การมีส่วนร่วมของเภสัชกรในการป้องกันความคลาดเคลื่อนจากการสั่งใช้ยาในผู้ป่วยเอชไอวี/เอดส์

นางสาวฐิติมา พยัฆศิริ

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PHARMACIST PARTICIPATION IN PRESCRIBING-ERROR PREVENTION AMONG HIV/AIDS PATIENTS

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A Thesis Submitted in Partial Fulfillment of the Requirements
for the Degree of Master of Science Program in Social and Administrative Pharmacy
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ฐิติมา พยัฆศิริ : การมีส่วนร่วมของเภสัชกร ในการป้องกันความคลาดเคลื่อนจากการสั่งใช้ยาในผู้ป่วยเอชไอวี/เอดส์ (PHARMACIST PARTICIPATION IN PRESCRIBING-ERROR PREVENTION AMONG HIV/AIDS PATIENTS) อ.ที่ปรึกษาวิทยานิพนธ์หลัก : รศ.ดร. วิทยา กุลสมบูรณ์, 84 หน้า.

การวิจัยนี้มีวัตถุประสงค์เพื่อ วิเคราะห์ความคลาดเคลื่อนทางยาของกระบวนการสั่งใช้ยาแก่ผู้ป่วยเอชไอวี/เอดส์ แยกตามประเภท อัตราการเกิด และความชุกของความคลาดเคลื่อน รวมทั้งประเมินการลดลงของความคลาดเคลื่อนจากการสั่งใช้ยา หลังจากเภสัชกรเข้าไปมีส่วนร่วมในการป้องกันความคลาดเคลื่อนจากการสั่งใช้ยา ทำการศึกษาในคลินิกเอชไอวี โรงพยาบาลสมุทรสาคร การศึกษาแบ่งเป็น 3 ช่วง ช่วงที่ 1 ศึกษากระบวนการสั่งใช้ยาและประเมินความคลาดเคลื่อนในการสั่งใช้ยาโดยผู้สังเกตการณ์ ระหว่างวันที่ 1 ตุลาคม ถึง 15 พฤศจิกายน ปี พ.ศ. 2550 ช่วงที่ 2 เภสัชกรร่วมกับแพทย์และพยาบาลพัฒนาระบบโดยการให้เภสัชกรเข้าไปมีส่วนร่วมในการลดความคลาดเคลื่อนในกระบวนการสั่งใช้ยาและทดสอบระบบ เป็นระยะเวลา 1 เดือน ช่วงที่ 3 ประเมินบทบาทของเภสัชกรในระบบดังกล่าวและความคลาดเคลื่อนในการสั่งใช้ยา ระหว่างวันที่ 15 ธันวาคม ปี พ.ศ. 2550 ถึง วันที่ 31 มกราคม ปี พ.ศ. 2551 ผู้ป่วยที่ถูกศึกษาในช่วงที่ 1 มีจำนวน 249 คน และในช่วงที่ 3 มีจำนวน 254 คน พบความคลาดเคลื่อนจากการสั่งใช้ยา 123 ครั้งในช่วงที่ 1 แต่พบเพียง 8 ครั้งในช่วงที่ 3 อัตราการเกิดความคลาดเคลื่อนของช่วงที่ 1 คิดเป็นร้อยละ 19.19 และช่วงที่ 3 คิดเป็นร้อยละ 1.20 ประเภทความคลาดเคลื่อนที่พบมากที่สุดคือ การสั่งใช้ยาผิดเวลา (ไม่เป็นตามช่วงเวลา) คิดเป็นร้อยละ 44.72, การสั่งยาไม่ระบุความแรง คิดเป็นร้อยละ 21.14 และการสั่งใช้ยาป้องกันโรคติดเชื้อฉวยโอกาสผิดข้อบ่งใช้ คิดเป็นร้อยละ 13.01 ประเภทของแพทย์ที่สั่งจ่ายยาคลาดเคลื่อนคือ แพทย์เสริมทักษะร้อยละ 45.45, แพทย์ตรวจโรคทั่วไปร้อยละ 23.17 และแพทย์เฉพาะทางร้อยละ 13.61 ทุกคำแนะนำของเภสัชกรได้รับการยอมรับจากแพทย์ ซึ่งได้แก่ การตรวจสอบคำสั่งใช้ยาให้ชัดเจนอีกครั้ง การเปลี่ยนเวลาใช้ยา และ การงดยาบางรายการ

ผลที่ได้จากการศึกษาบ่งชี้ว่า อัตราการสั่งจ่ายยาคลาดเคลื่อนที่ลดลงเป็นผลจากการมีส่วนร่วมของเภสัชกรในการป้องกันความคลาดเคลื่อนก่อนที่แพทย์จะมีการสั่งใช้ยา ซึ่งได้แก่ การทบทวนสูตรยา, การใช้ตราปั๊มสำเร็จรูปที่มีชื่อยาต้านไวรัส, การคำนวณปริมาณยา, และการจัดเตรียมยาล่วงหน้า

ข้อเสนอแนะจากการศึกษานี้ คือ การร่วมมือกับแพทย์และพยาบาลในการพัฒนาระบบโดยให้เภสัชกรเข้าไปมีส่วนร่วมในการป้องกันความคลาดเคลื่อนจากการสั่งใช้ยา ซึ่งจะทำให้เกิดความมั่นใจได้ว่า ผู้ป่วยจะได้รับยาที่ปลอดภัยและเหมาะสม

ภาควิชาเภสัชศาสตร์สังคมและบริหาร.....ลายมือชื่อนิสิต.....ฐิติมา พยัฆศิริ.....

ปีการศึกษา.....2551.....ลายมือชื่อ อ.ที่ปรึกษาวิทยานิพนธ์หลัก.....Vitaya K.....

##4976858733: MAJOR SOCIAL AND ADMINISTRATIVE PHARMACY
KEY WORDS: PRESCRIBING ERROR/ PHARMACIST PARTICIPATION/
PRESCRIBING ERROR PREVENTION/ HIV/AIDS

THITIMA PAYAKSIRI : PHARMACIST PARTICIPATION IN
PRESCRIBING-ERROR PREVENTION AMONG HIV/AIDS PATIENTS. THESIS
PRINCIPAL ADVISOR : ASSOC. PROF. VITTHAYA KULSOMBOON, 84 pp.

The objectives of this study were to analyse prescribing errors in the prescribing process of HIV/AIDS patients in term of types, rate and prevalence of error, and to assess the reduction of prescribing error after pharmacist participation on prescribing error prevention. The study was conducted in the HIV clinic at Samutsakhon Hospital. The study was divided into three phases. In phase 1, the prescribing process was observed and prescribing errors were assessed by the investigator during October 1, 2007 to November 15, 2007. In phase 2, pharmacists with physicians and nurses develop the model of pharmacist participation in prescribing error prevention and the model was tested for a 1-month period. In phase 3, The role of pharmacist in the model and prescribing errors were evaluated during December 15, 2007 to January 31, 2008. A total of 249 patients in phase 1 and 254 patients in phase 3 were evaluated. There were 123 prescribing errors in phase 1 but only 8 prescribing errors in phase 3. The error rates were 19.19% in phase 1 and 1.20% in phase 3. Types of errors most commonly found were prescribing medication with the incorrect time (not around the clock)(44.72%), do not specified strength (21.14%), and incorrect indication of opportunistic infections (13.01%). Types of physician associated with prescribing errors were internist (45.45%), general practitioner (23.17%), and medical specialist (13.61%). All pharmacists' recommendations to physician were accepted, including clarification of order, time changing, and cessation of drug.

The results indicated that substantial reduction of prescribing error rate came from pharmacist participation prior to physician prescribing which included reviewing the regimen, identifying the name of antiretroviral regimen using self-inking stamp, calculating the quantity of medication, and preparing the medication.

This study recommended that collaboration with physicians and nurses to develop the system that enhances pharmacist participation in prescribing error prevention will ensure that patients are safe and receive appropriate drug therapy.

Field of study: Social and Administrative Pharmacy Student's signature Thitima Payaksiri

Academic year: .....2008.....Principal advisor's signature Vitthaya Kulsom

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LIST OF ABBREVIATIONS

3TC	=	lamivudine
ADR	=	adverse drug reaction
Ag	=	antigen
AIDS	=	acquired immunodeficiency syndrome
ALT	=	alanine aminotransferase
ART	=	antiretroviral therapy
ARV	=	antiretroviral
AST	=	aspartate aminotransferase
AZT	=	zidovudine
CD4 count	=	CD4+ T-cell (T-lymphocyte bearing CD4 receptor)
CNS	=	central nervous system
d4T	=	stavudine
ddI	=	didanosine
EFV	=	efavirenz
FDC	=	fixed-dose combination
FTC	=	emtricitabine
HAART	=	Highly Active Anti-Retroviral Treatment
HB	=	hepatitis B
HIV	=	human immunodeficiency virus
IDV	=	indinavir
INH	=	isoniazid
LFT	=	liver function test

LPV	=	lopinavir
MTCT	=	mother-to-child transmission (of HIV)
NFV	=	nelfinavir
NNRTI	=	non nucleoside reverse transcriptase inhibitor
NRTI	=	nucleoside reverse transcriptase inhibitor
NVP	=	nevirapine
OI	=	opportunistic infection
OPD	=	out patient department
PCP	=	pneumocystis pneumonia
PI	=	protease inhibitor
q	=	every
/r	=	low-dose ritonavir
RTV	=	ritonavir
TB	=	tuberculosis
TDF	=	tenofovir disoproxil fumarate
TOE	=	total opportunities for error
WHO	=	World Health Organization

CHAPTER I
INTRODUCTION

The human immunodeficiency virus (HIV) is a retrovirus that infects cells of the human immune system, destroying or impairing their function. In the early stages of infection, the person has no symptoms. However, as the infection progresses, the immune system becomes weaker, and the person becomes more susceptible to opportunistic infections. The most advanced stage of HIV infection is acquired immunodeficiency syndrome (AIDS). It can take 10-15 years for an HIV-infected person to develop AIDS; antiretroviral drugs can slow down the process even further.

About 33 million people are now living with HIV, of whom more than 30 million live in low and middle income countries. WHO estimates that at least 9.7 million of these people are in need of antiretroviral treatment (ART). As of December 2007, there are 3 million people had access to ART in low- and middle-income countries.[1]

Several studies have shown that antiretroviral treatment reduces both mortality and morbidity rate of HIV infection, but routine access to antiretroviral medication is not available in every country. Current treatment for HIV infection that is widely acceptable is consists of highly active antiretroviral therapy, or HAART. This has been highly beneficial to HIV-infected individual since its introduction in 1996 when the protease inhibitor-based HAART initially became available. Current optimal HAART consists of at least three ARV drugs. These ARV drugs belong to, at least, two types of anti-retroviral agents. Typical regimens consist of two nucleoside analogue reverse transcriptase inhibitors (NRTIs) plus either a protease inhibitor or a non-nucleoside reverse transcriptase inhibitor

(NNRTI). HAART stabilizes of patient's symptoms and viremia, but it neither cures the patient of HIV, nor alleviates the symptoms, and high levels of HIV-1, often HAART resistant, return once treatment is stopped. Moreover, it would take more than the lifetime of an individual to be cleared of HIV infection using HAART. Despite this, many HIV-infected individuals have experienced remarkable improvements in their general health and quality of life, which has led to the plummeting of HIV-associated morbidity and mortality. In the absence of HAART, progression from HIV infection to AIDS occurs at a median of nine to ten years and the median survival time after developing AIDS is only 9.2 months. HAART is thought to increase survival time between 4 and 12 years. HAART achieves far less than optimal results. This is due to a variety of reasons such as medication intolerance/side effects, prior ineffective antiretroviral therapy and infection with a drug-resistant strain of HIV. However, non-adherence and non-persistence with antiretroviral therapy are the major reasons most that individuals fail to get any benefit from HAART. The reasons for non-adherence and non-persistence with HAART varied. Major psychosocial issues, such as poor access to medical care, inadequate social supports, psychiatric disease and drug abuse, contribute to non-adherence. The complexity of these HAART regimens, whether due to pill number, dosing frequency, meal restrictions or other issues along with side effects, create non-adherence resulting in adverse consequences. The side effects include lipodystrophy, dyslipidaemia, insulin resistance, an increase in cardiovascular risks and birth defects.[2]

In Thailand, about 700,000 people out of a population of 63 million are infected with HIV. It is estimated that 2 % of men and 1 % of women are currently living with HIV. There are 30,000 to 50,000 new AIDS and HIV infected patients each year. As a result of successful prevention campaign, the incidence of newly HIV infected has stabilized.[3]

There are 22 ARV agents within the four classes which were approved for the treatment of HIV infection by the US Food and Drug Administration (FDA). Prescribing ARV therapy can be complex since the medications have multiple names, abbreviations, dosing strategies, and regimen permutations. In addition, the nationwide shortage of pharmacists places extra time constraints on careful filling, double-checking, and counseling of any complicated medication regimen-including ARVs. People who are infected with HIV may not be familiar with the number of tablets per dose, frequency of administration, dietary requirements of their regimens, side-effect management, and the dangers of nonadherence-despite multiple educational sessions. These factors as well as others make the ARV agents be a target for potential medication errors.[4]

Improved understanding of the type, frequency, and associated factors of medication errors should assist in the implementation of more effective error prevention strategies. Medication error may be detected and prevented by a multidisciplinary team, including physicians, pharmacists, nurses, supportive personnel (e.g., pharmacy assistants), patients, and others.

