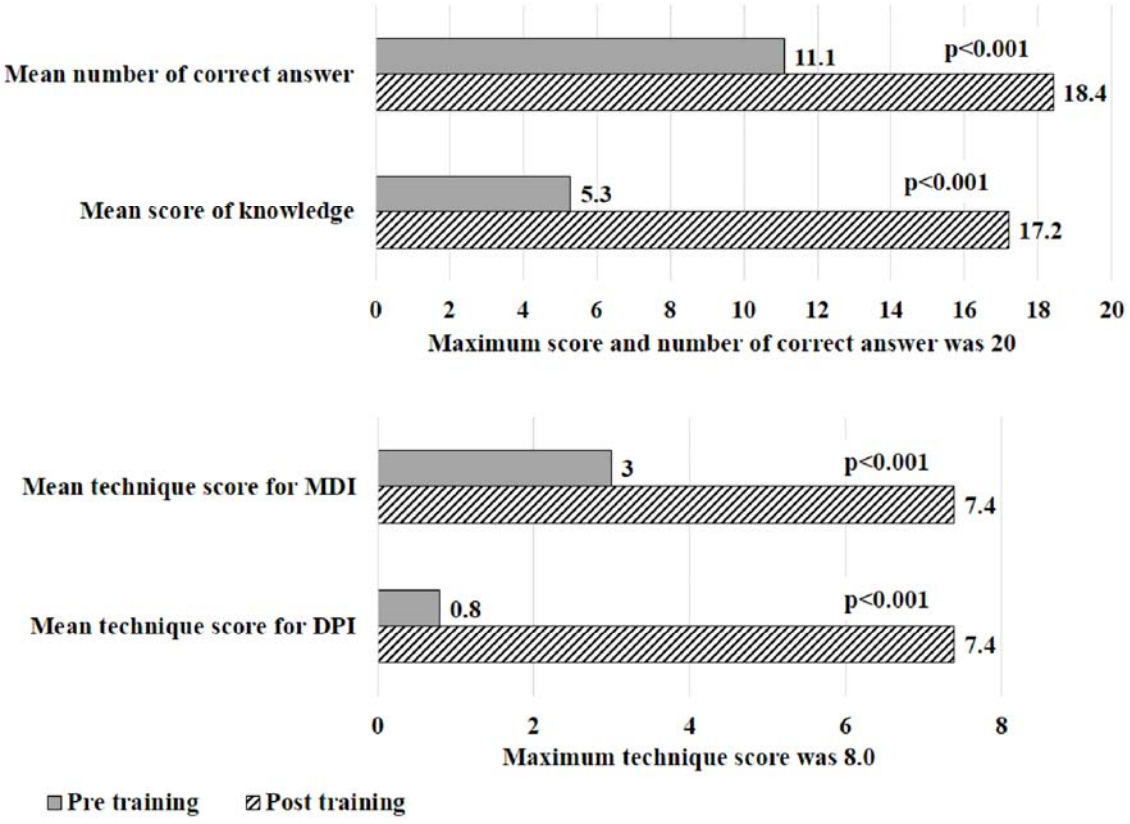

Figure 2. Improvement of knowledge about asthma and inhaler technique after the training (Part 2 of the study, n=103). Note: p value of paired-samples T test

Table 5. Comparison of pre- and post-training knowledge and technique scores between the two study groups

	Not attending training group (n=197)[a]	Attending training group (n=103)	
		Pre- training	Post-training
Mean knowledge score	4.4	5.3	17.2
Mean technique score for MDI	2.8	3.0	7.4
Mean technique score for DPI-Turbuhaler	0.9	0.8	7.4

Note: [a] participant who did not know how to use inhaler devices was given "0" for technique score

Evaluating the effectiveness of the training program using a simulated patient study

There was no significant difference in the demographics of the study participants in both groups, irrespective of attendance in the training program (Table 6). Similarly, the results from Part 1 of the study showed no difference in both knowledge and technique scores in both groups at baseline ($p>0.05$). Pharmacists that had completed the training program were significantly more effective at correctly counselling about relievers and controllers, medication adherence, and common side effects compared to the untrained group ($p<0.001$) (Figure 3). This was further supported by the counselling scores (Table 7), which showed that the trained pharmacists achieved significantly higher scores for all results in the simulated patient case study ($p<0.001$). In particular, there was an overall increase of 215% in total counselling scores for the group that had attended the training program when compared with the untrained group (5.4 vs 1.7, $p<0.001$). There was also a significant difference in mean MDI technique scores

between the two groups (6.1 vs 4.3, p<0.001). When investigating whether there were other influencing factors on the outcomes, we found no differences between the demographics of the study participants and the counselling scores in the subgroup analysis, with pharmacists at different educational levels achieving almost identical counselling scores (p>0.05).

