# PHARMACEUTICAL CARE FOR PATIENTS WITH TUBERCULOSIS AND DIABETES MELLITUS IN MALAYSIA: A COMPLEX INTERVENTION

SHUBASHINI GNANASAN

B.Pharm (Hons), M.Pharm (Clin. Pharm.)

Thesis submitted to the University of Nottingham for the degree of Doctor of Philosophy

JANUARY 2012

# ABSTRACT

The increasing comorbid burden of tuberculosis (TB) and diabetes mellitus (DM) worldwide requires the management of all stakeholders including pharmacists. This raises the question whether current single disease management system fulfils patients' health needs and whether pharmacists could effectively play a role in enhancing the joint management of these two commonly associated diseases. Pharmacists have begun to provide pharmaceutical care through pharmacist-led medication therapy adherence clinics and clinical pharmacy services for several diseases and conditions (e.g. DM, asthma) in some public hospitals in Malaysia but are yet to be involved in the management of TB. The management of TB has been largely delivered through directly observed treatment (DOT) as high level of adherence to treatment is vital. However, little is known on how TB patients with DM are being managed and how these patients cope with their medication. The aim of this study was to develop a pharmaceutical care service for patients with TB and DM.

The first three phases (preclinical, phase 1 and phase 2) of the UK Medical Research Council framework for the development of complex interventions to improve health was applied to develop a pharmaceutical care service for patients with both TB and DM in a tertiary hospital in Malaysia. First, literature relating to TB and DM was reviewed (preclinical). Second, the pharmaceutical care needs of TB and DM patients were explored using semi-structured interviews with twenty patients, three physicians, three nurses, and a focus-group with four pharmacists (phase 1). Third, action research was conducted to assess the feasibility of providing a pharmaceutical care service for patients with TB and DM (phase 2). This study received ethical approval from the Medical Research and Ethics Committee (MREC), Ministry of Health, Malaysia.

Patients and health care professionals reported several medication-related issues in the phase 1 study. Patients were most inclined to discuss their concerns about their medication. Patients also tended to display different attitudes towards medication-taking, depending on their beliefs, the severity of illnesses, perceived efficacy of the treatment, and the severity of

medication-related problems. The findings also revealed that many of these concerns had not been discussed with their physicians. This was also caused by the patients' and physicians' tendencies to prioritise the management of TB, and unintentionally neglecting other comorbidities especially when patients were primarily managed at the chest clinic. Other difficulties identified in comorbid management included delayed initiation of both TB and DM treatment, chest physicians' lack of confidence in managing 'difficult' DM in TB patients and the burden of attending multiple clinics for patients. Health care professionals believed that pharmacist-led medication therapy adherence clinics (MTACs) encouraged the provision of patient-centred care, enhanced pharmacist-patient communication, created opportunities for inter-professional interactions and could be used as a model to provide pharmaceutical care services. Health care professionals urged pharmacists to play a role in the management of TB and DM by providing patient education and counselling.

The phase 2 study revealed that the prevalence of DM in TB patients was 15%. Action research allowed the researcher, together with a hospital pharmacist, to identify pharmaceutical care needs in TB and DM patients, and fulfilled some of them. Pharmaceutical care issues identified included lack of medication adherence, poor management of DM, the need to manage adverse drug reactions, and the lack of frequent monitoring of certain monitoring parameters for TB, DM and other comorbidities at the chest clinic. Many patients had uncontrolled DM, however, many were more likely to be adherent to TB medication than medication of DM and/or other conditions. As a follow-up action, pharmacists advised these patients to place equal importance to TB and non-TB related management. Additionally, pharmacists also made treatment recommendations and referred patients to their chest physicians for further management of medication-related problems. Nevertheless, there were barriers that impinged the provision of pharmaceutical care service. The barriers include the lack of space with privacy to provide education and counselling to patients; the unavailability of medication records and other clinical information for comorbidities at the chest clinic; and the lack of time to develop inter-professional relationship. Despite the need to address the barriers, the provision of pharmaceutical care service to TB and DM patients was feasible as pharmacists were able to integrate TB and DM management by identifying, communicating, and resolving some medication-related problems.

In summary, this study provided the groundwork by conducting phase 1 and phase 2 study prior to developing a full-fledged pharmaceutical care service for TB and DM patients. Future work can be done to improve the service through critical analysis of the challenges faced in the developmental phase with the effectiveness of the service care plan assessed through a randomised controlled trial (RCT).

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# ACKNOWLEDGEMENTS

There are so many people without whom this project would not have been possible who I would like to thank.

I would like to start with thanking my supervisors, Professor Claire Anderson, Dr. Ting Kang Nee and Associate Professor Dr. Salmiah Mohd Ali for giving me their time and support throughout the course of this PhD. Their input and comments have been invaluable. A special thanks to Associate Professor Wong Kok Thong for his suggestions and encouragement.

I owe a deep gratitude to Dato' Dr. Abdul Razak Muttalif. Without his support, I would not have been able to complete this study. I would also like to extend my heartfelt gratitude to the hospital's staff for assisting me during the data collecting process.

I thank the Higher Education Ministry of Malaysia and Universiti Teknologi MARA for providing the scholarship for this PhD. They have allowed me to fulfil my dream by providing the much needed financial support that was required.

I take this opportunity to thank my family members and friends for their abundance of love, encouragement and support. My family has and always will be the greatest pillar of support in my life. My friends have been my best critiques, they were ever willing to help and their assistance has been invaluable. I would like to acknowledge all of them for their support, in particular Mahmathi Karuppannan, Dr. Nde-Eshimuni Salema, Naseeba Alozaibi, Asam Latif, Zoe Lim, and Harpreet Kaur. Thank you.

Finally, a deep appreciation goes out to all the participants of this study. Without them this study would not have been possible.

# DEDICATIONS

This thesis is dedicated to the Almighty Lord for giving me the strength to complete my PhD, my parents who gave me the most support by sacrificing their time to look after my sons while I spent my time writing, my children (Prakaladhan and Sithaarthan) for inspiring me, and my husband for allowing me to embark on this PhD programme that took me away from him for some time. Thank you!

# TABLE OF CONTENTS

# LIST OF TABLES

# LIST OF FIGURES

# ABBREVIATIONS AND ACRONYMS

| | |
|---|---|
| A/G ratio | Albumin globulin ratio |
| ADR | Adverse drug reaction |
| AFB | Acid fast bacilli |
| AIDS | Acquired Immunodeficiency Syndrome |
| Ba | Basophil |
| BCG | Bacille Calmette Guérin |
| BMQ | Beliefs about medication questionnaire |
| BP | Blood pressure |
| CDC | Centres for Disease Control and Prevention |
| CrCl | Creatinine clearance |
| DM | Diabetes Mellitus |
| DOT | Directly Observed Treatment |
| DOTS | Directly Observed Treatment, Short- course |
| EHRZ | Ethambutol, Isoniazid, Rifampicin, Pyrazinamide |
| Eo | Eosinophyl |
| ESR | Erythromycin sedimentation rate |
| HbA1c | Glycated haemoglobin |
| HCT | Haematocrit |
| HDL | High density lipoprotein |
| HGB | Haemoglobin |
| HIV | Human Immunodeficiency Virus |
| HRZ | Isoniazid, Rifampicin, Pyrazinamide |
| IC | Identification card |
| IDF | International Diabetes Federation |
| IUATLD | International Union against Tuberculosis and Lung Disease |
| LDL | Low density lipoprotein |

| | |
|---|---|
| Ly | Lymphocyte |
| MCH | Mean corpuscular haemoglobin |
| MCHC | Mean corpuscular haemoglobin concentration |
| MCV | Mean corpuscular volume |
| MDG | Millennium Development Goals |
| MDR-TB | Multi-drug resistance tuberculosis |
| MMAS | Morisky Medication Adherence Scale |
| Mo | Monocyte |
| MOH | Ministry of Health Malaysia |
| MRC | Medical Research Council |
| MTAC | Medication therapy adherence clinic |
| Ne | Neutrophil |
| NGO | Non-government organisation |
| NTP | National tuberculosis control programme |
| PC | Pharmaceutical care |
| PK-PD | Pharmacokinetics-pharmacodynamics |
| PLT | Platelet |
| PTB | Pulmonary tuberculosis |
| R/N | Registration number |
| RBC | Red blood cell |
| RDW-CV | Red blood cell distribution width-coefficient variation |
| SHRZ | Streptomycin, Isoniazid, Rifampicin, Pyrazinamide |
| TB | Tuberculosis |
| TBDM | Tuberculosis and Diabetes Mellitus |
| TCA | To come again |
| UK | United Kingdom |
| WBC | White blood cell |
| WHO | World Health Organisation |

# GLOSSARY

| | |
|---|---|
| Action research | It is a form of research that describes, interprets and explains social situations while executing a change intervention aimed at improvement and involvement. |
| Adherence | The extent to which the patient's behaviour matches agreed recommendations from the prescriber. |
| *Bomoh* | Malay traditional healer |
| Comorbidities | The presence of one or more disorders (or diseases) in addition to a primary disease or disorder. |
| Complex intervention | Complex interventions are usually described as interventions that contain several interacting components. |
| Euglycaemia | Normal level of glucose in the blood. |
| *Hempedu Tanah/Hempedu Bumi/ Daun Cerita* | *Andrographis paniculata.* A herb that is used by locals especially for treating DM. |
| Medication-related problems | Any problem experienced by a patient that may impact on their ability to manage or use their medicines effectively. |
| *Misai Kuching* | *Orthosiphon staminues.* A herb that is used by locals for treating DM. |
| *Mohroo* | Indian salted yoghurt drink with spices. |
| *Panas* | *Hot*. It is a cultural belief that certain food or drink contains *hot or cold* properties. These properties were believed to cause certain symptoms (e.g. cough). |
| Pharmaceutical care | Pharmaceutical care involves the process through which a pharmacist cooperates with a patient and other professionals in designing, implementing, and monitoring a therapeutic plan that will produce specific therapeutic outcomes for the patient. |
| *Sinseh* | Chinese medicine practitioners |

# CHAPTER 1: INTRODUCTION

## 1.1 Introduction to the thesis

This thesis is about developing a pharmaceutical care service for patients with tuberculosis (TB) and diabetes mellitus (DM) in Malaysia. The purpose of this introductory chapter is to provide a background to this thesis. It begins with the problem statement followed by an explanation of how I became interested in the topic. The chapter concludes with a brief overview of the chapters in this thesis.

## 1.2 The problem statement

There has been a growing interest in identifying strategies to reduce the joint burden of TB and DM (Harries et al., 2010; Ottmani et al., 2010). The significance of these two chronic diseases is threefold.

Firstly, the already high global burden of DM is estimated to rise. The global burden of DM is expected to rise from an estimated 180 million prevalent cases currently recorded to a predicted 366 million by 2030 (Wild, Roglic, Green, Sicree, & King, 2004). The greatest increase is projected for developing countries (Wild, et al., 2004), where TB is highly endemic.

Secondly, DM has been known to be a risk factor for TB infection (Jeon & Murray, 2008). The association and the negative impact of the convergence of TB and DM have been extensively reviewed (Dooley & Chaisson, 2009; Ruslami, Aarnoutse, Alisjahbana, van der Ven, & van Crevel, 2010). A study conducted in India revealed that the increased prevalence of DM in urban areas was associated with a 15% greater smear positive TB incidence in urban than in rural areas (Stevenson et al., 2007). A systematic review of TB and DM showed that DM was associated with a three-fold increased risk of TB (Jeon & Murray, 2008).

Thirdly, the management of TB is highly challenging when a patient presents with DM as co-morbidity (Dooley & Chaisson, 2009; Ruslami, Aarnoutse, et al., 2010). DM has also been associated with higher mortality rates in patients with TB and DM compared to TB only patients; an increased risk of TB treatment failure or relapse, and diminished 2-month and 6-month culture conversion rates (Dooley & Chaisson, 2009; Dooley, Tang, Golub, Dorman, & Cronin, 2009; Ruslami, Aarnoutse, et al., 2010). It was also found that TB and DM patients take longer to respond to treatment (Nissapatorn et al., 2005), and are more likely to develop multi-drug resistant TB (MDR-TB) (Bashar, Alcabes, Rom, & Condos, 2001).

Malaysia is one of the top ten countries in Asia which has the highest number of people living with type 2 DM (Chan et al., 2009). In 2006, the prevalence of DM in Malaysia was 11.6% in those above 18 years and 14.9% in those above 30 years (Letchuman et al., 2010). The International Diabetes Federation (IDF) has predicted that the number of individuals with DM in Malaysia will increase from 1.5 million in 2007 to 2.7 million in 2025 (Chan, et al., 2009). There has been a continuous increase in the number of new TB cases reported in Malaysia with 14,908 cases in 1999 (MOH, 2002) to 18,102 cases in 2009 (WHO, 2010a). Due to the rising prevalence of DM a parallel increase of TB could be anticipated.

The treatment of either DM or TB requires a patient to take a large number of medicines which has been known to impact medicine adherence (Munro et al., 2007; Odegard & Gray, 2008). The directly observed treatment (DOT) for TB that was introduced in 1990s as a means of combating non-adherence has been shown to be a good strategy to enforce adherence to TB treatment (WHO, 1994b). In Malaysia, patients with conditions such as DM, asthma and human immunodeficiency virus (HIV), and patients on methadone and warfarin therapy are able to attend a medication therapy adherence clinic (MTAC) run by hospital pharmacists in a few public hospitals to assist with medicine adherence (Clinical Pharmacy Practice; Lim & Lim, 2010; Loganadan et al., 2010; Loganadan et al., 2008). To date, pharmacists in Malaysia have not been involved in the management of TB patients, especially in an out-patient setting. Although, DOT and MTACs are good strategies in promoting adherence to TB and DM treatment respectively, there is a lack of clinical guideline on the co-management of TB and

DM patients. In addition, little is known about the overall pharmaceutical care needs of patients with TB and DM.

Efforts to develop an intervention that is tailored to patients with TB and DM requires an understanding of particular barriers and facilitators in the health care system as well as to understand how best to deliver them in the context of patients' complex lives. Whilst there have been a number of qualitative investigations on experiences of TB patients (Munro, et al., 2007) and DM patients (Campbell et al., 2003; Mohd Ali, 2009; Vermeire et al., 2007), most of them focused on the consequences of a single disease state and less is known on the challenges of dealing with both diseases concurrently. As such, there is a need to investigate patients' and health care professionals' experiences in managing TB and DM in order to understand the pharmaceutical care issues of these patients prior to the development of a pharmaceutical care service.

## 1.3 How I became interested in the topic?

I received undergraduate and postgraduate trainings in pharmacy and clinical pharmacy respectively. Prior to beginning my PhD, I worked as a clinical pharmacy lecturer and my research interest was in developing pharmaceutical care services. From my own experience, a good inter-professional relationship is important not only in developing a new service but also in getting support from physicians in order to conduct research within their practice environment. My previous experience and exposure had directed me towards this research topic in this study.

When I was doing a masters degree in clinical pharmacy, I was acquainted with a chest physician who was involved in teaching clinical aspects of infectious diseases which included TB. I remembered this physician in particular because he was open and receptive to suggestions and recommendations given by pharmacy students. He had emphasised the importance of health care professionals working in collaborative practice.

I knew pharmacists were not involved in the management of TB and since I had a pre-established contact with the chest physician, I thought it would be easier to approach him and express my desire of developing a pharmaceutical care service for TB patients. The physician concerned was a chest consultant and head of the respiratory department of a tertiary public hospital in the northern region of Malaysia. I informed him about my interest and asked his permission to conduct a preliminary observational study in his out-patient clinic.

Upon his approval, I observed how DOT was given at the chest clinic. This helped me to familiarise myself with the clinic environment. I reviewed 30 newly diagnosed TB cases reported in January 2007. I wanted to find out whether I could identify pharmaceutical care issues by reviewing TB patients' medical records. However, I experienced difficulties in identifying those issues due to poor documentation of medication history especially for co-

morbidities in the patients' medical records. More than half of the patients had comorbidities (n=16) and DM (n=7) was the most common comorbid condition in TB patients. Nevertheless, this preliminary finding intrigued me to investigate the management of comorbidities in TB patients.

At that time, I assumed adherence to TB treatment might not be a problem with DOT in place but I wondered how comorbidities of TB patients were managed and whether pharmacists will have a role to play. In order to have a homogenous group, I decided to focus on TB patients with comorbid DM.

## 1.4 Organisation of the study

This thesis is divided into seven chapters. The current chapter provided an introduction to the thesis.

**Chapter 2** begins with a description about Malaysia, TB and DM in Malaysia and its health care system. Subsequently, it discusses the concept of pharmaceutical care and complex intervention. Then, it presents the literature review on TB and DM, the role of pharmacists in the management of TB and DM and patients' and providers' perspective on medication-related issues. The chapter ends with the rationale for the study and presents the aim and objectives of the study.

**Chapter 3** describes the methodology and methods underpinning the phase 1 study. It describes the qualitative methods that were chosen and how validity and reliability can be assessed. It illustrates the data collecting process and methods of analysis in detail.

**Chapter 4** presents and discusses the patients' and health care professionals' experiences in managing TB and DM; health care professionals' perceptions on pharmacist-led MTAC and the potential role of a pharmacist in managing TB and DM.

**Chapter 5** describes the methodology and methods used in phase 2 study. It provides explanation on action research and describes the data collection process and methods of analysis in detail.

**Chapter 6** presents and discusses the feasibility of providing a pharmaceutical care service to TB and DM patients. It presents the prevalence of DM in TB patients, describes the

pharmaceutical care issues of TB and DM patients and discusses the factors hindering the provision of service.

**Chapter 7** summarises the overall findings and concludes with the implications for practice, policy and research.

# CHAPTER 2: LITERATURE REVIEW

## 2.1 Introduction

This chapter has three important components. Firstly, it provides the background information about Malaysia. Secondly, it describes the concept of pharmaceutical care, why pharmaceutical care is a complex intervention and how a complex intervention can be carried out. Thirdly, it provides a literature review on TB and DM, the role of pharmacists in the management of TB and DM, the patients' and providers' perspectives on managing medication-related issues and, a summary of the literature review and the rationale for the study. The chapter ends by presenting the aim and objectives of the thesis.

## 2.2 Malaysia

Malaysia is located in Southeast Asia, between 2 and 7 degrees north of the Equator and occupies an area of 330,803 square kilometres (Department of statistics Malaysia, 2011). Malaysia consists of a federation of 13 states and the Federal Territories of Kuala Lumpur, Labuan and Putrajaya. Peninsular Malaysia, is bordered by Thailand in the north and Singapore in the south. The South China Sea separates the states of Sabah, Sarawak from Peninsular Malaysia. Sabah and Sarawak are bordered by Indonesia. Sarawak also shares a border with Brunei.

In 2010, the Malaysian population was estimated to be around 28.3 million (Department of Statistics Malaysia). The population density is approximately 86 persons per square kilometre with the annual population growth rate projected to be 2.0% annually. Malaysia has an ethnically diverse population consisting of 67% Bumiputeras (Malays and ethnic minorities), 25% Chinese and 7% Indians. In general, Malaysia is a very young country with 27% of the population below the age of 15, 67% between the age of 15 and 64, and 5% of the population is 65 years and above (Department of Statistics Malaysia). Over the years, the life expectancy at birth of males and females increased to 71 years and 77 years respectively in 2010 (Department of Statistics Malaysia) from 55 years and 58 years in 1957 (Merican & Yon, 2002). Basic immunisation coverage of infants improved to 100% (Merican & Yon, 2002). Bacille Calmette Guérin (BCG) vaccination is given to all newborns in Malaysia.

Islam is the most common religion in Malaysia with the proportion of 61.3 %. Other religions embraced are Buddhism (19.8%), Christianity (9.2%) and Hinduism (6.3%) (Department of

Statistics Malaysia). The Malay language is the official language in Malaysia. Other spoken languages include English, Chinese[1] and Tamil.

[1] There are various spoken Chinese dialects which include Mandarin, Hokkien and Cantonese.

### 2.2.1 TB in Malaysia

TB is one of the ancient infectious diseases which remain a major public health problem till today. Despite the availability of effective anti-TB drugs, it has been estimated that TB accounts for 1.7 million deaths every year and 9 million new cases worldwide which is more than any other time in history (WHO, 2009). Pulmonary TB is the commonest form of TB and the symptoms include cough persisting for more than two weeks, cough with sputum which is occasionally bloodstained, loss of appetite, loss of weight and fever (Schaaf & Zumla, 2009).

TB was the number one cause of death in Malaysia in the 1940s and 1950s (Iyawoo, 2004). Prior to the availability of anti-TB drugs in the late 1950s, patients were isolated in sanatoria and were managed by surgical means (Iyawoo, 2004). The Malaysian government launched its National TB control programme (NTP) in 1961 (Iyawoo, 2004). The National TB centre functioned as the headquarters of the NTP, and the state general hospitals with their chest clinics functioned as the state directorates (Iyawoo, 2004). Every state has its own State TB Managerial Team which is responsible for the implementation of the activities of the NTP at the state and district levels. In 1995, the national TB directorate has been shifted to the Public Health Division of the Ministry of Health (MOH) and is now under the director of disease control. The National TB centre is now known as the Institute of Respiratory Medicine (Iyawoo, 2004).

The aims of TB treatment are to reduce morbidity, prevent mortality, prevent relapse, decrease transmission and prevent the emergence of MDR-TB (MOH, 2002). The essential first line drugs include isoniazid (H), rifampicin (R), pyrazinamide (Z), streptomycin(S) and ethambutol (E). A-six-months course of chemotherapy has proven highly effective and reliable. These drugs should be able to cure almost all newly diagnosed patients if the treatment regimen is prescribed for an adequate period of time and if the patient consumes the prescribed medication without fail. The treatment regimens are divided into intensive and maintenance phases. During the intensive phase, three or four drugs are given daily for two

months. This will lead to rapid sputum conversion and amelioration of clinical symptoms. However, during the continuation phase, two or three drugs are usually given intermittently for the subsequent four months. The duration of treatment is extended for severe forms of extra pulmonary TB and immunocompromised patients.

