EVALUATION OF THE IMPACT OF HOME MEDICATION REVIEW PROGRAM ON ADHERENCE AMONG PATIENTS DIAGNOSED WITH SCHIZOPHRENIA AT KINTA DISTRICT, MALAYSIA

TAN YEE MUN

UNIVERSITI SAINS MALAYSIA
2015

EVALUATION OF THE IMPACT OF HOME MEDICATION REVIEW PROGRAM ON ADHERENCE AMONG PATIENTS DIAGNOSED WITH SCHIZOPHRENIA AT KINTA DISTRICT, MALAYSIA

By

TAN YEE MUN

Thesis submitted in fulfillment of the requirements for the Degree of Master of Science (Clinical Pharmacy)

July 2015

DECLARATION OF ORIGINALITY

I hereby declare that this thesis is my own work and none of the contents in this thesis contains substantial proportions of material which has been submitted and accepted for the reward of any other degree or diploma at tertiary educational institutions or organizations. To the best of my knowledge, the information derived from the previously published work or written by any person has been acknowledged in the text and a full list of references is given in this thesis.

Tan Yee Mun

ACKNOWLEDGEMENTS

It is my pleasure to convey my deepest gratitude to many individuals and parties who have involved directly and indirectly to make this study a success.

First and foremost, I would like to express my deepest gratitude to my supervisor, Dr. Chong Chee Ping for his supervision, encouragement and valuable advices throughout the research study. His constructive comments and suggestions in the preparation and completion of this research successfully are much appreciated.

I would like to extend my sincere thanks to my field-supervisor, Dr. Cheah Yee Chuang, a consultant psychiatrist for her precious time to guide, support and showering me with her perpetual optimistic spirit. Her kind input has contributed a lot throughout the progress of this research.

Thank you to my other co-supervisor, Dr. Chooi Wing Tink from Advance Medical and Dental Institute, USM for her guidance and assistance throughout the study.

I would like to express my gratitude to the director of HBUK, Dr. Hjh Rabai'ah bt Mohd Salleh for granting me the permission to conduct and proceed my data collection in HBUK, Perak.

My sincere thanks are extended to the home care staff in HBUK for their constant help and support to bring me along to visit patient's home. Their dedication in supporting this research study is really appreciated.

Many thanks to all patients and families who were willing to share their precious time and take part in this study otherwise this project would not have been possible without them.

CRC Ipoh, thank you for providing assistance on sample size calculation and statistical analysis for this research.

Special thanks to the librarians in USM for their technical support provided to enable me completing my thesis writing smoothly.

I feel truly grateful to my lovely colleagues, clinical and outpatient pharmacy department, HBUK for their encouragement and mental support as well.

Last but not least, a special appreciation to my beloved family members for their constant support, understanding and encouragement all these while. Much immense thanks to Mr. Neow Boon Jiann who stood by me through thick and thin in this journey.

TABLE OF CONTENTS

LIST OF TABLES

LIST OF FIGURES

LIST OF ABBREVIATIONS

ACT	Assertive Community Treatment
BMI	Body Mass Index
CBI	Clinic-based Intervention
CHF	Chronic Heart Failure
DAI	Drug Attitude Inventory
DALY	Disability-adjusted Life Years
DSM-IV	Diagnostic and Statistical Manual of Mental Disorders IV
FDA	Food and Drug Administration
GHS	German National Health Interview and Examination Survey
GP	General Practitioner
GSS	General Social Survey
HBI	Home-based Intervention
HBUK	Hospital Bahagia Ulu Kinta
HCT	Home Care Team
HMR	Home Medication Review
HUKM	Hospital Universiti Kebangsaan Malaysia
ICM	Intensive Case Management
IQR	Interquartile Range
MARS	Medication Adherence Rating Scale
MBS	Medicare Benefits Scheme
MHA	Mental Health Act
MHR	Mental Health Regulations
MOH	Ministry of Health
MREC	Medical Research Ethics Committee
NHMS	National Health and Morbidity Survey
NICE	National Institute for Health and Care Excellence
NMHR	National Mental Health Registry
NMRR	National Medical Research Register
NSF	National Service Framework
PILL	Prescription Intervention and Lifelong Learning
QoL	Quality of Life
RCT	Randomized Controlled Trial
SD	Standard Deviation
SDS	Sheehan Disability Scale
SF-36	Short Form Health Survey
SPSS	Statistical Package for the Social Sciences
T	Tablet
US CATIE	United States Clinical Antipsychotic Treatment for Intervention Effectiveness
WHO	World Health Organization
XR	Extended Release

LIST OF APPENDICES

PENILAIAN IMPAK PROGRAM PEMANTAUAN UBAT-UBATAN DI RUMAH PESAKIT TERHADAP PEMATUHAN UBAT DI KALANGAN PESAKIT YANG DIDIAGNOS DENGAN SKIZOFRENIA DI DAERAH KINTA, MALAYSIA