Pharmacist can bring such changes to establish measurement and to monitor of medication-use process. These changes will also make pharmacist more possible to use the information gained from monitoring to work collaboratively with nurses and physicians in order to improve patient safety.

The improvement of prescribing process of HIV clinic in Samutsakhon Hospital, a provincial hospital of 509 beds, the process of HIV care starts from the patient met the nurse for measuring vital sign and gathering patient's data. After that patients met with a physician who prescribes ARV medication. Then, patients met the nurse again. The nurse write lab request and make an appointment date for next follow up. Finally

patients receive medicine from pharmacy department. In such process, if there are some problems about prescribing error, pharmacist will discuss with physician to solve the error. Previous approach to prevent medication error is inadequate owing to insufficient data about the prevalence, types, and cause of errors. In order to increase the quality of treatment, medication analysis is established in the HIV clinic. Risk management to reduce and prevent such error is organized. This study was thus performed to obtain the following objectives. The prescribing process at the HIV clinic was analyzed and pharmacist participation was implemented as a model.

Objectives of the study

1. To describe type and prevalence of prescribing errors occurring in pharmacist participation on prescribing error prevention among HIV/AIDs patients.
2. To assess the reduction of prescribing error after pharmacist participation on prescribing error prevention among HIV/AIDs patients.

Expected benefit

1. The well-established role of pharmacist in HIV/AIDs patients care team will be described.
2. Preventable adverse drug events occurring among HIV/AIDs patients receiving anti-retroviral treatment will be minimized.
3. Appropriate and correct treatment in the medication use process could result in substantial improvement in patient safety.

CHAPTER II
LITERATURE REVIEW

Antiretroviral Therapy[5-6]

Potent combination antiretroviral therapy (ART), consisting of 3 or more antiretroviral drugs (ARV), has greatly improved the health and survival rates of HIV-infected patients in the areas around the world that need the access to ARVs.

More than 20 individual ARV regimens are available in the resource sufficient world, in addition to several fixed-dose combination preparations. These can be combined to construct a number of effective regimens for initial and subsequent therapy. ART is not without limitations, however. ART does not cure HIV infection and it requires that multiple medications be taken for very long periods of time (usually for the duration of life). It is very expensive, and may cause a variety of adverse effects. It requires effective adherence in order to prevent the emergence of resistance, and treatment failure. The failure of an ARV regimen from drug resistance usually means that subsequent regimens are less likely to succeed.

The process of initiating ART involves assessing patient readiness to commence therapy and understanding of its implications including lifelong therapy, adherence, and toxicities. Obtaining nutritional and psychosocial support, and receiving family and peer support groups are important when decisions are being made about the initiation of ART.

The optimum time to commence ART is before patients become unwell or present with their first opportunistic infection. Immunological monitoring (CD4 testing) is the ideal way to approach this situation. A baseline CD4 cell count not only guides the decision on when to initiate

ART but is also essential if CD4 counts are to be used to monitor ART. Table 1 summarizes the immunological criteria for the initiation of ART.

Table 2.1 CD4 criteria for the initiation of ART in adults and adolescents [5,67]

Clinical symptom	CD4 (cells/mm^3)	Treatment recommendation
AIDS-defining illness	any	Start ART
Symptomatic*	any	Start ART
Asymptomatic	<200	Start ART
Asymptomatic	200-350	Do not initiate treatment, follow symptom and CD4 every 3 months
Asymptomatic	>350	Do not initiate treatment, follow symptom and CD4 every 6 months

*symptomatic such as: oral thrus, Pruritic Popular Eruptions (PPE), fever, diarrhea.

The use of standardized regimens has been an essential factor in expanding access to ART. First line regimen for adults and adolescents contains two NRTIs plus one NNRTI, which is efficacious and is generally less expensive than other regimens. These ARV regimen are available as fixed-dose combinations and do not require cold chain. In addition, a potent new class, protease inhibitors for second-line treatments is preferred. Disadvantages include different drug half-life resulting in the complicated ART stopping process. The fact, that a single mutation is associated with resistance to some drugs, and cross-resistance within the NNRTI class.

The preferred NRTI backbone is composed of AZT or TDF combined with either 3TC. Didanosine (ddI) is an adenosine analogue NRTI recommended to be reserved for second-line regimens. Finally an NNRTI, either EFV or NVP, should be added.

Choice of NRTIs

Lamivudine (3TC) has been and remains pivotal to all first-line ARV regimens in resource limited settings. It is a core component of the dual NRTI backbone in all ARV combinations. It has proved safe, has a favourable toxicity profile, nonteratogenic, effective against hepatitis B infection, relatively cheap to produce and widely available, including in fixed-dose combinations (FDCs).

Emtricitabine (FTC) is a new NRTI that has recently been included in WHO's recommended first-line regimens. FTC is an equivalent alternative to 3TC as it is structurally related to 3TC shares the same efficacy against HIV and hepatitis B virus and has the same resistance profile. It is available as an FDC with TDF and, recently, a formulation with TDF, and EFV as a single, "three-in-one" pill was approved for clinical use. FTC is not yet on the WHO list of essential medications.

Zidovudine (AZT) is included as a preferred first-line NRTI. It is generally well tolerated and widely available in some FDCs. Initial drug-related side effects are headache and nausea, and it can also cause severe anemia and neutropenia. Hemoglobin monitoring is recommended before and during treatment with AZT. This is particularly important in areas with a high prevalence of malaria, where anemia is common. AZT is associated with metabolic complications, such as lactic acidosis and lipoatrophy, but to a lesser extent than d4T.

Tenofovir (TDF) is now included as a preferred first-line NRTI, because of its efficacy, ease of use and safety profile. This is a change from the 2003 guidelines, which recommended reserving the use of TDF as part of second-line regimens. TDF has long intracellular half-life and can be used as part of once daily regimens. It is generally well tolerated and studies suggest that it is not more frequently associated with renal insufficiency in patients receiving TDF, the occurrence of renal dysfunction in this contest is usually attributable to other causes. The dose of TDF should be reduced in patients with underlying renal insufficiency.

Stavudine (d4T) is recognized as a life-saving drug that has played a crucial role in ART rollout, especially because of its availability in fixed-dose combinations, the low cost of these FDCs and the clinical efficacy of the regimens recommended. d4T has also been preferred over AZT because of the requirement for limited or no laboratory monitoring. However, d4T has been consistently the NRTI most associated with lactic acidosis, lipoatrophy and peripheral neuropathy. The latter toxicities are cumulative and often irreversible, and have the potential to affect adherence in the long term. The stigmatization associated with lipoatrophy can result in withdrawal from or refusal to enroll in ART programs.

Choice of NNRTIs

NNRTIs are potent and the key ARV class to be combined with a dual NRTI backbone in first-line therapy and facilitate the construction of relatively simple initial regimens.

Nevirapine (NVP) is widely available (including in several FDCs) and is less costly than EFV. Moreover, significant experience has been gained with this drug at country leveling resource-limited settings. However, a higher incidence of rash is associated with it than with

EFV. NVP-related rash may be severe and life-threatening, and Stevens-Johnson syndrome may occur. NVP is also associated with a rare but potentially life-threatening risk of hepatotoxicity. This makes the drug less suitable for treating patients who use other hepatotoxic medications. In the case of severe hepatic or skin reactions, NVP should be permanently discontinued and not restarted. NVP is the preferred NNRTI for women if there is potential for pregnancy or during the first trimester of pregnancy, when EFV can not be used because of its teratogenic effect. However, symptomatic NVP-associated hepatic toxicity or serious rash, while uncommon, is more frequent in women than in men.

Efavirenz (EFV) can be used once daily and is generally well tolerated. However, it is relatively costly and currently less widely available than NVP. It is primarily associated with toxicities related to the central nervous system (CNS), teratogenicity and rash. Rash is generally mild, self-resolving and usually does not require the discontinuation of therapy. EFV should be avoided in patients with a history of severe psychiatric illness, when there is a potential for pregnancy and during the first trimester of pregnancy. In these situations, NVP may be the better choice. EFV is the NNRTI of choice in individuals with TB/HIV coinfection who are receiving rifampicin-based TB therapy.

Use of protease inhibitors

The key element in the construction of an effective second-line regimen for treatment failure is the PI component, as this represents a potent drug from an entirely new class of agents. Maximizing the potency of the PI component is critical for successful virological suppression and durability of response. For this reason, a ritonavir-boosted PI is recommended as the core of the second-line regimen.

There are insufficient data on the differences between ritonavir-boosted PIs to allow the recommendation of one agent over another. Ritonavir-boosted Lopinavir (LPV/r) has the advantage of being available as an FDC; moreover, the recent approval of a heat-stable tablet formulation eliminates the need for refrigeration. For other PIs to be boosted, ritonavir in heat-stable formulation is also desirable, particularly in countries with hot climates, but it has not been developed. If LPV/r is not an option, Ritonavir-boosted Indinavir (IDV/r) is effective but the incidence of nephrolithiasis and the daily fluid requirement make this choice less attractive. In the absence of a cold chain and in advance of the availability of the new formulation of LPV/r, nelfinavir (NFV) is an acceptable alternative choice for the PI component, although it is less potent than a boosted PI.

ARV combinations to be avoided or used with caution

Monotherapy or dual therapy should not be used to treat chronic HIV infection; they may only be used in the setting of prevention of MTCT and post-exposure prophylaxis. Certain dual NRTI backbone combinations should not be used within three-drug therapy. These are d4T+AZT (proven antagonism). d4T+ddI (overlapping toxicities) and 3TC+FTC (interchangeable, but should not be used together). The combinations of TDF+3TC+ABC and TDF+3TC+ddI select for the K65R mutation and are associated with high incidences of early virological failure. The combinations of TDF+ddI+any NNRTI are also associated with high rates of early virological failure. However, the use of ddI should be reserved for second-line treatment, in which situation it is possible to consider TDF+ddI with boosted PIs, provided that caution and close monitoring are practiced,

until more data become available. The ddI dose should be adjusted when used concomitantly with TDF in order to reduce the toxicity risk.

Definition of medication error

The National coordinating Council for Medication Error Reporting and Prevention (NCCMERP) defines a medication error as any preventable event that may cause or lead to inappropriate medication use or patient harm while the medication is in the control of the health care professional, patient, or consumer. Such events may be related to professional practice, health care products, or procedures, and systems, including prescribing; order communication; product labeling; packaging, and nomenclature; compounding; dispensing; distribution; administration; education; monitoring; and use.[7]

Type of medication errors

The problems and sources of medication errors are multidisciplinary and multifactorial.[8-9] Medication errors are divided into four main categories, namely prescribing error, transcribing error, dispensing error, and administration error.[10] These errors can be caused by many factors, including system failure, human failure, or a combination. System factors may be related to the complexity of medication-use process, the type of drug and route of administration, and the physical appearance and availability of the drug product, Human factors may involve a health professional' s knowledge, experience, and education; interruptions; distractions; and fatigue.[11]

Frequency of medication errors

The overall rate of errors was 3.99 errors per 1000 medication orders, and the error rate varied among medication classes and prescribing services. The most common specific factors associated with errors were decline in renal or hepatic function requiring alteration of drug therapy (97 errors, 13.9%), patient history of allergy to the same medication class (84 errors, 12.1%), using the wrong drug name, dosage form, or abbreviation (total of 79 errors, 11.4%, for both brand name and generic name orders), incorrect dosage calculations (77 errors**,** 11.1%), and atypical or unusual and critical dosage frequency considerations (75 errors, 10.8%). The most common groups of factors associated with errors were those related to knowledge and the application of knowledge regarding drug therapy (209 errors, 30%); knowledge and use of knowledge regarding patient factors that affect drug therapy (203 errors, 29.2%); use of calculations, decimal points, or unit and rate expression factors (122 errors, 17.5%); and nomenclature factors (incorrect drug name, dosage form, or abbreviation) (93 errors, 13.4%). By improving the focus of organizational, technological, and risk management educational and training efforts using the factors commonly associated with prescribing errors, risk to patients from adverse drug events should be reduced.[12]

Medication error prevention by pharmacist

The overall error rates of pharmacist intervention in preventing potential harm by record the frequency and potential harm caused by errant medication orders at two large pediatric hospitals were 1.35 and 1.77 per 100-patient days, and 4.9 and 4.5 per 1,000 medication orders, respectively. The most type of error was incorrect dosage, and the most prevalent type of

error was over dosage. Antibiotic was the class of drugs for which errant orders were most common. At both institutions, physicians with the most training were least likely to write errant medication orders. This may result simply from their increased skill and experience.[13]

In a general hospital in Israel during a 6-month period. A total of 160 medication order errors were detected at the hospital of which 60.6% were prescription errors and 39.4% were therapy ones. Principal types of errors detected were incorrect dosage (27.5%), interactions between drugs (20%), incorrect drug (12.5%), route (11.2%) and frequency (11.2%). Medication error rate by degree of severity was calculated per 100 patient days. The highest rate was found in Hemato-Oncology (2.48), followed by Intensive Care (0.82), Surgery (0.48) and Internal Medicine (0.26). Anti-infective drugs were the most prevalent class of drugs in which errors occurred (38.7%) followed by total parenteral nutrition preparations (21.8%), antineoplastics (15.6%) and anticoagulants (11.3%). Changes in medication orders due to pharmacists' intervention only occurred in 73.8% of error cases, most referring to dosage or route change (37.5%).[14]

Medication errors were detected using self-report by pharmacists, nurse review of all patient charts to classify errors by type during a 51-day. Over the study period, 10,070 medication orders were written, and 530 medications errors were identified. Of the medication errors; 53% involved at least one missing dose of a medication, 8% frequency errors, and 5% route errors.[15]

HAART errors

HAART errors included the following: incomplete regimen, incorrect dosage, incorrect schedule, medication-disease interaction,

incorrect formulation, incorrect antiretroviral, duplication of therapy, and drug-drug interaction.