Malaysia adopts the Directly observed treatment, short-course (DOTS) strategy, which has been recommended by the WHO (MOH, 2002). DOT is one of the key elements of DOTS. As such, all anti-TB drugs are administered under supervision whereby patients are directly observed by a health personnel or trained person. Each dose of medication taken by the patient under supervision is recorded. However, supervision of treatment need not necessarily be confined to health care facilities. The other four elements of DOTS include:

1. The government's commitment to a National TB Control Programme
2. Case detection through sputum smear microscopy examination of TB suspects in general health services
3. A regular, uninterrupted supply of quality TB medication
4. A monitoring and reporting system to evaluate treatment outcome for each and every patient with proper documentation.

Although efforts were taken to increase DOTS coverage to 100%, 10-15% of TB cases were being managed by private medical practitioners where DOT may not be practiced (Iyawoo, 2004).

The number of new TB cases rose from 14,908 in 1999 (MOH, 2002) to 18,102 in 2010 (WHO, 2010a). Despite being a curable disease, 1,600 TB deaths were recorded in 2010 (The Star, 2011). Although TB is the second highest infectious disease in Malaysia after dengue, it is the

main cause of deaths from infectious diseases in 2010 (Tan, 2011). The current notification rate of 64 cases for every 100,000 people categorised Malaysia as an 'intermediate TB burden' country (Lee, Abd Rahman, Loh, & Yuen, 2010). Among the states in Malaysia, Sabah recorded the highest notification rate with 110 cases for every 100,000 people (Lee, et al., 2010). The rise in the notification rate could be linked to many factors such as the increase in population, the increase in immigrants, urbanisation, and other risk factors like smoking and the HIV epidemic as well as the increase in the number of health facilities that enabled a higher degree of detection and diagnosis (Lee, et al., 2010).

Under the Millennium Development Goals (MDG) set by the World Health Organisation (WHO), the number of TB cases should be reduced by half by 2015 in comparison with 1990. The goal for Malaysia would be 31 cases for every 100,000 people by the end of 2015 compared with 61 cases for every 100,000 people in 1990 (Lee, et al., 2010). However, the current notification rate is higher than what was found in 1990. This trend indicates that Malaysia might not achieve the desired target by 2015. Drastic measures need to be undertaken in order to reverse the incidence rate.

The increasing number of HIV patients is another factor for the surge in the number of TB cases. Out of 15,192 TB patients who were screened for HIV in 2009, 11% (n=1644) of TB patients were HIV positive (WHO, 2010a). Collaboration between National TB programme and HIV programme resulted in the formation of a National Committee for TB-HIV strategic plan (MOH, 2010). The government health care facilities provide TB and HIV screening and offer TB-HIV patients universal access to anti-retroviral treatment for free.

MDR-TB is a worldwide concern. Globally, the proportion of MDR-TB among new TB cases ranges from 0% to 28.3% (WHO, 2010b). In 2009, 7664 TB patients in Malaysia were tested for MDR-TB and 55 patients were confirmed to have MDR-TB which is equivalent to 0.7% (WHO, 2010a). The prevalence of MDR-TB indicates an increasing trend when compared with 0.1% in 1996 (Iyawoo, 2004). Data on treatment adherence to DOT revealed that in 2008, 3.7 % of

newly diagnosed TB patients defaulted on TB treatment and 4.7 % were lost to follow-up or referred out (MOH, 2010). Poor adherence to treatment may contribute to the increase of drug resistance.

It was found that men make up a larger percentage of TB patients compared to women with a 2:1 ratio (Lee, et al., 2010). It has been reported that many Malaysians are not aware that TB has made a comeback and this has resulted in late treatment seeking behaviour (The Star, 2011). This is a huge concern for public health because people who do not seek treatment early are risking others by spreading the disease. Many Malaysians who developed TB visited *bomohs* (traditional Malay healers) and *sinsehs* (Chinese medicine practitioners) and only sought medical treatment when their conditions became worse (The Star, 2011). As such, there is a clear need to increase the nation's awareness with regards to TB and its treatment.

## 2.2.2 DM in Malaysia

DM is a chronic metabolic disorder with hyperglycaemia and other metabolic abnormalities. It is due to insulin resistance and/or deficiency as well as increased hepatic glucose output. DM can be either type 1 or type 2. Type 1 DM is an autoimmune disease, whilst type 2 DM is associated with older age, obesity, family history of diabetes, previous history of gestational diabetes and physical inactivity. Type 2 DM is far more common than type 1 DM. There is currently no known cure for DM but it can be controlled. The aim of DM management is directed at reducing the complications of DM. Acute complications of DM include hypoglycaemia and hyperglycaemia. The common symptoms include polyuria, polydipsia, tiredness and weight loss and other precipitating factors such as infections. Macrovascular and microvascular complications are chronic complications. Cardiovascular, cerebrovascular, and peripheral vascular diseases are all macrovascular complications. Microvascular complications include nephropathy, neuropathy and retinopathy.

Rapid socio-economic growth, urbanisation, sedentary lifestyle, changes in nutritional habits with high intake of carbohydrates and saturated fats, and increased proportion of the population who are overweight and obese have all contributed to DM epidemic in Malaysia (Ismail et al., 2002; Letchuman, et al., 2010; Noor, 2002). The National Health and Morbidity Survey (III) showed that the overall national prevalence of DM among Malaysians aged 30 years and above had increased from 8.3% in 1996 to 14.9% in 2006 (Letchuman, et al., 2010). Forty-eight percent of patients above the age of 30 were not aware that they had DM (Letchuman, et al., 2010). Among those who were previously diagnosed with DM, only 84.3% were under treatment (Letchuman, et al., 2010). Another national study carried out by Rampal et al. in 2004 showed that among those receiving treatment for DM, only 25.1% had their fasting blood sugar under control (Rampal, 2010).

There were no significant difference in the prevalence of DM among males and females in Malaysia (Letchuman, et al., 2010; Rampal, 2010). Among the ethnic group, the Indians had

the highest prevalence of DM which is at 19.9% for those aged 30 years and above (Letchuman, et al., 2010). Prevalence of DM was also higher among urban population compared to the rural population (Letchuman, et al., 2010). The risk of having DM increases with increasing age, positive family history of DM, increasing BMI, and lower levels of education (Rampal, 2010). The majority of DM patients with suboptimal glycaemic control had inadequate self-management skills and lacked DM-related knowledge (Tan & Magarey, 2008).

Previous studies in Malaysia indicated a high prevalence of suboptimal glycaemic control and that DM complications were common (Chuang, Tsai, Huang, Tai, & The Diabcare-Asia 1998 Study Group, 2002; Ismail et al., 2001; Ismail et al., 2000; Mafauzy, 2005; Mimi, Teng, & Chia, 2003). It was found that 4.3% of DM patients had amputations (Letchuman, et al., 2010). Studies that evaluated the prevalence of stroke found that 55% of patients who had stroke were DM patients (Hamidon & Raymond, 2003; Wong & Asian Acute Stroke Advisory Panel, 1999). More than half of the patients (57%) who required dialysis in Malaysia had diabetic nephropathy (Lim & Lim, 2006). Late presentation to the hospital and delayed treatment were other reasons for complications and poorly controlled DM (Rampal, Loong, Azhar, & Sanjay, 2010). On the other hand, active screening for DM complications (e.g. screening for microalbuminuria and neurology testing) were not routinely practiced by many health care providers in Malaysia (Rampal, et al., 2010). Fifty-five percent of DM patients never had an eye examination (Letchuman, et al., 2010). This indicates a high level of complications among patients with DM in Malaysia.

When it comes to the treatment of DM, 77% of patients were on oral hypoglycaemic agents , 7% were on insulin alone or in combination with oral hypoglycaemic agents and the rest was not on any treatment (Letchuman, et al., 2010). The progressive nature of DM indicates that patients will eventually need insulin to reach the targeted blood glucose level. However, the lack of insulin usage is a major concern and one of the reasons reported was the fact that physicians were prolonging a failing treatment (Letchuman, et al., 2010).

In summary, DM care is far from satisfactory with the majority not achieving targeted blood glucose levels and presenting with complications. There is lack of awareness about DM in the community, lack of intensification of DM treatment through the use of insulin, lack of screening for complications and lack of emphasis on self-management of DM. More efforts need to be taken to address these issues.

## 2.3 The health care system in Malaysia

Health care in Malaysia is provided by the public and private sectors and non-governmental organisations (NGOs). Public health services are heavily subsidised by the government. The Ministry of Health (MOH) is the major provider of health services and is responsible for the health of the population, as stated in the Federal Constitution. Primary care services at health clinics are delivered almost free of charge, whereby each patient is charged a nominal fee of RM 1 (equivalent to £0.2) for each outpatient visit (Yu, Whynes, & Sach, 2008). From January 2012, all senior citizens aged 60 years and above are exempted from paying the nominal fee of RM1 and they are entitled to receive free outpatient treatment in all government hospitals, health clinics and dental clinics (MOH, 2011b). Secondary and tertiary care services provided at hospital facilities are also highly subsidised by the government.

The government provides primary, secondary and tertiary care through various types of health facilities. These facilities include hospitals, special medical institutions, national institutes of health, dental clinics, health clinics, mobile health and dental clinics and flying doctor stations (MOH, 2011a). There are 131 government hospitals (with a total of 33,211 beds) and six special medical institutions (with 4,582 beds) (MOH, 2011a). Patients can go to any general outpatient services and hospitals for medical emergency and admissions at the public health sector. However, access to specialist services is controlled through a national system of referral (Yu, et al., 2008). Specialist services are available at certain hospitals such as national referral hospitals in the capital, the state hospitals and selected district hospitals. Referral to specialist services will be made if patients cannot be managed at general outpatient facilities.

Other government agencies like the Ministry of Education, Ministry of Human Resource, Ministry of Defence, Ministry of Rural Development and the Ministry of Housing and Local Government also complement the role of the MOH (Merican & Yon, 2002; Thomas, Beh, & Nordin, 2011). There are eight hospitals (3,690 beds) under the non MOH government agencies (MOH, 2011a). The Ministry of Education is responsible for the running of university

or teaching hospitals and the training of technical health personnel for the country. The Ministry of Human Resources is responsible for the enforcement and regulations in relation to the safety and health of industrial workers as well as the estate plantation workers. The Ministry of Defence provides health services for its personnel and dependants as well as the surrounding local population living within its territory. The Ministry of Housing and Local Government is responsible for the licensing and enforcement of some specific health legislation in areas under its control. The Ministry of Rural Development was previously responsible for the aborigine's health, through its jungle services and a hospital for aborigines but recently these services are being provided by the MOH.

The private health sector is the second major provider of health services which have been on the rise, especially in urban areas. Private health providers complement the medical services provided by the government (MOH, 2011a). In 2010, there were 217 private hospitals (with a total of 13,186 beds), 22 maternity homes, 12 nursing homes, three hospices, 36 ambulatory care centres, 6,442 medical clinics and 1,512 dental clinics (MOH, 2011a).

The increasing demand for high quality health services has contributed to the growth of the private health sector. The quality of care at private facilities was perceived to be of high quality with reduced waiting time (MOH, 2000). The quick service at a private general practitioner's clinic also offers convenient medical services, in particular to the nearby population.

The private sector charges user fees on patients for utilising health services in order to operate and maintain their facility. Access to private health services is inevitably limited to the affluent population that can afford to pay high user fees as out-of pocket payments or co-payments (with coverage of private insurance) (MOH, 2000; Thomas, et al., 2011). Private health insurances provide premiums according to the risk of having illness (Merican & Yon, 2002). Patients who have pre-existing diseases may not be selected to the scheme or they may have to pay higher premiums (Merican & Yon, 2002).

Other providers of health care include the traditional complementary medicine practitioners and the NGOs. Traditional complementary medicine in Malaysia includes traditional Malay, traditional Chinese and Ayurvedic treatments and is well accepted by both rural and urban communities (Merican & Yon, 2002). Currently, guidelines and the passing of the Traditional and Complementary Medicine Bill for the various fields in traditional medicine are being studied carefully by various organisation in Malaysia (Thomas, et al., 2011). The NGOs (e.g. Malaysian AIDS council) contribute towards the provision of health care on a voluntary basis and are not profit oriented.

Lack of integration between the public and private health sectors is a problem (Merican & Yon, 2002). At present, patients can go to any health care facilities but their medical records are not shared. The private sectors are centred mainly in the urban areas, leading to inequitable distribution of health services and resources (Merican & Yon, 2002). In addition, only those who could afford to pay higher fees could go to private hospitals. The charges from private hospitals on services component range from 15% to 28% of the hospital bills and medication whereby 15% of this bill is not declared to patients (Thomas, et al., 2011). The charges for professional fees take up almost 50% of the total bill (Thomas, et al., 2011). The attractive salary in private health sector has triggered the out flow of senior doctors and specialists from the public sector to the private sector which led to varied distribution of workforce in public and private sectors in Malaysia (Merican & Yon, 2002; Thomas, et al., 2011). In 2000, 46% of all doctors in Malaysia were in the private sector and were responsible for 20% of hospital beds while the rest of the doctors were in the public sector looking after 80% of the beds (Thomas, et al., 2011). When compared with private sector, 71% of hospital admission occurs in public sector (MOH, 2011a). The main difference between the private and public hospitals with regards to TB care provision is that the treatment of TB is free of charge in public hospitals. As for DM, a nominal fee of RM1 is charged for DM treatment for patients under 60 years of age at any outpatient clinics in the public sector.

### 2.3.1 Pharmacy practice in Malaysia

Pharmacists in Malaysia practise under two different sets of legal-historical framework (Wong, 2001). Pharmacists working in government hospitals have complete control over the supply of medicines. However, pharmacists at the private sectors especially in community pharmacies are yet to have full dispensing rights as medical doctors in the private sectors still dispense medicines to their own patients. This doctor-dispensing practice has been allowed since the colonial era when Malaysia suffered from an acute shortage of all professionals (Wong, 2001). Nevertheless, these practices are more likely to change with the increasing number of pharmacists in Malaysia.

Almost 7000 pharmacists were registered with the Malaysian Pharmacy Board in 2009, giving a pharmacist to general population ratio of about 1:6000 (Hasan et al., 2010). In line with the WHO recommendation, the MOH expects to achieve a ratio of 1:2000 (pharmacists to general population) by 2020 (Hasan, et al., 2010). The increase in the number of graduates in pharmacy allowed the MOH and Pharmacy Board to implement a new registration process in 2005, whereby the registration is dependent on a period of mandatory government service (Hasan, et al., 2010). The registration process consists of one year as a provisionally registered pharmacist and three years of mandatory service as a fully registered pharmacist in public hospitals. However, this led to a surplus of pharmacists in public hospitals and the three years of mandatory service has been reduced to one year since October 2011.

Over the years, the pharmacy practice in Malaysia has shifted its focus from product-oriented services to patient-centred services. Pharmacists today work alongside other medical professionals in an increasingly cohesive environment and together they play an active role in patient care. Pharmacists provide pharmaceutical care services during ward rounds and through Medication Therapy Adherence Clinics (MTAC). The aim of MTAC is to optimise medication therapy in chronic diseases such as DM, retroviral disease, asthma and chronic kidney disease. MTAC services have also been expanded to cover warfarin management, pain

management, medication management in patients with neurological disorders, psychiatric problems and hypertension (MOH, 2009). Pharmacists educate patients on their medications, promote adherence to drug therapy and monitor safety and effectiveness of the treatment (Rahman, 2010). MTAC was started in 2004 and has grown ever since. In 2009, there were 187 MTACs in the country (MOH, 2009; Rahman, 2010). MTAC is practised in 150 hospitals and 37 health clinics and these clinics did follow-up sessions with 23,447 patients in 2009 (Rahman, 2010). 21.5% from the total 345,903 number of outpatients counselled in hospitals and health clinics were done through the MTAC services (MOH, 2009). Despite the growing number of these clinics, little is known about the perceptions of pharmacists and other health care professionals regarding the service. Feedback from the healthcare professionals as well as from patients may help to improve the provision of service.

Besides MTAC, specialised clinical pharmacy services such as clinical pharmacokinetics services, the nutritional support services, and cytotoxic drug reconstitution services have provided the opportunity to individualise treatment based on patient needs. These services are provided for inpatients.

The increasing number of pharmacists in Malaysia encouraged the development of new pharmacy services in the public health sector. Pharmacists are already being placed in health clinics (Rahman, 2010) and pharmacists are also beginning to do home visits to monitor adherence to treatment (Merican, 2010). Technology and telecommunications have been integrated through innovative and creative ideas by the pharmaceutical services at the MOH to further improve drug delivery system. Some of the new services include the Integrated Drug Dispensing System, Drive through Pharmacy, 'Short Message Services (SMS) and Take' as well as the appointment card system (Merican, 2010). These new services have enabled patients to collect repeat medications at their own convenience. The Integrated Drug Dispensing System allows patients to collect their medications at any government hospital or clinic of their choice and this system enable patients to save time and travel expenses. The drive through pharmacy system was introduced in two hospitals in Malaysia whereby patients can drive directly to the dedicated counter and collect their medicines without having to wait. Other innovative

approaches taken include the Home Delivery service which enables patients to receive their repeat medication through post at a minimal charge. In addition, these services will help to reduce the waiting time at public hospitals. However, these services are limited and yet to be fully established in all hospitals in Malaysia.

Many pharmacists also practice in the private sector which include the community pharmacies (chain pharmacies and independent pharmacies), pharmaceutical industry as well as in academic institutions. Community pharmacists in Malaysia are yet to have the full control over the supply of medicines as general practitioners are legally allowed to dispense medicines in their clinics. This doctor-dispensing practice has been allowed since the colonial era due to a shortage of health care professionals. Pharmacists have been seeking full dispensing rights and this issue has not been resolved till now. However, the growing number of pharmacists may lead to positive changes in the future. Besides dispensing medication, community pharmacists provide other services such as patient education and counselling, blood glucose monitoring, and finger prick testing of blood glucose and cholesterol.

## 2.4 Pharmaceutical care: a philosophy for pharmacy practice

Hepler and Strand (1990) formulated the most widely used definition of pharmaceutical care: 'Pharmaceutical care is the responsible provision of drug therapy for the purpose of achieving definite outcomes that improve a patient's quality of life'. The outcomes are cure of a disease; elimination or reduction of a patient's symptoms; arresting or slowing a disease process; or preventing a disease or symptoms (Hepler & Strand, 1990). Barber (2001) argued that the outcome measures refer to the patient's clinical condition whereby the goals are stated in terms of the disease. It was felt that this original definition of pharmaceutical care was not adequately conceived which led to the development of many other definitions (Barber, 2001).

In 1998, Strand, Cipolle and Morley approached the topic from a humanistic perspective and proposed the following definition: 'Pharmaceutical care is a practice in which the practitioner takes responsibility for a patient's drug-related needs and is held accountable for this commitment' (Cipolle, Strand, & Morley, 1998). In other words, pharmacists should practice in a patient-centred manner whereby pharmacists' decisions should be made based upon the wants and needs of the patients, who may have specific drug-related needs.

The European understanding of pharmaceutical care is basically the professional care for the individual patient in a pharmacy (van Mil, Schulz, & Tromp, 2004). It is the way pharmacists coach individual patients about their medication. The concept also includes the responsibilities of pharmacists, medication surveillance, counselling and the evaluation of all the outcomes of care.

Despite the various definitions, pharmaceutical care is generally regarded as a philosophy for pharmacy practice in many countries across the globe (van Mil, et al., 2004). Not only the definitions of pharmaceutical care differ, the terminologies used to describe pharmacy

services that embrace the concept of pharmaceutical care vary. For example, in the United States, the term medication therapy management services refers to a strategy to incorporate the philosophy of pharmaceutical care into everyday pharmacy practice for a defined patient population or patients with certain diagnoses (McGivney et al., 2007; Pellegrino, Martin, Tilton, & Touchette, 2009). In Malaysia, pharmacists provide pharmaceutical care services through MTACs for various disease in some public hospitals (Gnanasan, Wong, Mohd Ali, Ting, & Anderson, 2010; Lim & Lim, 2010; Loganadan, et al., 2010; Loganadan, et al., 2008). Besides MTAC, pharmaceutical care is also an embedded concept in many other clinical pharmacy services that are being provided in hospitals and community pharmacies in Malaysia.

### 2.4.1 Development of a pharmaceutical care service

The expansion of pharmaceutical care services in various disease management settings calls for more pharmaceutical care research to be conducted. Pharmaceutical care research falls under the umbrella of health services research. Research in this area is context specific as it depends on the local health care system.

It has been reported that it is vital to first conduct a need assessment study as the first phase in developing a pharmaceutical care service (van Mil, 2004). Needs assessment is a basic research which tries to identify the types of care required in a given patient in terms of pharmaceuticals which will eventually lead to the development of a proposal for a pharmaceutical care intervention. Impact assessment is the second phase of the research which tries to investigate whether the provision of pharmaceutical care improves the patients' clinical, humanistic and economic outcome (van Mil, 2004). However, most pharmaceutical care studies focus mainly on the second phase of the research in determining whether the pharmaceutical care intervention leads to the expected outcomes with a lack of consideration or explanation given to the mechanisms by which those outcomes are mediated. For example, the impact of a pharmaceutical care intervention in improving patients' health lies on the assumption that the intervention worked as planned; that the pharmacists were comfortable with their new roles; that patients welcomed the service and that the necessary collaboration with other health care professionals had taken place. In reality, there could be many barriers that hinder the provision of service. As such, there is a need to understand the components that are most likely to affect the provision of pharmaceutical care prior to finalising the design of the pharmaceutical care service or in evaluating the outcome of the service.