ABSTRAK

Program pemantauan ubat-ubatan di rumah adalah untuk memberikan kesinambungan penjagaan pesakit dari institusi penjagaan kesihatan ke rumah pesakit. Namun demikian, impak sebenar program HMR di Malaysia adalah kurang diketahui. Kajian ini adalah untuk menilai impak program HMR terhadap pesakit skizofrenia dari segi pematuhan dan pengetahuan ubat, kualiti hidup, kepuasan kepada program dan jumlah penjimatan kos daripada stok lampau ubat-ubatan. Kajian prospektif longitudinal ini dijalankan dari September 2012 hingga Disember 2013 dan melibatkan satu pensampelan mudah sejumlah 133 pesakit skizofrenia di bawah jagaan 'Home Care Team' Hospital Bahagia Ulu Kinta. Selepas mendapat persetujuan bertulis, pesakit-pesakit telah dilawati oleh pegawai farmasi untuk menjalankan kajian komprehensif penggunaan ubat dan memberikan kaunseling ubat secara individu di rumah. Borang pengumpulan data yang standard telah digunakan untuk mengumpul data dari pesakit semasa lawatan pertama (garis asas), lawatan kedua (selepas sebulan), lawatan ketiga (selepas tiga bulan) dan lawatan keempat (selepas enam bulan). Pematuhan ubat telah dinilai dengan skala 'Medication Adherence Rating Scale' (MARS) yang telah disahkan dan juga kaedah kiraan pil. Pengetahuan pesakit pada ubat antipsikotik dan kepuasan terhadap program HMR telah dinilai dengan borang soal selidik yang standard digubal oleh

penyelidik bagi projek ini. Kualiti hidup pesakit telah dinilai dengan skala “Sheehan Disability Scale” (SDS). Sebarang penyimpanan ubat-ubatan yang berlebihan telah dikumpul dan direkod untuk analisis penjimatan kos. Purata umur untuk 133 pesakit-pesakit adalah 41.76 (SD 8.86) tahun dan nisbah lelaki kepada perempuan adalah lebih kurang sama (54.9% vs 45.1%). Skor MARS menunjukkan pematuhan ubat telah bertambah baik dengan nyata pada setiap lawatan [lawatan pertama: median MARS = 9 (IQR 3) vs lawatan keempat: median MARS = 10 (IQR 1), p <0.001] manakala kaedah kiraan pil juga menunjukkan bahawa peratusan dos yang diambil mempunyai pencapaian yang sangat ketara selepas lawatan keempat [lawatan pertama: median = 67.1% (IQR 92.1%) vs lawatan keempat: median = 97.5% (IQR 14.3%), p <0.001]. Skor pengetahuan juga telah bertambah baik dengan nyata selepas implementasi program HMR [lawatan pertama: 5 (IQR 2.5) vs lawatan keempat: 8 (IQR 1.0), p <0.001]. Dari segi kualiti hidup pesakit, terdapat peningkatan yang nyata bagi komponen ‘sosial’ dan ‘keluarga’ selepas enam bulan susulan (p < 0.001). Namun demikian, tiada perbezaan yang nyata didapati pada keseluruhan kualiti hidup pesakit (p = 0.600) dan pada komponen ‘kerja’ (p = 0.486). Pengurangan pembaziran ubat adalah sebanyak 26.5% selepas enam bulan program HMR. Pada akhir kajian, pesakit-pesakit menunjukkan kepuasan positif dan penerimaan terhadap program HMR yang diberikan oleh pegawai farmasi. Secara kesimpulan, program HMR mempunyai impak positif pada pesakit dari segi pematuhan ubat, pengetahuan ubat antipsikotik, pengurangan pembaziran ubat, kepuasan perkhidmatan dan kualiti hidup pada komponen 'sosial' dan 'keluarga'.

EVALUATION OF THE IMPACT OF HOME MEDICATION REVIEW PROGRAM ON ADHERENCE AMONG PATIENTS DIAGNOSED WITH SCHIZOPHRENIA AT KINTA DISTRICT, MALAYSIA

ABSTRACT

Home medication review (HMR) program is to provide continuity of patient's care from healthcare institutions to patients' home. However, little is known about the actual impact of the HMR program in Malaysia. This study was to evaluate the impact of HMR program on schizophrenia patients' medication adherence, knowledge, quality of life, satisfaction to the program and the total cost saving from overstocked medications. This prospective longitudinal study was conducted from September 2012 to December 2013 and involved a convenience sampling of 133 schizophrenia patients under follow up of the home care team of Hospital Bahagia Ulu Kinta. After attaining written informed consent, patients were visited by the pharmacist to perform comprehensive medication review and provide individualized medication counseling at home. Standardized data collection forms were used to collect data from patient during the first visit (baseline), second visit (after one month), third visit (after three months) and fourth visit (after six month). Medication adherence was evaluated by validated medication adherence rating scale (MARS) and pill count method. Patient's knowledge of antipsychotics and satisfaction towards HMR program were assessed by standardized questionnaires formulated by the researcher of this project. Quality of life was measured by the Sheehan Disability Scale (SDS). Any overstocked medications were collected and recorded for cost saving analysis. Friedman ANOVA test was used to compare the differences of the

outcome measured at baseline, one month, three months and six months follow up visit. The mean age of 133 patients was 41.76 (SD 8.86) years, with approximately equal ratio of males to females (54.9% vs 45.1%). MARS score showed medication adherence was significantly improved at all time points [first visit: median MARS = 9 (IQR 3) vs fourth visit: median MARS = 10 (IQR 1), $p < 0.001$] while pill count method also revealed that percentage of doses taken had a highly significant improvement after the fourth visit [first visit: median = 67.1% (IQR 92.1%) vs fourth visit: median = 97.5% (IQR 14.3%), $p < 0.001$]. The knowledge score had also improved considerably after the implementation of HMR program [first visit: 5 (IQR 2.5) vs fourth visit: 8 (IQR 1.0), $p<0.001$]. Regarding patient's quality of life, there was a significant improvement for 'social' and 'family' components after fourth visit ($p < 0.001$). However, no difference was seen for overall quality of life of the patients, $p=0.600$ and for the 'work' component ($p = 0.486$). The reduction of medication wastage was 26.5% after six months of HMR program. At the end of the study, patients generally showed positive satisfaction and acceptance towards HMR program provided by pharmacist. In conclusion, the HMR program has positive impact on schizophrenic patient's medication adherence, knowledge of antipsychotics, medication wastage reduction, service satisfaction and quality of life on 'social' and 'family' component.