A total of 73 HAART errors were confirmed in 41 patients in 651 beds tertiary care teaching hospital between August 4, 2005 and February 4, 2006. The most common type of error was incomplete regimen. There was no significant difference in the frequency or type of prescribing when comparing the pre-intervention and intervention phases.[16]

The analysis of medication errors involved at least one single or combined HIV antiretroviral product revealed that 3% of the errors were harmful. Most of the errors (45%) occurred in the dispensing phase of the medication use process, a finding that differs significantly from many published studies. The most frequent types of errors were wrong dose (37.5%) and wrong medication (32%). Lamivudine was the most commonly identified product to be involved in the errors. Community hospitals were more likely to have prescribing errors than teaching hospitals. Similar brand and generic names were associated with many of the errors. With frequent dosing of many HIV medications, health care organizations must have a process to clarify orders rapidly and maintain current references of antiretrovirals. Prescribers should clearly spell out the intended product and avoid abbreviations.[17]

A total of 108 clinically significant prescribing errors involving antiretrovirals were detected during the 34-month study period. The most common errors were overdosing and underdosing. Overall, errors occurred in 5.8% of admitted patients prescribed antiretroviral medications. The rate of error increased from 2% of admissions in 1996 to 12% of admissions in 1998. The most common likely related factors associated with errors were confusion/lack of familiarity regarding appropriate dosing frequency (30.3%) or dosage (25.5%), and confusion due to need for multiple dosage units per dose (13%). This information should be considered in the

development of medication error prevention strategies necessary to prevent adverse patient outcomes resulting from such errors.[18]

Persons with HIV have compromised immune systems and often take many medications. Thus, the risk and consequences of medication errors are severe, and both providers and patients should carefully monitor drug regimens to ensure that they are both safe and efficacious.[19]

HAART-related medication-prescribing errors; the causes of these errors are often multifactorial and include lack of knowledge about HIV treatments, complexity of regimens, and sound-alike/look-alike names of medications. Clinicians caring for HIV-infected patients should be aware of the potential for prescribing errors associated with HAART and employ strategies to prevent them.[20]

Several published reports describe medication errors in patients with HIV, which appear to be related to a lack of knowledge, inexperience, complexities of the antiretroviral regimens, and sound-alike and look-alike names.[21]

Errors identified with ordering protease inhibitors included the incorrect frequency, the incorrect dose, and the ordering of protease inhibitor as a monotherapeutic agent instead of in combination with other recommended antiretroviral agents.[22]

Contributing factors of prescribing errors

Many factors have been associated with prescribing errors, including knowledge and the application of knowledge regarding drug therapy, inadequate patient history, calculations, decimal point errors, medication with sound-alike or look-alike names, use of abbreviations.

Systematic evaluation type and frequency of identifiable factors associated with prescribing errors. Of every third prescribing error was

detected and averted by pharmacists in a 631-bed tertiary care teaching hospital during the 1-year study period. Each error was retrospectively evaluated by a physician and two pharmacists and a factor likely related to the error was identified. A total of 2.103 confirmed clinically significant medication prescribing errors were detected. Of the 696 potentially significant prescribing errors were evaluated for a likely related factor. The most common specific factors associated with errors were the presence of pathophysiological status or disease (renal impairment, hepatic failure) that required alteration of drug therapy (13.9%), patient history of allergy to the same medication class (12.1%), using the wrong drug name, dosage form, or abbreviation (11.4%), and incorrect dosage calculations (11.1%).[12]

Numbers containing decimal points are a major source of errors.[23] They can easily be missed, especially on on-lined order sheets, carbon forms, and faxes. If a decimal point is missed, an overdose may occur. Decimal expressions of less than 1 should always be preceded by a zero to enhance the visibility of the decimal. A space should appear between the name of the medication and the dose, as well as between the dose and the units.[24]

Patient-specific information (e.g., height, weight, age, and body system function) should be used to calculate the correct dose for an individual patient if the medication in question is influenced by these factors. [26] Dosages of medications for infants and children may be calculated on the basis of age, status of prematurity, weight, and body surface area (height and weight). Children are at particular risk for calculation errors, as the broad range of patient age and size requires dosage individualization, most often using dosage equations.[25]

The risk for error is particular concern for chemotherapeutic agents to treat cancer, for which very complicated and atypical dosage regimens are used.[26] Study of Lesar shown errors involving children resulted in

overdose 56.1% and underdose 43.9%. Dosage calculation errors most commonly involved in antimicrobial agents (53.5%); the class of electrolytes, minerals, and vitamins (8.0%); and gastrointestinal agents (5.5%). Errors in decimal point placement, mathematical calculation, or expression of dosage regimen accounted for 59.5% of dosage errors. The use of an errant dosage equation resulted in 29.5% of all errors. The most common errors were the wrong dose or frequency used in the equation.

Abbreviations are convenience, a time saver, a space saver, and a way of avoiding the possibility of misspelling words. Abbreviations are sometimes not understood, misread, or are interpreted incorrectly

The existence of confusing drug names is one of the most common caused of medication error and is of concern worldwide. Contributing to this confusion are illegible hand-writing , incomplete knowledge of drug names, newly available products, similar packaging or labeling, similar clinical use, similar strengths and dosage forms authorities to recognize the potential for error. To reduced the potential for error requiring “read back” clarification of oral orders and improvements in communications with patients.[27]

Poor handwriting by physician is a common cause of medication error. Illegible prescriptions can easily be misinterpreted, resulting in patient injury or death. Physicians must take responsibility in ensuring their prescription order is clearly communicated by taking the time to write or print carefully.

Potential problems existed in the order-writing process for inpatients were reviewed for a seven-day period in 1997. More than 10% of all orders had illegible handwriting or were written with a felt-tip pen, which makes copies difficult to read. Other potential errors were also identified. Following educational programs for physicians and residents focusing on the importance of writing orders clearly, physician orders were reviewed

for a 24-hour period. The use of felt-tip pens decreased to 1.37% of all orders, and no orders had illegible handwriting.[28]

Error management is based on understanding the nature and extent of error, changing the conditions that induce error, and determining behaviors that prevent or mitigate error. Physician computer order entry represents a major system change with great potential for reducing serious medication errors. In physician order entry, physicians write orders using the computer. Drug orders will require a drug name, dose, route, and frequency which will eliminate errors of omission. All orders will legible, and transcription errors will be eliminated. Computerized dose checking and guided dose algorithms should decrease the occurrence of orders with incorrect dosages. Computers can also store relevant information regarding drug-drug interactions, known allergies, and appropriate dosage schedule according to the patient's characteristics.[29-33] Other strategies is the enhancement of the role of clinical pharmacist by increasing his or her participation in physicians' rounds.[10][34-35] When screening prescription orders before dispensing, pharmacists maintain the four stages to problem solving.[35] The first responsibility is to verify the completeness and legality of the prescription order. Fulfilling this responsibility requires that the pharmacist know all state and federal laws relating to the distribution of prescription drug products. The pharmacist's second responsibility is to ensure the appropriateness of the dose, route of administration, and duration of therapy. Third, the pharmacist must assess the ingredients of the prescription order for physical and chemical compatibility with each other, and with other food and drug products the patient is using. Finally, the pharmacist is responsible for ensuring the appropriateness of the prescription order within the context of the patient's medication history and ongoing drug therapy.

Type of prescribing error

Prescribing error is defined as incorrect drug selection (based on indications, contraindications, known allergies, and existing drug therapy), dose, dosage form, quantity, route, concentration, rate of administration, or instructions for use of a drug product ordered or authorized by physician (or other legitimate prescriber); illegible prescriptions or medication orders leading to errors that reach the patients.[11,36]

Prescriptions that are missing an essential information are considered to have errors of omission.[34][37-38] The most commonly reported errors of omission are as follows:

-Incomplete specification of dosage form or strength

-Failure to specify the quantity to dispense or duration of therapy

-Failure to specify the dose or dosage regimen

-Failure to write the prescription legibly.

Prescriptions that contain incorrect information concerning the drug therapy or those that duplicate existing therapy are judged to contain errors of commission.[34][37-38] The most common errors of commission are as follows:

-Incorrect dose or dosage regimen

-Incorrect drug or indication for use

-Incorrect dosage form

-Incorrect quantity or duration of therapy

-Therapeutic duplication

-Incorrect patient name on the prescription order

-Prescription orders containing drug interactions

Frequency of prescribing errors

Errors in the prescribing step are common and account for a large proportion of the preventable adverse drug events in hospitals. Studies carried out in US hospitals suggest that prescribing errors occur in 0.4-1.9% of all medication orders written.[39] Mandal et al [40] evaluated the number of errors of prescribing during a 4 week period at an eye hospital in UK. Overall 144/1952 (8%) prescription sheets had errors. 7% of the total errors were errors of prescription writing while 1% were drug errors. The majority of errors were made by junior doctors and no drug errors were made by senior doctors.

Prescribing problems reported by nine community pharmacists for 1-month period. 32,403 items dispensed, pharmacists reported 196 prescribing problems (0.6%). The reporting rates ranged from 0.2%-1.9% between pharmacists and were inversely correlated to dispensing volume. Prescriptions containing incomplete or incorrect information accounted for two-thirds of the problems. Lack of information on the prescriptions and transcribing / typing errors were the most frequently cited proximal causes. [41]

905 prescribing errors from a total of 289,411 medication orders were detected and averted in a tertiary-care teaching hospital. During the 1-year period, of which 522 (57.7%) were rated as having potential for

adverse consequences. The overall detected error rate was 3.13 errors for each 1000 orders written and a rate of 1.81 significant errors per 1000 orders. The error rate (4.01 per 1000 orders) was greatest between 12 p.m. and 3.39 p.m. First-year postgraduate residents were found to have a higher error rate (4.25 per 1000 orders) than other prescriber classes.[42]

Problems in prescribing medicines to children in the UK and Ireland between January 1997 and March 2005. Of which 615 HIV infected children aged 2-12 years were prescribed antiretrovirals. Actual doses standardized to weight or surface area varied widely across individual drugs, antiretroviral class, and calendar time, with children underdosed (prescribed less than 90% of current recommended doses) from 6-62% child time at risk. Three serious issues in prescribing antiretrovirals, which may also be relevant to paediatric prescribing in general, were identified. Firstly, dosing was inadequate before correct recommendations at licensing were later revised when important pharmacokinetic results emerged. Secondly, guidelines stating dosage alternatives (by weight / surface area) for the same drug led to different and inconsistent doses. And, thirdly, ongoing growth was not adjusted for.[43]

The number of prescribing errors occurred among HIV-positive people receiving highly active antiretroviral therapy who were admitted to a single hospital over one year. According to the study, errors in drug dosage of antiretroviral occurred in 34 (16.3%) admissions; errors in combining antiretrovirals with a contraindicated medication occurred in 12 (5.2%) admissions; errors in the number of different antiretrovirals received occurred in 8 (3.8%) admissions; and 7 (3.3%) of HIV-positive people admitted experienced delays in receiving antiretrovirals.[44]

Study in Songklanagarind hospital, evaluated prescriptions filled in the outpatient pharmacy service, during 1-31 July 2000. Among the 25,247 prescriptions filled (61,574 items), errors were detected in 445 items (0.72%). The most common type of prescribing errors was missing information (60.7% of errors detected). Drug strength omission was the most common type of missing information (44%).[45]

Routine discussion of identified medication errors will lead to prevention of future problems. Prevention is a key because a serious medication error that causes harm can lead to significant financial loss to the hospital.[46-47]

Strategies to prevent prescribing error

1. Computerized Physician Order Entry (CPOE)

Physician computer order entry represents a major system change with great potential for reducing serious medication errors. In physician order entry, physicians write orders using the computer. Drug orders will require a drug name, dose, route, and frequency which will eliminate errors of omission. All orders will legible, and transcription errors will be eliminated. Computerized dose checking and guided dose algorithms should decrease the occurrence of orders with incorrect dosages. Computers can also store relevant information regarding drug-drug interactions, known allergies, and appropriate dosage schedule according to the patient's characteristics.[10][29-33][48]