This shows that pharmaceutical care is actually a 'complex intervention' as there are various factors contributing to the success of the delivery and it is difficult to measure specific outcomes (MRC, 2000; Tulip & Campbell, 2001). A systematic review showed that it is difficult to replicate and evaluate pharmaceutical care research as there are various interconnecting

factors or components that need to be considered (Kennie, Schuster, & Einarson, 1998). For example, some components of pharmaceutical care may involve the need to improve therapeutic outcomes while other components may work through psycho-social or behavioural modifications in an individual patient through patient education and counselling (Wong, 2004). In addition, some components have an organisational nature whereby inter-professional communication between pharmacists, physicians and other health care professionals is important in the delivery of pharmaceutical care (Wong, 2004). All these factors reveal the multifaceted nature of a pharmaceutical care intervention.

The UK Medical Research Council (MRC) has defined 'complex interventions in health care' as "interventions comprising separate elements which seem essential to the proper functioning of the intervention although the active ingredient is difficult to specify" (MRC, 2000). In fact, not only the number of elements in the intervention package are complex, there are other dimensions of complexity which include the range of possible outcomes, the behavioural differences of those delivering and receiving the intervention and the variability in the target population (Craig et al., 2008). For example, the *active ingredients* of pharmaceutical care could consists of many elements such as the pharmacist's personality and expertise, whose skills, patient characteristics and behaviours, inter-professional relationships and organisational culture (Tulip & Campbell, 2001). These factors highlight the complex nature of a pharmaceutical care service and research in pharmaceutical care should consider these elements (Tulip & Campbell, 2001).

The MRC has designed a framework for the development and evaluation of RCTs for complex intervention to improve health care services which is applicable to pharmacy practice (MRC, 2000; Watson, 2006). The framework provides a flexible guide for devising complex interventions (see Figure 2-1). In 2006, the MRC reported that the process of development and evaluation of complex intervention may not follow a linear sequence as suggested in 2000 (Craig, et al., 2008) which resulted in alteration of the model to a cyclical design. However, the content was more or less the same and it is still applicable.

Other models such as the Reach, Effectiveness, Adoption, Implementation and Maintenance (RE-AIM) framework has also been suggested to be applied for designing, implementing and evaluating practice-based interventions and complex interventions (Planas, 2008). The **RE-AIM** framework suggests that all interventions need to be designed and evaluated in terms of their **R**each to the intended target population, **E**ffectiveness or efficacy, **A**doption by target settings or institutions, Implementation with consistent delivery and **M**aintenance of intervention effects in individuals and settings over time. The Multiphase Optimisation Strategy (MOST) framework (Collins, Murphy, Nair, & Strecher, 2005), National Institute for Health and Clinical Excellence (NICE) public health guidance on behavioural change (National Institute for Health and Clinical Excellence (NICE), 2007) and research steps for public health interventions (de Zoysa, Habicht, Pelto, & Martines, 1998) are examples of other frameworks that are tailored for behavioural and public health interventions.

Although both MRC and the RE-AIM framework appear to be more relevant for developing complex interventions, the MRC framework has been widely used in health care services research (Bradley, Wiles, Kinmonth, Mant, & Gantley, 1999; Byrne et al., 2006; Murchie, Hannaford, Wyke, Nicolson, & Campbell, 2007) and has been suggested to be applied in pharmaceutical care interventions (Tulip & Campbell, 2001; Watson, 2006; Wong, 2004). Therefore, for this study the MRC framework was thought to be the most feasible with regards to its generic approach than other specific evaluation guidelines. In this study, stepwise implementation of the development of a pharmaceutical care service for TB and DM patients is guided by the MRC framework (see Figure 2-1) because of its applicability towards pharmacy practice research (Montgomery, Kälvemark-Sporrong, Henning, Tully, & Åsa Kettis-Lindblad, 2007; Wong, 2004).

As RCTs can be expensive and time-consuming, preliminary development work is important to identify the components of RCT intervention, the mechanism that will influence the intervention and the feasibility of the protocol before embarking on a RCT (Horne. R., Weinman, Barber, Elliott, & Morgan, 2005; MRC, 2000). This PhD project, which is explorative in nature, therefore serves as a preliminary development work by applying the first three

phases of the MRC framework prior to designing and evaluating a full-fledged pharmaceutical care service for TB and DM patients that could be evaluated through a RCT in the future.

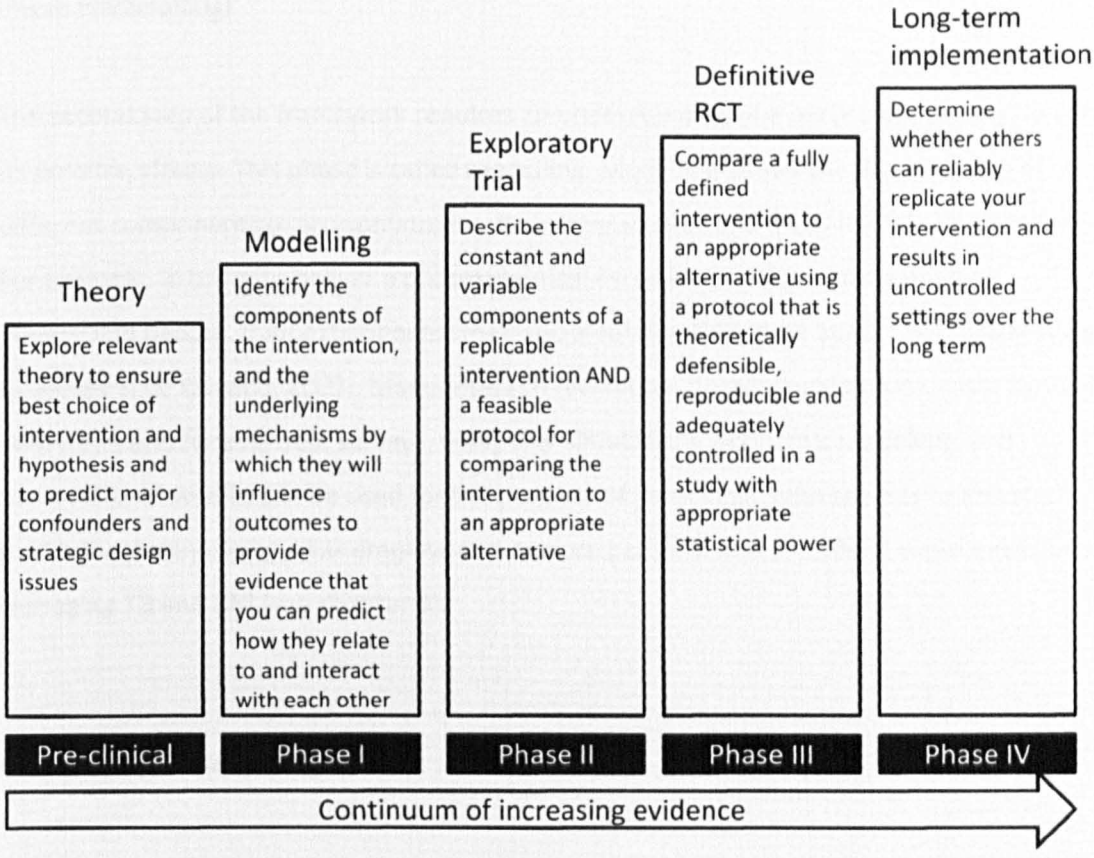


Figure 2-1 The MRC framework for the development and evaluation of RCTs for complex interventions to improve health (MRC, 2000)

There are five stages in MRC Framework (see Figure 2-1).

**Pre-clinical (Theory)**

The first step of the MRC framework emphasises the importance of identifying existing evidence by carrying out a literature review and establishing a theoretical basis for an

intervention (Craig, et al., 2008; MRC, 2000). 'Pharmaceutical care', as explained in section 2.4 was chosen as the theoretical basis for this study and a literature review on TB and DM was conducted (see section 2.5) in order to gather relevant background information.

**Phase I (Modelling)**

The second step of the framework requires an understanding of a particular intervention and its possible effects. This phase is called modelling. Modelling allows the identification of different components of an intervention, their interactions, and their effect in the outcome. For example, in order to deliver a pharmaceutical care service, pharmacists need to understand people, their experiences, their social relationship, their culture and belief systems (Dupotey & de Oliveria, 2009). Many research techniques such as qualitative testing through interviews and focus group, surveys, computer simulations, economic modelling, and observational studies can be used for the purpose of modelling. With regards to this study, qualitative methodology was employed to explore patients' and providers' experiences in managing TB and DM (see chapter 3).

**Phase II (Exploratory trial)**

Exploratory trials are used to evaluate whether the evidence gathered in the previous phases is effective in achieving the desired outcome. This includes the implementation of testing procedures to assess the feasibility of the intervention, the estimation of the likely recruitment and retention rates of the research subjects and the calculation of an appropriate sample size (Craig, et al., 2008). In this study, the feasibility of providing a pharmaceutical care service for TB and DM patients was investigated. Furthermore, the prevalence of DM in TB patients was determined to estimate the likely recruitment of patients (see chapter 5).

**Phase III (Definitive RCT)**

This phase relates to the conduct of a definitive RCT of the intervention. Phase III trials should have adequate statistical power, adequate randomisation and blinding (where feasible), appropriate outcome measures and informed consent of participants. All aspect of phase III trial should be tested in the exploratory trial (phase II) prior to their inclusion in the RCT. This phase is beyond the scope of this PhD project. However, future work will concentrate on evaluating the effectiveness of the pharmaceutical care service through a RCT.

**Phase IV (Long-term implementation)**

The final stage of a complex intervention is the implementation stage by getting the evidence into routine practice or policy. Surveillance, monitoring an long-term follow-ups are needed to determine whether short term changes that were seen in a RCT persist and whether benefits that was previously recommended were sustained (Craig, et al., 2008; MRC, 2000).

The following section represents the preclinical phase of the MRC framework as it presents the review of literature on TB and DM; the role of pharmacists in the management of TB and DM; and patients' and providers' perspectives on the management of TB, DM and comorbid conditions with regards to medication-related issues.

## 2.5 The convergence of TB and DM epidemic

### 2.5.1 Association of TB and DM

A link between TB and DM has long been recognised. Richard Morton's *Phtisiologia: or a treatise on consumption* which was published in 1694, stated that an association between TB and DM was suggested even in Roman times (Dixon, 2007). An Indian physician Susruta was aware about the association in 600CE and Avicenna reported that phthisis frequently complicated DM (Guptan & Shah, 2000). Early studies have shown that patients with DM had threefold to fourfold increased risk of developing TB (Boucot, Dillon, Cooper, Meier, & Richardson, 1952; Root, 1934). In 1934, Root revealed that "in the latter half of the 19$^{th}$ century the diabetic patient appeared doomed to die of pulmonary TB if he succeeded in escaping coma" (Root, 1934). Bouchardat commented "at autopsy every case of diabetes had tubercles in the lungs" (Younger & Hadley, 1971).

Before the advent of insulin, TB was the most common cause of death in DM patients (Himsworth, 1938; Skavlem, Castle, & Moore, 1942). Case series in 1930s showed that insulin was used as an aid in the treatment of TB (Day, 1940; Ellman, 1932; Heaton, 1932 ; Himsworth, 1938). Insulin was used to help TB patients gain weight and build up their natural resistance to fight illness (Heaton, 1932 ). Similarly, insulin was a must in TB patients with DM (Banyai, 1959; Himsworth, 1938; Skavlem, et al., 1942). An expert clinic was established half a century ago for "tuberculous diabetics" in Birmingham, UK and successfully reduced the mortality rate (Luntz, 1954).

However, the availability of treatment for both diseases in the second half of the 20$^{th}$ century led to separate management of diseases and the association between TB and DM was not much of a concern. Nevertheless in the last decades, the soaring DM epidemic globally has

called for a renewed interest in understanding the link between TB and DM (Ruslami, Aarnoutse, et al., 2010). The importance of addressing the risk factors of TB including DM in order to reduce the growing burden of TB has been highlighted (Lönnroth, Jaramillo, Williams, Dye, & Raviglione, 2009). The high prevalence of DM in developing countries is a major concern because these are the countries that harbour TB the most (Harries, et al., 2010).

Many studies have shown that 5-30% of TB patients present with DM (Alisjahbana, van Crevel, & Sahiratmadja, 2006; Feleke, Abdulkadir, & Aderaye, 1999; Pablos-Mendez, Blustein, & Knirsch, 1997; Ponce-De-Leon, Garcia-Garcia, Garcia-Sancho, Gomez-Perez, & Valdespino-Gomez, 2004; Singla et al., 2006; Wang, Lee, & Hsueh, 2005). A meta-analysis that was conducted in 2008 revealed that DM patients were 3 times more likely to contract TB compared to people without DM (Jeon & Murray, 2008). Studies from Ethiopia (Feleke, et al., 1999) and Tanzania (Swai, McLarty, & Mugusi, 1990) showed that patients with type 1 DM had a threefold to fivefold higher risk of contracting TB than patients with type 2 DM.

### 2.5.1.1 **The global burden of TB and DM**

Socio-economic and lifestyle changes in the developing countries have led to an upsurge of type 2 DM. The total number of people with DM worldwide is projected to rise from 285 million in 2010 to 439 million in 2030 (IDF, 2009). It has been estimated that 70% of patients with DM in 2030 will live in TB-endemic countries (Harries, et al., 2010). Although it has been predicted that the incidence of TB in most parts of the world will stabilise or drop in the coming decades, the rising prevalence of DM will contribute to the TB epidemic. India, China, and Indonesia will be the most affected due to the rising prevalence rates for DM (Ruslami, Aarnoutse, et al., 2010). It was estimated that new TB cases attributable to DM will increase from 11.4% to 14.1% in 2030 in the top ten countries with the highest burden of DM (Ruslami, Aarnoutse, et al., 2010).

DM appears to be a more important risk factor at the population level as compared to HIV, although HIV is the strongest risk factor for TB at an individual level. It was estimated that DM contributed to 14.8 % of pulmonary TB cases in India, while HIV contributed to 3.4% of pulmonary TB cases (Stevenson, et al., 2007). A study in California showed that the estimated risk of TB attributable to DM in Hispanic people was 25% and it was equivalent to that of HIV (Pablos-Mendez, et al., 1997).

A Tanzanian study showed that among 34 TB and DM patients, 73% of DM was newly diagnosed (Mugusi, Swai, Alberti, & McLarty, 1990). Similarly, an Indonesian study showed that among 94 TB and DM patients, 61% of DM was newly diagnosed (Alisjahbana et al., 2007). This indicates the importance of screening for DM in TB patients.

The chance of detecting TB in DM patients will depend on the incidence of TB in a particular country (Ruslami, Aarnoutse, et al., 2010). It is equally important to diagnose DM at early stage, as DM is a time-dependent risk factor for TB (Ruslami, Aarnoutse, et al., 2010). It has

been documented that long duration of DM and poor glucose control may increase the risk of TB (Banyai, 1959; Swai, et al., 1990).

### 2.5.1.2 **Effect of DM on therapeutic outcomes of TB**

It has been reported that TB patients with DM were usually 10-20 years older than those without DM and have a higher body weight before the initiation of treatment, and even more after treatment (Ruslami, Aarnoutse, et al., 2010). A study from West Africa showed that 23% of TB patients with DM were obese as compared to 3% of patients without DM (Baldé et al., 2006). In Indonesia, 53% of TB patients with DM weighed more than 50kg before the initiation of TB treatment as compared to 16.5% in patients without DM (Alisjahbana, et al., 2007). Patients with TB and DM might have lower plasma concentrations of anti-TB drugs, contributing to higher rates of treatment failure (Ridzon et al., 1998; Sahai et al., 1997; Weiner et al., 2005). A pharmacokinetic study that was conducted in Indonesia showed that exposure to rifampicin ($AUC_{0\text{-}6h}$) was 50% lower in heavier TB patients with DM compared to patients without DM during the continuation phase of treatment (Nijland et al., 2006). This finding is a concern because low concentrations of anti-TB drugs can cause treatment failure or resistance. Therefore, TB and DM patients with higher body weight may need dosage modifications of anti-TB drugs.

DM patients with MDR-TB are at risk for poor outcomes (Bashar, et al., 2001). Besides, the presence of DM may potentiate the adverse effects of anti- TB drugs, especially renal dysfunction and peripheral neuropathy (The Francis J. Curry National Tuberculosis Center, 2009). Pyridoxine should be given with isoniazid during TB treatment in DM patients to prevent peripheral neuropathy (American Thoracic Society, Centers for Diseases Control and Prevention, & Infectious Diseases Society of America, 2003). Serum creatinine and potassium levels in patients with MDR-TB should be monitored more frequently, often weekly for the first month and then at least monthly thereafter (WHO, 2006a). It has been recommended that DM must be managed closely throughout the treatment of drug-resistant TB and TB care providers should be in close communication with the physician who manages the patients' DM (WHO, 2006a).

In terms of therapy, patients with TB and DM were approximately eight times more likely to be culture positive after six months of standard therapy compared with TB only patients (Alisjahbana, et al., 2007). A Malaysian study reported that patients with DM were more often treated longer than 6 months, but the bacteriological outcome was not reported (Nissapatorn, et al., 2005). The median time for culture conversion after two months of TB treatment was longer in DM than TB only patients (Dooley, et al., 2009; Restrepo et al., 2008; Singla, et al., 2006).

DM can also cause changes in oral absorption, decreased protein binding of drugs, renal insufficiency or fatty liver with impaired drug clearance (Gwilt, Nahhas, & Tracewell, 1991). Although, the effect of DM on TB drug concentrations are yet to be thoroughly investigated, it has been recommended that therapeutic drug monitoring should be considered if poor response to treatment is observed in patients with TB and DM (Peloquin, 2002; Yew, 2001).

Studies have also indicated that DM increases the risk of death in patients with TB (Dooley, et al., 2009; Wang et al., 2009).

In summary, DM affects therapeutic outcome of TB, delays sputum conversion, increases the risk for MDR-TB and mortality.

### 2.5.2 The pharmacological issues in the management of TB and DM

Like all infections, TB infections could worsen DM control. Although TB can cause glucose intolerance and might predispose patients to DM, the drugs used to treat TB might also worsen glycaemic control in patients with DM.

The standard treatment regimen for drug-susceptible TB has not changed in decades. Isoniazid, rifampicin, and pyrazinamide, are still the key anti-TB drugs. The most important drugs for DM are classified as insulin secretogogue (sulphonylureas and metiglinides), biguanide (metformin), thiazolidinediones (TZD) and insulin. Sulphonylureas and TZDs are metabolised by cytochrome P450 enzymes in the liver.

Rifampicin is a very potent inducer of cytochrome P450 enzymes (Burman, Gallicano, & Peloquin, 2001; Niemi, Backman, Fromm, Neuvonen, & Kivisto, 2003; Venkatesan, 1992). Induction of these enzymes can accelerate the metabolism of a number of drugs given together with rifampicin and reduce the therapeutic effect. Treatment with rifampicin can cause direct or indirect hyperglycaemia with oral hypoglycaemic drugs (Atkin, Masson, Bodmer, Walker, & White, 1992; Niemi, Backman, Fromm, Neuvonen, & Kivisto, 2001). Plasma levels of several drugs for DM (tolbutamide, glibenclamide, gliclazide, glimepride, glipizide, repaglinide, nateglinide, rosiglitazone, pioglitazone) were significantly lower when co-administered with rifampicin (Ruslami, Aarnoutse, et al., 2010). However, oral hypoglycaemic agents are not contraindicated during the treatment of both TB and drug-resistant TB but patients may require higher doses. Insulin requirements might increase when rifampicin is administered in patients with type 1 DM (Hatorp, Hansen, & Thomsen, 2003). Rifampicin also caused early-phase hyperglycaemia with associated hyperinsulinemia even in non-DM patients (Takasu et al., 1982 ; Waterhouse, Wilson, White, & Chowdhury, 2005). Due to rifampicin's direct and indirect effects on glycaemic control, careful monitoring with appropriate dose adjustment of DM medications is crucial in patients with TB and DM. It has been

recommended that blood glucose levels should be monitored after the initiation and discontinuation of rifampicin in patients using oral hypoglycaemic agents (Ruslami, Aarnoutse, et al., 2010). It takes about one week to reach full induction of drug-metabolising enzymes upon the initiation of rifampicin treatment and it takes about two weeks for the induction to dissipate upon the discontinuation of rifampicin (Niemi, et al., 2003).

Isoniazid is an inhibitor of some of the enzymes that are induced by rifampicin. However the inductive effect of rifampicin overshadows the inhibitory effect of isoniazid on the same enzyme, so the overall effect of isoniazid plus rifampicin may decrease the concentrations of other drugs (Venkatesan, 1992). The effect of rifampicin and isoniazid on metabolism of insulin is unknown. However, insulin might not be affected as it is mostly degraded in the liver by hydrolysis of disulphide connections between the A and B chains through the action of insulin degrading enzymes (Duckworth, Bennett, & Hamel, 1998).

Metformin is not metabolised by rifampicin and might be a good alternative to sulphonylureas. Metformin is a first choice drug for type 2 DM (Nathan et al., 2006) as it has several mechanisms to control hyperglycaemia and does not lead to hypoglycaemia (Campbell, White, & Saulie, 1996). It is relatively cheap, widely available and associated with less weight increase than other oral anti-diabetic drugs. However, the disadvantage of metformin when it is given together with anti-TB drugs is that up to 30% of patients may experience gastrointestinal side effects (Campbell, et al., 1996), which may lead to non-adherence and poor treatment outcome.