Table 6. Comparison of the demographics of the study participants (Part 3 of the study)

Characteristics		**Attending training group (n=87)**	**Not attending training group (n=99)**	**p value[a]**
Age (years)	Mean (±SD)	33.94 (9.96)	33.91 (11.05)	0.983
Gender	Female /Male	78/9	85/14	0.507
Years since graduating from pharmacy school	> 10	16	17	0.984
	6-10	25	31	
	3-5	26	29	
	< 3	20	22	
Pharmacy qualification[b]	BPharm or higher	11	9	0.880
	CDPharm	25	28	
	SDPharm	47	57	
	EDPharm	4	5	
Work experience in community pharmacy (years)	> 10	22	28	0.915
	6-10	23	22	
	3-5	21	25	
	< 3	22	28	
Knowledge score before training	Mean (±SD)	5.08 (4.55)	4.85 (4.78)	0.736
Technique score before training	Mean (±SD)	3.03 (2.00)	3.05 (2.02)	0.957

Note: [a] p value of Chi-square test and independent-T test when appropriate; [b] EDPharm: elementary diploma in pharmacy (1.5-year program), SDPharm: secondary diploma in pharmacy (2-year-progam), CDPharm: college diploma in pharmacy (3-year-progam), BPharm: bachelor of pharmacy (5-year-progam).

Table 7. Comparison of the counselling scores for the simulated patient study

Counselling scores	Attending training group (n=87)	Not attending training group (n=99)	p value[a]
Score for counselling simulated patients (mean (±SD), maximum score of 7.0)	5.4 (±2.2)	1.7 (±2.9)	< 0.001
Score for MDI technique (mean(±SD), maximum score of 8.0)	6.1 (±1.6)	4.3 (±1.4)	< 0.001