Several recent studies in hospitals have shown that computerized physician order entry (CPOE) improvements in medication error rates. CPOE is an application in which physicians write orders online. Computerization of ordering improves safety in several ways: firstly, all

orders are structured, so that they must include a dose, route, and frequency; secondly, they are legible and the orderer can be identified in all instances; thirdly, information can be provided to the orderer during the process; and fourthly, all orders can be checked for a number of problems including allergies, drug interactions, overly high doses, drug-laboratory problems , and whether the dose is appropriate for the patient's liver and kidney function.[49] One noteworthy example found a 55% reduction in errors with potential for harm; the program greatly reduced the need for transcription, and it minimized misinterpretations caused by illegibility. [50-51]

The effect of computerized physician order entry for prevention of serious medication errors during a 15-month period. Comparing between phase 1 (baseline) and phase 2 (after intervention), serious medication errors decreased 55%, from 10.7 events per 1000 patient-days to 4.86 events per 1000 patient-days. The rate of ordering errors decreased 19% overall. The number of transcription errors fell by 84%. The rates of dispensing and administration errors also fell between phased 1 and 2, 68% and 59%, respectively.[51]

1,879 prescriptions reviewed the rates, types, and severity of outpatient prescribing errors. Of these, 62 represented potential ADEs, 3 led to preventable ADEs, and 78 were errors with no potential for harm. The most frequent errors were incorrect or missing dose or frequency. Advanced computerized prescribing could have prevented 138 of 143 (97%) prescribing error and 59 of 62 (95%) potential ADEs.[52]

In the Brigham and Women's hospital, which in a 726-bed tertiary referral centre, the use of a physician computer order entry (POE) system was evaluated. The study comparing between baseline period and

implementation of the POE system. Use of the POE system prevented more than half of the serious medication errors. There were just under 11 of these per 1000 patient days at baseline, and under 5 per 1000 patient day during use of the POE system. Potential errors which had not been intercepted fell most, by 84%. Preventable errors fell by 17%.[53]

2. Role of pharmacist in error prevention

Other strategy is the enhancement of the role of clinical pharmacist by increasing participation in physicians' rounds.[10][34-35] When screening prescription orders before dispensing, pharmacists maintain the four stages to problem solving.[38] The first responsibility is to verify the completeness and legality of the prescription order. Fulfilling this responsibility requires that the pharmacist know all state and federal laws relating to the distribution of prescription drug products. The second is to ensure the appropriateness of the dose, route of administration, and duration of therapy. Third, the pharmacist must assess the ingredients of the prescription order for physical and chemical compatibility with each other, and with other food and drug products the patient is using. Finally, the pharmacist is responsible for ensuring the appropriateness of the prescription order within the context of the patient's medication history and ongoing drug therapy.

The effect of pharmacist participation on medical rounds in the Intensive Care Unit on the rate of preventable adverse drug events (ADEs) caused by ordering errors comparison between phase 1 (baseline) and phase 2 (after intervention). The rate of preventable ADEs decreased by 66% from 10.4 per 1000 patient-days before the intervention to 3.5 after

the intervention. A total of 398 pharmacist interventions were recorded. Of these, 366 were related to ordering, of which 362 (99%) were accepted by the physicians. Nearly half (46%) were pharmacist-initiated clarification or correction of a proposed or previous order. These errors included incomplete orders, wrong dose, wrong frequency, inappropriate choice, and duplicate therapy.[54]

In hospitals in Nottingham, 769 interventions were made, of which 60 concerned prescriptions rated as having a major potential for medication harm. Errors of dosage were the commonest reason for intervention by pharmacists. They comprised 280 prescriptions and included 32 of those judged to have a major potential for medical harm. In 639 cases (83%) the pharmacist's intervention was accepted, resulting in an alteration of the prescription in 575 (75%); in 92 the prescription was unaltered; in 8 the information was already know; and in 5 the pharmacist considered that the intervention was inappropriate; a further 25 interventions were considered inappropriate by the medical assessor.[55]

A study of the consultation performed by pharmacists at a tertiary care teaching hospital under a documentation system during July 1990 through June 1991. During the study period, 1031 clinically significant consultations were documented. The rate of acceptance by prescribers was 83%. Orders with potentially fatal or severe consequences accounted for 18.4% of the consultations. The medical service had the larges percentage of consultations, followed by the psychiatric, surgical, and obstertrics and gynecology services.[56]

3. The use of preprinted order

The use of a preprinted order form significantly reduces medication errors. Preprinted orders are often used in hospitals and health systems to deal with common, recurring clinical situations and offer many advantages. They guide the prescriber to appropriate ordering, enhance the clarity and accuracy of the prescription by minimizing illegible handwriting and the use of inappropriate abbreviations, and ensure the presence of all elements of a prescription required by law, as well as all information needed to dispense the drug and save time.[57-59]

The use of a structured order sheet in a pediatric Emergency Department (ED) comparing between regular form and preprinted order sheets. Within the study period, a total of 2058 (95.4%) charts were available for review. A total of 411 (52.2%) orders for drugs in the ED were ordered on the regular form, and 376 (47.8%) were given on the new form. Drug errors were identified in 68 (16.6%) orders when the regular form was used and in 37 (9.8%) of the orders on the new form. Using the new form was associated with a significant reduction in the risk for an error.[57]

The use of cancer chemotherapy prescription form comparing before and after implementation of a preprinted form. During the baseline period, orders for 143 patients were evaluated. Only two prescription components, dose and route, were present is more than 90% of the orders. Educational intervention led to some improvement in order completeness, but only dose and route appeared in at least 90% of the 87 orders evaluated. The components necessary to verify physicians' calculations for body surface area and dose-height, weight, and dosage, were absent in 29 of the orders, and a pharmacist spent 420 minutes clarifying them. After the order form

was implemented, orders for 77 patients were reviewed. Compliance exceeded 90% for eight of the nine components, and 12 medication errors were prevented by the form. A pharmacist spent 70 minutes clarifying five orders.[60]

The decrease incomplete handwritten prescriptions by preprinted prescription forms comparing before and after introduction of preprinted medication order forms. Using the preprinted forms increased inclusion of prescription time from 86% to 98%, patient weight from 57% to 98%, weight-based dose from 37% to 91%, route of administration from 89% to 98%, and prescriber's name or pager number from 70% to 99%.[61]

Prescribing is an early point at which medication errors can arise. The physicians should be legible when prescribed orders. Drug orders should be complete. They should include patient name, generic drug name, trademarked name, route and site of administration, dosage form, dose, strength, quantity, frequency of administration, and prescriber's name. A handwritten order should be completely readable (not merely recognizable through familiarity). Prescribers should review all drug orders for accuracy and legibility immediately after they have prescribed them. To prevent prescribing errors, organization-wide interventions and cultural changes are likely to be required. However, useful first steps suggested include reporting prescribing errors identified, formally reviewing pharmacists' interventions and developing increased 'error awareness' amongst all health care professionals.[62-63]

CHAPTER III

METHODOLOGY

The methodology of the study was categorized into six parts including 1) definition of term 2) study design 3) study population 4) scope of study 5) step of investigation and 6) data analysis.

1. Definition of terms

The following terms were defined and used for this study.

Medical specialist

Medical specialist was defined as a branch of medical science, other than general practice. After completing medical school, physicians usually further their medical education in a particular field of medicine.

General Practitioner (GP)

General practitioner was defined as a physician whose practice is based on a broad understanding of all illnesses and who does not restrict his/her practice to any particular field.

Internist

Internist was defined as a physician who had completed medical school and was engaged in a year of additional training under supervision of experienced physicians at a hospital before residency.

Pharmacist's Participation

Pharmacist's Participation was defined as an act of pharmacist in medical history analysis, patient counseling, regimen recommendation, and physician consultation.

Pharmacist's recommendation

Pharmacist's recommendation was defined as an activity of pharmacist in consult and suggest appropriate regimen to the physician in which case had prescribing problem before dispensed drug.

Prescribing error

Prescribing error was defined as incorrect drug selection [based on indications, contraindications, known allergies, and existing drug therapy], dose, dosage form, quantity, route, concentration, rate of administration, or instructions for use of a drug product ordered or authorized by physician [or other legitimate prescriber].[9,28]

Prescriptions that were missing an essential information were considered to have errors of omission[26,30]. The most commonly reported errors of omission follows:

- Incomplete specification of dosage form or strength
- Failure to specify the quantity to dispense or duration of therapy
- Failure to specify the dose or dosage regimen
- Failure to write the prescription legibly

Prescriptions that contain incorrect information concerning the drug therapy or those that duplicate existing therapy were judged to contain errors of commission. The most common errors of commission follows:

- Incorrect dose or dosage regimen
- Incorrect drug or indication for use
- Incorrect dosage form
- Incorrect quantity or duration of therapy
- Therapeutic duplication
- Incorrect patient name on the prescription order
- Prescription orders containing drug interactions

2. Study design

This study was a descriptive and quasi-experimental study.

3. Study population

Study population was patients at outpatient HIV clinic at Samutsakhon hospital during October 1, 2007 to January 31, 2008. All prescriptions consisting of anti-retroviral and opportunistic infections (OIs) drug were screened except prescriptions which did not contain anti-retroviral drug. Based on the series of clinical trials, chemoprophylaxis to prevent initial episodes of certain opportunistic infections (primary prophylaxis) and subsequent episodes (secondary prophylaxis) became the standard of HIV care, thus OIs drug were also investigated.

Inclusion criteria:

-Patients who received anti-retroviral medicine

Exclusion criteria:

-New HIV/AIDs patient who first received anti-retroviral medicine

4. Scope of study

Period of data collection was only on Friday during 1.30 p.m. and 4.00 p.m.

5. Step of investigation

5.1 Pre-study period

5.1.1 Articles related to the analysis of prescribing errors in HIV/AIDS were reviewed.

5.1.2 Prescribing error collecting forms were designed (Appendix A)

5.2 Study period

5.2.1 Phase 1 : Analysis of prescribing error in the former system of prescribing process

Prescribing process of outpatient at HIV clinic was monitored which was prescribed in the following:

-The investigator observed the hospital pharmacist counseling with HIV/AIDS patient every Friday during 1.30 p.m. to 4.00 p.m. The workflow of prescribing process was demonstrated in Figure 1.

-All prescriptions which contained anti-retroviral and opportunistic infections drugs were screened to check for the prescribing error. The errors were then classified for their types and calculated for the prevalence of prescribing errors.

-Information related with demographic data, medication use, and relevant laboratory data were collected from OPD card.

Prescribing error

-Medication prescribing orders that were incorrect were recorded. These incorrect medication prescribing orders included drug selection [based on indications, contraindications, known allergies, and existing drug therapy], dose, dosage form, quantity, route, concentration, rate of administration, or instructions for use of a drug product ordered or authorized by physician [or other legitimate prescriber].

-Prescribing errors were reconfirmed. Prescribing order was considered to contain a prescribing error if any aspect was not in accordance with National ARV Treatment Guideline, Ministry Of Public Health 2006/2007[64].

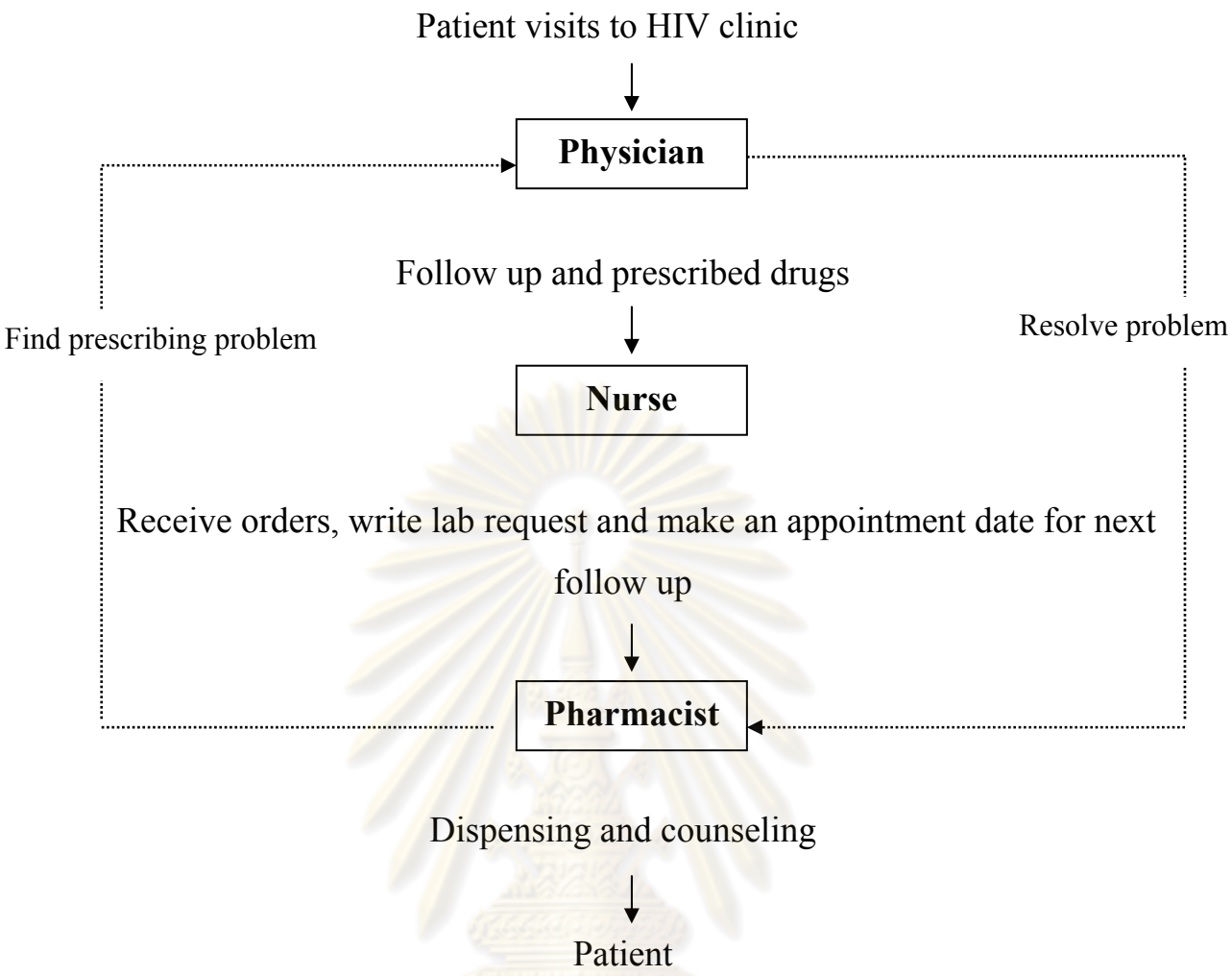

Figure 1 The workflow of the former prescribing process at HIV clinic, Samutsakhon Hospital

5.2.2 Phase 2 : Implementation of pharmacist's participation on prescription error reduction.

-The investigator presented and discussed the results of prescribing error analysis in phase 1 with pharmacy staff. The pharmacist made conference with the physician to find the way to prevent errors. Role of pharmacist's participation to reduce prescribing error were then set up.