It has also been argued that better glycaemic control in TB and DM patients can only be achieved with intensive insulin treatment regimens and patients on oral hypoglycaemic agents should be converted to insulin (Rao, 1999). Marked weight loss, adversity of aging, longer duration of diabetes, higher insulin and calorie needs in TB patients are all important indications for withholding oral hypoglycaemic agents in TB patients. Insulin has anabolic action, lowers pill burden, improves appetite and promotes weight gain. Biguanides are

contraindicated in hepatic disease, and therefore may not be suitable for tuberculosis patients since hepatotoxicity is a common adverse reaction of anti TB drugs. High doses of biguanides promote weight loss and might not be suitable in TB patients.

A study from India, showed that almost 90% of patients achieved fair to good glycaemic control with the use of insulin in TB and DM patients (Kotokey, Bhattaharya, Das, Azad, & De, 2007). Conversely, another study from India reported that TB and DM patients were treated with oral hypoglycaemic agents and dosage adjustment was made based on fasting blood sugar levels, while insulin injections were only given upon completing TB treatment (Balasubramaniam et al., 2007). The authors stated that although insulin injections should be recommended for TB and DM patients, as a policy, these patients were treated only with oral hypoglycaemic agents. However, it was unclear why insulin injections were allowed to be initiated after completing TB treatment and not during the course of TB treatment. The study showed that it was not easy to control DM although TB and DM patients responded to TB treatment through DOT.

In December 2009, a national web-based seminar on TB and DM was conducted in the United States (The Francis J. Curry National Tuberculosis Center, 2009). Richard Brostrom, a Public Health Medical Director and TB controller in the Commonwealth of the Northern Mariane Islands (CNMI) provided his recommendations with regards to DM management in TB patients in the seminar. The following is the excerpt from the seminar's transcript:

> *I think we would rely on common sense, which is that optimising glucose control would seem very likely to promote more rapid resolution of the TB infection. And so I would tend to approach this patient like we've approached patients with let's say gestational diabetes, where you really want to try to achieve euglycaemia for the benefit of the fetus, here we're trying to achieve euglycaemia for the benefit of killing the microbe. And so I would suggest that adding metformin, while an absolute wonderful and first line drug for the*

*treatment of early diabetes, would not give you the bang for the buck that you need. If he's running blood sugars in the 300 to 400s his HbA1c is going to be 11, let's say, and that's really going to accelerate the progression of his TB disease. So I think almost certainly one would recommend initiating insulin for this gentleman. Now there is a school of thought that says, 'Oh, difficult patients will never start insulin.' And there certainly is a subset of patients that I have for whom I just can't get through to them. However, the overwhelming majority of our patients, once they understood, once they experience it, once it's been done with the help of a skilled diabetes educator, can succeed with insulin therapy. And there are multiple modalities of insulin. There is once a day, long-acting. There are insulins that can be used around mealtime. One could work with gentleman over time to achieve more optimal glucose control (The Francis J. Curry National Tuberculosis Center, 2009)*

Richard Brostrom highlighted the importance of insulin to achieve tight glycaemic control in TB patients with DM. So far, the Brazilian Thoracic Association has considered replacing oral hypoglycaemic agents with insulin during TB treatment to keep fasting blood glucose below 160mg/dl (8.89 mmol/l) (Conde et al., 2009).

Recent population pharmacokinetic studies have shown the importance of individualised dosing of isoniazid, pyrazinamide, and rifampicin (Ronald, Richard, & Gumbo, 2009). Isoniazid serum clearance differs depending on the patient's number of *N*-acetyltransferase 2 gene *4 (*NAT2*4*) alleles (Ronald, et al., 2009). The relationship between gene dose and serum clearance (AUC: MIC ratio) provide an example of how dosing can be adjusted for different patient genotypes (Ronald, et al., 2009). Pyrazinamide serum clearance has been shown to increase in patients with higher body weight (Ronald, et al., 2009). In order to maximise efficacy and minimise toxicity of pyrazinamide, it is important to individualise dosing based on each patient's weight (Ronald, et al., 2009). Rifampicin's volume of distribution, clearance, and absorption has wide between-patient and within-patient variability (Ronald, et al., 2009). Rifampicin's action is concentration-dependent and the recommended dose of rifampicin is

10mg/kg body weight (Blumberg et al., 2003), which might be at the lower end of the dose-response curve. Higher daily doses are probably more effective and reduce treatment duration (Mitchison, 2000). In practice, most guidelines advise 450mg/day for patients below 50kg and 600mg/day for patients above 50kg. Since patients with DM are usually heavier and gain more weight during TB treatment, it has been recommended that dose adjustment must be made, especially in the later phase of treatment (Ruslami et al., 2010).

Microbial pharmacokinetic-pharmacodynamic (PK-PD) indexes and targets to optimize microbial killing and minimize resistance have been identified for rifampin, isoniazid, pyrazinamide, and the fluoroquinolones. These PK-PD indexes suggest that different doses and dosing schedules than those currently recommended could optimize therapy and perhaps shorten the duration of TB treatment (Ronald, et al., 2009). Since DM has been associated with significantly worse patient outcomes, treatment for TB and DM patients need to be improved due to the PK-PD variability by providing individualised treatment (Hall II, Leff, & Gumbo, 2009). It has been recommended that pharmacists should utilise their skills in pharmacogenomics and pharmacokinetics to individualise TB treatment (Ronald, et al., 2009).

In short, conversion to insulin and individualised TB treatment are a recognised pharmacological need for TB and DM patients.

### 2.5.2.1 The recent expert recommendations and research priorities

In order to develop a policy document on TB and DM, the International Union Against Tuberculosis and Lung Disease (IUATLD), World Diabetes Foundation (WDF) and the WHO Stop TB Department started off a series of consultation in January 2009 (Ottmani, et al., 2010). Based on these consultations, the experts recommended that additional literature review were needed to address many unanswered questions in the area of TB and DM (Harries, Billo, & Kapur, 2009; Harries, et al., 2010; Ottmani, et al., 2010). Previous studies that were published between 1965 and 2009 were reported to have limitations as many studies were health facility-based case-control studies using medical chart diagnoses of DM which could be subjected to confounding and most studies were conducted in developed countries (Harries, et al., 2010).

As such additional systematic review and meta-analysis was conducted from May to August 2009 by experts from the Harvard School of Public Health to address key questions such as screening for TB and DM, TB chemoprophylaxis and the impact of DM on the management of TB (Harries, et al., 2010; Ottmani, et al., 2010). Subsequently, an expert meeting was held in November 2009 at IUATLD, Paris, France to discuss the findings; to determine whether there was sufficient evidence to make policy recommendations about joint management of TB and DM; and to address research gaps and develop a research agenda for TB and DM. The meeting ended with the following four main recommendations and four main priority areas for research (Ottmani, et al., 2010):

1. **Collaboration between TB and DM care and control initiatives**

   The health ministries, technical agencies, funding agencies and donors should recognise the link between TB and DM and encourage closer collaboration between the National TB programmes and stakeholders involved in national DM prevention and care.

2. **Screening for active TB among DM patients**

   In high TB burden countries, DM patients should be routinely asked about TB symptoms and recent exposure to TB as part of regular clinical check-ups. For example, DM patients with persistent cough for more than two weeks should be screened for TB.

3. **Screening for DM among TB patients**

   People with newly diagnosed TB should be screened for DM especially in countries with medium to high prevalence of DM.

4. **Management of TB and DM comorbidity**

   Treatment and monitoring of TB and DM patients should be optimised as recommended in national guidelines and/or international best practice. Cross-referrals of TB and DM cases should be ensured and integrated approaches for diagnosis, management and prevention should be explored. TB health workers should deliver DM health education, behaviour modification messages and interventions as part of the routine health education.

Harries et al. (2010) identified four key priority areas for research which include: 1) the need to screen DM patients for active TB and vice versa, 2) the impact of DM and non-DM hyperglycaemia on TB treatment outcome and mortalities, 3) the implementation and evaluation of the TB DOTS strategy model for managing and monitoring DM, and 4) the development of better point-of-care diagnostic and monitoring tests, including the measurements of glycosylated haemoglobin (HbA1C) for DM patients.

In December 2009, Richard Brostrom shared his experience in managing TB and DM patients in CNMI in a web-based seminar (The Francis J. Curry National Tuberculosis Center, 2009). He provided four steps to integrate TB and DM care which he named as the 'Saipan standards' (The Francis J. Curry National Tuberculosis Center, 2009). The four steps include: 1. Diagnose DM in TB patients; 2. Adjust TB treatment in DM patients; 3. Help manage DM during TB treatment and; 4. Prevent TB in DM patients. These standards aim to assist TB care providers to prevent, identify, evaluate and manage patients with TB and DM (Brostrom, 2010).

Huge projects are being conducted in China and India to create the awareness of the link between TB and DM (World Diabetes Foundation, 2010, 2011). The projects aim to: 1) train TB health care workers in diagnosing and managing DM through capacity building workshops and, 2) screen TB patients for DM. These projects started in 2009 and will be completed in 2012. Protocols and guidelines on treatment for patients with TB and DM will be developed based on the findings of these projects (World Diabetes Foundation, 2010, 2011).

Recently, IUATLD and WHO have developed a collaborative framework which aims to guide national programmes, clinicians and others engaged in care of patients and prevention and control of TB and DM on how to establish a coordinated response to both diseases, at organisational and clinical levels (WHO, 2011).

## 2.5.3 Role of pharmacists

### 2.5.3.1 Pharmacists' role in TB management

In 1993, WHO declared TB as a 'global emergency' (WHO, 1994a) and promoted the DOTS strategy to manage TB (WHO, 1994b). Kanyok (1997) urged pharmacists to promote adherence by getting involved in DOTS programme. Prior to the introduction of DOTS, three studies reported pharmacists' role in the management of TB (Coleman, 1983; Dayton, 1978; Taylor, 1992).

Coleman (1983) described the role of clinical pharmacist as a primary care provider in a TB clinic. The role of the clinical pharmacist include obtaining the medical and drug history; explaining the pathophysiology and epidemiology of tuberculosis to the patients; monitoring side effects and managing problems during follow-up visits with physical assessment techniques and laboratory tests (Coleman, 1983). Dayton (1978) explained the role of a pharmacist in improving adherence to anti-TB treatment in a rural TB out-patient clinic. The pharmacist was responsible for maintenance of patient records, patient consultation, onsite drug preparation and dispensing, and teaching responsibilities (Dayton, 1978). There was increased pharmacist-physician interaction as the pharmacist had the opportunity to contribute drug-related information (Dayton, 1978).

However, except for Kanyok (1997), there was a lack of studies on the contribution of pharmacists in TB management after the introduction of DOTS. Nurses began to play a major role as DOT providers and pharmacists' expertise were somehow underused. Even the recent study by Clark et al. (2007) was conducted in TB patients who were not on DOT. Less is known about pharmacists' role in a DOTS setting especially in the clinics or hospitals.

Mismanagement of MDR-TB by using too few drugs or less effective second-line drugs and failure in educating patients on the importance of adherence have been cited to be the reasons for the emergence of extensively-drug resistance TB (XDR-TB) (Mitrzyk, 2008). The WHO and the United States Centers for Disease Control and Prevention (CDC) have identified XDR-TB as a serious public health threat and are calling for increased efforts in managing TB (Gandhi et al., 2010; Mitrzyk, 2008). It has been suggested that pharmacists should play a key role in the prevention and treatment of TB by promoting adherence, assessing patients for risk factors for resistant disease, providing information about disease control and prevention, and monitoring for effectiveness, adverse effects, and drug interactions (Mitrzyk, 2008; Mkele, 2010). Clark et al. (2007) demonstrated that patients' adherence to TB treatment improved when a pharmacist provided patient education on medication used and addresses patients' pharmaceutical care issues. The study also identified the pharmaceutical care needs and issues of first-time TB and MDR-TB patients.

After decades of managing TB via DOTS, the WHO launched the 'Stop TB strategy' in 2006 in response to a number of challenges (e.g. MDR-TB, TB-HIV epidemic, weak health systems, and lack of engagement of private providers) that have not been fully resolved through DOTS (Stop TB Partnership, 2006; WHO, 2006b). This strategy called for the engagement of all stakeholders including pharmacists within public and private sectors (Stop TB Partnership, 2006; WHO, 2006b). Private pharmacies are often the first point of contact when people with early unspecific symptoms of TB like cough and fever seek help from the health services. As such, community pharmacists can play an important role in the early detection and refer patients for TB screening.

The Indian Pharmaceutical Association has integrated private pharmacies with DOTS programme. Community pharmacists who participated in the TB Fact Card project in Mumbai, India played important roles such as providing TB information, referring patients for diagnosis, providing DOTS medicines boxes, administering anti-TB treatment, and in following up on patiens who defaulted treatment by phone calls ("*DOTS TB Pharmacist Project–Public-private Initiative in Mumbai*; FIP, 2011a; Gharat, Bell, Ambe, & Bell, 2007).

Recently, the WHO and FIP have signed a joint statement which was launched at the World Pharmacy Congress in Hyderabad in September 2011 on the role of pharmacists in the management of TB (FIP, 2011b). This WHO/FIP Joint Statement emphasised the need for engaging pharmacists in TB care and control. It calls on TB programmes and pharmacy associations to engage pharmacists and utilise their expertise to: 1) increase awareness of TB, and refer people with TB symptoms to facilities with quality diagnosis and treatment; 2) provide patient-centered treatment supervision to promote adherence and help prevent multidrug-resistant TB; 3) promote the rational use of anti-TB medicines through procuring and dispensing quality-assured medicines and fixed-dose combinations recommended by WHO; and by prohibiting the sale of anti-TB medicines over the counter, or without prescription; and 4) support health-care providers to rationalise and strengthen their TB management practices (FIP, 2011b).

### 2.5.3.2 **Pharmacists' role in DM management**

There is a growing body of literature supporting the roles of pharmacist in DM care. Studies conducted in various settings around the globe have shown that pharmacists' interventions improved HbA1C values and other clinical outcomes in DM patients (Al Mazroui et al., 2009; Anaya et al., 2008; Armor, Britton, Dennis, & Letassy, 2010; Choe et al., 2005; Clifford, Davis, Batty, & Davis, 2005; Davis, Clifford, Davis, & Batty, 2005; Fornos, Floro Andre´s, Carlos Andre´s, Mercedes Guerra, & Egea, 2006; Kiel & McCord, 2005; Lim & Lim, 2010; Loganadan, et al., 2010; Loganadan, et al., 2008; Machado, 2007; Nowak, Singh, Clarke, Campbell, & Jaber, 2002; Scott, Boyd, Stephan, Augustine, & Reardon, 2006; Turnacilar, Sancar, Apikoglu-Rabus, Hursitoglu, & Izzettin, 2009; Wubben & Vivian, 2008). Some studies have also reported improvements in both clinical and economic outcome (Cranor, Bunting, & Christensen, 2003; Cranor & Christensen, 2003).

A systematic review on the effects of pharmacists' interventions showed that pharmacists managed to build strong relationship with DM patients and were regarded to be a reliable source of information (Wubben & Vivian, 2008). The review showed that pharmacists ensured continuity of care by having on-going relationships with other health care professionals and served as a 'bridge' between these health care professionals and the patients. In addition, pharmacists provided recommendations to patients and their health care professionals to optimise therapeutic outcomes. Another review of pharmacist contribution to DM care in the United States indicated that pharmacists working as educators, consultants or clinicians in partnership with other health care professionals or working in a collaborative-practice model were able to contribute to improved patient outcomes (Armor, et al., 2010). Pharmacists played important roles by following-up patients between physician visits, utilising their clinical expertise to monitor and manage DM medication plans, and educating patients on disease, lifestyle and adherence (Smith, 2009).

A study conducted in a hospital outpatient clinic in United Arab Emirates indicated that a comprehensive pharmaceutical care programme (consisting of patient education and advice on medication adherence, metabolic control and life style ) delivered by a clinical pharmacist over a 12-month period significantly improved glycaemic control and health-related quality of life (Al Mazroui, et al., 2009). A 12-month randomised controlled trial of pharmaceutical care in community-based DM patients revealed that regular face to face and telephone interviews with an experienced clinical pharmacist improved HbA1c and reduced blood pressure (Davis, et al., 2005). Davis et al. (2005) suggested that pharmaceutical care strategies can be easy to implement and time-efficient when telephones and emails are used to facilitate communications (Davis, et al., 2005).

Pharmacist-coordinated DM management programme has been shown to be effective in improving clinical markers and adherence (Kiel & McCord, 2005). Similarly, Malaysian studies have also shown that pharmacist-led MTAC for DM patients were successful in improving adherence and glycaemic control (Lim & Lim, 2010; Loganadan, et al., 2010; Loganadan, et al., 2008). Another study reported that provision of pharmaceutical care service through pharmacist-led clinics significantly reduced the risk of cerebrovascular accidents and coronary heart disease in DM patients (Lowey et al., 2007).

In summary, it has been suggested that pharmacists can be involved in the direct care of patients with DM by screening, encouraging self-management and education, monitoring for preventive care and comorbid conditions, providing expertise on medication management and forming collaborative relationships with other health care providers (Brooks & Prevost, 2007).

### 2.5.4 Patients' and providers' perspectives on medication-related issues

One of the important components in the provision of pharmaceutical care is to understand patients' needs and experiences (van Mil, 2004). Most pharmaceutical care studies do not report medication-related issues from the patients' perspectives. Patients' perspectives of their diseases may differ from those of health professionals. Qualitative studies provide rich descriptions and insights that are valuable in understanding these factors (The PloS Medicine Editors, 2007). For example, Gordon and colleagues explored medication-related problems in patients with cardiovascular disease (Gordon, Smith, & Dhillon, 2007). They found that patients were: 1) concerned about adverse effects of medication and its management, 2) having different views with regards to the use of medicines, 3) concerned about declining ability to use their medicines due to cognitive, physical and sensory problems, 4) lacking information or understanding about the use of medicines, and 5) having problems attributed to access to, and organisation of services.

Stack (2009) suggested that it is important to identify patients' perspectives on specific co-morbid conditions. However, qualitative studies that explored patients' and providers' experiences and perspectives on managing both TB and DM treatment are lacking. As such, individual qualitative studies on TB and DM treatment as well as studies on people's experiences in managing multiple medicines due to comorbidities are presented in the following sections.

### 2.5.4.1 **Patients' and providers' experiences in managing TB treatment**

A systematic review of qualitative studies on patients' adherence to TB treatment identified eight factors that was considered to be important by patients, caregivers and health care providers (Munro, et al., 2007). These factors include: 1) organisation of treatment and care; 2) interpretations of illness and wellness; 3) the financial burden of treatment; 4) knowledge, attitudes, and beliefs about treatment; 5) law and immigration; 6) personal characteristics and adherence behaviour; 7) side effects; and 8) family, community and household support. Patients' adherence to treatment was believed to be influenced by the interplay of these factors.

Medication issues were one of the themes identified in a qualitative study that explored factors affecting quality of life of TB patients (Marra, Marra, Cox, Palepu, & Fitzgerald, 2004). Patients reported that adverse effects of medication (e.g. gastrointestinal disturbances and itchiness), large size of tablets and the high number of medicines were bothersome (Marra, et al., 2004). Similarly, other qualitative studies have also reported that patients who experienced or anticipated adverse effects of medications tended to default TB treatment (Munro, et al., 2007; Noyes & Popay, 2007) and that patients expressed difficulties in consuming multiple medication (Hansel, Wu, Chang, & Diette, 2004; Marra, et al., 2004; Munro, et al., 2007). In fact, patients have expressed their desire to reduce the amount of medicines or decrease the duration of therapy (Hansel, et al., 2004).

Studies have shown that patients stop taking their treatment if they do not believe in the efficacy of the treatment (Munro, et al., 2007; Noyes & Popay, 2007). One study found that adherence appeared to be better during the initial acute phase of the illness, when the patients were more symptomatic and they defaulted TB treatment as soon as their symptoms improved (Naidoo, Dick, & Cooper, 2009). Patients could also be non-adherent if they were taking other traditional medicines and perceived there to be negative consequences if these

were taken concurrently with TB medication (Munro, et al., 2007). Naidoo et al. (2009) showed that patients also stopped TB treatment after visiting traditional healers.

Many health care providers stated that patients found DOT intrusive and an imposition on lifestyle (Hansel, et al., 2004). Furthermore, responsibilities in the home may be given priority over treatment adherence (Munro, et al., 2007). Patients appeared to have less choice or flexibility concerning their treatment as they had to give up part of their working day to attend and had to wait to receive and be observed taking their drugs (Munro, et al., 2007; Noyes & Popay, 2007). Noyes & Popay (2007) highlighted that there is a need for locally tailored, patient centred programmes rather than a single world-wide intervention like DOT. Self-supervision was found to be the preferred option by most people (Noyes & Popay, 2007).

The quality of health care the participants received is another factor that influenced adherence (Naidoo, et al., 2009). Noyes & Popay (2007) highlighted the crucial need for more effective exchange of expertise and knowledge between patient and the DOT provider. They cited that the 'experiential knowledge' from TB patients should inform the medical practice. For example, patient reported issues like "the hunger induced by getting better, different 'lay' understandings about the nature of 'cure', the debilitating effects of TB and TB medication, and the 'meaning' of the side effects of medicines" should be taken into account (Noyes & Popay, 2007).

Family support, including financial assistance, collecting medication, and emotional support, were found to be very important to ensure patient adherence to treatment (Munro, et al., 2007). TB patients who experienced family instability or social isolation were less likely to comply with medical treatment (Naidoo, et al., 2009).

In summary, adverse effects of medications, multiple medicines, treatment beliefs and concerns, inconveniences caused by DOT, poor patient-provider communication and lack of family support were found to be the factors affecting TB treatment.