CHAPTER 1

GENERAL INTRODUCTION

1.1 Introduction

Schizophrenia is a chronic and serious mental illness, profoundly affecting patient's emotions, thinking and behavior. It is presented with positive symptoms of delusions, hallucinations and negative symptoms of affective flattening, alogia or avolition. Patients with schizophrenia can have cognitive deficits and impaired psychosocial functioning as well (American Psychiatric Association, 2000a). Information from World Health Organization stated that schizophrenia affects about 21 million people across the world (World Health Organization, 2014). Patients with schizophrenia have high risk for suicide. Out of one-third of patients who attempted suicide, about one out of ten took their own lives eventually (Centers for Disease Control and Prevention, 2013). The patients who have deterioration in psychosocial functioning and risk of harming themselves or others will be admitted to the hospital (Ministry of Health Malaysia, 2009). In Malaysia, there are increasing trend of patient newly diagnosed with schizophrenia. The prevalence of new cases of schizophrenia is about 100/100,000 per year (National Mental Health Registry, 2008). Comprehensive psychiatric services are available to mental illness patients such as outpatient care, inpatient care, rehabilitative services and hospital-based outreach community psychiatric services (Ministry of Health Malaysia, 2011b). For instances, home care service in Hospital Bahagia Ulu Kinta was formalized since year 2002 with ongoing improvements in line with of Mental Health Act (MHA) 2001 and Mental Health Regulations (MHR) 2010. The MHR 2010 Part III, Section 16 has stated that the medical director or a license personal in charge shall ensure

the establishment of a community mental health team for community mental healthcare services in a psychiatric hospital or community mental health centre. The community mental health team shall consist of multidisciplinary personal. Thus, the concept of assertive community treatment is applied and customized to the local needs.

Despite the availability of various psychiatric services and effective treatment for schizophrenia, low adherence rate to the prescribed antipsychotics is a major cause of psychotic relapse. The non-adherence rate is about 50 percent for people with schizophrenia who were discharged after one year and 75 percent after two years (Young et al., 1986, Weiden et al., 1991, Serban and Thomas, 1974, Barkhof et al., 2012, Klingberg et al., 2008). Indeed, the average risk of relapse is 3.7 times greater in patients who were not adhering to the treatment compared with patients who adhered to antipsychotic regimens (Fenton et al., 1997). There are many factors that influence patient adherence to antipsychotic treatment, which include lack of insight, medication side effects, complexity of prescribed drug regime as well as the degree of family or social support (Young et al., 1986, Perkins, 2002).

Antipsychotic drugs are identified as most frequently contributed to overall medication problems at the community setting such as nursing home. The common problems were adverse drug reactions, inappropriate treatment and underuse of beneficial treatment (Ruths et al., 2003). The rate of inappropriate prescription of psychoactive drugs was approximately 50% had been seen in US and Northern Ireland homes (Patterson et al., 2010). Side effects of antipsychotics that developed early in treatment can cause non-adherence to the medication. This is because

antipsychotics have delayed onset of action whereby patients experience side effects of antipsychotics before the intended positive outcomes from the treatment (Van Putten et al., 1984). The extrapyramidal motor symptoms, sexual disturbances and weight gain are significant side effects of antipsychotics that patients worried with (Fleischhacker et al., 1994). Further compounding this problem is the inadequate clinical information on medications received by the patients and care givers. This is usually too complicated for them to understand the information in the product leaflet especially for those from low levels of education or non-English educational backgrounds (Hussainy et al., 2011). Therefore, patients and care givers will normally search for other primary and secondary sources of information such as personal's opinions or experiences, occasionally information from the internet of undetermined sources. This will influence the decision of the patients and may lead to patients choosing for inappropriate treatment or discontinue the medications by themselves with subsequent potentially harmful outcomes (Hussainy et al., 2011).

Pharmacy practice has now shifted towards patient care (Hassali et al., 2014, Pharmaceutical Services Division and Ministry of Health Malaysia, 2013) by increasing medication knowledge and enhancing treatment adherence so as to improve their social and occupational functioning, with better quality of life. One of the advancement is the development of home medication review (HMR) service conducted by pharmacist to identify and facilitate problem solving skills regarding the issue of medication non-adherence at patient's home (Ministry of Health Malaysia, 2011a). Patient's inability to manage medications properly is a common problem at home, particularly for patients taking multiple medications (Stuck et al., 1994). Inadequate medication management often stems from poor medication related

knowledge and understanding (Armes and Addington-Hall, 2003), and can lead to non-concordance with medication regimens which include medications not being taken, taken the wrong way or in the wrong dose. These in return can result in substantial treatment issues for the patients with impacts on their quality of life as well as indirect expenditures, such as psychological, social and economic burdens on patients, care givers and the healthcare system. These indirect expenditures are generally much greater than the costs of pharmacological and non-pharmacological treatments for the government (National Cancer Control Initiative, 2003).

HMR program conducted by pharmacist is one of the options available to help patients who are at risk of experiencing medication-related problems at their home. Patient's medication adherence was assessed though patient's feedback, pill counts and identification of expired or unused medications (Papastergiou et al., 2013). It empowers and encourages the patients to take responsibility for their medicines and health by feeling comfortable enough to ask pharmacists about anything of which they are unsure. Patients play a key role in decision-making regarding their treatment and self-management strategies (Carter et al., 2012a). The program involves a team approach, whereby the doctor, pharmacist and other relevant members of the health care team working together to provide care for the patients. Pharmacist is part of a multidisciplinary team and plays a proactive role in ensuring medication adherence of all patients under the home care team. The pharmacist will visit the patients at their home, performs a comprehensive review of medication regime (including over-the-counter and complementary medicines) in the home setting and feedback to the doctor via a report or during daily review. The doctor will discuss any recommendations with pharmacist and may make appropriate

changes to patient's medication regime (Ministry of Health Malaysia, 2011a). Although time consuming, HMR gives patients satisfaction through a better pharmacist-patient relationship which is worth the effort. The pharmacist's involvement and contributions can potentially improve the patients' medication management and reduce their risk of non-concordance and hospital admissions (Carter et al., 2012a, Roberts et al., 2001, Hanlon et al., 1996, Borgsdorf et al., 1994, National Health Service UK, 2000).