-The system to provide regimen preparation to individual HIV/AIDs patients by pharmacist was established by the collaboration with healthcare professional including physicians and nurses :

a) Self-inking stamp was chosen as a model to prevent medication error in this study.

b) The content of self-inking stamp consisted of drug regimen and quantity.

c) Pharmacist discussed with physicians to approve each stamp regimen for routine use.

d) Any pharmacist who was trained about HIV/AIDs disease and medication was assigned to have role in prescribing error prevention.

e) There were 2-4 pharmacists working for prescribing error prevention at the same time.

f) Regimen preparation was performed on Thursday before HIV clinic. Pharmacist reviewed the regimen and recommended OIs medication if necessary which were prescribed to an individual patient at the last visit.

g) OIs drug might be prescribed or discontinued based on CD4 count result. (Appendix E)

h) The quantity of medication was calculated based on duration from this visit to the next visit.

i) Then, pharmacist prepared the medication for dispensing in the next day.

On the HIV clinic visit day, the pharmacist performed counseling and dispensed the medication after a patient met with the physician.

Pharmacist's counseling includes :

a) Asking for compliance by checking if patient forgot to take the medication. Forgetting to take medication three times in one month indicates treatment failure. Pharmacist encouraged patient to complete all medication and taking the medication on time.

b) Discussing with the patient about the ADR and resolve the ADR problem when occurred.

c) Checking dose of medication base on patient's weight. If incorrect dose was found, the pharmacist provide drug information and discuss with the physician to resolve.

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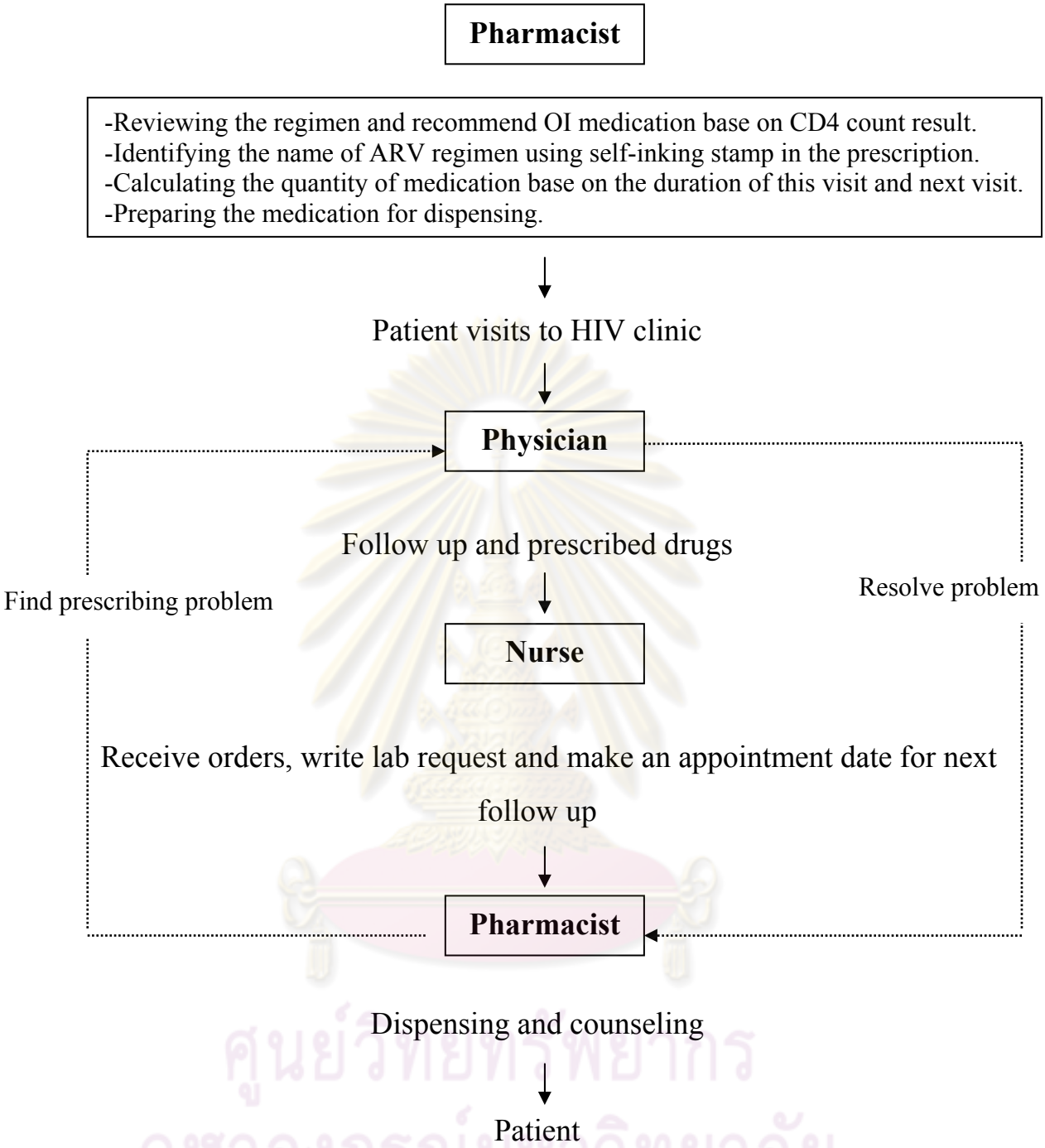

Figure 2 The new workflow of prescribing process at HIV clinic including pharmacist participation in prescribing error prevention, Samutsakhon Hospital

-The workflow of new prescribing process was demonstrated in Figure 2. The workflow in Figure 2 differed from the former one. Pharmacist had several activities to do on the day before HIV clinic visit day. These activities are :

1) Reviewing the regimen and recommend OIs medication base on CD4 count result.

2) Identifying the name of ARV regimen using self-inking stamp in the prescription.

3) Calculating the quantity of medication base on the duration of this visit and next visit.

4) Preparing the medication for dispensing

5.2.3 Phase 3 : Analysis of prescribing error after pharmacist's participation.

After the system to provide regimen preparation to individual HIV/AIDs patient by pharmacist was established by collaboration with healthcare professional including physicians and nurses, the prescribing process was assessed as in phase 1.

6. Data analysis

The following data collected from phase 1 and phase 3 were analyzed:

6.1 Demographic data of patient was described by descriptive statistics. The mean differences of age in phase 1 and phase 3 were analyzed by Unpaired t-test. The difference was considered to be statistically significant at p-value <0.05.

6.2 Error types and frequency were calculated in percentage.

6.3 For prescribing error rate calculation, were counted cumulatively every visit during use period as total opportunities for error [TOE]. Prescribing error rate was reported as % error of total opportunities for error [TOE]

$$\% \text{ Error} = \frac{\text{errors X 100}}{\text{TOE}}$$

TOE was the sum of all HAART regimen and OIs medication prescribing orders.

Prevalence (P) was calculated by

$$P = \frac{\text{errors}}{\text{TOE}}$$

CHAPTER IV
RESULTS

The results of the study are presented in five parts including 1) demographic data 2) prescribing errors 3) types of physician associated with prescribing error 4) pharmacist's recommendations and 5) factor associated with medication errors.

1. Demographic data

Characteristics of all patients are presented in Table 1. The number of patients in phase 1 were 249. There were 138 males and 111 females. A age ranged from 23 to 65 years and the average (Mean age ± SD) of age was 37.24 ± 7.97 years. The number of patients in phase 3 were 254. There were 126 males and 128 females. Age ranged from 17 to 66 years and the average (Mean age ± SD) of age was 37.65 ± 7.38 years. The mean of age was not significantly different between phase 1 and phase 3 (p-value = 0.349). The majority of regimens for treatment in both phases were GPO-VIR 30, followed by d4T+3TC+EFV, and AZT+3TC+NVP. The types of physician in both phase were medical specialist, general practitioner, and internist. The opportunistic infections prophylaxis was similar in both phase including pneumocytis pneumonia, cryptococosis, and mycobacterium avium complex. The first three co-diseases of patient in both phase were endocrine and metabolism, cardiovascular, and respiratory.

Table 4.1 Characteristics of patients and relating factors in phase 1 and phase 3.

Characteristic	Number of patients (%)	
	Phase 1	**Phase 3**
Age (years)		
10-19	0 (0)	1 (0.4)
20-29	36 (14.5)	26 (10.2)
30-39	126 (50.6)	141 (55.5)
40-49	70 (28.1)	68 (26.8)
50-59	14 (5.6)	16 (6.3)
≥60	3 (1.2)	2 (0.8)
Total	**249 (100)**	**254 (100)**
Mean age ± SD	37.20 ± 7.69	37.46 ± 7.25
Sex		
Male	138 (55.42)	126 (49.61)
Female	111 (44.58)	128 (50.39)
Total	**249 (100)**	**254 (100)**
Major regimen for treatment		
GPO-VIR 30	177 (63.21)	176 (61.11)
d4T+3TC+EFV	30 (10.71)	41 (14.24)
AZT+3TC+NVP	22 (7.86)	27 (9.38)
GPO-VIR Z	17 (6.07)	10 (3.47)
GPO-VIR 40	13 (4.64)	14 (4.86)
AZT+3TC+EFV	13 (4.64)	13 (4.51)
d4T+3TC+IDV+RTV	5 (1.79)	2 (0.69)
AZT+3TC+RTV+IDV	2 (0.72)	1 (0.35)
DDI+IDV+RTV+NFV	1 (0.36)	1 (0.35)
3TC+EFV+IDV+RTV	0 (0.00)	2 (0.69)
AZT+DDI+RTV+IDV	0 (0.00)	1 (0.35)
Total	**280 (100)**	**288 (100)**

Table 4.1 Characteristics of patients and relating factors in phase 1 and phase 3. (cont.)

Characteristic	Number of patients (%)	
	Phase 1	**Phase 3**
Types of physician		
Medical specialist	157 (56.07)	163 (56.60)
General practitioner	113 (40.36)	101 (35.07)
Internist	10 (3.57)	24 (8.33)
Total	**280 (100)**	**288 (100)**
The opportunistic infections prophylaxis		
Pneumocytis pneumonia	119 (59.20)	121 (58.74)
Cryptococcosis	74 (36.82)	76 (36.89)
Mycobacterium avium complex	5 (2.49)	3 (1.46)
Toxoplasmic encephalitis	3 (1.49)	4 (1.94)
Penicillosis	0 (0.00)	2 (0.97)
Total	**201 (100)**	**206 (100)**
Major co-disease of patient		
Endocrine and metabolism	23 (30.67)	22 (27.85)
Cardiovascular	19 (25.33)	17 (21.52)
Respiratory	15 (20.00)	14 (17.72)
Gastrointestinal	10 (13.33)	15 (18.98)
Dermatology	2 (2.67)	3 (3.80)
Neurology	2 (2.67)	3 (3.80)
Psychiatric	1 (1.33)	2 (2.53)
Other	3 (4.00)	3 (3.80)
Total	**75 (100)**	**79 (100)**

2. Prescribing errors

2.1 Number, error rate, and prevalence of prescribing errors

Prescribing error occurred in 103 patients in phase 1 and 7 patients in phase 3. The number, error rate, and prevalence of prescribing errors are presented in Table 4.2. In phase 1, a total of 123 prescribing errors were identified from 641 prescription orders. The error rate and prevalence were 19.19% and 0.1919, respectively. During phase 3, there were 8 prescribing errors detected from 673 prescription orders, giving an error rate and prevalence of 1.20% and 0.0120, respectively.