### 2.5.4.2 **Patients' and providers' experiences in managing DM treatment**

Al-Qazaz and colleagues from Malaysia explored DM patients' knowledge about the disease and its medication. It was reported that patients lacked knowledge on adverse effects of DM medication and had not received sufficient information from their physicians. Forgetting to take medication and modification of treatment regimen were also reported (Al-Qazaz, Hassali, Shafie, Syed Sulaiman, & Sundram, 2011). Another qualitative study from Malaysia also showed that many patients lacked awareness about DM and its treatment (Mohd Ali, 2009). Many patients were unaware that they had DM until complications sets in (Mohd Ali, 2009). Concurring with Al-Qazaz et al. (2011), patients reported that they were not given adequate information and wanted to know more about their disease (Mohd Ali, 2009). Pharmacists who participated in the study reported that some patients had erroneous beliefs such as DM can be cured and that they could eat anything if they took their insulin (Mohd Ali, 2009). It was also reported that patients' education level was another factor that contributed to their understanding about the disease and its management (Mohd Ali, 2009). Multiple medication taking was felt to be problematic for patients with comorbidities especially when multiple dosing was involved (Mohd Ali, 2009).

A qualitative meta-analysis on obstacles to adherence in type 2 DM patients revealed that the factors affecting adherence were less related to the health care system and more to patients' knowledge about DM, beliefs and attitudes, and their relationship with health care professionals (Vermeire, et al., 2007). It has been reported that patient-provider communication was one of the factors that affected adherence to DM treatment regimens (Matthews, Peden, & Rowles, 2009). Matthews et al. (2009) reported that providers did not acknowledge the importance of their patients' autonomy and did not encourage active participation in disease management. Many patients denied that their DM symptoms were serious and admitted that they would consider their condition to be serious and would be more likely to adhere to treatment if the symptoms worsened (Matthews, et al., 2009).

Lawton and colleagues explored perceptions and experiences of taking oral hypoglycaemic agents among people of Pakistani and Indian origin (Lawton, Peel, Parry, & Douglas, 2008). The study found ambivalent views about oral hypoglycaemic agents. Despite believing the importance of oral hypoglycaemic agents, some patients reduced their tablet intake without consulting their physicians. The patients felt that the drugs worked by providing relief of symptoms and that it was detrimental to take the medication for a long period as well as in combination with other medication (Lawton, et al., 2008).

A synthesis of qualitative research in lay experiences of DM and DM care showed that patients employ 'strategic non-compliance' by monitoring and observing symptoms and manipulate dietary and medication regimens in order to live a normal life rather than limiting social and work activities in order to adhere to medical advice (Campbell, et al., 2003). In other words, DM patients self-manage by making modification to their medication regimen and lifestyle according to the severity of illness.

In summary, qualitative studies have shown that many DM patients: lacked knowledge about their disease and its treatment; believed that their disease was not serious in the absence of complications; modified treatment regimens; had difficulties in complying with dietary recommendation; were burdened with multiple medicines; and had not raised some of their medication-related concerns with their physicians.

### 2.5.4.3 **Patients' and providers' experiences of managing comorbidities and its treatment**

As there were no studies conducted in patients with TB and DM, this section provides a general review on patients' and providers' experiences in managing comorbidities.

Studies have shown that patients with comorbidities had a higher risk of dying, a poorer functional status or quality of life (Fortin, Bravo, Hudon, Lapointe, Almirall, et al., 2006), psychological distress (Fortin, Bravo, Hudon, Lapointe, Dubois, et al., 2006), longer hospital stay and a higher cost of care (Fortin, Soubhi, Hudon, Bayliss, & Akker M, 2007; Gijsen et al., 2001).

It has been widely reported that patients with comorbidities prioritise their health conditions and its treatment (Bayliss, Steiner, Fernald, Crane, & Main, 2003; Beverly, Wray, Chiu, & Weinger, 2011; Elliott, Ross-Degnan, Adans, Safran, & Soumerai, 2007; Jowsey et al., 2009; Stack, 2009). Some health issues could be neglected or compromised when patients prioritise health conditions by selectively attending to the management of those conditions based on perceived severity or importance (Bayliss, et al., 2003; Beverly, et al., 2011; Jowsey, et al., 2009). Some patients found management of all their conditions to be challenging and in some cases financial barriers led to prioritisation of treatment (Beverly, et al., 2011). On the other hand, Elliot et al. (2007) reported that people prioritised their medicines based on their experiences of side effects, cost , beliefs on treatment necessity and concerns about medicines (Elliott, et al., 2007).

Stack (2009) explored the way patients with comorbid DM perceived and managed multiple medicines and their multiple conditions. Some of the findings revealed that patients wanted to avoid additional medicines; compared between medications and alternative methods of treatment; believed medicine taking and lifestyle management were different issues; were

concerned about adverse effects; and expressed a range of emotional responses to multiple medicine taking. Other studies have also shown that patients were reluctant to take medication and preferred to reduce the number of medications (Elliott, et al., 2007; Townsend, Hunt, & Wyke, 2003). Studies have shown prevalent cultural belief that medication should be minimised (Britten, 1994; Townsend, et al., 2003).

Another study showed that comorbidities reduced patients' ability to act on risk factors; complicated the process of detecting the early symptoms of deterioration of each condition, and complicated their capacity to manage multiple medication (Jowsey, et al., 2009). The study reported that patients found managing medication for their numerous conditions to be complicated, time-consuming, inconvenient and confusing. Another study found that some patients felt that they had insufficient knowledge about drug interactions and side-effects (Jowsey, et al., 2009). Bayliss and colleagues reported that some people expressed difficulties in managing comorbidities, especially when each disease had a different management and some believed that medicines for one condition would worsen the symptoms of other conditions (Bayliss, et al., 2003).

Given the challenges of managing comorbidities, it has been suggested that future practices should move away from single disease orientation and move toward strategies that meet the needs of people with comorbid conditions and strengthen their capacity to self-manage (Fortin, et al., 2007; Jowsey, et al., 2009). Specialised education and services that cater to the needs of people with clusters of comorbidities need to be developed (Gijsen, et al., 2001; Jowsey, et al., 2009). Jowsey et al. (2009) called for more research to address specific combinations of diseases that are known to be comorbid and highly prevalent. In addition, there is a need for optimal coordination among health care professionals (Gijsen, et al., 2001). Increased understanding of comorbidites among health care professionals and increased communication between specialities are vital to improve coordination of care (Fortin, et al., 2007).

Piette & Kerr (2006) highlighted that there is a need to know more about how physicians prioritise DM management goals relative to the management of comorbidities, how health systems affect these choices, and the ways in which patients' multiple providers either share goals or coordinate care. Less is known about how DM patients rate the importance of their diabetes-specific self-management behaviours, treatments, and outcomes when compared with other comorbid conditions (Piette & Kerr, 2006). As comorbid conditions and their treatments often interact, it is vital that treatment be coordinated by a single provider or a team of providers with an understanding of the patient's many challenges (Piette & Kerr, 2006). It has been suggested that care managers and clinical pharmacists can assist in coordinating activities within a patient's complex medical care regimen (Piette & Kerr, 2006).

In summary, studies on patients and providers perspectives in managing comorbidities revealed that patients prioritised treatment; wanted to reduce the number of medicines and had many challenges in managing multiple diseases and its treatment. Coordination of care is vital in order to manage people with comorbidities.

## 2.6 Summary of the literature review

- Malaysia
  - The increasing prevalence of DM and the continuous surge in the number of TB cases reported in Malaysia is a huge concern.
- Pharmaceutical care research
  - Pharmaceutical care is a complex intervention and the MRC framework provides a guideline for developing complex interventions.
- Association of TB and DM
  - DM triples the risk of developing TB, increases mortality and severity of TB, and slows the response to effective TB treatment.
- The pharmacological issues in the management of TB and DM
  - TB and its treatment can worsen DM control. Rifampin interacts negatively with commonly used oral hypoglycaemic drugs like sulfonlyureas and thiazolidinediones. Blood levels of these drugs are lower when rifampin is being used and can affect DM control. It is important to monitor blood glucose and adjust DM medication while on rifampin. DM patients also have a higher incidence of peripheral neuropathy while taking isoniazid.
  - TB and DM patients consume multiple medicines which may have an impact on adherence.
- Role of pharmacists
  - Pharmacists have been urged to participate in the management of TB.
  - Pharmacists have played important roles in the management of DM and improved clinical outcomes.
  - Pharmacists in Malaysia are providing pharmaceutical care service through MTAC and other clinical pharmacy services.
- Patients' and providers' perspectives on medication-related issues
  - There is a need to understand the problems faced by people with specific combination of comorbid conditions like TB and DM.
  - Qualitative studies have provided various insights on patients' experiences in managing TB, DM and comorbid conditions but less is known about the experiences of people with TB and DM.
  - There is a need to integrate the management of comorbid condition.
- More research is currently needed in the area of TB and DM.

## 2.7 Rationale for study

The gaps in the literature with regards to the scarcity of research in TB and DM, the call for integrated management for comorbid conditions, and the lack of involvement of pharmacists in the management of TB resulted in the idea of developing a pharmaceutical care service for patients with TB and DM. It is envisaged that this study could contribute to the body of knowledge in relation to 1) patients' and providers' experiences and perceptions in managing TB and DM, 2) identification of medication-related problems in patients with TB and DM and 3) the role of pharmacist in the management of TB and DM.

## 2.8 Research aim and objectives

This study aimed to develop a pharmaceutical care service for patients with TB and DM. The specific objectives of the study were divided into two phases.

Phase 1:

i. To identify the pharmaceutical care needs of patients with TB and DM in Malaysia.
ii. To explore health care professionals' views on the existing pharmacist-led medication therapy adherence clinic and the potential role of pharmacists in the joint management of TB and DM.

Phase 2:

i. To investigate the feasibility of providing a pharmaceutical care service for patients with TB and DM.

# CHAPTER 3: METHODOLOGY AND METHODS (PHASE 1)

## 3.1 Introduction

This chapter describes how the phase 1 study was carried out. It presents the research methodology, describes the data collection methods, explains how the data was analysed and discusses how the validity and reliability of the phase 1 findings detailed in this thesis can be assessed.

## 3.2 Objectives

The objectives of the phase 1 study were:

i. To identify the pharmaceutical care needs of patients with TB and DM in Malaysia.

ii. To explore health care professionals' views on the existing pharmacist-led medication therapy adherence clinic and the potential role of pharmacists in the joint management of TB and DM.

## 3.3 The methodology of Phase 1 study

This section explains how the methodology for this study was derived from the research questions. In order to explore the pharmaceutical care needs of TB and DM patients, it is important to understand the experience of both patients and health care professionals in managing TB and DM and whether pharmacists have a role to play. Therefore, three research questions were identified as the starting point of this phase 1 study.

- What are the experiences of patients and healthcare professionals in managing TB and DM?
- How do health care professionals perceive the existing pharmacist-led MTAC service?
- How can pharmacists play a role in the management of TB and DM?

As there was no prior information about medicine taking experiences of patients with both TB and DM and lack of reported evidence on health care professionals' perceptions on pharmacist-led MTAC service in Malaysia, there was the need to explore these issues. Hence, a qualitative research approach was chosen.

The next section describes the nature of qualitative research.

## 3.4 Qualitative research

Qualitative methods are gaining recognition in health care research and by policy-makers too as they provide detailed and contextual explanation to a complex phenomenon. Qualitative research investigates *how* and *why* things happen rather than quantifying them (Murphy, Dingwall, Greatbatch, Parker, & Watson, 1998; Pope & Mays, 2006). It allows in-depth exploration of issues pertaining to individuals' experiences (Bowling, 1997) and *how* and *why* similar events are conceived in a different way by other stakeholders (Murphy, et al., 1998; Sofaer, 1999). This strategy is helpful in the exploratory stages of a research project as it forms the base for subsequent explanatory research.

Qualitative research allows the adoption of a flexible framework for data collection. Therefore, rather than being fixed at the start, the study design can be modified as the research progresses in response to the researcher's understanding of the issues (Lincoln & Guba, 1985). This is a key attribute of qualitative research because the researcher does not usually have a complete understanding of the issues under investigation. Furthermore, the aim is to learn from every step and as the understanding increases, the study design can be modified (Dahlgren, Emmelin, & Winkvist, 2004).

## 3.5 Data collection and sampling methods

In qualitative research, interview is one of the most important data collection tools (Morse & Field, 1995). It is a very effective way of accessing people's perceptions, meanings, and constructions of reality (Morse & Field, 1995). It is a complex social process and there are many different types of interviews. Interviews can be structured, semi-structured and unstructured (Minichiello, Aroni, & Timewell, 1995).

Interviews can be conducted on a one-to-one or group basis. The latter include techniques such as group interviews, community interviews and focus groups. Focus group discussions allow a small group of people to discuss a subject of common interest with the guidance of a moderator or facilitator. The facilitator plays an important role to control the scope of the discussion and to make sure that everybody gets the chance to voice their opinions on the subject matter (Krueger & Casey, 2000). Focus group are not the same as group interviews as it utilises group dynamics to access peoples' concerns, group norms and knowledge (Kitzinger, 1994, 1995; Krueger & Casey, 2000). Group members influence each other by responding to ideas and comments of others. Focus group discussions produces large amount of data within a short period (Krueger & Casey, 2000).

Interviews can be administered face-to-face, over the telephone an on-line. However, face-to-face interviews are good for establishing rapport and also for capturing the body language of the participants.

The actual data generated by interviews are words. Interviews are generally audio-recorded and then transcribed verbatim to produce transcripts for analysis but they can also be video recorded to capture non-verbal communication.

### 3.5.1 Selection of interview type for this study

This study employs semi-structured interviews. Face-to-face interviews were conducted with patients and health care professionals from the respective TB and DM setting. This interview method was chosen because some of the aspects to be addressed were already identified from the literature and also to ensure that key issues pertaining to the research question were covered with all participants.

On the other hand, focus group discussions were used to gather information from pharmacists in order to utilise group dynamics. The other reason is, pharmacists in this context are not involved in the care of TB and therefore, they were not subjected to the same questions raised in the semi-structured interviews. Different sets of questions were posed to pharmacists in the focus group discussions, to facilitate the expression of ideas and encourage pharmacists' to voice their perspectives within a homogenous group (Pope & Mays, 2006). To avoid hierarchy within the health care professionals affecting the data, focus group discussions were not carried out with all the health providers (Pope & Mays, 2006). For example, nurses might not share their opinion freely in the presence of a physician hence, one-to-one interviews with physicians and nurses were conducted.

## 3.6 Qualitative Sampling

Qualitative research does not require large or statistically representative samples as the norm for quantitative research. Qualitative samples are generally small and the 'richness' of the data relevant to address a specific problem is more important than the number of participants recruited into a study. Nevertheless, effective sampling strategy is equally important in qualitative research.

In this study, purposive, convenience and snowball sampling strategies were used. Purposive sampling was used to select adult patients with TB and DM from all the three main ethnic groups (Malay, Chinese, Indian) in Malaysia. Convenience sampling was used to recruit the physicians and nurses. Snowball sampling was used to recruit pharmacists for the focus group discussion. The researcher contacted the chief pharmacist of the hospital and requested him to introduce pharmacists especially those who led the MTACs to participate in this study.

## 3.7 Interview Guide

Two interview guides and one focus group guide (see Appendix 5 and 6) were developed to lead the interview and discussion process. Topics that were covered in the interview guide for patients include the experiences of living with TB and DM, adherence to medications and medication-related problems. The topics for physicians and nurses included experiences in managing patients with TB and DM, potential role of pharmacists, DOT and health system barriers. The topics for the focus group were experiences in managing MTAC and the potential role of pharmacist in managing TB and DM. The interview guide was developed following a literature search.

## 3.8 Process and Procedures

### 3.8.1 Ethical Approval

Prior to the commencement of the interviews, ethical approval was sought. The phase 1 study was registered with the Malaysian National Medical Research Register. All the required documents were submitted to the ethical committee of the Ministry of Health, Malaysia. Ethical approval was obtained (reference number: NMRR-08-10-1165) two months after submission (see appendix 2).

### 3.8.2 Recruitment setting

The study was mainly conducted at a tertiary public hospital in the northern region of Malaysia. Patients were recruited for semi-structured interviews from the Hospital's Chest clinic as well as from three other district hospitals from the state. Initially, it was not intended to recruit patients from the district hospitals but coincidently, the first few interviews conducted in the Hospital's Chest clinic were all with Chinese patients. The nurses suggested the researcher follow the health care professionals (TB health care team) to district hospitals in order to have higher chances of interviewing Malay and Indian patients. Hence, the researcher joined the health care professionals' weekly visits to the district hospitals. It also provided an opportunity to observe how DOT was done in those settings.

Physicians, nurses and pharmacists who participated in the study were recruited from one tertiary public hospital. Physicians and nurses were first recruited from the chest clinic. Pharmacists were recruited from the pharmacy department. Upon completing interviews with the physician and nurses from the chest clinic and a focus group discussion with the

pharmacists, it was felt that more information was needed to clarify some issues and therefore, a physician and a nurse from the endocrine clinic were recruited.

### 3.8.3 Participant identification and recruitment

Patients with TB and DM could be identified from patient medical charts and registers as well as from their attending doctors and nurses. The nurses said that they were in a better position to identify potential patients with TB and DM due to their daily interaction with TB patients who attend the clinic for DOT. They informed the researcher that although patients could be identified from the registers, not all patients were having their DOT at the hospital's chest clinic as they can have DOT at any government health clinics close to their homes. Such patients only visit the hospital's chest clinic during their follow-up. As such, the researcher relied on the nurses in identifying the patients for this study. As for the patients at the district hospitals, the researcher contacted and informed the nurses prior to the visit in order to enable them to identify and refer potential patients.

The patient inclusion criteria for this study are listed below and those who matched the criteria were invited to participate in the interview.

**Inclusion criteria:**

- Adult patients ( 18 years and above) with clinically diagnosed TB and DM
  (For safety reasons, only those who had been on TB treatment for more than 2 months were recruited)
- English, Malay or Tamil language speaking patients
- Patients prescribed with both TB and DM medications

**Exclusion criteria:**

- TB only patients
- TB and DM patients who were terminally ill or unable to provide written informed consent

The patient information sheet (see Appendix 3) was provided to patients identified as suitable participants for the study. Patient recruitment and interviews continued until new themes ceased to emerge. This was achieved after interviewing 20 patients.

On the other hand, it was not possible to expect saturation of themes to be reached with the limited number of health care professionals within the context of this study. Therefore, health care professionals who were believed to be able to produce 'rich' information were approached and recruited for in-depth interviews. The details of how they were recruited were already explained in section 3.8.2.

### 3.8.4 Interview setting

Patients were interviewed at the chest clinics. It was held in a quiet location (e.g. empty nurse's room, counselling room) that was suitable for an interview within the clinic setting. Health care professionals were interviewed in their respective rooms or offices in the hospital. One focus group discussion was conducted with a group of pharmacists in the pharmacy department.

### 3.8.5 Interview process

Patients were given options to be interviewed alone or in the presence of their family members. The purpose of the study and process of the interview were explained to all patients. Patient's permission to audio record the interview was obtained. They were also reminded that they were able to withdraw their participation with no resulting consequences at any point of the process and that they only need to answer questions that they feel comfortable to answer. This process was aimed to provide a non-threatening environment which encouraged patients to tell their own story. Demographic data including gender, age, ethnicity, and occupation were also collected from each patient.

The researcher is a trilingual and is able to speak in English, Malay and Tamil languages. All Chinese and Malay patients chose to communicate in Malay which is the national language. Indian patients were comfortable to be interviewed either in Tamil or English. Among health care professionals, the nurses from the Chest clinic spoke in Malay while the rest preferred English. The focus group discussion was conducted in English.

## 3.9 Data collection and data management

Data collection began in April 2008 and continued till July 2008. All the interviews were conducted by the researcher. However, the focus group discussion was facilitated by the researcher's main supervisor who was in Malaysia at that time. The researcher made the arrangement for the focus group discussion and played the role of a note taker. Refreshments were provided after the focus group session.

### 3.9.1 Interview and focus group data

All interviews and focus group discussion were audio recorded using a digital interview recorder. The recorded materials were downloaded to a personal computer. The recordings were played via Windows media player and it facilitated the transcribing process.

### 3.9.2 Field notes

The researcher's field notes were documented in individual patients' data collecting form. Field notes were documented after each interview session. These notes were useful during the data analysis as it helped the researcher to recollect the events that took place during the interview. The field notes were reviewed with the interview transcripts to help recall and clarify a particular event.

### 3.9.3 Transcription

Audio-recordings were transcribed verbatim. In order to ensure the study was rigorous and trustworthy, the audio-recorded and written verbatim versions of the interviews were assessed for accuracy and completeness of data by three Malaysian pharmacists who were pursuing a doctoral degree in pharmacy and were familiar with the local languages. For example, interviews that were conducted in Tamil were verified by a Tamil speaking pharmacist and interviews that were conducted in Malay were verified by the other pharmacists.

### 3.9.4 Translation

In order to ensure consistency (Twinn, 1997), all non- English transcripts were translated to English by the researcher. As there was only a single translator in this study, the translation was consistent and reliable (Twinn, 1997), but it took a huge amount of time to do it. It takes nearly two hours to translate one transcribed page (Squires, 2008). However, translation was needed because one of the researcher's supervisor is British and does not speak Malay and Tamil and the other two supervisors do not speak Tamil. Factors which affect the quality of the translation include the linguistic competence of the translator and the translator's knowledge of the people under study (Birbili, 2000). As mentioned earlier, the researcher is trilingual and is familiar with the local people.