HMR program had been incorporated into the Malaysian public health care system since 2004. In fact, the World Health Organization (WHO) and the European Council have stressed the importance of including community pharmacists, considered the health professional most readily accessible to patients, as an active member of the multidisciplinary HMR team with the aim of benefiting patients' health (World Health Organization, 1994, Council of Europe, 2001), including those suffering from mental disorders (World Health Organization, 2005). Pharmacist is responsible to provide systematic assessment of the patients' medications at their home which is effectively to identify, resolve and prevent drug-related problems (Roughead et al., 2009, Sorensen et al., 2004). However little is known about the impact of HMR program since its implementation in Malaysia particularly among the patients diagnosed with schizophrenia (World Health Organization, 2003).

1.2 Justification for this study

Non-adherence and inappropriate medication use in the community and institutional settings has been reported to be a common and continuing problem in both local and overseas setting, particularly in patients taking multiple types of medications

(Rubio-Valera et al., 2009, Chen et al., 2012b, Ramli et al., 2012, Razali and Yahya, 1995). Under-utilization of psychiatric services and non-adherence to the medications are the common issues at home for psychiatric patients which subsequently lead to a failure in achieving treatment goals. One of the methods to address medication-related problems is to conduct comprehensive medication reviews and related interventions by pharmacist as part of a multidisciplinary team process (Sorensen et al., 2004). Visiting patients in the home by pharmacist indicates pharmacy service has shifted traditionally from product centered towards patient care. HMR program is assisting individuals living at home to maximize the benefits of the treatment as well as to detect, resolve and prevent medication-related problems. Patients' and care givers' medication-related knowledge and understanding of the illness also improved after pharmacist's domiciliary visit (Hussainy et al., 2011, Carter et al., 2012a). Studies of pharmacist medication reviews at home in Australia had positive impacts on medication care (Sorensen et al., 2004). This best practice approach which involves cooperation of the doctor, pharmacist, other relevant health professionals, patient and care taker facilitates cooperative working relationship between members of the health care team in the interests of patient health and wellbeing which is advocated by MHA 2001 and MHR 2010.

To the best of our knowledge, there is limited study conducted to evaluate the impact of HMR program in Malaysia. As patients with schizophrenia are among the group of patients with higher tendency to use psychotropic medications inappropriately (Everard, 2005), there is a strong need to assess the effect of HMR service targeting at this population. This study therefore aims to evaluate the impact

of HMR program performed by pharmacist on the patients diagnosed with schizophrenia. The patients' adherence, knowledge, quality of life and the cost saving from declining medications wasted were assessed in this study. The findings of this study will help in providing recommendations to improve the standard Home Medication Review Protocol and its implementation in the Home Care Team, Hospital Bahagia Ulu Kinta, Perak, Malaysia.

1.3 Objectives of this Study

1.3.1 General Objective

To evaluate the impact of the home medication review program conducted by the pharmacist for patients diagnosed with schizophrenia enrolled under the home care team, Hospital Bahagia Ulu Kinta, Perak, Malaysia.

1.3.2 Specific Objectives

1) To assess the impact of HMR program by pharmacist on medication adherence for patients diagnosed with schizophrenia.
2) To evaluate the patients' knowledge towards antipsychotic agents before and after the HMR program conducted by pharmacist.
3) To calculate the total cost saving resulting from the unused antipsychotic agents collected from patient's home during the pharmacist HMR visit.
4) To determine the effect of HMR program on the quality of life of the patients by using Sheehan Disability Scale (SDS).
5) To evaluate patient's satisfaction towards HMR service.

CHAPTER 2

LITERATURE REVIEW

2.1 Overview

A systematic literature search was conducted by using ScienceDirect, Scopus, SpringerLink, Wiley online library, SAGE Journals, Lippincott Williams & Wilkins Journals@Ovid, Cochrane Library, Medline (Abstracts) and Pubmed (Abstracts) electronic databases from year 1974 to 2014 to identify all relevant articles. Keywords for the search terms were ‘‘mental health’’ or ‘‘psychiatry’’ or ‘‘psychiatric’’ or “schizophrenia” in combination with “home medication review” or “domiciliary medication review” or “pharmacist-led medication review”. The references section of the articles obtained were used for further search too. The articles that published in English language were included. The most recent publication was chosen if abundant abstracts of the same topic were obtained.

2.2 Medication Misadventure at Home

Globally, medication misadventure is a leading public health issue which covers broad array of negative drug experiences. It is defined as any iatrogenic hazard or incident associated with drug therapy (Kaboli et al., 2010). For instance, medication errors, adverse drug reactions and the harms resulting from the errors are associated with medication misadventures (Manasse, 1989). Serious, harmful, poor clinical response and life threatening medication misadventures at home can lead to hospital admission. A systematic review by Runciman and colleagues in Australia revealed about 2 to 4% of all hospital admissions were drug-related which stemmed from medication misadventure (Runciman et al., 2003). Based on the findings of the

authors, up to three quarter of the admissions were either definitely or potentially preventable (Runciman et al., 2003). Another review on 15 studies on this topic in 2002, Winterstein et al. reported a median of 7.1% were medication-related hospital admissions (Winterstein et al., 2002). Other observational studies in different countries also estimated the percentage of drug-related admissions were between 2.3% to 16.2% and more than half of the cases actually can be prevented (Jha et al., 2001, Howard et al., 2003, Nelson and Talbert, 1996). While in Malaysian context, a recent prospective study conducted by Karuppannan et al. in two medical wards in Malaysia reported as high as 36.9% (n = 443/1200) of admissions were related to adverse drug events (Karuppannan et al., 2013).