Note: [a] Student T test

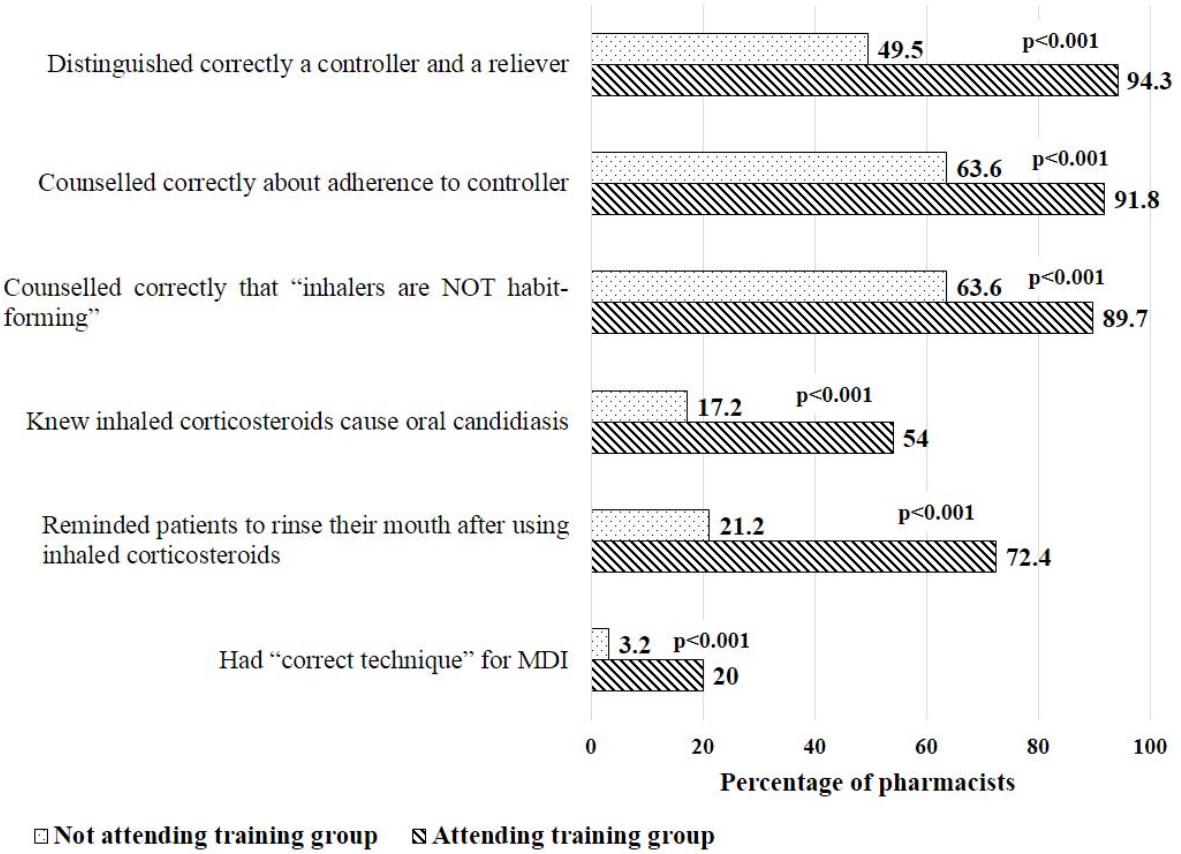

Figure 3. Comparison of the counselling by pharmacists who attended the training program (n=87) with pharmacists who did not attend the training program (n=99) using a simulated patient study. Note: p value of the chi-square test for the difference of percentage

Discussion

The positive contribution of community pharmacists in the management of patients with asthma is well-established in the literature, with the majority of studies conducted in developed countries [9, 19-21]. Community pharmacists are able to identify patients with poor asthma control, improve medication adherence and inhaler technique, and reduce the frequency of acute attacks [7, 8, 19, 21]. The interventions were shown to improve both the clinical status and quality of life of asthmatic patients [8, 19]. However, there have been limited studies that have focused on establishing effective and specific strategies to meet the needs of community pharmacists in asthma management in developing countries. In Vietnam, the national programs for the prevention and management of asthma and other non-communicable diseases are mostly run in a few large hospitals in major cities. Like most developing countries, these hospitals generally suffer from overcrowding of patients, limited facilities, and overworked healthcare professionals [15, 22]. Therefore, the present study was conducted to develop and evaluate new strategies that can be implemented for pharmacists in the community sector to assist in improving the management of asthma in Vietnam [1, 11]. The number of community pharmacies meeting good pharmacy practice (GPP) standards is increasing rapidly in Vietnam, especially in the major cities. However, GPP standards mainly focus on conditions surrounding appropriate facilities (e.g. pharmacy store and medication storing conditions), with currently no requirement for continuing professional education for pharmacists [23]. Despite this, community pharmacies are still more accessible for the majority of patients in the community with chronic medical conditions. Thus, a decentralized approach away from hospitals may be a feasible solution to improve the management of asthma and other non-communicable diseases in the community, by taking advantage of the under-utilized resource of community pharmacists in the healthcare system in many developing countries, such as Vietnam. To implement this approach successfully, the fundamental requirement is that the community

pharmacists possess sufficient professional skills and expertise to manage these diseases. Hence, our study aimed to evaluate and improve the professional skill level of community pharmacists in a developing country.

This is the first study in Vietnam to implement strategies to improve the knowledge and skills of community pharmacists to enhance their role in counselling asthmatic patients. Part 1 of the study clearly demonstrated that the baseline knowledge of the community pharmacists participating in the study was inadequate for counselling asthmatic patients to manage their medications. Lack of knowledge and skills can lead to negative consequences in asthma management. For example, 40.3% of the study participants were incorrect to consider asthma as an infectious respiratory disease. This may result in the supply of unnecessary antibiotics for patients, which is concerning in countries like Vietnam where antibiotics are commonly supplied illegally without a prescription. This potential misuse of antibiotics would contribute to the already high level of antibiotic resistance in Vietnam [24]. In addition, approximately half of the community pharmacists were unable to distinguish between a reliever and preventer in the study, which may lead to significant consequences for patients during an acute asthma attack. Nearly 60% of the participants also did not understand the role and side effects of inhaled corticosteroids in the management of asthma and incorrectly advised patients to stop these preventers at any time. Similarly, there was a high percentage of participating pharmacists who overemphasized the potential side effects of asthma medications. Again, this can negatively affect patients' compliance with the medications.