However, it must be acknowledged that there is the potential for modification of the data through mistranslation, partial omission or oversimplification which is unavoidable during translations (Escott & Walley, 2005; Wong & Poon, 2010). Such modification could be intentional or unintentional, but the reliability of translation to reflect the participants' intended response will influence the validity of the data (Escott & Walley, 2005). Although, all the transcripts were translated to English for verification purpose, the data was analysed in the original language. Furthermore, it was easier to cross check certain data with the audio recordings, especially when there was a need to consider the voice modulations of the participants in certain circumstances. This helped to reduce the misinterpretations. In this study, the translation was meant to capture the meaning of the statements, rather than giving a literal translation (Esposito, 2001). For example, one Indian participant mentioned that 'he had no appetite' and if those words were to be literally translated as he said it in Tamil, it would be 'my tongue died'.

During the data analysis, the selected themes and sub-themes were translated to English again. The retranslated themes were checked against the earlier version of the translated

transcripts. Although only the selected themes were translated, repeating the translation process helped the researcher to check whether there were any discrepancies between the first and second translations, thus avoiding misinterpretations.

Comparing the first and the second version of the translation showed that better translation in terms of preserving the actual meaning was produced in the second version. Thus, it is better to translate selected themes rather than translating the whole transcript. In fact, it has been recommended that verbatim transcription and data analysis can be done in the original language and only the emergent concepts and categories (themes and sub-themes) needed translations to English (Chen & Boore, 2009).

Some researchers may raise the issue of back translating translated interviews as a way to validate the translation (Chen & Boore, 2009; Maneesriwongul & Dixon, 2004). Chen & Boore suggest that another translator should take the English version and back translates the concept and categories from English to the original language. Subsequently, they suggest the involvement of an expert panel committee in reaching final agreement on the translation in order to gain conceptual equivalence and the words used by native speakers (Chen & Boore, 2009). However, it has been argued that back translations can incur additional time and costs to the study (Squires, 2008). It was also argued that back translation does not necessarily ensure the trustworthiness of the results and therefore, a qualified bilingual individual competent in the qualitative researcher's discipline can easily validate the conceptual equivalence of the translation (Squires, 2008). Therefore, back translation was not done in this study. To ensure accurate translation from Malays to English, assistance was procured from the researcher's supervisor. The researcher revisited and retranslated some of the excerpts until agreement was reached between the researcher and the researcher's supervisor. Similarly, a Tamil speaking PhD student (pharmacist) assisted the process of verifying the translations from Tamil to English. Consensus validation was the finalisation point with the supervisor and the PhD student for all the translations.

## 3.10 Data analysis

Thematic analysis was used to analyse these interview data, informed by a constant comparison approach (Boyatzis, 1998; Braun & Clarke, 2006). It involves identifying, analysing, and reporting patterns or themes within data (Boyatzis, 1998; Braun & Clarke, 2006). The transcripts were read repeatedly while listening to the audio recording and emerging topics were coded and constantly compared and contrasted with other transcripts (Braun & Clarke, 2006).

The data was analysed with the aid of the qualitative computer software NVivo (version 8). This software allows handling of large amounts of data and enables useful comparisons to be carried out (Bazeley, 2007). It facilitates constant comparison between interpretations and illustrative statements from the original transcript (Bazeley, 2007). The documents containing the transcripts and field notes were imported from Microsoft Word into NVivo for analysis. The documents can then be opened in NVivo and coded for analysis (Bazeley, 2007).

Data analysis began with the themes that have guided the research design. These themes are called 'nodes' in NVivo (Bazeley, 2007). These themes can be anticipated or emergent. NVivo stores tree type of nodes: free nodes, tree nodes and case nodes (Bazeley, 2007). The free nodes are stand alone nodes and usually the analysis begins by identifying the free nodes (Bazeley, 2007). Free nodes can later be moved to tree nodes and vice versa. Tree nodes are organised into hierarchy and can be used to show the relation between nodes. Case nodes are used to organise coding according to cases. Tree nodes and free nodes were used in this study.

Coding is a process of which a researcher identifies and labels text that relates to a node (Bazeley, 2007; Miles & Huberman, 1994). The transcripts were read line by line and key nodes were identified (Miles & Huberman, 1994). The identified nodes were used to develop a coding framework for coding the data. The coding process involved reading, linking and

connecting texts to the represented nodes. Newly identified nodes were added to the coding framework. Coding is an iterative process whereby previously coded texts were revisited and checked whether the assignment of the data to specific nodes were correct or could be moved to other nodes. At times the same texts were coded with different nodes, as they embraced different meanings.

Tree nodes were arranged into parent nodes (themes) and child nodes (sub-themes) which showed the hierarchical organisation (Bazeley, 2007). This process continued until all transcripts had been analysed and the coding was compared until no new themes emerged especially in patients' interviews. The number of interviews with health care professionals was limited by recruitment and saturation could not be assessed.

The next section explores the concept of reliability and validity.

## 3.11 Reliability and validity of data and methods

Qualitative research is often subject to validity and reliability criticism. The weaknesses of qualitative research are the potential for bias and the lack of generalisability due to smaller samples which are selected through non-random means. Nevertheless, unbiased, in depth, valid, reliable, credible and rigorous data can be produced if the research was carried out appropriately (Anderson, 2010). The claims made in qualitative research needs to be supported by convincing evidence (Murphy, et al., 1998).

### 3.11.1 Validity

The validity of research findings refers to the extent to which the findings are true representations of the phenomena (Anderson, 2010; Smith, 2002). Validity can be demonstrated by a number of strategies including triangulation, use of contradictory evidence, respondent validation, and constant comparison (Anderson, 2010).

Triangulation is using two or more methods to study the same event. This enables the researcher to compare different perspectives of the same event or experience and build a more comprehensive understanding of the subject matter. If both sources confirm the same findings, then the research is thought to be valid (Smith, 2005). In this study, some of the issues were triangulated using different strategy of inquiry (e.g. focus group and interviews) and sources (e.g. medical records) in order to substantiate the findings.

Respondent validation allows participants to read through the data and analyses and provide feedback on the researcher's interpretations of their responses. It is also a suitable method of checking for inconsistencies, challenges the researcher's assumptions, and provides them with

an opportunity to revisit their data (Anderson, 2010). First, this strategy was not feasible due to the low literacy level of some patients and the fact that the researcher was not able to see the patients again. Respondent validation was conducted using a different approach in this study. The findings of the study were presented in an oral presentation session (see Chapter 5) to the health care professionals after completing the study. The session provided an opportunity for the health care professionals to check for consistencies and provided further information on certain issues. Additional issues were raised during the question and answer session which was held after the presentation and that led the researcher to revisit the transcripts and field notes to confirm some of the issues.

The use of constant comparison means the data from one participant was compared to another participant to generate a complete understanding rather than presenting a single view. In this study, constant comparison method helped to identify both the emergent and the unanticipated themes.

Qualitative study relies on those who conduct the research and therefore, the acknowledgement of what they bring into the research is important as it influence what they see and how they analyse their data (Charmaz, 2006). Validity can be compromised if participants do not feel free or comfortable to express their thoughts or opinions (Smith, 2002). Although, the necessary steps had been taken to make sure the interviewees were comfortable to talk about their experience, some unavoidable factors could have affected the validity of the data.

Being a novice, the validity of the study could have been compromised due to lack of interviewing skills especially at the beginning stage of the study. There were some cues that were not grasped during the initial interviews in which further probing could have led to a deeper understanding about the phenomena. However, the researcher was only able to reflect on it after gaining a deeper understanding on the nuances of qualitative research which happened at the later stages of the PhD project.

For example, it was observed that health care professionals especially physicians responded in a *clinical* way. Although this might not affect the validity of the study, the fact that the identity of the researcher (pharmacist) was known could have affected the way the health care professionals responded to the questions.

On the other hand, the majority of the patients informed the researcher that they had not met a pharmacist before which means that they do not know the role of a pharmacist. Nevertheless, these patients knew that they were talking to someone who is equivalent to a doctor as the researcher was wearing a white coat and that might have impacted the data to a certain extent. Patients might have provided answers which are socially acceptable and avoided actions or behaviours that could be negatively judged. Again, their account are not considered invalid but the potential influence of the context should be considered (Murphy, et al., 1998).

Language barrier was another aspect that could have compromised the validity of this study. Some of the Chinese patients had difficulties in articulating their views in Malay language resulting in short replies. They would have been able to provide detailed explanation if they were interviewed by a Chinese speaking interviewer.

This study was conducted in a clinic environment and that could have also affected the way patients responded in the interview. Participants would have been more comfortable and relaxed if they were interviewed in their choice of place (e.g. patient's home). It was decided not to conduct the interview in patients' homes for health and safety precautions.

### 3.11.2 Reliability

The reliability of a study refers to the reproducibility and stability of the findings. Internal reliability relates to consistency of application of themes to the data and can be addressed by the use of inter-rater reliability checks. Different researchers' applications of the themes can be compared and adjustments made if and where necessary. This can be time consuming, labour intensive and it can be facilitated by the use of NVivo.

In order to check the reliability of the data analysis in this study, sections of the coded transcript was presented to my supervisors to establish agreements on the codes assigned to each section of the data.

The data within each code were also assessed to confirm that the code represented the data. The summary of all interviews and discussion were presented to the researcher's supervisors in order to allow them to get a complete understanding of the study. Consensus validation was used to confirm themes and the matching of the transcribed quotes with the themes and sub-themes derived from the analysis.

## 3.12 Ethical issues

It is important to make sure that the study was conducted in an ethical manner whereby the participants' identities were protected. The section below discusses the three important aspects (anonymity, confidentiality and informed consent) (Goodwin, Mays, & Pope, 2006) of research ethics in qualitative research.

### 3.12.1 Anonymity

The identities of all participants were removed and pseudonyms were assigned. The settings from which the participants were recruited were not reported as health care professionals stood a higher chance of being recognised based on their professions and due to the limited number of health care professionals in the clinic.

### 3.12.2 Confidentiality

Participants' contact details were not obtained during the data collecting process. The audio-recorded data and transcripts were saved in a password protected personal computer. Patients' name and health care professionals' demographic data that might reveal the participants identity were removed before the data analysis and will not be included in any publications.

### 3.12.3 Informed Consent

Written informed consent (see Appendix 4) for participating and audio recording of the interviews and discussions was obtained from each patient and health care professional prior to the start of any research activity.

The findings and discussion of phase 1 study are presented in Chapter 4.

# CHAPTER 4: EXPLORING THE PHARMACEUTICAL CARE NEEDS OF TB AND DM PATIENTS (PHASE 1)

## 4.1 Introduction

The findings of the phase 1 study are presented in two sections in this chapter. Firstly, patients' and health care professionals' experiences of managing TB and DM are explained. Secondly, health care professionals' views on the expanding role of pharmacists are presented. The chapter concludes with the discussion of key findings.

## 4.2 Participants characteristics

In total, 20 patients, three physicians and three nurses were interviewed. Four pharmacists participated in a focus group discussion. The characteristics of patients are shown in Table 4-1. Detailed characteristics of patients are provided in Appendix 8. The mean age of patients with TB and DM was 57 years (range 42-78 years). The majority of patients were male (n=18). There were seven Malay, eight Chinese and five Indian patients. All Malay and Chinese patients preferred to be interviewed in Malay, four Indian patients were interviewed in Tamil and one Indian patient preferred English. All patients were diagnosed with pulmonary TB and three of them had a relapse of pulmonary TB. One out of the three participants who relapsed developed MDR-TB and was isolated in a TB ward. Fourteen patients had history of chronic DM preceding the diagnosis of TB and six were newly diagnosed with DM while on TB treatment. Eight patients reported to have other concurrent health problems such as hypertension, hyperlipidemia, osteoarthritis, cholelithiasis, diabetic foot, and pneumonia. Five patients had history of cataract surgery.

Out of six health care professionals who participated in the interviews two physicians (a consultant and a specialist) and two nurses were attached to the chest clinic whilst the rest (a consultant and a nurse) were from the endocrine clinic. The two nurses from the chest clinic had more than six years of working experience and the nurse from the endocrine clinic had

eight years of working experience. As for the pharmacists who participated in the focus group discussion, two were running the MTAC for DM patients; one was running the MTAC for human immunodeficiency virus (HIV) patients whilst the fourth pharmacist was responsible in providing pharmaceutical care services to in-patients at the respiratory wards, which includes TB patients. Pharmacists had four to five years of working experiences. Demographic data for the health care professionals are not presented to protect their identities due to the small number of participants. All names used below are pseudonyms.

Table 4-1 Characteristics of TB and DM patients (n=20)

| Patient characteristics | Number of patients |
|---|---|
| **Age[a], mean ± SD (range)** | 57.3 ± 9.2 years (42-78 years) |
| 40-59 | 13 |
| 60-79 | 7 |
| **Gender** | |
| Male | 18 |
| Female | 2 |
| **Ethnicity** | |
| Malay | 7 |
| Chinese | 8 |
| Indian | 5 |
| **History of DM** | |
| Newly diagnosed DM[b] | 6 |
| Previously diagnosed DM (range 1-30 years) | 14 |
| **Classification of TB** | |
| Newly diagnosed pulmonary TB | 17 |
| Relapsed pulmonary TB[c] | 3 |
| **Other concurrent health problems[d]** | 8 |
| **Social history** | |
| Ever smoked | 8 |
| Alcohol consumer | 2 |
| **Marital status** | |
| Single | 0 |
| Married | 20 |
| **Occupational status** | |
| Employed | 8 |
| Unemployed | 6 |
| Retired | 6 |

[a]This is age (mean and standard deviation) and range of age rather than number of patients
[b]DM was diagnosed at the chest clinic
[c]One of the patient who had a relapse of pulmonary TB also had MDR-TB
[d]Other concurrent health problems include hypertension, hyperlipidemia, osteoarthritis, cholelithiasis, diabetic foot, and pneumonia

## 4.3 Patients' and health care professionals' experiences in managing TB and DM

As the focus of this study was to explore the pharmaceutical care issues of TB and DM, issues related to the treatment of TB and DM were regarded to be relevant. Concerns about medication and issues related to the management of TB and DM were the two major themes identified in this study. Summary of themes and subthemes are presented in Table 4-2.

Table 4-2 Themes and subthemes related to the experiences of managing TB and DM

| Themes | Subthemes |
|---|---|
| **Concerns about medication** | Adverse effects of medication<br>Burden of multiple medication<br>Concerns about drug interactions<br>Medication confusion<br>Necessity and efficacy of medication |
| **Management of TB and DM** | Longer duration of TB treatment in DM patients<br>Delayed initiation of TB and DM treatment<br>Poor record keeping<br>Patient-physician communication barrier<br>The ambiguity of DM management in TB patients<br>DOT and the burden of attending multiple clinics<br>Self-management and incorporation of traditional remedies |

### 4.3.1 Concerns about medication

Concerns about medication relate to the adverse effects of medication; the burden of consuming multiple medicines; concerns about drug interactions; medication confusion; and the necessity and efficacy of medication.

#### 4.3.1.1 Adverse effects of medication

One physician believed that nausea and vomiting was the only medication-related problem observed in patients with TB and DM that was different from TB only patients.

> *The only problem ... I notice that if I see patients with DM with TB, they tend to have a bit more of nauseatic symptom... (Rahmat, physician, chest clinic)*

Rahmat also reported the measures that he took to manage patients who vomited during TB treatment. The option of prescribing TB treatment at night (before bedtime) was considered in order to reduce the occurrence of nausea and vomiting.

> *So all these patients with DM and TB, when they are vomiting, normally I admit them to the ward. They must hold on with TB and diabetes treatment side effects... a few patients what I do is that because they have lot of nausea, vomiting, I give them their TB treatment at night...so, they sleep off with the tablet so they don't have much nausea vomiting at night (Rahmat, physician, chest clinic)*

Similar to physicians, nausea and vomiting was the most common complaint and was reported by eight patients. Patients also speculated about the reasons they felt to be the causes for nausea and vomiting. Many said that the vomiting was more severe when they took medication on an empty stomach. While others thought strong medication odour and concomitant use of TB and DM medication were causing the problem. For example:

> *...cause when I take the medicines for my diabetes, it disturbs the TB medicines, very fast, I'll feel like vomiting (Choo, 53 years, Chinese male patient)*

Patients also mentioned their strategies to alleviate nausea and vomiting. For example, they avoided taking TB medication and DM medication simultaneously, taking food before consuming TB or DM medication. One patient adjusted the dosage of DM medication to prevent vomiting without first consulting his physician.

> *Doctor asked me to take two tablets of gliclazide but now I'm only taking one. I feel like vomiting, feel ill. Since I'm experiencing it, I can't follow doctor's instruction. (Ejass, 64 years, Malay male patient)*

However, unlike physicians, patients discussed their experiences with a range of additional adverse effects of medication. Five patients experienced painful toes and ankles. One patient described the episode:

> *When I take my TB medicines, my leg hurts, it's similar to how I used to have pain for gout, if you get it, it's very difficult, toes till here (ankle) will ache, happens a lot in the morning (Choo, 53 years, Chinese male patient)*

Four other patients reported visual disturbances. Other adverse effects that were reported by patients include swelling of the limbs, itchiness, palpitation, drowsiness and fatigue.

Some patients talked about developing other problems that they perceived to be related to multiple medicines taking such as losing appetite, feeling depressed and lethargy.

### 4.3.1.2 **Burden of multiple medication**

Having to consume a high number of medicines was considered burdensome for many patients. One patient reported that he took about 21 tablets a day, which included treatment for TB, DM and other presenting comorbidities. Four patients said that they had some reservations or fear of taking a large quantity of TB medication at the initial stage of the treatment but found it to be tolerable after some time. Another patient reported that it was easier to take DM medication since the number of medication was lesser when compared with TB medication.

> *Insyallah (God willing), I can take the DM medicines, twice a day only and the medicines are not a lot but if you compare with TB medicines, 13 pills, that's a lot, even just looking at it, it's frightening. I am really scared of taking medicines, but what can I do. (Nusa, 53 years, Malay male)*

Some feared that multiple medicines can lead to other health problems. For example:

> *I'm afraid. If I have to take so many medicines, definitely I'll be scared...I might end up with other problems. (Yuen, 64 years, Chinese male patient)*

Many expressed difficulties of consuming multiple medicines on an empty stomach.

> *When I had to come (for DOT), I had to fast. When I take the medicines in empty stomach, I always vomit. (Badrul, 55 years, Malay male patient)*

Conversely, some patients expressed that they did not find multiple medication taking a problem as they have "got used to it" or they did not have any option as they had to take the medication to improve their well-being.

One physician affirmed that the recent availability of fixed-dose combinations of TB medication in Malaysia would be able to reduce the burden of multiple medicines.

> *But now we got the fixed-dose combination...We are already starting in patients now with TB...So patients need to take four to five tablets a day. Last time they take twelve tablets a day. (Rahmat, physician, chest clinic)*

On the other hand, another physician mentioned that despite the availability of fixed- dose combinations, not all patients were privileged to get the fixed-dose combination due to the higher cost, and reiterated the burden of multiple medicines.

> *We manage to bring the fixed- dose combination in... it is not very popular...we are not giving to everybody...so the pill loads... is always a problem. (Chong, physician, chest clinic)*

According to the same physician, only certain patients who have problems tolerating multiple medicines were given the fixed-dose combination of TB medication.

### 4.3.1.3 **Concerns about drug interactions**

Some patients were concerned about drug interactions when multiple medicines were consumed. For instance:

> *When I take the medicines for diabetes, it disturbs the TB medicines. Very fast, I'll feel like vomiting. (Zaman, 50 years, Malay male)*

Some believed that drug interactions may cause other health problems. For instance, one patient perceived that the pain-killer that he used to take became ineffective after he started taking TB medication.

> *Last time, when it is painful, I go to the pharmacy to buy the small pill, in two hours it will be okay. Now after taking the TB medication, there is no effect...I even had to take two pills. (Choo, 53 years, Chinese male patient)*

When health care professionals were asked about whether they experienced any drug interactions in TB and DM management, a physician said *'I'm not aware of any drug interactions in TB and DM'*. Similar account was given by another physician.

> *...what differences from diabetes TB patient to other TB patients? Well, I don't know whether they are different in the developing side effects or drug interactions ... not sure about that... (Chong, physician, chest clinic)*

### 4.3.1.4 **Medication confusion**

Despite receiving labelled medication, most of the patients do not know the name of their medication. However, they were able to describe their medication based on the shape and colour with limited knowledge on indications of the medication.

> *I'm not sure what is it for, I just take them (Ooi, 63 years, Chinese male patient)*

> *The diabetic medicine is elongated in shape and it is white in colour and another one is white round tablet. There is another one for cholesterol which is a heart shape tablet (Ramamany, 56 years, Indian female patient)*

Since there are many medicines that have the similar colour and shapes, patients reported that they were confused with some of the medication (e.g. glibenclamide and perindopril have similar colour and shape). Although some may know medicines by name, confusion arose due to the strength of the medicines. A higher number was equated with a stronger medicine for which the patient believed a smaller amount should be taken. One patient said that he was confused when a different prescription for DM was issued but he did not voice or discuss his concerns with his physician.

> *I was recently prescribed with gliclazide and metformin. Prior to gliclazide, I was taking glibenclamide. I don't know why the dosage of gliclazide was 80mg when the glibenclamide was 5mg. I think the physician had made a mistake, so I only take one tablet instead of two (Ejass, 64 years, Malay male patient)*

Researcher's reflection

I felt that it was important to clarify that gliclazide and glibenclamide are two different drugs and therefore the doses are not equivalent. I spoke to the patient after completing the interview. He said that he did not realise that the medication were different and that he now understood and would start taking his medication as prescribed by the physician.

### 4.3.1.5 **Necessity and efficacy of medication**

Despite all the challenges with having to take medication, patients talked about the importance of medication especially TB medication in curing their disease. They expressed the efficacy of TB medication which was based on the improvement in their health condition. They gained appetite and some felt energised. They also reported that they started to trust TB medication due to the fast recovery.