The burden of mental illness is about twelve percent of the global burden of disease and most of the mental illness cases are managed in the community (World Health Organization, 2013). Antipsychotic medication is one of the main effective treatments for mental illness. However, psychotropic medications are always used incorrectly which causes medication misadventure (Mort and Aparasu, 2002). Based on a multidisciplinary review of drug utilization among nursing home residents, antipsychotic agents were mostly involved in medication problems such as adverse drug reactions which was the highest reported (Ruths et al., 2003). The expanding of pharmacist's role to provide community-based services to mentally ill patients who are at high risk of medication misadventure is an approach to improve psychotropic medication use (Bell et al., 2005). The systematic review by Bell et al. provided evidence that pharmacist conducted medication review can optimize the use of antipsychotic medications in the community setting (Bell et al., 2005).

By preventing medication misadventure, it is believed that this will reduce the health care cost burden besides improving patient's health outcomes and reducing medication-related hospital admissions. Among the studies which evaluated the cost burden caused by medication misadventures, one of the biggest studies involving 18820 patients in two large general hospitals in Merseyside, England revealed that such admissions cost up to 466 million pounds annually (Pirmohamed et al., 2004). Another data from nested case-control study in 1997, reported that a total of $5.6 million annually had been attributed from the admissions caused by adverse drug events (Bates et al., 1997). Medication misadventure can happen in patients' home upon discharged due to the confusion with the treatment and medication non-adherence. For instances, patients might take the medications wrongly in improper dose because of lack of knowledge and poor adherence to the medications (The Pharmacy Guild of Australia, 2009, Procyshyn et al., 2010). Subsequently, they were at high risk to encounter medication problems and might cause an admission if in serious case. This issue has become a worldwide concern and is preventable, better preventive efforts are urgently needed in order to avoid the problems from worsening. The development of the continuity care would be a good strategy to facilitate the continuum of the quality use of medicines from hospital to community setting.

2.3 Risk of Medication Misadventure with Patients diagnosed as Schizophrenia

Person with mental illness are known with diminished cognitive capacity and are similarly exposed to the risk of medication misadventure (Campbell Research & Consulting, 2008). In addition, all psychotropic drugs are common with adverse

drug reaction which is an example of medication misadventure (Ruths et al., 2003). This in return will increase the risk of medication misadventure among the mentally ill patients. There are bundle of studies which had shown the incidence and causes of medication misadventure among individuals with mental illness. (Maidment et al., 2006, Procyshyn et al., 2010).

Maidment et al. conducted a systematic review on hospital-based psychiatry service and the medication dispensing process by pharmacist. The review pointed out that psychiatric patients are at higher risk of medication misadventure as this group of patients are putting responsibilities on mental health staff with less articulate and question about the potential side effects, change of the treatment regimen and the monitoring requirement (Maidment et al., 2006). The review was focused on process based and not on outcome based studies. Outcome based studies were retrospective review on historical medical notes that had reported harm to the patients caused by medication. While process based studies were prospective review on prescriptions by pharmacist to prevent harm and error caused by medication. Therefore, the systematic review on process based studies noted there were errors reported which did not reach patients with serious harm such as adverse drug events and iatrogenic injury. Most errors reported were prescribing errors (illegibility, incomplete prescriptions and transcription errors) and administration errors (wrong time, wrong dose and missed dose) (Maidment et al., 2006). Another comprehensive review by Procyshyn et al. identified the contributing factors to the medication errors in psychiatry. The review noted that the misadventure can be originated from patient, mental health care provider and system. The patient-related factor would be poor medication adherence, failure to tell the presented psychiatric symptoms and inform

their mental health care providers about their latest treatment (Procyshyn et al., 2010). Both reviews from Maidment et al. and Procyshyn et al. highlighted the need of seamless continuity of care and adequate clinical pharmacy practice (Maidment et al., 2006, Procyshyn et al., 2010).

2.4 The Causes of Medication Misadventure in Patients with Schizophrenia

2.4.1 Poor Medication Adherence

The previous reported mean non-adherence rate to antipsychotics among schizophrenia patients was about 49.5% (Lacro et al., 2002). It is often associated with potentially severe clinical outcomes. For instances, it shows an increased risk of relapse and is seen as a major problem which prevents patients with schizophrenia from living independently in community settings. Based on a recent update from a systematic review by Zipursky et al., a mean of 77% relapse rate following one year of stopping antipsychotic medications by patients were found. The risk had increased to 90% after two years (Zipursky et al., 2014). According to a prospective study, around one third of the patients who had poor insight were tended to stop the treatment within six months of their first psychotic episode during early stage of the illness (Kamali et al., 2006). The finding was also supported by a two years prospective study by Linden et al., which reported 34.4% of the patients refused psychiatry follow up and stopped the medications. These patients were from young age group and with shorter duration of mental illness. They were more likely to miss the follow up after discharged from hospital and not keeping mental health outpatient appointments regularly (Linden et al., 2001).