The study also indicated that the majority of the participating community pharmacists had poor knowledge of appropriate inhaler technique and did not know about using spacers for optimizing inhaled medication delivery. These results are consistent with those in other published studies on community pharmacists, regardless of the method of assessment [11, 14, 25-27]. For example, over half of community pharmacists classified themselves as having a low

level of asthma knowledge in a national survey conducted in Turkey [14]. In another study in Turkey, Gemicioglu et al. also showed that community pharmacists possessed insufficient and often incorrect knowledge about asthma and inhaler devices [11]. Using a simulated patient method, Van Sickle reported that asthmatic patients were often provided inappropriate advice and unnecessary medications in private pharmacies in an urban area in India [27]. Furthermore, two other studies (Sudan and Nigeria) using mystery customers also demonstrated that the majority of the community pharmacists did not know how to use inhaler devices properly [25, 26]. A study in Sudan showed that only one in 300 community pharmacists was categorized as having optimal inhaler technique when demonstrating its use for simulated patients [25]. Lack of basic skill to use MDI among community pharmacists was also reported by Nduka et al in a simulated patient study in two major cities in Nigeria [26]. The community pharmacists in the study only achieved less than 50% of the maximum inhaler technique score when performing MDI [26]. Taken together, these studies highlight an inadequacy in professional skill level among community pharmacists in many developing countries.

For Part 2 and Part 3 of the study, the results supported that a well-organized training program would have notable changes in the knowledge and practice of community pharmacists in the management of asthma. In particular, both the knowledge and inhaler technique scores improved significantly after the study participants attended the training program (see Table 5). The post-training knowledge score was nearly 3 times higher than the corresponding pre-training score. Similar results were seen with the inhaler technique scores, with a significant improvement after practicing with placebo inhalers in the training program (7.3 out of 8.0) compared to pre-training (3.0 out of 8.0). There was also a 289.8% increase in knowledge scores in the study group that attending the training program in comparison to the untrained study group. The training program also had a positive impact in the simulated patient study, with pharmacists that attended the training program achieving significantly better scores in

counselling (5.4 vs 1.7 out of a maximum score of 7.0) and inhaler technique (6.1 vs 4.3 out of a maximum score of 8.0) than the pharmacists that had not attended the training program.

Overall, our study supports the effectiveness of implementing a short training program for community pharmacists to improve their practical skills and knowledge for counselling asthmatic patients. By reviewing the guidelines [5, 28] and reference materials [8, 10, 11, 16] and consulting health professional experts, we have developed a questionnaire and training tool that embrace the core knowledge and skills needed by pharmacists for the effective management of asthma in the community. Based on the results of our study, we may state that asthmatic patients will receive more valuable and relevant advice from community pharmacists who attended the training program. This may possibly be considered a test model for organizing continuing professional education programs in Vietnam, which presently has no compulsory education programs for community pharmacists. The training program has been also shown to be effective for upskilling community pharmacists with heterogeneous qualifications in pharmacy to an optimal level of practice for asthma counselling. In Vietnam, pharmacy qualifications include four levels: elementary diploma in pharmacy, secondary diploma in pharmacy, college diploma in pharmacy, and bachelor of pharmacy and higher – with all qualifications able to work independently in private community pharmacies [29, 30]. Importantly, the results of the study showed no significant difference in knowledge and practice scores of the community pharmacists across all qualification levels in post-training.

The duration of the training program was considered an important factor for implementation as a continuing professional education program, due to the busy environment in pharmacies and busy schedules of pharmacists. Our training program of four hours was sufficient to provide the necessary asthma knowledge and skills for community pharmacists to appropriately counsel on asthma management. The time taken for training in other published studies varied from 2 h [31], 3 h and 40 min [32], 4 h [33], and 20 h [34]. However, the studies

were focused on different target groups for the continuing professional education program and varied from providing only knowledge [31] to incorporating both knowledge and practice [32, 34]. Role-play and case discussion were also applied to improve knowledge and attitude of pharmacists [34]. Regardless of the content of the training program, pharmacists were not willing to attend or more likely to discontinue the training if it were conducted over several days, especially when countinuing professional education programs are not mandatory in Vietnam. Therefore, the short training program we have developed in our study appears to be a practical solution for upskilling both the knowledge and practice of asthma management for pharmacists in Vietnam.