> *When I was first diagnosed with TB, I just don't feel like doing anything. I feel very lazy. But now after taking the medicines, I'm feeling much better. (Sharon, 42 years, Chinese female patient)*

> *Oh yes, I take my medication daily. I'm excited now. I can eat. There's no blood anymore. I'm so relieved. (Nusa, 53 years, Malay male patient)*

Pavithran talked about how his physician linked the necessity of taking DM medication to avoid the relapse of TB.

> *Doctor said lot of improvement (chest x-ray)...He told me to continue my TB medication. Then he said "Diabetic one, you must strictly take, you leave it you will get back to TB". (Pavithran, 49 years, Indian male patient)*

When health care professionals were asked whether patients tended to prioritise their treatment given the presence of other comorbidities, one physician reported that he did not know what patients prioritise but the message that TB can be cured had been stressed.

*I don't actually know what they prioritise. But I think we already told them that TB is curable and TB is infectious...so we stress that they should be taking medicines regularly and should be compliant to the medication. And we mentioned that whatever disease that they already have, TB is also very important because it is curable. But what the patient prioritise, I'm not so sure. (Rahmat, physician, chest clinic)*

Patients talked about the necessity of TB medication in greater depth as compared to DM medication. Although, they reported that they took their DM medication regularly, they did not disclose how they felt after taking DM medication in detail as compared to how they described the improvement in their health after taking TB medication.

### 4.3.2 Management of TB and DM

#### 4.3.2.1 Longer duration of TB treatment in DM patients

Physicians reported that because TB and DM patients presented with more cavities in their lungs as compared to TB only patients, the former group had to undergo a longer duration of TB treatment. Unlike patients with TB alone who mostly required six months treatment, those with TB and DM were reported to need an additional three months.

> *...my patients are always taking the same TB dose and everything. Only thing I notice about TB and diabetes is that I give them longer treatment. Nine months...Prognosis if you ask me is good. Only thing patients with TB and DM, DM patients tend to have very bad x-rays when they come and see me. They have got lots of cavities... (Rahmat, physician, chest clinic)*

Most of the patients did not express any difficulties with regards to longer duration of treatment. However, some patients informed that they did not know that they had to take their medication for nine months. Some patients took comfort with their improving health condition and that motivated some of them to continue their treatment.

On the other hand, those who had a relapse of TB believed that they were unlucky and had no other choice rather than repeating the treatment process.

> *It's my bad luck, I've got it (TB) again for the third time. (Ooi, 63 years, Chinese male patient)*

Some believed that consuming medication for a long duration will be detrimental for health. As one mentioned:

> *If you take medicines for a long period, you may fall ill. (Goh, 51 years, Chinese male patient)*

### 4.3.2.2 **Delayed initiation of TB and DM treatment**

Late treatment-seeking behaviour was reported to be a major obstacle for early initiation of TB treatment. A physician reported how he regularly observed patients presenting with severe stages of TB. He also believed that the awareness to seek early treatment is lacking.

> *...I go to the district hospital every month and I can see four to six new cases. Probably half of them are at very severe stage...they have high tolerance in their symptoms...they seek other sort of treatment before they come to us and those who smoke they usually cough with or without infection. So they think it is part of their smoker culprits and that don't seem to alert them that much... they have been in their house, coughing for months, come with very bad destroyed lungs, even young population, I think education play a very important role... the awareness definitely not good enough. (Chong, physician, chest clinic)*

TB and DM patients in this study confirmed that they were diagnosed with TB at the hospital after coughing for a long period of time. They also mentioned that they first sought treatment for cough from private clinics or pharmacies.

> *When I first had TB, I coughed, coughed blood, real fresh blood... after one week I went (private clinic), he (doctor) said 'panas' (hot), he gave medicines, but it never went off, only then I went to see the doctor in the health clinic, x-ray, he said I had TB. (Nusa, 53 years, Malay male patient)*

When the same patient was asked of why he did not present to the hospital despite coughing blood. He replied:

*Oh you know, I thought it will disappear on its own. I thought the pain will be gone in a day or two. I am still young. (Nusa, 53 years, Malay male patient)*

Another patient revealed how he prioritised family affairs than seeking early treatment.

*Never mind, that's what I thought. After a few days I can go, because my son is about to get married. I would like to wait until the big day is over. I can always go and check. I was just worried that I may not make it for the wedding if I go to the hospital so as long as I could tolerate it, why must I check first. (Yuen, 64 years, Chinese male patient)*

Many patients reported that DM was diagnosed only when they presented to the hospital for some other problems. For example:

*I didn't know. I only knew when my leg was injured. I do not have any sensation on the other leg. Since I injured my leg, I came for a check-up. They told me that this whole area (pointing to his leg) was gone. Then, they amputated my leg. (Jeyaraj, 52 years, Indian male patient)*

Four patients reported that they discovered that they had DM when they went for their eye check-up or surgery. Another four patients were diagnosed with DM when they were screened at the chest clinic following the diagnosis of TB. Therefore, many did not know that they had DM until it was detected at the later stages.

Some patients lived in denial and doubted the diagnosis of TB. For example, Veeramuthu did not inform his family members regarding the diagnosis of TB, although he had been on TB treatment for 2 weeks.

> *I yet to tell anybody at home...I have not brought anyone for check-up. (Veeramuthu, 50 years, Indian male patient)*

Prior to the diagnosis, he had been coughing for more than a month. He kept saying that he could not understand how he developed TB. He said that he had quit smoking 5 years ago and he was still doubtful whether the diagnosis of TB was correct or not. Therefore, he was reluctant to inform his family members. Denial about the disease could also lead to delayed initiation of treatment in affected family members.

Nurses also reported that Malay and Indian patients tended to be more secretive about their disease and do not refer family members for screening.

> *But when it comes to some of the Malay and Indian community, there are many incidences where patients do not give correct contact address and they also don't refer their family members for screening. In fact they tend to hide them...Even when the whole family is infected, there will be some who will be quiet and silent about it. (Ros, nurse, chest clinic)*

Nurses reported that Chinese patients were generally more vigilant and took extra precautions to make sure that all family members were screened for TB.

*The Chinese are very afraid of TB, so they are extremely careful...sometimes when there is one family member who developed TB, we usually tell them that close family members should be screened, at times 20 or 30 people will come for screening, even those who do not stay together will come...they are very scared. But the Malays and Indians are not like that. The Malays, they will go and see the 'bomoh' (Malay traditional healer) based on their own beliefs. (Rohana, nurse, chest clinic)*

### 4.3.2.3 **Poor record keeping**

Poor medical and medication history taking and poor record keeping were observed. Three patients had previous history of cataract surgery but they did not inform their physicians treating their TB as they were not asked about it. However, one patient reported that he had informed his physician that he had had an eye surgery before the initiation of TB treatment but he was prescribed with ethambutol and he was on treatment for one month. It was only when the eye physician came to know about it, the recommendation to stop ethambutol was made through a letter to the respiratory physician.

> *I informed the doctor that I had an eye operation...Even that day, the doctor told me that this medicine (ethambutol) can cause eye problem. But the medicine was given to me. Then one day, I went for an eye check-up and the doctor said 'Don't take this medicine, you can't take this medicine'. So he wrote to the doctor over here...Only then the medicine was stopped. Even after stopping it, it took me nearly one week to get my vision improved (Yuen, 64 years, Chinese male patient)*

Similarly, two patients informed that they had history of gout but it was not documented in their medical records.

Researcher's reflection

As I also viewed patient's medical record prior to the interview, I realised that medical and medication history was incomplete. I managed to gather further information about medication especially for comorbidities during the interview session.

### 4.3.2.4 **Patient-physician communication barrier**

When physicians were asked whether patients complain about their medication, one physician reported that patients prefer to communicate their problems to the nurses. Physicians believed that patients communicate better to nurses since they provide DOT and also due to time limitation during medical consultation.

> *They don't complain to me. Probably they complain to my nurses but not to me. Because the treatment is given by the nurses...To them probably I suppose they complain. They never tell me anything probably we do not have much time to talk to the patients. We see them in appointment. They probably might tell the nurses about all the side effects. (Rahmat, physician, chest clinic)*

Nurses explained that although they advise patients to tell their health problems when they visit their physician, patients tended to complain about their problems to them rather than informing their physicians.

> *Before seeing the doctor they will tell us. 'Nurse, I feel itchy, I feel this and that'. We tell them to tell the doctor whatever they feel, but after seeing the doctor, they come back and tell us again. Sometimes we ask them why they did not tell the doctor? That's the problem, patients prefer to tell us. (Ros, nurse, chest clinic)*

### 4.3.2.5 **The ambiguity of DM management in TB patients**

Two physicians from the chest clinic were asked whether they treat DM in TB patients. It seemed that physicians managed DM based on the criteria of 'simple' DM or 'difficult' DM. Both had similar notions that they were capable of treating 'simple' diabetes or in other words manage 'non-insulin' patients.

> *We try not to treat the diabetes here as we are not the real experts. There are experts out there, and if it is simple diabetes which can be easily controlled sugar, then probably we will treat here. Otherwise, people with diabetes especially with complications like chronic kidney disease or some other problem, we will refer them. (Chong, physician, chest clinic)*

> *Diabetes can be treated by me. It shouldn't be a problem. Unless they have difficult kind of diabetes and need insulin therapy and then I refer them to the endocrine clinic. If their diabetes can be given in oral therapy, then I treat them in my clinic. (Rahmat, physician, chest clinic)*

It was felt that more information about the management of DM in TB patients could be obtained if the health care professionals from the endocrine clinic could provide their point of view. Therefore, the idea to interview health care professionals from the endocrine clinic came after completing the interviews with patients and healthcare professionals from the chest clinic. Nevertheless, the physician from the endocrine clinic also mentioned that DM can be treated by the chest physicians and were only referred to them when it was 'difficult'. However she was unsure about the types of assessment that patients with TB and DM receive when they were not treated by the endocrine physicians.

*They (TB and DM patients) should get the same thing...because sometimes, the chest physicians themselves can treat diabetes, and sometimes unless it is very difficult then they will call us. At the time, usually when we see, we will send for assessment, to assess the leg, check the renal profile...that has been our practice. But other physicians attending to these patients, I can't say... Well, if it is not a difficult diabetes, they may remain on the same oral hypoglycaemic agents that they are on, if they are difficult then we will put them on insulin. (Adilah, physician, endocrine clinic)*

Being unclear about the meaning of 'simple' and 'difficult' DM, further questions were posed to Adilah.

*Interviewer: How do you differentiate between simple and difficult because the physicians from the Chest clinic used that as well?*

*Adilah: Yes, it depends on the HbA1c. Most of the time, if their starting HbA1c is more than 9, usually there will be a need of at least two oral hypoglycaemic agents with insulin on board...it's just that if they are already on maximum oral hypoglycaemic agents and the HbA1c is still not well control, still not achieving targets, we would introduce insulin therapy. The aim is to reduce HbA1c to less than 7. So if they are already a diabetic and they have TB, the chances are the glucose control will deteriorate, so it makes more logic to add insulin.*

The importance of HbA1c in order to differentiate 'simple' and 'difficult' DM relates to the importance of having the data in patients' medical records at the TB clinic. Based on the preliminary findings, minimal documentation of medication history as well as laboratory findings was seen. It was indeed unknown how physicians interpret 'simple' and 'difficult' DM

if the HbA1C was not recorded. This issue was also raised during the interviews with the physicians from the Chest clinic.

> *We are doing HbA1c if the patient is only following-up here. We do HbA1C at least 3 to 4 months once...If it's not done then probably it's done in the clinic where they follow-up. (Rahmat, physician, chest clinic)*

The issue of non-documentation or absence of non-TB related data was also mentioned by another physician from the chest clinic. Chong informed that relevant information for non-TB drugs might not be available at the Chest clinic.

> *If you are here, you can get the information for TB, we have all the records here. But the others, we don't keep the records here. (Chong, physician, chest clinic)*

Issues regarding insulin were discussed with the endocrine physician.

> *Interviewer: Is it true that only the physicians from the endocrine department can prescribe insulin?*
>
> *Adilah: Under the general specialties, they can let other doctors to prescribe as well. Yeah we cannot handle too many patients.*
>
> *Interviewer: Is it better to put them on insulin?*
>
> *Adilah: Our patients are very resistant...but if they get TB and they are little bit concerned about their health, then it might be easier to convert them to insulin.*

### 4.3.2.6 **DOT and the burden of attending multiple clinics**

Discussions regarding the management of TB via DOT revealed that almost all health care professionals felt that DOT was a good strategy to ensure adherence to TB medication.

> *DOTS is good for many things ...When they come and see the doctors or nurses, they can get the medicines everyday for compliance and at the sometime also the nurses can ask the patients for side effects of the drugs too and the third thing this can also prevent MDR-TB in this patients. So in general, if you ask me definitely it is good for the patients. (Rahmat, physician, chest clinic)*

> *As for me, I can see patient taking medicine every day, make sure they take medicine every day, it's good, if they don't take medicine for one day we can trace and we prevent the disease from spreading... (Ros, nurse, chest clinic)*

Unlike health care professionals, not all patients were in favour of DOT. Some patients expressed that they will be able to self-supervise their treatment. The following quotes express how strongly patients feel about the necessity of TB medication and how they would like to negotiate with the health care professionals to allow self-supervision of TB treatment.

> *Because I asked. Earlier when I asked, they say cannot, they say that I'll throw my medicines. But I take my medicines daily. I won't forget, because I know how it is after I take the medicines...I want to ask the doctor, at least give me (TB medication) every three or four days. It will be easier for me. (Long, 63 years, Chinese male patient)*

*Even though I'm poor, my life is very important, so definitely I'll take my medicines. I won't lie, some may just collect the medicine, not to eat but to keep. I would like to discuss and see. I'll say my life, I'll take care of it. I'll definitely take my TB medication. It is like God giving me to take. If I don't take, I'll die. (Tim, 78 years, Chinese male patient)*

Few patients reported that it was important to visit the clinic daily for DOT due to the complex treatment regimen. One patient said:

*I feel that this is a very effective method. Because the medication is a lot. Even if I take it at home, it is difficult for us to follow the prescription (Zainal, 50 years, Malay male patient)*

Another patient stressed that DOT provided the opportunity to get better care.

*Doctors must check weekly and let us know, doctors must get to know what is going on and we want to discuss with doctors too (Yuen, 64 years, Chinese male patient)*

The same patient also expressed willingness to travel to the general hospital for DOT although there was a health clinic closer to his home. This was due to the impression that nurses at the general hospital were better trained and were more knowledgeable about multiple diseases compared to nurses in health clinics, which meant that more information could be obtained from the general hospital nurses.

*They (nurse at health clinic) also provide DOT in the health clinic, but sometime the missy (nurse) can't answer, she doesn't know anything, if there's a lot of disease, she can't take care of all. (Yuen, 64 years, Chinese male patient)*

Yuen also viewed DOT as an avenue that provides peer support through meeting other patients.

*It is much better to come over to GH (general hospital)... to meet other friends (TB patients), we have to take good care, we get to see others getting better (Yuen, 64 years, Chinese male patient)*

Health care professionals preferred patients to have DOT at the clinic. However, patients will be assessed whether they were suitable candidates for DOT.

*I prefer that they take their medicines everyday in the clinic...I feel if they take in their house, somebody responsible must be there to see the patients taking their medicines every day. Unless those who are ill and they can't come to the clinic everyday (Rahmat, physician, chest clinic)*

*We try to ensure DOTS for everybody but sometimes it's not quite possible if they are crippled by disease or...(Chong, physician, chest clinic)*

Some patients accepted DOT although there were some strong resentments projected. For example:

*I do not have any problem with that (DOT) because I'm self-employed. But I feel like being punished because I have to come every day. I'm not a small kid anymore. I'm a grown-up (Najip, 54 years, Malay male patient)*

Nevertheless, some health care professionals and patients also reported that DOT was felt to be inconvenient as patients have to visit the clinic everyday and it also involves the participation of other family members.

*I think DOT is a good way to control TB but again it's not very convenient or patient friendly kind of treatment. Patients have to come to clinic every day. Get the family involved to bring them (Chong, physician, chest clinic)*

Although it was agreed that DOT could be troublesome to some patients, one physician reported that patients were given the flexibility to choose their appointment time.

*We are flexible of the patient's time to make sure that patient can come every day for DOT and the time is up to them to decide (Rahmat, physician, chest clinic)*

Nevertheless, health care professionals also acknowledged the burden of having to attend multiple clinics due to comorbidities. One physician reported that patients have long waiting time in other clinics as compared to chest clinic.

*The only barrier is...for TB it is not a problem because TB patients they come to my clinic everyday and they don't have to wait. They get the treatment and they go home straightaway. So there's no waiting time, there's no wasting*

*time there for the patients. Only problem is that when they come to other clinics, they have to wait for a long period. They may have to take their diabetic medicines in medical clinics or cardio medicines in cardio clinic. There they have to wait very long. So the barrier is the long waiting time. That's all... Long waiting time to see the doctor and long waiting time to get the medication in the pharmacy. (Rahmat, physician, chest clinic)*

*Our clinic days do not coincide, sometimes they have to come on different days. (Adilah, physician, endocrine clinic)*

Nurses also reported that patients complained about having to make various visits to different clinics on different days.

*You know they have to come so many times, if they can make it on the same day, like in the morning they come to chest clinic and in the evening they go to cardio clinic or something, then they will only have to come once which will be easier for them but unfortunately clinic days are different. (Ros, nurse, chest clinic)*

From my own observation, patients came for their DOT and then went back home to take their food before consuming their DM medication. Some of them expressed that they experienced giddiness which could have been due to hypoglycaemia. Some patients had to walk back home after their DOT or follow-up visits. Nurses reported that some patients complained that it was difficult to come for daily DOT as they could not afford to pay for the transportation.

*Sometimes there are patients who will tell, ' Nurse no money'...to come by taxi it will cost RM 30 and they can't afford it. (Rohana, nurse, chest clinic)*

### 4.3.2.7 **Self-management and incorporation of traditional remedies**

Unlike TB, DM management depended on self-management. Some patients reported that they sometimes forget to take their DM medication especially at night. Health care professionals reported that non-adherence to DM medication were commonly seen.

> *Some patients still don't like to take drugs, they are not regular, we have patients that they will come and tell us that they take their medicines for 3 to 4 days, they feel better then they off it...But there are quite a number of patients, that we do know that they are not taking their medicines on regular basis, or not compliant to injections, you know from three they might drop the injections to two and try to get away with it, so HbA1C control is very difficult especially patients who are not well motivated (Adilah, physician, endocrine clinic)*

A nurse reported that patients feared insulin injections and preferred insulin pens as compared to conventional needle and syringes.

> *Most of the patients at the beginning, they are reluctant to take insulin, because they have the fear oh every day I must inject, they got this fear, they prefer taking tablets, even though there are many tablets they don't mind. Some will get used to injections...but some still so reluctant...they will complain to us that problem this problem, even when there is no problem they will complain that they cannot use the needle...There will be a reason for them to make the doctor stop the insulin...but now I think few patients ... we switch to pen, they are okay with it, because it is easy to carry, it is already there...just take and then inject. Whereas the needle and the syringe, the old fashion type,*

*they have to keep it clean, you know all that basic procedure... (Manjit Kaur, nurse, endocrine clinic)*

One patient reported how he requested for changing insulin to oral hypoglycaemic agents after a bad experience with the use of insulin.

*I used to take insulin injections. There was once the needle broke. I told them (doctors) that I dare not take insulin any longer. So they replaced it with pills. (Veeramuthu, 50 years, Indian male patient)*

None of the patients interviewed reported owning a self-monitoring glucometer. The majority of patients indicated that their blood sugar was only checked during their follow-up visits at the DM clinic. Two patients reported that they have checked their blood sugar at the community pharmacy. For example:

*Interviewer: Do you check your sugar regularly?*

*Mydin: Not really. But I take my medicines regularly. At times, I check in the pharmacy. If I pay them RM5, they will check for me (Mydin, 72 years, Indian male patient)*

When patients were asked whether they knew their current blood sugar level, some reported that they don't know, some said that their sugar level was lower than what it was when they were first diagnosed with DM but the blood sugar level was still uncontrolled and only two patients reported that their blood sugar level was normal during their last check-up.

*I think that time, slightly high about 16...Now I don't know (Pavithran, 49 years, Indian male patient)*

*Last time it was 12 to 13, recently it was about 9 plus (Hakim, 55 years, Malay male patient)*

*When I first checked, it was 19, I think now it is about 4 or 5 (Jeyaraj, 52 years, Indian male patient)*

Some patients talked about the fluctuating nature of their blood sugar levels based on food intake and exercise.

*Those days the sugar level fluctuates because I used to eat a lot and it will be high, if I eat less then it will be low, so it goes up and down, it was never quite the same, so it all depends on what I eat, when I eat more the sugar goes up so I have to be careful with what I eat (Long, 63 years, Chinese male patient)*

*Now it is about 9 or more, previously it was more than 12. Then once I started exercise and worked hard, it went really low and the doctor said that I don't have diabetes any longer... but later I got it again (Choo, 53 years, Chinese male patient)*

Some reported that they had changed their diet and began to exercise.

*I exercise and control my food. Morning, I take oats, afternoon I take brown rice and at night, I take oats (Sharon, 42 years, Chinese female patient)*

Some patients said that they abstained themselves from eating certain food items (e.g chicken, pork, eggs, potatoes) that they believed could worsen either their TB or DM. When patients were asked about their diet, many reported that they reduced their intake of rice. Some patients claimed that they only ate rice in the afternoon and had a light diet at night. When they were asked of what they meant about light diet, some said that they ate noodles or burgers. For example:

> *Now I don't take much rice. Even if I take, I only take it once a day...At night, I eat chicken burger. (Badrul, 55 years, Malay male patient)*

A physician explained that patients have difficulties in sticking to diabetic diet recommendation.