A comprehensive review by Acosta et al. postulated a number of risk factors associated with medication non-adherence, for instances, history of poor adherence, poor rapport with the psychiatrist, shorter duration of illness, without an adequate follow up plan upon discharge, distress with the side effects, inadequate treatment with residual symptoms and believing the illness does not need a long term treatment (Acosta et al., 2012). For patients with younger age and shorter duration of illness, they may distrust the diagnosis and the importance for treatment, and show poorer tolerance to adverse effects caused by the medications at the beginning of the illness (Acosta et al., 2012, Mahaye et al., 2012). Besides, the disease severity and the unique characteristics of schizophrenia such as cognitive impairment were associated risk factors for medication non-adherence as well. These disease related factors can be explained by the deficiency of memory and concentration which led to the difficulty of comprehension and organization of their medication schedules (Acosta et al., 2012, Higashi et al., 2013).

As a consequence of antipsychotics non-adherence, patients are posed at a higher risk of medication misadventure which can lead to poorer prognosis, relapse, readmission and longer remission time (Acosta et al., 2012). Furthermore, the antipsychotic non-adherence has a definite relationship with the incurred economic costs. The significant direct costs would be the issue of rehospitalization (Thieda et al., 2003, Weiden and Olfson, 1995). In the UK, the predicted excess total inpatient service cost for non-adherent psychiatric patients as compared to the adherent psychiatric patients was over 5000 pounds per year (Knapp et al., 2004). Since patients with severe mental illness such as schizophrenia have complex cognitive features, a specific intervention to improve their medication adherence is required.

2.4.2 Poor Insight

Insight into illness is a determinant value for the treatment outcomes in schizophrenia, particularly to improve the medication adherence, and to reduce the risk of relapse and rehospitalization. According to the Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition (DSM-IV), lack of insight is a common phenomenon among mental illness patients and it may be one of the best predictors of poor outcome. This is because it predisposes the patients to non-adherence with treatment (American Psychiatric Association, 2000a). Literatures reported that higher level of insight into illness correlates with better treatment adherence and medication response (Schwartz et al., 1997, Schennach et al., 2012). People tend to view mental illnesses in different ways. For example, in Chinese culture, they hold an integrated point of view that supernatural attributions are usually causing mental illness (Song et al., 2005, Lauber and Rossler, 2007). Two studies conducted in Taiwan in 1981 and in 1991 showed that up to 15% of the population linked spiritual explanations to mental illnesses, and with that they opted and believed in folk therapy rather than sought for psychiatric treatment (Chen et al., 2012a). These cultural attitudes can affect patient's insight towards mental illness and their acceptance to the medication significantly. For instances, some literatures suggest that Chinese culture imposes greater stigmatizing attitudes to mentally ill patients compared to other cultures such as the Western culture (Hsiao et al., 2006, Lauber and Rossler, 2007, Mellor et al., 2012). Patients in this Chinese stigmatizing culture tend to deny their illness, refuse to be admitted when in need of hospitalization and discontinue prescribed medications after discharge. This is consistent with a study finding which demonstrated significant lower levels of insight and less positive attitudes towards medication among Chinese sample from Guangzhou, China as

compared to the United States Clinical Antipsychotic Treatment for Intervention Effectiveness (US CATIE) sample (Mohamed et al., 2014). Furthermore, patients with perception of their antipsychotics treatment is ineffective and causes lots of side effects are likely not to fill their prescription and take the medications as prescribed. Study by Kamali et al. claimed that poor insight is a strong predictor which caused 33% of patients who encountered first episode of schizophrenia had stopped their treatment within 6 months (Kamali et al., 2006). Atkinson et al. also postulated that bad medication experience increases the risk of poor medication adherence (Atkinson et al., 2004). A study by Amador et al. showed deficits of self awareness in patients with schizophrenia were much more severe than patients with schizoaffective or major depressive disorders with or without psychosis (Amador et al., 1994). Therefore, a critical look at the relationship between awareness of mental disorder and its impact on patient's outcomes is utmost important.

2.4.3 Lack of Medication Knowledge

Managing medications wrongly is the major problem patients encounter at home which can lead to misadventure and rehospitalization (Hussainy et al., 2011). Medication taking decision and awareness of the illness are influenced by the patient's level of understanding on the illness and treatment. This is especially important for the younger patients who encounter recent onset of schizophrenia as compared to the multi-episode patients. The treatment normally will involve both patients and their families who are lacking of information in this field (Grubic and Tavcar, 1999, Robinson et al., 2002). Their poor understanding about the important benefits and possible side effects of the antipsychotics may lead to medication refusal and relapse. This proves the need of information and the two-way

communication between mental health care provider and patients. In addition, cognitive deficiencies will affect patients' ability of judgment and master new knowledge about their illness and treatment as well (Acosta et al., 2012).

Implementing education program to the patients and their families may provide related information about the illness and treatment to increase their understanding and promote medication adherence. The efficacy of a comprehensive educational program such as psychoeducation had been proven to improve patient's knowledge, reduce psychotic symptoms and relapsing rate (Li and Arthur, 2005, Chan et al., 2009). A Malaysian study had reported positive outcomes on insight and reduction of admission rate after evaluating the impact of psychoeducation to patients with schizophrenia (Ruzanna et al., 2010). Such program can decrease the patients' negative thoughts of medication side effects, increase patients' confident on medication and subsequently improve the medication adherence. Further, younger generation of schizophrenia patients gain more from psychoeducation as compared to those with advanced age. This is because of the cognitive and memory issue around the older patients which suggesting that they have illness related limitation to learning (Ruzanna et al., 2010).

In short, the potential medication misadventure resulting from poor knowledge about illness and treatment for schizophrenia can be avoided by implementing education program such as psychoeducation program.