Several limitations should be noted in this study. Firstly, we selected the pharmacists who accepted the invitation to attend the training program for Parts 2 and 3 of the study, which may lead to potential selection bias. Although there was no significant difference between the trained and untrained groups at baseline, the community pharmacists that attended the training program may be more motivated to improve their knowledge and more willing to be trained compared to the pharmacists who did not accept the invitation. This may have led them to achieve better scores compared to baseline. The second limitation is that we had to develop our own questionnaire tailored for our study objectives and the context of the country, as there was no formal questionnaire for asthma knowledge evaluation available. In this development process, we had referred to publications such as the necessary knowledge required of pharmacists [10], published questionnaires [11, 16], current guidelines [5, 17], and opinions of experienced experts and advisers who are working in clinical settings and community pharmacy to reduce subjective bias. Furthermore, our questionnaire was not validated using a formal method – it was, however, tested on pharmacy students and small groups of community pharmacists before being implemented in the study. In addition, we did not evaluate how long the effectiveness of the training would last. The effectiveness of the education program was evaluated 6-8 weeks

post-training in the simulated patient study, but this may be an inadequately short period for assessing the long-term effects of the training. Therefore, we plan to assess this in future studies, especially when taking into account that regular updating of knowledge and skills are the main objectives of continuing professional education programs. Nevertheless, these programs have been reported to improve pharmacists' attitude and confidence toward the management of other chronic diseases [13, 31, 34]. Finally, as our study was performed only in one single city in Vietnam, some caution must be taken when generalizing our results to different settings, particularly in other jurisdictions. Despite this concern, our study included community pharmacies that were representative of community pharmacies in Hanoi and in Vietnam. Considering also the fact that educational training is rather generic, it is most likely to produce effects in other jurisdictions too.

Conclusions

The study demonstrated that our short training program was highly effective in providing community pharmacists with the necessary knowledge and practical skills to effectively counsel patients with asthma about the management of their condition and medications in Vietnam. It is suggested that such education programs should be promptly implemented and made compulsory for community pharmacists in Vietnam to improve the quality of counselling for patients with asthma and other non-communicable diseases. Our training program may be relevant to other countries similar to Vietnam, which may lack in formal quality use of medicines education during tertiary qualifications and/or do not have continuing professional education programs for community pharmacists. The approach and solution methodology addressed in the present study may also be applicable for improving the role of community pharmacists in the management of other chronic diseases such as cardiovascular diseases and diabetes.

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Conflict of interest statement

All authors have declared that they have no conflict of interest to declare for this manuscript.

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Appendix A. Questionnaire for assessment of knowledge about asthma and medications

No	Statement/question	Answer
1	Asthma is an infectious disease of the airways	Wrong
2	Asthma is a chronic, inflammatory disease of the airways	Right
3	Frequent wheezing or coughing (especially at night or in the early morning) are signs of asthma	Right
4	The majority of patients with asthma are cigarette smokers	Wrong
5	A patient requires reliever medications more than twice/week, his/her asthma is under well control	Wrong
6	Night waking due to asthma is one of the signs of uncontrolled asthma	Right
7	It is appropriate to use cough suppressants to treat coughing caused by asthma	Wrong
8	Inhaler medications containing salbutamol could be used as a rescue at home for patients with acute asthma attack	Right
9	Inhaler medications containing salbutamol could cause oral candidiasis	Wrong
10	Medications containing salmeterol could be used as a rescue at home for patients with acute asthma attack	Wrong
11	Inhaler medications containing corticosteroid can be used as a reliever for patients	Wrong
12	Inhaled corticosteroids are associated with many side-effects, therefore they should only be used in patients with severe asthma	Wrong
13	Patients with asthma can stop using inhaled corticosteroids whenever they feel better to reduce side effects	Wrong
14	Long-term use of inhalers can be habit-forming	Wrong
15	Herbal medications such as Hen P/H* could be used alone for asthma treatment	Wrong
16	Inhaled medicines generally cause more side effects than oral medicines	Wrong
17	The most appropriate medication for the long-term maintenance of asthma is inhaled corticosteroids	Right
18	Patients need to rinse their mouth with water and spit out after using inhaled corticosteroids	Right