Table 4.2 The number, error rate, and prevalence of prescribing error classified by type of error

Type	Phase 1 (total orders=641)			Phase 3 (total orders=673)		
	Number of error	Error rate (%)	Prevalence	Number of error	Error rate (%)	Prevalence
Incorrect time	55	8.58	0.0858	0	0	0
Not specified strength	26	4.06	0.0406	0	0	0
Incorrect indication						
-drug used without indication	12	1.87	0.0187	0	0	0
-untreated indication*	4	0.62	0.0062	1	0.15	0.0015
Adverse drug reaction (ADR)	7	1.09	0.0109	2	0.30	0.0030
Drug interaction	5	0.78	0.0078	3	0.45	0.0045
Incorrect dose	5	0.78	0.0078	1	0.15	0.0015
Incorrect regimen	5	0.78	0.0078	1	0.15	0.0015
Incorrect quantity	3	0.47	0.0047	0	0	0
Incorrect drug	1	0.16	0.0016	0	0	0
Total	**123**	**19.19**	**0.1919**	**8**	**1.20**	**0.0120**

* having indication but no treatment

2.2 Type and percentage of prescribing errors

Type and percentage of prescribing error are shown in Table 4.3. In phase 1, a total of 123 prescribing errors were identified. The majority types of error were incorrect time (44.72%), not specified strength (21.14%), and incorrect indication (13.01%). In phase 3, there were 8 prescribing errors. Most types of error were drug-drug interaction (37.50%), adverse drug reaction (25.00%). While, errors of incorrect regimen, incorrect indication, and incorrect dose, were equally (12.50%).

Table 4.3 Number and percentage of error based on type of prescribing error

Type	Phase 1		Phase 3	
	Number of error	Percentage	Number of error	Percentage
Incorrect time	55	44.72	0	0.00
Not specified strength	26	21.14	0	0.00
Incorrect indication				
-drug used without indication	12	9.76	0	0
-untreated indication*	4	3.25	1	12.50
Adverse drug reaction (ADR)	7	5.69	2	25.00
Drug interaction	5	4.06	3	37.50
Incorrect dose	5	4.06	1	12.50
Incorrect regimen	5	4.06	1	12.50
Incorrect quantity	3	2.44	0	0.00
Incorrect drug	1	0.82	0	0.00
Total	**123**	**100**	**8**	**100**

* having indication but no treatment

2.3 Details of detected prescribing errors

The most common prescribing error detected was prescribing incorrect time. Physician prescribed drug for bid instead of around the clock. The HAART regimens require patients to take them on time and around the clock to promote less variation in peak and trough serum level.[65-66,68] For example, physicians normally prescribed bid which means the drugs should be taken after breakfast and dinner. However, ARV drugs should be taken 12 hours interval. In this case physicians must specify the exact time to take the medicines such as 8.00 a.m. and 8.00 p.m. or 9.00 a.m. and 9.00 p.m. The errors included GPO-VIR 30 which was prescribed bid pc (31 errors), AZT [100]+3TC+NVP bid pc (7 errors), AZT [100]+3TC bid pc and EFV hs (7 errors), GPO-VIR 40 bid pc (4 errors), d4T+3TC bid pc and EFV hs (4 errors), GPO-VIR Z bid pc (2 errors).

The next most common error was not specifying strength. Twenty-six errors occurred in phase 1. There were 13 errors of d4T 1 cap. q 12 hr. (drug strength used in hospital are 15 mg, 20 mg, 30 mg, and 40 mg. The order was not identified which strength to be used). Also, there were 8 errors of AZT which was prescribed 1 cap. q 12 hr. and 2 cap. q 12 hr. (drug strength used in hospital are 100 mg and 300 mg. The order was not clearly identified between 100 mg or 300 mg strength). And the last one, there were 5 errors of EFV 1 tab OD hs. (drug strength used in hospital are 200 mg and 600 mg. The order was not specified either 200 mg or 600 mg strength to be used).

Incorrect indication was the third frequent type of prescribing error. This study classified incorrect indication into two groups which were drug used without indication and untreated indication. Most errors were related with drugs regimen for prophylaxis opportunistic infections. In phase 1, there were 12 cases of drug which was prescribed without indication. Nine cases occurred among patients with a CD4 count ≥100 cells / mm^3 for 6

months. It is not necessary to have fluconazole for prophylaxis cryptococcal meningitis. Three cases were patients with a CD4 count ≥ 200 cells / mm^3 for 6 months. It is not necessary to have co-trimoxazole for prophylaxis PCP.

The next error was untreated indication which was occurred among patients with a CD4 count <200 cells / mm^3. Patients need co-trimoxazole for prophylaxis PCP, but the physician failed to prescribe (2 cases). The other case was patients with a CD4 count <100 cells / mm^3. They need fluconazole for prophylaxis cryptococcal meningitis, but the physician, again, fail to prescribed (1 case).

The last error of untreated indication was forgetting to prescribe both co-trimoxazole and fluconazole (1 case in phase 1 and 1 case in phase 3) to patient with a CD4 count <100 cells / mm^3. In fact, patients need fluconazole and co-trimoxazole for prophylaxis cryptococcal meningitis and PCP.

The fourth frequent types of errors were adverse drug reaction (ADR). Seven cases occurred in phase 1 and two cases occurred in phase 3, but there was no harm to the patients. There were six cases in phase 1 and one case in phase 3. All of them were lipodystrophy from stavudine. The main clinical features of lipodystrophy syndrome are peripheral fat loss and central fat accumulation within abdomen, breast (gyneacomastia) and dorsocervical spine (buffalo hump). The overall prevalence is about 50% after 12-18 months of therapy but it can reversible if withdrawal or substitution of ARV. [70] Study of McComsey,G.A. reported that the improvement of lipodystrophy was associated with ARV in patients who were switched from stavudine to abacavir or zidovudine.[71] These ADR was discussed with physician, then the physician changed to zidovudine. One case in phase 1 had skin rash from nevirapine after starting ARV about 3 weeks. The physician prescribed antihistamine drug and calamine lotion,

but the symptom did not recover. From the incidence report, NVP had incidence of skin rash >10% and occurs most frequently within the first 6 weeks of therapy.[66] After pharmacist discussed with physician, the physician stopped NVP and changed to EFV.

The remaining case of ADR was in phase 3. The patient had abdominal pain and crystalluria after starting regimen, d4T [30] 1 cap q 12 hr, 3TC 1 tab q 12 hr, IDV [400] 2 cap q 12 hr, and RTV [100] 1 tab q 12 hr, for 2 months. About 12.4% of nephrolithiasis from IDV were reported in clinical trials (4.7%-34.4% in different trials).[72] After pharmacist discussed with physician, the physician reduced IDV's dose to 400 mg 1 cap q 12 hr.

Drug-drug interactions were the fifth frequent type of error including indinavir-simvastatin (1 error in phase 1 and phase 3), ritonavir-simvastatin (1 error in phase 1 and phase 3), zidovudine-rifampicin (1 error in phase 1), indinavir-omeprazole (1 error in phase 3), and zidovudine-clarithromycin (1 error in phase 3). In these cases the physician did not change medications, but followed up the ADE in every visit. (Appendix B)

One case of drug-drug interaction occurred in phase 1 and physician changed medication. NVP was prescribed to patient who received TB drugs consisting of isoniazid, rifampicin, ethambutol, and pyrazinamide. NVP metabolized by the hepatic p450 isozyme system. Rifampicin is an inducer of CYP3A4 and NVP induces CYP2B6 > CYP3A4. Thus both have potential to generate an important interactions with each other. Rifampincin can decrease serum concentrations of nevirapine by 20% to 55%. The preferred treatment regimen for patients with HIV infection and tuberculosis is EFV-base antiretroviral. The pharmacokinetic effect of rifampicin is modest and well-characterized. The antiviral activity of the EFV is excellent when used with rifampicin. Tolerability is good with low

rates of discontinuation.[73] This information was discussed with the physician. At the end, physician replaced NVP with EFV.

The sixth frequent type of error was incorrect dose. Error in calculating dose came from patient's weight. In phase 1, errors resulted in higher dose (3 errors) and lower dose (2 errors). Two case of higher dose and one lower dose of AZT. One "higher dose" error was prescribing GPO VIR 40 instead of GPO VIR 30 and the latter one was prescribing "lower dose" GPO VIR 30 instead of GPO VIR 40. In phase 3, the errors came from prescribing the lower dose of GPO VIR. The patient's weight increased, thus higher dose was required. Pharmacist consulted with the physician to prescribe GPO VIR 40 instead of GPO VIR 30. (Appendix C)

Incorrect regimen was the seventh frequent type of error. Five errors occurred in phase 1. Three errors associated with drugs regimen for prophylaxis opportunistic infections included prescribing fluconazole (2 errors) 200 mg OD for primary prophylaxis of cryptococcal meningitis, and one error from prescribing fluconazole 400 mg "per week" to patient with a history of cryptococcal meningitis, in fact it should be prescribed OD.

The next error occurred to patient who had LFT elevated. The former regimen was d4T+3TC+EFV. The physician suspected hepatitis B viral infection then he prescribed only d4T+3TC in order to protect liver from damage. After HB Ag test, the result was negative. LFT elevated may be from EFV. Physician still prescribed only d4T+3TC. This was incorrect because ARV regimen should be combined with 2NRTIs+NNRTI or 2NRTIs+PI.

The other incorrect regimen was occurred to patient recovering from TB drugs. Former ARV regimen was d4T+3TC+EFV which was use for HIV patients who had TB. After recovering form TB, physician prescribed GPO VIR 30 1 tab. at 8.00 a.m., NVP 1 tab. at 8.00 p.m., and 3TC 1 tab. at 8.00 p.m. for two weeks. This was incorrect because regimen should be

only GPO VIR 30 1 tab. q 12 hr. One error occurred in phase 3. The error was prescribing fluconazole 1 cap. on Monday and Thursday instead of prescribing it for use every day in patients with a history of cryptococcal meningitis (Case 4, Appendix D)

The next frequent type of error was incorrect quantity. There were 3 errors occurred in phase 1. Most of the errors were prescribing quantity of drug which was not enough until the next visit. These two errors were from GPO VIR 30 1 tab q 12 hr. Physician prescribed 60 tab. instead of 120 tab. for two months. The remaining error was prescribing AZT [100 mg] 2 cap. q 12 hr. 112 tab for 56 days. The error was discussed with physician. Physician changed quantity to 224 tab.

The last error is incorrect drug occurred in phase 1. The physician prescribed GPO VIR 30 to the patient who had lipodystrophy. In fact, GPO VIR 30 had d4T which must not be given to patient who had lipodystrophy. Pharmacist consulted with the physician and then changed regimen to GPO VIR Z.

3. Type of physician associated with prescribing errors

The type, number, and error rate of physicians associated with prescribing errors are shown in Table 4.4. During phase 1 and phase 3, the most frequent prescribing error was internist (40.91% and 3.64%, respectively). The second was general practitioner (24.71% and 1.26%, respectively). Medical specialist (13.89% and 0.79% respectively) was the third.

In phase 1, the types of error frequently found were “incorrect time” and “do not specified strength” which occurred in every type of physicians. Considering the internist, this group of physician generates higher incorrect

indication errors than other types of errors. Internist may have less experience and knowledge in therapeutic decisions.

Eight errors in phase 3 included prescribing drug-drug interaction (2 cases from GP and 1 case from medical specialist) (Appendix B), ADR (2 case from internist), incorrect dose (1 case from GP), incorrect indication (1 case from medical specialist), and incorrect regimen (1 case from medical specialist) (Appendix D)

Table 4.4 The type, number, and error rate of prescribing error associated with type of physician

Type of error	Internist		General practitioner		Medical specialist	
	Phase 1	Phase 3	Phase 1	Phase 3	Phase 1	Phase 3
Incorrect time	2	0	28	0	25	0
Not specified strength	1	0	17	0	8	0
Incorrect indication						
-drug used without indication	2	0	3	0	7	0
-untreated indication*	1	0	2	0	1	1
Adverse drug reaction (ADR)	1	2	4	0	2	0
Drug interaction	0	0	2	2	3	1
Incorrect dose	0	0	5	1	0	0
Incorrect regimen	0	0	2	0	3	1
Incorrect quantity	2	0	0	0	1	0
Incorrect drug	0	0	1	0	0	0
Total errors	9	2	64	3	50	3
Total orders	22	55	259	239	360	379
Error rate (%)	40.91	3.64	24.71	1.26	13.89	0.79

* having indication but no treatment

4. Pharmacist's recommendations for modifying physician order on HIV clinic visit day

Pharmacist's recommendations were recorded after pharmacist discussed with the physicians and modifying physician order. Role of pharmacists and their participation in prescribing error prevention was well accepted by physicians, as evidence by the fact that all of the recommendations were accepted. The number and type of pharmacist's recommendation in phase 1 and phase 3 are shown in Table 4.5. Seventy-one of 123 errors were recommended in phase 1. The three common types of pharmacist recommendation were clarification of order (30.99%), changing time (25.35%), and cessation of drug (16.90%). Fifty-two of the errors were not recommended, because they had less effect in patient, or the physician allowed pharmacist to modify the orders. During phase 3, there were 5 recommendations. Type of pharmacist recommendations included changing dose (40.00%), drug addition (20.00%), substitution of drug (20.00%), and clarification of order (20.00%).