2.4.4 Poor Family Support

Rejection and poor family support is the main perpetuating factor which causes inadequate treatment of schizophrenia (Chen et al., 2012a). Family members or caregiving relatives have important role in facilitating patient's adaption to illness, improving medication adherence and promoting recovery (Magliano et al., 2005). However, Chatterjee and colleagues found out there were 31% of families which had been rated as not being supportive when they were collecting study sample characteristics for their study. They reported that poor family support was correlated with longer duration of illness (Chatterjee et al., 2009). Previous studies had found that expressed emotion from the families can predict the repeatedly relapse in patients with schizophrenia. Expressed emotion is an adverse family environment in which the patients received a number of critical comments and marked degree of emotional over involvement from family members. This would cause patients to be more likely to have symptoms exacerbation and relapse (King, 2000, King and Dixon, 1999).

Lack of family's supervision on patient's treatment is another commonest factor associated with poor prognosis of the disease and longer duration of untreated psychosis. Due to the frequent psychotic symptoms at home, patients are more likely to be rejected by their overburdened family (Chen et al., 2012a), and subsequently lead to homelessness. Hence, studies showed patients with schizophrenia are having greater risk of homelessness as compared to the other psychiatric patients (Bebbington et al., 2005, Brekke et al., 2001, Chatterjee et al., 2009).

There is growing recognition of family intervention as an adjunct to the treatment of antipsychotic. One of the recent Cochrane review on 53 randomized controlled trials (RCTs) revealed that the family support on patients with schizophrenia can lead to the improvement of medication adherence, the reductions of psychotic symptoms, relapse and rehospitalization (Pharoah et al., 2012). In a Malaysian study, provision of psychoeducation program to the family members or caregivers demonstrated significant improvement in their knowledge of the illness symptoms, the importance of the treatment and the early warning signs. Moreover, the defaulter rate for patient's follow up was reduced after the psychoeducation program (Paranthaman et al., 2010).

In conclusion, many studies in the past have ascertained the value of family support and involvement for the treatment of schizophrenia patients. In addition, patients who stay with their families would have more contact and support from the family members. This would be an advantage for the patients' recovery. Thus, the preference of families to participate into mental health care of the patients should be reinforced to prevent the illness deterioration.

2.4.5 Stigmatization

The stigma of mental illness is a well documented cause of a person's reluctance or delay to seek effective mental care treatment, social withdrawal, lower self-esteem, poor self-care and substance misuse (O'Reilly et al., 2013, Sartorius, 2007). In a long run, mental illness patients with a low treatment effect will increase the probability of the illness relapse. Stigma comes from the public towards person with mental illness such as schizophrenia is high, particularly due to the perception that this

group of people is dangerous (Lauber and Rossler, 2007). According to the General Social Survey (GSS) 1996 conducted in United States, more than half of the 1444 surveyed adults were not willing to socialize, work next to or have a family member marry to a person with mental illness. Nearly 50% of the GSS 1996 sample agreed that patients with schizophrenia should be forced to get treatment (Pescosolido et al., 1999). A recent meta-analysis of international studies done by Schomerus et al. had shown that mental health stigma towards people with mental illness remained unchanged for the past two decades although public's level of mental health literacy had increased in recent years (Schomerus et al., 2012). Negative attitudes can raise the stress to the mentally ill patients and rob their opportunities to deserve better quality of life, good jobs and satisfactory health care (Song et al., 2005, Patrick et al., 2002). They not only struggled with the discrimination from the public but also challenged by the symptoms from the disease as well as from family members. A study by Thornicroft et al. on 729 patients with schizophrenia across 27 countries found that about 50% of them experienced and anticipated discrimination from family members, in making or keeping friends, in finding or keeping a job and in intimate or sexual relationships. The discrimination rate was high and consistent across countries (Thornicroft et al., 2009). In addition, numerous studies revealed that Chinese community put heavily stigmatizes on mentally ill patients. They labeled mentally ill people as useless, incompetent, failure to fulfill cultural expectations and familial obligations. Consequently, the mentally ill patients experienced rejection and interpersonal disharmony (Hsiao et al., 2006, Lauber and Rossler, 2007, Mellor et al., 2012, Yang et al., 2007, Yang, 2007).

2.5 The Consequences of Medication Misadventure in Patients with Schizophrenia

2.5.1 Psychosis Severity and Relapse

For patients who are discharged from hospital to their home, maintenance treatment with antipsychotics is important to prevent patients from relapse. The NICE guidelines also stated about the importance of long term maintenance of antipsychotics in relapse prevention (National Institute for Health and Clinical Excellent, 2014). However, patients who missed appointments have high prevalence of dropout from treatment and subsequent poor prognosis. It is supported by a prospective study on 365 patients who received mental healthcare, the result showed that patients who missed an appointment were more functionally impaired, unwell and subsequent more admissions than those who attended appointments (Killaspy et al., 2000). A study carried out by Jaeger et al. found that patients who discontinued the psychiatric maintenance treatment had the highest rate of being rehospitalized compared to patients who adhered to the treatment during the six months follow up (Jaeger et al., 2012).

Apart from distressing rehospitalization, relapse cases were also associated with the positive and negative symptoms exacerbation which required more intensive case management, changed of antipsychotic agent and appeared to have lower QoL (Almond et al., 2004, Briggs et al., 2008, Chabungbam et al., 2007). Not surprisingly, relapse cases were generating higher cost to the health care system compared to the stable patients. Although not all relapsing patients were admitted, the changed of the treatment cost, increased psychiatric outpatient visits and intensive community psychiatric service should be taken into account as well.

Almond et al. found that the relapse cases cost four times higher than the stable patients (Almond et al., 2004).