19	Spacers reduce the risk of oral candidiasis from inhaled corticosteroids	Right
20	Spacers are only suitable for children	Wrong

Note: *: *Hen PH is a herbal cough medication in Vietnam*

Appendix B. Scenario for simulated asthma patients

A simulated patient (SP) role-plays as an asthma patient (22-25 year old), having been diagnosed with asthma for 3 months. The SP goes to see the pharmacist at the community pharmacy to buy a Ventolin because the Ventolin bought last month was empty. The SP also brings 2 medicines with the doctor's prescription to seek advice:

1. Ventolin ®[a] (Metered Dose Inhaler containing salbutamol): *on an as-needed basis*
2. Seretide ®[b] (Metered Dose Inhaler containing fluticasone and salmeterol): *use everyday*

The SP tells the pharmacist that these medicines were prescribed 3 months ago. However, she/he just uses Ventolin when the asthma symptoms appear because she/he feels more comfortable after using it. For Seretide, the SP says that she/he is still having one box from last month. She/he often uses in 5 to 10 days and stops because she/he thinks both medications are similar. Moreover, because Seretide need to be used every day, she/he feel not comfortable and afraid of being depended on the medicine and other side effects.

The mystery shopper (simulated patient) would need to record down the following information using the table (appended in Part 3):

- What is the response of the pharmacist when the SP intends to use Ventolin alone and stops Seretide?

- What is the response of the pharmacist when the SP tells them about the fear of side effects from using both medications together: dependence and side effects of inhaled medicines?

- The SP also asks the pharmacist to instruct her/him on how to use the inhaler device because she/he is not sure how to use the inhaler/device correctly.

Note: [a,b] Ventolin ® and Seretide ® are brand name e of GlaxoSmithKline, UK. These medicines are approved by Mistry of Health in Vietnam for selling in pharmacies.

Appendix C. Scenario checklist for simulated patients (SP)

1. Distinguish relievers and controllers

Distinguish relievers and controllers	Check
The pharmacist is CORRECT about the role of Ventolin[a] (a reliever used for urgent asthma symptoms)	
The pharmacist is CORRECT about the role of Seretide[b] (a controller)	
The pharmacist is WRONG about the role of Ventolin	
The pharmacist is WRONG about the role of Seretide	
The pharmacist tells the simulated patient (SP) to see doctors	
Other response:…… ……	

2. Counselling for medication adherence

Counselling for medication adherence	Check
The pharmacist tells SP should NOT stop using Seretide even when the patient feels better	
The pharmacist explains CORRECTLY the role of Seretide and patient needs to use it everyday	
The pharmacist agrees with the SP to STOP using Seretide (no more detail or explanation)	
The pharmacist tells SP to use medicines as doctor's prescription (no more detail or explanation)	
The pharmacist says he/she doesn't know/ tell SP to ask doctor	
Other response:……..	

3. Counselling for side effects of asthma medicines

For the side effect of dependence, pharmacist's response	Check
Tell SP that dependence may happen	
Tell SP that the medicines do NOT cause dependence	
Tell SP that she/he doesn't know	
The pharmacist tells the SP to go and discuss with the prescribing doctor	
Other: …….	

For the side effect of oral candidiasis, pharmacist's response	Check
Mentioned oral candidiasis may occur when using Seretide	
Does not mention oral candidiasis	
Tell the SP to go and discuss with the prescribing doctor	
Tell the SP that he/she doesn't know about other side effects	
Other:…….	

4. Instructions on how to use MDIs

When SP ask how to use the MDI, pharmacist's response	Check
Pharmacist doesn't know to use MDI	
Pharmacist says that it is not her/his role. It is the role of prescribing doctor	
Pharmacist tells SP to open the instruction in the leaflet	
Tell the SP to ask the prescribing doctor	
Pharmacist agree to show how to use MDI => check the box below	

Checklist of Metered Dose Inhaler	Correct	Incorrect or miss
Step 1: Remove the cap		
Step 2. Shake inhaler		
Step 3. Hold inhaler upright		
Step 4. Breath out all the way		
Step 5. Place the inhaler mouthpiece between your lips (and teeth); keep your tongue down and out of the way of the mouthpiece.		
Step 6. Press the inhaler just after starting a **very slow** and **very deep** breath in (until the lung is full)		
Step 7. Remove the inhaler from your mouth and hold your breath while counting to 10 or as long as possible		
Step 8. Breathe out slowly		
Remind patient to need to rinse the mouth after using Seretide		

Note: [a,b] Ventolin ® and Seretide ® are brand name e of GlaxoSmithKline, UK. These medicines are approved by Mistry of Health in Vietnam for selling in pharmacies.