Table 4.5 The number of pharmacist's recommendations classified by type

Type of recommendation	**Number (%)**	
	Phase 1	**Phase 3**
Clarification of order	22 (30.99)	1 (20.00)
Changing time	18 (25.35)	0 (0.00)
Cessation of drug	12 (16.90)	0 (00.00)
Substitution of drug	9 (12.68)	1 (20.00)
Changing dose	5 (7.04)	2 (40.00)
Drug addition	5 (7.04)	1 (20.00)
Total	71 (100)	5 (100)

5. Factor associated with medication error

5.1 Type of regimen related to the errors

The regimens for treatment in this study were 11 regimens which can be found in Table 4.1 page 39. The 11 regimen were classified into 2 groups. First group included one tablet combination regimen (GPO VIR 30, GPO VIR 40 and GPO VIR Z). The remaining regimen was in the other group. When testing the error associated with the types of regimen by using chi-square test, the result showed that the group of regimen which contained one tablet combination regimen had error less than other group significantly ($p<0.05$, $\chi^2 = 24.89$)

Table 4.6 Type of regimen related to errors

Type of regimen	Medication Error		Total
	Yes	No	
One tablet combination regimen	62	145	**207**
More than one tablet regimen	46	27	**73**
Total	**108**	**172**	**280**

$p<0.05$, $\chi^2 = 24.89$

5.2 Type of physician related errors

The physicians who prescribed in this study were 3 types (medical specialist, general practitioner, and internist). Then three types were classified into 2 groups. First group included medical specialist and the remaining types were in the other group. When testing the error associated with the type of physician by using chi-square test, the result show medical specialist made error less than the other group significantly ($p<0.05$, $\chi^2=14.81$)

Table 4.7 Type of physician related to errors

Type of physician	Medication Error		Total
	Yes	No	
Medical specialist	45	112	**157**
Others	63	60	**123**
Total	**108**	**172**	**280**

$p<0.05$, $\chi^2=14.81$

CHAPTER V
DISCUSSION

Medication error analysis is one indicator for quality assurance of hospital service. In this study, prescribing process of HIV clinic was assessed by pharmacist. The results of the two-phase study, phase 1 which was during the former prescribing process and phase 3 which was the new prescribing process in which pharmacist prepared regimen for individual patient by reviewing the former order and laboratory value, were compared.

High error rate compared to other studies

Error rate in phase 1 and phase 3 were 19.19% and 1.20%, respectively. These error rates were higher than error rate reported in the other literature, which ranged from 0.3% to 2.7%. The error rate exists because HAART regimen have more than 20 individual drugs, in addition to multiple names, abbreviations, dosing strategies, and regimen permutations.[3] In this study, after pharmacist's participation in phase 3 the error rate was lower than the error rate in phase 1. Several reasons explained the results. During phase 3, it was possible that physicians received more information on prescribing error analysis. Therefore, they paid more attention for drug information consultation with the pharmacist before prescribing drug. Regimen preparation by pharmacist prior to physician's prescribing provide the opportunity for pharmacist to solve the problem which came from the physician in term of poor handwriting, lack of drug knowledge, prescribing incorrect drug or dose, or forgetting to prescribed drug.

Errors of incorrect time

A majority of prescribing errors in phase 1 was “incorrect time”. Physician usually prescribed drug for bid in term of 1X2 pc, in general it means after meal but do not specify the time. HAART regimen usually includes a combination of three or more HIV medications. Including a non-nucleoside reverse transcriptase inhibitor (NNRTIs), or a protease inhibitor (PI) plus two nucleoside, or nucleotide reverse transcriptase inhibitors (NRTIs). For all the NNRTI class and NRTI class, the dosing interval was 12 hr. (around the clock). Taking medication not on time or skipping a dose can have several possible effects, such as increasing viral load and resistance to treatment.[68,71] After implementing regimen preparation, this type of error was not found in phase 3.

Errors of not specified strength

“Do not specified strength” was the second frequent type of error. Because of the large amount of patient visits and numerous medications prescribed, physician did not have enough time to specify the strength of medication. Failure of specifying strength may cause drug toxicity from dispensing large strength, or drug resistant from subtherapeutic dose. Regimen prepared by pharmacist was suitable for solving this problem because the former order was reviewed and drug strength was calculated by weight. Therefore, every order is clearly specified for drug strength.

Error of incorrect indication

Incorrect indication of this study associates with drug regimen for prophylaxis opportunistic infections. After AIDS was first described, it became clear that opportunistic infections occurred with remarkable frequency and caused substantial morbidity and mortality among patients with AIDS. Chemoprophylaxis to prevent initial episodes of opportunistic

infections and subsequent episodes became the standard of care.[70] During phase 1, physician forgot to prescribe OIs drug 4 cases. Pharmacist discussed with the physician and OIs drug were added. Twelve cases were OIs drug prescribed without indication. These did not cause any harm to the patients but hospital's or patient's expenditures would increase. One error occurred in phase 3, this case was caused by pharmacist trainee, the prepared regimen did not covered OIs drug.

Regimen associated with errors

According to this study, there were many types of regimen for the treatment. The statistic test showed that regimens which were one tablet combination regimen having less error than more than one tablet regimen. In addition, dose, drug-drug interaction, contraindication, and allergies in each item of regimen were needed to be considered. Thus, physicians might make more error than prescribing one tablet combination regimen.

Errors caused by polypharmacy

Concerning polypharmacy in HIV/AIDs' patients, these groups of patient usually received more than three drugs unless they have co-disease, therefore they would be at risk in medication use. Consequences of polypharmacy included adverse drug effects, drug-drug interactions, disease-drug interactions, food-drug interactions, and medication cascade effect.[77] In this study, major co-diseases of patient were endocrine and metabolism, cardiovascular, and respiratory. There were four cases of interaction between HIV drug and other group of drugs. The strategies to prevents the problem from polypharmacy are pharmacist's counseling with the patient, closely monitoring the appearance of the patient after a changing dosage or medication, and receiving the information from the patients about their use of medication.[78]

Computerized Physician order entry (CPOE)

The other preventative measures should be tried such as computerized physician order entry can be used to notify the physician about drug-drug interaction, history of allergies, overdose, underdose, etc. A study of Bates et al[32] demonstrated a decrease of 19% of prescribing errors after implementing computerized physician order entry.

Several studies have shown that Computerized Physician order entry (CPOE) reduced prescribing error rates. However, many factors should be considered for implementing CPOE in hospital system such as vision and leadership of administrator, motivation for implementing POE, values to users costs, health service process, technical considerations, and management of program etc.

In this study, CPOE is another way to reduce prescribing error especially for the type of incorrect time and not specified strength. Our study did not recommend this method because of several reasons in the following:

1. CPOE systems can significantly increase physician workload. This can happen, for instance, by requiring that physician enter more information than the previous time or having them respond to an excessive number of alerts. These alerts may or may not contain useful information and will make physicians do not agree with the system.
2. The present information technology system (software) was not suitable for CPOE system and hospital workflows.
3. Emotional responses to change should be considered. Shifting from paper-based order generation to CPOE can make strong emotional responses as users are struggle in adapting to the new

technology. These responses can point out significant problems with the system design.

For Samutsakhon hospital, it may took a long time to plan and implement CPOE system but it may be possible to have CPOE in the future.

Checking regimen before physician prescribing by pharmacist could reduce prescribing errors

After establishing the system to check regimen before physician prescribing by pharmacist, almost every types of prescribing error decreased, especially the errors from prescribing medication with the incorrect time, do not specified strength, incorrect quantity, and incorrect drug. These types of errors were not found in phase 3. The incorrect indication and incorrect regimen still existed in this study because of human error including forgetfulness and carelessness. Error of drug-drug interaction should be prevented after establishing the system to prepare regimen. However, 3 cases still occurred in phase 3. These errors were found by the investigator after patient came back home. The investigator discussed with the hospital pharmacist for correction in the next visit. Occurrence of drug-drug interaction might be from pharmacist knowledge, workload of pharmacist, and lack of concurrent medication use of patient.

The important activities of pharmacist before patient visits HIV clinic included reviewing the regimen and recommending OIs medication based on CD4 count result. Additionally, there were the other two activities on the visits day included counseling and dispensing medication. All activities seem to take much time but the consequences of this process were to reduce prescribing error and save patient time because individual patient's medication were ready prepared on the day prior to HIV clinic.

Errors of the physician

In this study, there were many type of physician prescribed HAART regimen. Internist made more error in prescribing than medical specialist and general practitioner in both 2 phases. The reason that the internists may prescribe more error than medical specialist and general practitioner are their less accurate in estimating the risks and benefits of therapies in their field or their poor access to the data sources which can be the reference of their therapeutic decisions. It is similar to study of Ayanian, J.Z.[76] After implement regimen preparation, prescribing error significantly reduces in every type of physician.

Role and beneficial of pharmacist's recommendation

According to this study, the pharmacist has important role in the error prevention and alteration of physician's treatment decision. The benefit of pharmacist's recommendation is to prevent drug toxicity and enhance appropriate drug use. Some prescribing errors were not consulted because those errors had less effect. In some cases, physician allowed the pharmacist to modify the order such as setting the suitable time for each patient.

Anti-retroviral prescribing errors can also lead to significant consequences such as increasing toxicity or development of resistance to the HAART regimen. Prevention of the errors may ensure appropriate prescribing orders and patient safety. Pharmacist should have a role to detect error, discuss with physician, and resolve the prescription problems to patient safety.

Limitation of the study

However, this study had several limitations. Firstly, knowledge of individual pharmacists in ARV drugs might limit their ability to detect prescribing errors, because of the rapid changes in HIV treatment and the complexity of pharmacotherapy. Secondly, the short period of study might interfere the result. Because this study performed in 4-month period, while the patients were followed up only two or three months. Same patients might come back in the study period. Thirdly, because only one investigator collected data approximately 80 patients per visit some data might be missing.

CHAPTER VI
CONCLUSION

Medication errors are widely accepted among health care professional. Error reporting system is being established to prevent the problem. This system should be continuously improved to keep pace with medication error problem. This study was performed to analyze the errors in prescribing process and to assess the pharmacist role in participation in reducing prescribing error. The results might be used to improve the prescribing process in order to reduce and prevent the prescribing errors. The results can also guide another hospital for their detecting and preventing such errors.

The error rate detected in phase 1 and phase 3 were 19.19% and 1.2%, respectively. Most common types of error were prescribed drug incorrect time, do not specified strength, incorrect indication of regimen for prophylaxis opportunistic infection, and adverse drug reaction.

Physician who most frequently made prescribing errors was internist. After implementation of prescribing error prevention prior to physician prescribing, the prescribing errors decreased.

The need for pharmacist recommendations to prevent prescribing errors decrease from 71 times to 5 times after implementing pharmacist participation on prescribing error prevention.

The results indicated the substantially reduction of physician prescribing error rate came from pharmacist participation to the prescribing error prior to physician prescribing.

Role of pharmacist in prescribing error prevention included 1) pharmacist's role prior to physician prescribing and 2) pharmacist's role after physician prescribing. The activities on the day prior to physician prescribing were reviewing the regimen, identifying the name of

antiretroviral regimen using self-inking stamp, calculating the quantity of medication, and preparing the medication. The other two activities on the HIV visit day after the physician prescribing were dispensing and patient counseling.

Recommendations

All healthcare professions have their responsibility in identifying the contributing factors of medication errors. They can use such information to prevent the medication error. Medication use systems can be improved to prevent the error and by adding system to check and control error in prescribing and dispensing. The following recommendations for reducing and preventing prescribing errors included:

- Implement physician order entry in the CPOE system: This system will decrease illegible handwriting. It will help ensure that dose, form, and timing are accurate. Computer systems can be also easy to perform double-check for drug-drug or drug-allergy interactions.
- Implement pharmacist preparing regimen by using self-inking stamp: Self-inking stamp prevents error from poor handwriting. It ensures that patients received the correct regimen, save time from discussing with the physician when prescribing error occurred.
- Use drug information for dispensing software. The program should help pharmacist to check for duplicate prescriptions, patient allergies, drug-drug interactions, inappropriate doses (based on patient's weight and age), and drug-lab interactions.
- Set up group counseling to improve patient's knowledge about their treatment: Patients should know about their medication they received, its potential side effects, its appearance and how often they should receive it.

- Formulate one-tablet combination regimen: Drug's company should develop ARV regimens which contains one tablet, because it was convenient for the patients to take the medication. One-tablet combination regimen can also make less error in prescribing.

Through a systems-oriented approach, the pharmacist should collaborative with other health care professions and working as the multidisciplinary team to prevent, detect, and resolved drug-related problems. Pharmacist's roles on preventing prescribing error consisted of participation in prescribing process, disseminating drug information to the physician, and providing patient counseling on drug therapy.

Because, in this study, the investigator focused only the types and magnitude of errors. Further research should be explored to determine the effect of the prescribing error to the patient.