Chabungbam et al. found that medication misadventure is related to relapse in schizophrenia. Relapsed patients who reported with significant side effects of medications could be resulted from inappropriate dosage of the medications (Chabungbam et al., 2007). Discontinuing medication seems logical to many patients and is tempting when the psychotic symptoms subsided. Patients who tend to discontinue their treatment or partially adhere to the medications are a strong predictor to cause relapse as stated in a few studies (Kozma and Weiden, 2009, Olivares et al., 2013, Weiden et al., 2004).

2.5.2 Health Risk

Leaving patients with mental health problems untreated at home can worsen the patients' outcomes, such as committing suicide and mortality. Globally, there is increasing trend of suicides among patients with schizophrenia and their lifespan was reduced by an average of 10 years (Saha et al., 2007). According to Malaysian data, approximately 10-15 in 100 of schizophrenia patients were found to have committed suicide as compared to 10 out of 100,000 people only among those with no mental illness (Malaysian Psychiatric Association, 2007). This is also supported by a meta-analysis by Brown and a study by Osby et al. in Sweden. They found a linear increasing trend of mortality among patients with schizophrenia (Osby et al., 2000, Brown, 1997). The mortality rate for schizophrenia was highly associated with elevated suicide rate which attributed 28% of the total mortality rate (Brown, 1997). Increasing mortality from suicides was reported in a registry study from Denmark

and it shared the same conclusion in a Danish study which mentioned that the illness caused them to be less inclined to seek for treatment (Mortensen and Juel, 1993). Brown et al. found that one in four suicides were not in contact with psychiatric services (Brown et al., 2000). The mental disintegration resulting from rejecting psychiatric contact is the important predictor of suicide attempts. Hor and Taylor found an important finding in their systematic review that uncontrolled positive symptoms such as auditory hallucinations and delusions were associated with an increased risk of suicide among patients with schizophrenia (Hor and Taylor, 2010). Another protective factor that contributes to high suicide risk in schizophrenia is poor medication adherence (Hawton et al., 2005, Hor and Taylor, 2010). Tiihonen et al. reported a worrying 37-fold increase in mortality by suicides in a nationwide cohort of patients after a first episode of schizophrenia discharged from hospital and not taking antipsychotic medications (Tiihonen et al., 2006). Patients who were living alone or not staying with their families should be taken into account as it can affect the poor prognosis of the disease and increase the risk of suicide (Hawton et al., 2005). Prevention of suicide in schizophrenia will rely on patients adhere to the effective treatment and the support from family members. According to the review by Hor and Taylor, a smaller risk of committing suicide was found among individuals who were on treatment (Hor and Taylor, 2010).

2.5.3 Low Quality of Life

Quality of life (QoL) has been an important outcome measure to measure psychiatric patient's daily lives following deinstitutionalization (Xiang et al., 2007). The monitoring of symptoms recovery may not be adequate to understand and is insufficient to measure the efficacy of community care program. Indeed psychiatric

patients face many other challenges, such as marginalization and discrimination from the community, poor insight, limited rehabilitation resources available as well as the disabilities due to the disease (Xiang et al., 2007). In addition, the depressive symptoms in schizophrenia were significantly associated with poor quality of life that measured by Sheehan Disability Scale (SDS) (Rocca et al., 2005). Thus, the attempt to describe wider dimensions such as quality of life can provide better understanding of psychiatric patients living in the community. There are few studies which revealed that patients with schizophrenia had lower quality of life compared to the general population. For example, Lempp and colleagues recruited patients with schizophrenia found that they had significant impairments for their quality of life in physical and mental domains, assessed by the Short Form Health Survey (SF-36) compared to the general population (Lempp et al., 2009). The German National Health Interview and Examination Survey (GHS) showed that patients with mental disorder had poorer quality of life on all SF-36 subscales and component scores compared to the community without mental illness (Schmitz and Kruse, 2007). Pertaining to the community based psychotic patients in Penang, Malaysia, Mubarak et al. revealed approximately 50% of 174 patients faced social discrimination, isolation, acute poverty and exploitation in the working place (Mubarak et al., 2003). This phenomenon also happened in developed countries such as the urban areas in Australia (Jablensky et al., 2000). Another study on Chinese outpatients with schizophrenia living with their families reported significant poor QoL in physical, psychological and social domains compared to the general population in Hong Kong (Xiang et al., 2007, Chan and Yu Iu, 2004). It is important to know that patients with impending relapse risk with severe positive symptoms and higher readmission rate

were significantly correlated with poorer QoL (Xiang et al., 2007, Chan and Yu Iu, 2004).

Other than SF-36 which is comprehensive but lengthy, Sheehan Disability Scale (SDS) is another tool to measure patient's quality of life. This is a short, easy to use and sensitive tool to measure the functional impairment in psychiatric disorders (Sheehan et al., 1996). In a study involved 1,001 patients to evaluate the internal consistency reliability and validity for SDS, the result showed that more than eighty percent of the patients with mental disorder had significantly elevated SDS score (higher impairment) than those who were not mentally ill. The internal consistency reliability of the SDS found to be high, with a coefficient alpha of 0.89 (Leon et al., 1997). Meanwhile, according to American Psychiatric Association, the sensitivity and specificity for SDS are 0.83 and 0.69 respectively in identifying psychiatrically impaired patients (American Psychiatric Association, 2000b).

2.6 Continuity of Care - Community Psychiatry Service in Malaysia

Whilst patients with schizophrenia are clearly susceptible to medication misadventure, two interfaces between hospital and community services had been created as a crucial step to help patients at their home. Based on international mental health care standards, many Western mental health systems have included community mental health care in their contemporary health policies and guidelines. In response to this global phenomenon, many countries in the Asia-Pacific region such as Malaysia had established National Mental Health Policy and guidelines in 1998 to provide community mental health service (Ministry of Health Malaysia, 2011b). This mental health service is important to facilitate early discharge,