CHAPTER 6. CONCLUSIONS

Major findings

This is the first research project focused on the role of pharmacists in the management of COPD and asthma in Vietnam – a developing country with limited human resources. The overarching aim of the study was to develop strategies to support hospital and community pharmacists to improve the quality use of medicines for patients with chronic respiratory diseases. The role of pharmacists has significantly evolved over time to one that incorporates both product-oriented services and patient-oriented services. This is an international trend for developed countries and is gradually being established in more developing countries, including Vietnam. However, the transition is slow and pharmacists remain under-utilized in Vietnam. With the heavy pressure on the Vietnamese health care system due to a shortage of doctors and nurses, the studies conducted in this thesis would show an example of how to better utilize pharmacists to contribute to health care in a developing country such as Vietnam. The following is a summary of the key findings from this research project.

Chapter 1 provided an overview of the context of health care system, activities of pharmacists in hospital and community settings in Vietnam. The major issue in the health care system is human resource including shortage of staff and imbalanced regional distribution. The review also described the changes in population and disease pattern with rising number of elderly people and significantly increasing prevalence in non-communicable diseases. A bright spot is an increase in diversity of pharmacists' activities to improve quality use of medicines in Vietnam encompassed providing drug information, monitoring adverse effects, evaluating drug use and counselling patients. However, Vietnamese pharmacists are facing difficulties and challenges that prevent them from performing their roles in patient-focused works. That is the question of pharmacists' quality and quantity and the pharmacist's recognition as a medicine

counsellor, especially in community setting. Several strategies were discussed in Chapter 1 to address these issues. Firstly, new policies and law on the pharmaceutical field were promulgated to provide a legal platform for enhancing rational use of medicine both in community and hospital settings. These legal documents defined more clearly the role and responsibilities of pharmacists and clinical pharmacy activities. Secondly, educational strategies also were implemented by changing in curriculum in pharmacy education and promoting continuous training in clinical pharmacy. These strategies were considered as solutions to improve contributions of pharmacists to health care.

Chapter 2 is a literature review that determined why COPD and asthma are major health issues in Vietnam and worldwide, as well as the importance of inhaler technique and medication adherence in the management of these diseases. COPD and asthma are non-communicable diseases that cause significant morbidity and mortality worldwide. They place high pressure on the health care system and put a great burden on both society and economy, which is more evident in developing countries such as Vietnam. In addition, the review highlighted the importance of good inhaler technique and medication adherence to improving the quality of life, clinical outcomes, and financial costs of treatment for patients. Pharmacists can have a significant impact on improving inhaler technique and medication adherence for patients. The review also provided the rationale and approach for this research project which was conducted in both hospital and community settings in Vietnam.

Chapter 3 focused on developing and evaluating interventions for hospital pharmacists to improve inhaler technique for COPD patients in the national program. Our study showed that the pharmacist-led training program using an unbiased and simple scoring system can significantly improve the inhalation technique in COPD patients. The results demonstrated that the pharmacists' training initiative was a feasible service, as the training time for patients was between 3 to 6 minutes and could, therefore, be incorporated on top of their general activities.

We also identified that 3 months was the optimal time between training and re-training to maintain the perfect inhaler technique for patients following initial comprehensive training (three sessions). This study has shown our model of a pharmacist-led training program as an effective intervention for improving the inhalation technique of COPD patients and provides better utilisation of pharmacists in developing countries like Vietnam.

Chapter 4 describes our study on the impact of a pharmacist-led pharmaceutical care program on medication adherence, quality of life and clinical outcomes for COPD patients in the national program. Using a standardised Morisky Medication Adherence Scale, this study showed that pharmacists' counselling significantly improved medication adherence scores and the rate of "good" adherence in COPD patients. For quality of life, there was a significant increase in the percentage of patients having "no problems" and "little problems" as well as a decrease in the percentage of patients having "severe problems". Furthermore, the intervention also helped to stabilise the disease as determined by unchanged clinical symptom scores during the program. Stabilisation of the disease is a particularly important outcome for progressive and non-reversible diseases such as COPD.