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APPENDICES

Appendix A

Prescribing error collecting form

HN……Age……...Sex ☐ M ☐ F
Date of error detection…..……..Physician code……
Detail of errors
……
……
……
……
……
……
Type of error

☐ Incorrect drug/indication
☐ Incorrect dose/regimen/strength
☐ Incorrect dosage form
☐ Incorrect quantity/duration
☐ Incorrect time
☐ Drug interaction
☐ Duplicate therapy
☐ Dose/regimen not specified
☐ Dosage form/strength not specified
☐ Quantity/duration not specified
☐ Prescription illegible
☐ Allergy/Sensitivity/ADR
☐ Other…….

Pharmacist Recommendation :
……
……
……
……
…..……
……
☐ Addition ☐ Dose change ☐ Substitution ☐ Cessation ☐ Time change
☐ Clarification of order

Appendix B

Table B1. Drug-drug interactions* of prescribing errors.

Interaction-drug	Number of case		severity	Significance rating	Details
	Phase 1	Phase 3			
Nevirapine-Rifampicin	1		moderate	2	Rifampicin decrease serum concentration of nevirapine by 20% to 55% [73]
Indinavir-Simvastatin	1	1	major	1	Simvastatin plasma level may be elevated, increasing the risk of side effects (eg. Rhabdomyolysis)
Zidovudine-Rifampicin	1		moderate	4	The pharmacologic effects of zidovudine may be decreased
Ritonavir-Simvastatin	1	1	major	1	Simvastatin plasma level may be elevated, increasing the risk of side effects (eg. rhabdomyolysis)
Indinavir-Omeprazole		1	moderate	4	The antiviral activity of indinavir may be reduced.
Zidovudine-Clarithromycin	1		moderate	4	The pharmacologic effects of zidovudine may be decreased

* Clinical significance of drug-drug interactions were evaluated according to Drug interaction facts [74]
Significance rating =1, severity : major, documentation : established, probable, or suspected; Significance rating = 2, severity : moderate, documentation : established, probable, or suspected; Significance rating = 3, severity : minor, documentation : established, probable, or suspected: Significance rating = 4, severity : major/moderate, documentation : possible; Significance rating = 5, severity : minor, documentation : possible. [74]

Appendix C

Table C1. Incorrect dose due to miscalculation calculated by patient's body weight

Drug	Number of case		Details
	Phase 1	Phase 3	
Zidovudine	1		A 41-year-old woman, her body weight was approximately 45 kg. Physician prescribed AZT[100] 3 cap q 12 hr, 3TC 1 tab q 12 hr, NVP 1 tab q 12 hr. Dose therapy of AZT is . 200 mg twice daily in individual who weigh less than 60 kg. This patient should be treated with 400 mg. of AZT, so she should receive AZT 2 cap [100] q 12 hr. [75]
Zidovudine	1		A 42-year-old woman with approximated 41 kg weight was prescribed with AZT[150] 1 cap q 12 hr, 3TC 1 tab q 12 hr, EFV 1 tab hs. Dose therapy of AZT is 200 mg twice daily for less than 60 kg individual. Therefore this patient should be treated with 400 mg of AZT daily., so she should receive AZT 2 cap [100] q 12 hr. [75]
Zidovudine	1		A 29-year-old woman, her body weight was approximately 44 kg. Physician prescribed AZT[100] 3 cap q 12 hr, 3TC 1 tab q 12 hr, NVP 1 tab q 12 hr. Dose therapy of AZT is 200 mg twice daily in individual who weigh less than 60 kg. This patient should be treated with 400 mg. of AZT, so she should receive AZT 2 cap [100] q 12 hr. [75]
GPO VIR	1		A 34-year-old man with approximated 75 kg. weight was prescribed with GPO VIR 30. Dose therapy of GPO VIR is 30 mg for less than 60 kg individual, and 40 mg for whose weight is higher than 60 kg. Therefore, this patient should receive GPO VIR 40. [64]

Table C1. Incorrect dose due to miscalculation calculated by patient's body weight (cont.)

Drug	Number of case		Details
	Phase 1	Phase 3	
GPO VIR	1		A 41-year-old man, his body weight was approximately 58 kg. Physician prescribed GPO VIR 40. Dose therapy of GPO VIR is 30 mg for patients who are less than 60 kg, and 40 mg for those whose weight is higher than 60 kg. This patient should receive GPO VIR 30. [64]
GPO VIR		1	A 48-year-old man, his body weight was approximately 77 kg. Physician prescribed GPO VIR 30. Dose therapy of GPO VIR is 30 mg for patients who are less than 60 kg, and 40 mg for those whose weight is higher than 60 kg. This case should receive GPO VIR 40. [64]

Appendix D

Five cases of prescribing error association with type of physician in phase 3

Case 1.

A 49-year-old man was diagnosed AIDs for 2 years. At the last visit (three months ago), his weight was 57 kg. Physician prescribed GPO VIR 30 to take 1 tab q 12 hrs. On the observed day, hospital pharmacist prepared GPO VIR 30 for this patient. The general practitioner prescribed GPO VIR 30 followed the prepared regimen. Finally, the patient met hospital pharmacist to receive drug and counseling. Hospital pharmacist found that the body weight of patient was 65 kg. The pharmacist discussed with the physician. Then the physician changed to GPO VIR 40.

In this case, it is the error of incorrect dose associated with general practitioner.

Case 2.

A 39-year-old woman had the history of drug resistant to the first-line drug regimen. At the last visit (two months ago), her regimen was d4T(30) 1 cap q 12 hr, 3TC 1 tab q 12 hr, IDV (400) 2 cap q 12 hr, and RTV(100) 1 cap q 12 hr. On the observed day, hospital pharmacist prepared the same regimen for this patient. The internist prescribed regimen followed to the pharmacist's preparing for the regimen. Finally, the patient met hospital pharmacist to receive drug and counseling. The patient complained that she had abdominal pain and crystalluria. This was the sign of ADR from IDV (12.4% reported in clinical trial). After

pharmacist discussed with the physician, the physician reduced the dose of IDV to 400 mg 1 cap q 12 hr.

In this case, it was unpreventable ADR associated with internist but it can be detected during patient counseling with the pharmacist.

Case 3.

A 35-year-old man was diagnosed AIDs with TB. He received d4T+3TC+EFV and anti-TB drug. Furthermore, he received fluconazole and co-trimoxazole for OI prophylaxis. On the observed day, he finished the course of TB drug, the pharmacist trainee prepared only d4T+3TC+EFV but forgot to prepared OI prophylaxis. The medical specialist prescribed the medication followed the prepared regimen. After the patient had counseling with the hospital pharmacist, the pharmacist found that the patient didn't receive OI prophylaxis. The pharmacist discussed with the physician and then physician added OI prophylaxis.

In this case, there was incorrect indication of OI prophylaxis associated with medical specialist.

Case 4.

A 35-year-old woman had the history of cryptoccosis. Her regimen was GPO VIR 30. She received fluconazole and co-trimoxazole for OI prophylaxis. On the observed day, hospital pharmacist prepared GPO VIR 30 take 1 tab q 12 hr, fluconazole [200] 1 tab OD. and co-trimoxazole 2 tab OD. The medical specialist prescribed medication followed the prepared regimen but changed the time to take medication of fluconazole [200] to 1 tab at Monday and Thursday. Finally, the patient met hospital pharmacist to receive drug and counseling. The hospital pharmacist found that the

regimen of fluconazole was incorrect. The patient, with the history of cryptococcosis, should receive fluconazole 200 mg orally per day. The pharmacist discussed with the physician, then the physician changed fluconazole to 200 mg orally per day.

In this case, there was incorrect regimen of OI prophylaxis associated with medical specialist.

Case 5.

A 41-year-old woman was diagnosed AIDs and received GPO VIR 30 for 2 years. On the observed day, hospital pharmacist prepared GPO VIR 30 for this patient. The internist prescribed medication as the pharmacists prepared regimen. After that, the patient met hospital pharmacist to receive drug and have counseling. She complained that her arms and legs were atrophy and have bigger belly which is the sign of lipodystrophy from stavudine. The main clinical features of lipodystrophy syndrome are peripheral fat loss, central fat accumulation within abdomen, gyneacomastia, and dorsocervical spine (buffalo hump). The prevalence of lipodystrophy after taking stavudine is about 50% after 12-18 months of therapy. It could be reversible if withdrawing or substituting by other ARVs. The ADR was discussed with the physician and the physician changed stavudine to zidovudine.

In this case, it was unpreventable ADR associated with internist but could be detected while pharmacist provided counseling.

Appendix E

Table E1. Recommendation for initiating and discontinuing primary and secondary prophylaxis for adults and adolescents with HIV infection [69]

Pathogen	Primary prophylaxis		Secondary prophylaxis	
	start	stop	start	stop
Tuberculosis	Tuberculin skin test>5 mm and never treated, or contact with active case	NA	NA	NA
Pneumocytis pneumonia (PCP)	CD4 cell count <200 / mm^3 or oropharyngeal candidiasis	CD4 cell count ≥200 / mm^3 for 3-6 mo	Prior PCP	CD4 cell count ≥200 / mm^3 for 3-6 mo
Cryptococcal meningitis	CD4 cell count <100 / mm^3, cryptococcal antigen negative	CD4 cell count ≥100 / mm^3 for 3-6 mo	Prior cryptococcosis	CD4 cell count ≥100-200 / mm^3 for 6 mo
Penicillosis and histoplasmosis	CD4 cell count <100 / mm^3	CD4 cell count ≥100 / mm^3 for 6 mo	Prior penicillosis or histoplasmosis	CD4 cell count ≥100 / mm^3 for 6 mo
Toxoplasmic encephalitis	CD4 cell count <100 / mm^3 and IgG antibody to toxoplasma	CD4 cell count ≥200 / mm^3 and not detected HIV virus for 3 mo	Prior toxoplasmosis	CD4 cell count ≥200 / mm^3 and not detected HIV virus for 6 mo
Mycobacterium avium complex (MAC)	CD4 cell count < 50 / mm^3	CD4 cell count ≥100 / mm^3 for 3-6 mo	Prior MAC	CD4 cell count ≥100 / mm^3 and MAC treatment at least 12 mo

* NA denotes not applicable.

Table E2. Drug regimens for primary prophylaxis against opportunistic infections in patients with HIV infection. [67,69]

Pathogen	First choice	Alternative
Tuberculosis	Isoniazid, 300 mg orally per day for 9 mo.	Rifampicin 600 mg orally per day for 4-6 mo.
Pneumocytis pneumonia (PCP)	Co-trimoxazole, single-strength 2 tab. orally OD, or 1 tab. orally OD	Dapsone 100 mg orally OD, or dapsone 50 mg orally OD, plus pyrimethamine 50 mg orally OD, plus folinic acid 25 mg once a week; or dapsone 200 mg, plus pyrimethamine 75 mg, plus folinic acid 25 mg orally once a week; aerosolized pentamidine 300 mg monthly; atovaquone 30 mg/kg orally OD.
Cryptococcal meningitis	Fluconazole 400 mg orally once weekly	None
Penicillosis and histoplasmosis	Itraconazole 5 mg/kg or 200 mg orally OD	None
Toxoplasmic encephalitis	Co-trimoxazole single strength 2 tab. OD	Dapsone 50 mg orally OD, plus pyrimethamine 50 mg orally once a week, plus folinic acid 25 mg orally once a week; dapsone 200 mg orally , plus pyrimethamine 50 mg orally , plus folinic acid 25 mg orally once a week.
Mycobacterium avium complex (MAC)	Clarithromycin 500 mg orally twice a day, or azithromycin 1,200 mg orally once a week.	None

Table E3. Drug regimens for secondary prophylaxis against opportunistic infections after chemotherapy for acute infection in patients with HIV infection. [67,69]

Pathogen	First choice	Alternative
Candidiasis	Fluconazole or itraconazole 100-200 mg orally OD	None
Tuberculosis	Not recommend	None
Pneumocytis pneumonia (PCP)	Co-trimoxazole, single-strength 2 tab. orally OD, or 1 tab. orally OD.	Dapsone 100 mg orally OD, or dapsone 50 mg orally OD, plus pyrimethamine 50 mg orally OD, plus folinic acid 25 mg once a week; or dapsone 200 mg, plus pyrimethamine 75 mg, plus folinic acid 25 mg orally once a week; aerosolized pentamidine 300 mg monthly; atovaquone 30 mg/kg orally OD.
Cryptococcal meningitis	Fluconazole 200 mg/day orally.	Itraconazole 200 mg/day orally
Penicillosis and histoplasmosis	Itraconazole 200 mg orally OD.	Amphotericin-B 1.0 mg/kg IV once a week
Toxoplasmic encephalitis	Pyrimethamine 25-50 mg orally per day, plus sulfadiazine 500-1,000 mg orally 4 times a day, plus folinic acid 10-25 mg orally per day	Clindamycin 300-450 mg orally q 6-8 hrs., plus pyrimethamine 25-50 mg orally per day, plus folinic acid 10-25 mg orally per day.
Mycobacterium avium complex (MAC)	Clarithromycin 500 mg orally twice a day, plus ethambutol 15 mg/kg orally per day	Azithromycin 500-600 mg orally per day, plus ethambutol 15 mg/kg orally per day

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