Chapter 5 is based on our educational training program to improve the knowledge and skills of pharmacists to appropriately counsel asthmatic patients in a community pharmacy setting. The program was developed around core knowledge and skills recommended by respiratory physicians and senior pharmacists. We also evaluated the effectiveness of the training program in a real-life situation using a simulated patient study. The results showed that the pharmacists who attended the training program provided significantly better counselling with regards to the difference between relievers and controllers, the importance of medication adherence, common adverse effects and their prevention, and inhaler device training. Our short training program was highly effective in providing community pharmacists with the necessary knowledge and practical skills to effectively counsel patients with asthma about the

management of their condition and medications in Vietnam. It is suggested that such education programs should be promptly implemented and made compulsory for community pharmacists in Vietnam to improve the quality of counselling for patients with asthma and other non-communicable diseases.

In conclusion, this research project has demonstrated the significant impact of pharmacists in the management of COPD and asthma in Vietnam. In a hospital setting, pharmacists' interventions helped COPD patients to improve inhaler technique, medication adherence and quality of life, as well as to stabilise the disease. Our model should be considered an effective solution for the management of COPD and better utilisation of human resources in health care in a developing country like Vietnam. In a community setting, our training program provided pharmacists with the necessary knowledge and skills to effectively counsel asthmatic patients. The educational approach may be relevant to other countries similar to Vietnam, which may be limited in formal quality use of medicines training during tertiary qualifications and/or do not have continuing professional education programs for community pharmacists. The approach and solution methodology may also be applicable for improving the role of community pharmacists in the management of other chronic diseases such as cardiovascular diseases and diabetes.

Limitations

There are several limitations in our conducted studies, which is expected for trials in a clinical setting. These limitations have already been discussed in each individual chapter for each study. The following section is a summary of the limitations of the research project.

1. For the study in the hospital setting (Chapters 3 and 4):

- The study only included patients enrolled in the national program, which may overestimate the ability of the general COPD patients who would have less support than those in the program.
- Clinical outcomes in our study were only assessed by symptom score instead of other potential indicators such as respiratory function tests, days of hospitalization, and number of exacerbation periods. However, these indicators are only collected accurately and easily in a health care system with effective connections between hospitals. This is not feasible in a developing country like Vietnam with limited storing and sharing of patients' information among hospitals.

2. For the study in the community setting (Chapter 5):

- There was a potential selection bias when we selected the pharmacists who accepted the invitation to attend the training program for Parts 2 and 3 of the study. Although, there were no statistically difference between the two groups, the training group may have had more motivation to attend and learn. Therefore, they may get higher scores.
- We did not evaluate how long the effectiveness of the training would last. The effectiveness of the education program was evaluated 6-8 weeks post-training in the simulated patient study, but this may be an inadequately short period for assessing the long-term effects of the training.
- Generalisations of the results to different settings should be considered carefully because our study was performed only in one single city, albeit one of the largest cities in Vietnam.

Recommendations for future studies

By interpreting the findings and carefully analysing the limitations of this research project, there are some recommendations for future studies.

1. The model developed for pharmacist-led interventions should be evaluated in other settings and conditions such as: (1) patients with COPD and asthma in other hospitals and outside the national program, and (2) patients with other chronic conditions such as hypertension and diabetes. These studies will provide further support and evidence for the role of pharmacists in the management of non-communicable diseases, particularly in hospitals, and will encourage policy makers to integrate hospital pharmacists into the national programs as medication counsellors for patients with chronic diseases.
2. Future studies should also focus on the outcomes related to economic aspects. An effective model of intervention should be cost-effective for hospitals, patients and national programs.
3. It is recommended to evaluate the implementation of other training programs for community pharmacists in different settings and conditions. For example, incorporating pharmacies in rural areas and real patients with chronic diseases in the community. Different continuing professional education programs also should be developed and evaluated for other non-communicable diseases such as hypertension and diabetes. The results of these future studies would provide the foundation for policies regarding the involvement of pharmacists in the management of chronic diseases in the community setting.