> *I think the major factor especially in our local context here is food, our high carbohydrate diet is very difficult for our diabetes patients, asking them to change the lifestyle, reducing their food intake, carbohydrate intake is very difficult. (Adilah, physician, endocrine clinic)*

Some patients tried to self-medicate themselves by trying herbal or traditional remedies prior to being diagnosed with TB.

> *I look at my body, I'm not eating like before, the Chinese people will say that it is due to 'heat', try Chinese medicine first (Yuen, 64 years, Chinese male patient)*

Some patients believed that cough was caused by 'heat'. The term 'heat' is commonly used among Malaysian people regardless of their ethnic background. 'Heat' or 'hot' is assumed to be a condition that was caused by either the environment (hot weather) or the types of food that was consumed. Certain food was believed to have 'hot' or 'cold' properties. The example below shows, how another patient regarded that the cough was due to drinking something which had 'cold' properties and in order to reverse the condition he was recommended to consume beer which was believed to contain the 'hot' property.

> *I cough a lot at night. One day, I took 'mohroo' (Indian yogurt drink). Since I like it so much, I took 4 to 5 glasses. Due to that, my friend told me that I will keep on coughing and suggested that I should take Tiger (beer) to make myself warm and I will be able to sleep. So I took it and the coughing was less (Veeramuthu, 50 years, Indian male patient)*

Many patients stated that they had been using traditional or herbal remedies mainly for treating DM. Patients who perceived the benefit of using traditional or herbal remedies continued their practice. Mostly Malay patients reported consuming herbs like *Misai Kucing* (*Orthosiphon stamineus*) *and Daun Cerita/Hempedu Tanah/Hempedu Bumi* (*Andrographis paniculata*) to treat DM.

> *For diabetes, I drink Hempedu Tanah. That bitter Hempedu Tanah, I soak the leaves, drink weekly once...no bone pains, no tiredness, numbness, well, it might work for some but not for all. (Hakim, 55 years, Malay male patient)*

Only two patients spoke about using traditional or herbal medicines for TB. One patient explained that he boils the leaves that are used to wrap Malay 'ketupat' (rice cake) and he drinks the water in order to treat TB. Another patient said that he took Chinese Medicines

when he started TB treatment but has stopped taking it as he was unsure of its effectiveness. He informed that he did not know the name of the medicine.

> *When I had TB, I had to take. It is in a powder form, I'm not sure of the colour. I just consume the powder once daily (Yuen, 64 years, Chinese male patient)*

Similarly, some patients reported that they had stopped using traditional or herbal remedies as they were unsure of the benefits or believed that it could not be trusted.

> *I don't take Chinese Medicine anymore. Earlier I did try for diabetes. But I only drank a bit, I don't know can or cannot, but I can't trust the Chinese Medicine. This medicines (hospital medicines), yes I trust, but the one from the sinseh (Chinese Medical Hall Practitioners) I can't trust and the one on the streets, you can't take it, because it is dusty (Long, 63 years, Chinese male patient)*

## 4.4 Health care professionals' perspectives on the expanding role of pharmacist

The role of pharmacists in Malaysia is expanding with the introduction of new services such as MTAC. This section describes the views of the health care professionals on the existing pharmacist-led MTAC and followed by opinions on the potential role of pharmacist in the management of TB and DM. Themes and subthemes are presented in Table 4-3.

Table 4-3 Themes and subthemes regarding MTAC and the potential role of pharmacist

| Themes | Subthemes |
|---|---|
| **Perspectives on pharmacist-led MTAC** | Provision of pharmaceutical care<br>Pharmacist-physician interaction<br>Accessibility and timely delivery of service<br>Enhanced pharmacist-patient communication<br>Satisfaction |
| **Potential role of pharmacist in managing TB and DM** | Educate and counsel patients |

### 4.4.1 Views on pharmacist-led medication therapy adherence clinic

#### 4.4.1.1 Provision of pharmaceutical care

When pharmacists were asked about what they actually do in MTAC, they responded that they provided pharmaceutical care service and the main goal was to promote adherence to treatment. They described their activity that begins with a thorough medication history taking.

> *What we do is, we do a detailed patient medication history so that we know exactly how they are taking their medicines and not just following the prescriptions...First we see how they are taking it, why they are not taking it and problems with the medicines. (Elvin, pharmacist)*

Subsequently, they also described about having structured patient education and counselling programmes that they have developed for DM and HIV patients. The programme is delivered in 8 visits for DM patients and 10 visits for HIV patients.

> *They see us for eight visits. When they come here (MTAC), we will teach them something about diabetes, hypertension, cholesterol and all the essential things, which we have developed the syllabus, so that they can actually learn while they wait ...After four visits, we actually do revision and counter checking that patients know what they are taking. So after they complete these eight visits, hopefully their adherence will be better and their knowledge will be better and hopefully it translates to better results in HbA1c. (Elvin, pharmacist)*

*We have education kit to educate patients about HIV, what are the side effects, we have the drug chart, so the patient can show us which mediaction that their taking, whether the patient can identify what they are taking...(Ruhaila, pharmacist)*

Pharmacists also explained that they had to address patients' medication-related concerns.

*They always hear what other people say...they get confused and scared. For example, one patient said 'Perindopril is bad for kidneys. I've got kidney problem, I've microalbuminurea, so should I be taking this?' So we have to keep on explaining this sort of things. Because doctors don't explain this kind of things, so it's a bit hard for us. (Mei Ling, pharmacist)*

Another pharmacist reported how she managed patients with low literacy level and patients with visual impairment.

*Some patients, they can't read and we have to draw for them sun, moon...and then the problem is some of them progress to retinopathy and some become blind... I did have patients who were blind and on three types of insulin, mostly pens...So I drew certain shapes like round, moon and triangle and make sure it is something that the patients can touch and I stick it on a sticker cardboard and then stick it on the insulin pen and the box as well. (Mei Ling, pharmacist)*

When pharmacists were asked about the amount time spent in consultation, they replied that it ranges from ten to thirty minutes with longer sessions at the first visit and shorter sessions during follow-ups.

### 4.4.1.2 **Pharmacist-physician interaction**

Pharmacists believed that they have gained more knowledge, experience and confidence through practice and interactions with physicians. At the early stages of the MTAC programme, pharmacists did not have a separate counselling area or room. At this point, they used to share the clinic session with the physician. Although the lack of space was found to be a limiting factor, it provided the pharmacists an opportunity to observe how physicians communicate, counsel and do medication history taking.

> *Sometimes I observe how the doctors talk to patients, how they talk to the patient about their medication... (Ruhaila, pharmacist)*

Almost all pharmacists echoed that they *"learnt a lot from doctors"*. Being in the same setting with the physician provided the pharmacists with a unique inside look at how physician-patient interaction happened. Not only did the pharmacist learn from the physician, they also found areas where they could improve counselling for patients. In addition to picking up skills from the physician, a further benefit from this setup was pharmacists taking opportunities to improve patient adherence by filling in the gaps that occurred during physician-patient interaction.

It was also found to be convenient for the pharmacists and physicians to work as a team in making decision on patient's drug therapy. For example:

> *Double check of drugs. Here our pharmacist will tell the doctor, 'This patient is already on this and that' ...The doctor will say 'Ok... I'll cancel it or ok I'll add this'. So you see, they take away a big part of the doctor's role. So the doctor can see the patients for the other things and ... don't have to waste time*

*asking them these questions...He (doctor) can concentrate on something else to ask the patients. (Manjit Kaur, nurse, endocrine clinic)*

Despite the fact that these pharmacists are now 'independent' (having their own clinic/counselling area), the exposure and 'training' happened while they were sharing a clinic with physicians.

### 4.4.1.3 **Accessibility and timely delivery of service**

Most MTACs are strategically located next to the physicians' clinics and provided patients the convenience to access and consult the pharmacists. The main contribution of MTAC was the timely delivery of service that focused on effective utilisation of patients' waiting time. Patients were referred to pharmacists while they waited for their physicians' appointments and consequently patients waiting time was managed effectively. As one pharmacist mentioned:

> *We will see the patients before they see the doctor to assess the patients' adherence, compliance, especially for the follow-up counselling. (Ruhaila, pharmacist)*

Another pharmacist reported that they would usually go to the clinic earlier than the doctors to see patients and at times patients were referred to them.

> *We will go earlier than the doctor to the clinic and sometimes if there is too many patients and we can't really cover and see all the patients and those patients that the doctor thinks need to see the pharmacists first, then they will send them out for us. (Mei Ling, pharmacist)*

In addition, pharmacists were able to make immediate clinical recommendations and document pharmaceutical care issues in the patients' medical records before the patients were seen by their physicians. This helped the physician to take further action. The MTAC strategy of counselling patients while they waited to see the physicians was highly commended by health care professionals as patients do not have to spend additional waiting time at the outpatient pharmacy to consult the pharmacist there. However, it should be noted

that in most out-patient pharmacy settings, due to the high number of patients, pharmacist do not have the time to counsel patients in detail.

> *Although they have pharmacists to do counselling (at the pharmacy), is this available for the patients at this time? Patients have to wait, they have to go back to work...and those are hours they don't get paid, so when they are here (MTAC) while waiting to see the doctor, they see the pharmacist, then everything is done. (Manjit Kaur, nurse, endocrine clinic)*

#### 4.4.1.4 **Enhanced pharmacist-patient communication**

Enhanced pharmacist-patient communication was linked with a separate consultation area, a longer consultation period and regular follow-up counselling sessions. Pharmacists believed that pharmacist-patient communication was better as they had more time with the patients, and hence more in-depth information been gathered. In addition, pharmacists believed that patients felt more comfortable to share their thoughts and experience with the pharmacists when compared to their physicians. As one pharmacist narrated:

> *Probably they don't tell the doctor, but they tell us a lot these days. (Elvin, pharmacist)*

Pharmacists reported that prior to having a separate counselling area of their own they used to counsel the patients in the physician's clinic for more than a year. It was viewed that such setting inhibited the patients from communicating openly. During the consultation with the physicians patients were seen to be rather quiet. It was thought that some patients feared that they might be reprimanded by the physicians if they were found to be non-adherent. For example:

> *Actually our patients are more open to us. They can tell us whatever they have, I mean those problems and when they skip their medication or not comply or anything, they will actually tell us...Because they scared if they tell the doctor they will get scolded, so everything they will tell us. And sometimes when we are short of room, we will sit together with the doctor and the patients will just keep quiet without saying anything, then when we go outside, they will start talking. (Mei Ling, pharmacist)*

*But one thing, if pharmacist sits with the doctor in the same room, patients don't seem to talk much. Compared to if pharmacist sits in their room, its better, the patients tells us more... (Ruhaila, pharmacist)*

The provision of structured patient education and regular follow-up counselling sessions by pharmacists were seen to be effective in building a good pharmacist-patient relationship. As one said:

*We actually have more in-depth information because we spend more time...because they see us every month, become some sort of friends. (Elvin, pharmacist)*

Enhanced pharmacist-patient communication was observed when the pharmacists began their service in a separate clinic. Patients also showed a higher level of honesty in revealing issues related to adherence and that enabled pharmacists to provide more tailor made counselling for each patient.

#### 4.4.1.5 **Satisfaction**

Pharmacists narrated their experiences of running the MTACs with enthusiasm and satisfaction as they felt that their contributions were valued by patients and other health care team members.

> *I think the doctors appreciate what we did so far. (Ruhaila, pharmacist)*

> *Some of the patients have commented that pharmacists are concerned about them and therefore they take more responsibility towards their problem. (Adilah, physician, endocrine clinic)*

Pharmacists were also seen to be able to contribute to disease management by reinforcing education.

> *Yeah, I think it definitely improves patient care when we have the pharmacists here ...the pharmacists themselves can explain about the disease if we have not explain to the patients, diabetic education is reinforce at every step of the way...when we see the pharmacists, besides having the adherence to the medication is reinforced, the diabetic education as a whole gets reinforced. (Adilah, physician, endocrine clinic)*

The extended role of pharmacists in conducting the MTACs was well received in improving medication adherence. Both Adilah and Manjit Kaur reported that patients had informed them that they were satisfied with the service provided by the pharmacists. Patients were seen to be more adherent to their treatment. For example:

*Some of the patients have commented that they would like to come back to the clinic. Few minutes when they (patients) are with them (pharmacists), I think they appreciate that and compliance is better and follow up is better, they do not default compared to other clinic. (Adilah, physician, endocrine clinic)*

*After a few counselling sessions, I mean previously, the first time we saw them, their sense of compliance may be 20 or 30% but by the second visit most of them almost 100% compliant. So I think counselling is very important. (Mei Ling, pharmacist)*

### 4.4.2 Potential roles of pharmacists in the management of TB and DM

#### 4.4.2.1 Educate and counsel patient

Health care professionals believed that pharmacists could play a role in promoting adherence to TB treatment by providing patient education and counselling.

> *...we can inform the patient the importance of taking TB drug because some of them are not taking TB drugs properly even with DOT because some of them in the clinic, they give one week one week supply...some of them do not know the importance of TB drug or they just come to collect the medication and go back. Maybe the pharmacists have to educate about TB drugs...Because we do have HIV patients with TB but then they defaulted TB treatment and died because of TB. (Ruhaila, pharmacist)*

> *They can start of by educating patients about drugs, and then the compliance, side effects (Rahmat, physician, chest clinic)*

Although TB education is delivered by the nurses, pharmacists are expected to be able to provide education and counselling related to comorbidities management and resolve medication-related issues.

> *I think they should be involved. Only thing is that, like I said if it is just TB alone, shouldn't be a problem. My people can actually educate the patients... If they have other problem, I think the pharmacists are very important. Comorbidities, drug interactions and side effects (Rahmat, physician, chest clinic)*

Nurses felt that they were capable to manage TB but they lacked the knowledge in providing information regarding medication for comorbidities.

> *Information about drugs, like the diabetes medicines... We are not so knowledgeable you know, sometimes when the patients enquire we are not that sure. We ask the doctor, when we know we tell them, sometimes we are scared that we may give the wrong information. (Ros, nurse, chest clinic)*

> *Because some patients are taking so many medicines, for hypertension, diabetes, heart case. Sometimes when the patients ask, we do not know about the other medicines. For TB, it is ok, we have the charts to refer to, but the others we do not know much. (Rohana, nurse, chest clinic)*

When pharmacists were asked whether they have ever counselled TB patients who have comorbid conditions, some described their experiences of managing TB patients with comorbid DM and HIV.

> *Mei Ling: We do have a few, patients who were admitted in the ward, then when doctors check, it seems that they have this TB, then they will maximize their treatment and everything and then the patients will be sent to the chest clinic.*
>
> *Interviewer: So the chest clinic will look after them rather than the endocrine*
>
> *Mei Ling: Yes*
>
> *Interviewer: Ok. And same for HIV or?*

*Ruhaila: For me I'll see more cases of HIV with TB...I think pharmacist if they want to do something with TB patients, it's because of the toxicity of the TB drug is a lot, can cause hepatitis. This is something that we can start or do something, monitor the side effects, educate patient, drug interactions because TB drugs got interactions with some other drug also.*

*Interviewer: Do they interact with the HIV drug?*

*Ruhaila: Yes, they do. Ok like rifampicin, pyazinamide, ethambutol and isoniazid can cause hepatotoxicity, if you give together with nevirapine, which can also cause hepatitis it can worsen the liver function, so it's contraindicated to be given together. So we have to give the efavirenz. But since rifampicin is cytochrome P450 inducer, we actually have to cut the efavirenz, instead of...we have to give...*

*Interviewer: Quite complex*

*Ruhaila: Hmmm... yeah and then of course with the protein inhibitors, they have interactions as well, so if the patients are having TB, PI group is contraindicated as well. Or if we have to give the PI, then we have to increase the dose...something like that.*

*Interviewer: So it's quite complicated. And I think pharmacists will be a good person for this, yeah*

*Ruhaila: Yeah and I think pharmacists should do that.*

*Interviewer: So the diabetes people with TB, do they have problem with adherence because they have multiple medicines?*

*Mei Ling: But from those patients that I've seen in the ward, when they are first diagnosed with TB, very uncontrolled blood sugar, we will go for insulin first and once the control is very well, they switch back to oral.*

When pharmacists were asked about how pharmacists could contribute in the management of TB and DM, pharmacists proposed the MTAC model.

*Ruhaila: As for me, I know that we can help from what we have done earlier. So I think we can do something like MTAC...The pharmacist will be there to promote adherence, provide education and...*

*Interviewer: So, how do you propose this MTAC to be carried out?*

*Mei Ling: We can do it monthly*

*Ruhaila: Monthly visit is suitable, they will want to see you...If we see the patient every week, it's tough and time consuming. So every month we can see the progress*

*Interviewer: But TB patients come to clinic every day, it's a different dynamic isn't it?*

*Cheng: Probably we can have a meeting once a week, something like that. Because they are coming every day they can always drop by to see us. We can talk to the doctors and inform that pharmacists could help like that.*

Pharmacists believed that MTAC could be a good model that could be adapted for the pharmaceutical care management of TB and DM.

## 4.5 Discussion

This exploratory study has unveiled a number of pharmaceutical care issues related to TB and DM from the patients' and health care professionals' perspectives. It has also provided some insights into the perceptions held by health care professionals with regards to pharmacist-led MTAC clinics and the potential role of pharmacist in the management of TB and DM. The following discusses the key findings of this study.

Nausea and vomiting were the most commonly reported adverse effects that bothered TB and DM patients. Although, nausea and vomiting have been reported to be common adverse effects of TB treatment, a physician in this study confirmed that a higher incidence of nausea and vomiting were seen in TB and DM patients when compared to TB only patients. DM patients are more likely to have gastroparesis (delayed stomach emptying) that could induce nausea and vomiting (Park. M. I. & Camilleri, 2006). Metformin is also known to cause gastrointestinal problems (Bolen et al., 2007; Campbell, et al., 1996). As such, TB and DM patients might be at increased risk of developing nausea and vomiting due to the complex interplay between the underlying pathological condition and the combined adverse effects of both TB and DM treatment.

Besides nausea and vomiting, patients reported several other adverse effects (e.g. visual disturbances, painful toes and ankles) that may have not caught the attention of the physicians. This was evident when one of the physicians regarded nausea and vomiting to be the only problem associated with TB and DM while another physician reported that he was not aware of any adverse effects that was commonly seen in TB and DM patients. While some TB and DM patients may not have any specific adverse effects they may have some additional problems that may increase the risk of them developing adverse effects to medication. For example, complications in DM patients such as retinopathy could also potentiate the risk of developing adverse effects. A number of patients in this study had history of cataract surgery which might have been attributed to DM. Although all TB patients need to have their visual

acuity checked prior to the administration of ethambutol, failure to ask about the history of cataract surgery and the failure to document past medical history in patients' medical record may put the patients at risk of developing preventable adverse effect. This was obvious when one of the patients in this study with a history of cataract surgery reported blurring of vision due to ethambutol. This problem was detected by the patient's eye physician and recommendation to stop ethambutol was made. Patients may not disclose their past medical and medication history if they were not asked about it. Another patient in this study reported that he developed symptom that was similar to gout when he started TB treatment. However, he was not asked about his past medical history and he did not disclose his problem to his physician. This patient's gout could have been precipitated with the use of pyrazinamide. Therefore, health care professionals will need to be extra vigilant when it comes to managing TB patients with comorbidities. There is a recognised need for a thorough medication review.

The patients who experienced adverse effects of medication in this study learnt to cope with the medication or attempted to alleviate the adverse effects particularly nausea and vomiting by not taking their TB and DM medication together or administering medication with some food. One physician reported scheduling TB treatment to be administered at night to reduce the severity of nausea and vomiting. Likewise, another study conducted with HIV patients reported that patients eventually learnt to adjust their medication regimen in response to adverse effects like nausea and vomiting and developed strategies for alleviating the problem on their own or in consultation with their doctor, such as taking the medication at night (Remien et al., 2003). It is clear that patients need to be reassured to continue with their treatment and suggestions to reduce the severity of adverse effects are a necessity.

Besides having to take multiple medicines for TB, patients in this study were also on multiple medicines for DM and other comorbidities. Although fixed-dose combinations of TB medication may solve some of the burden of multiple medicines, they were not widely prescribed in the hospitals studied during the study period. The burden of consuming multiple medicines remains a major challenge to concomitant treatment. Concurring with the findings of this study, others had reported that patients have difficulties in consuming multiple

medicines on an empty stomach (Gebremariam, Bjune, & Frich, 2010; Hansel, et al., 2004; Marra, et al., 2004) and some were afraid of taking multiple medicines as some patients associated a high number of medicines with potential harm to the body and a higher risk of not tolerating the drugs (Gebremariam, et al., 2010; Townsend, et al., 2003).

Despite receiving medication with their names labelled on their packages, the majority of patients in this study were unable to name their medication. However, they were able to describe their medication based on shape and colour. A national survey on the use of medicines by Malaysian customer revealed that more than half of the respondents were unable to identify their medicines trade or generic name (Pharmaceutical Services Division., 2009). Low health literacy level and language barriers could also be a hindrance for patients to confidently discuss their concerns about medication with their physicians. Patients may feel inferior in terms of their knowledge and may not express their concern. The reason patients do not discuss issues with their physicians included embarrassment, assuming that the topic was less important, lack of trust and lack of time (Mohd Ali, 2009; Piette, Heisler, & Wagner, 2004). It is highly recommended that physicians spend more time discussing medication concerns with patients.

A number of patients in this study had not disclosed some of the adverse effects experienced, the use of traditional or herbal remedies and some of their past medical and medication histories to their physicians. There is a need for increased awareness among health care professionals to enquire about alternative practices used by patients according to their cultural background (consumption of traditional/herbal remedies) and the potential drug interactions or complications that may arise due to these practices. A study on the use of complementary and alternative medicine among patients with chronic diseases at outpatient clinics in Malaysia revealed that more than 60% of patients were using some form of complementary medicines and more than half of them were using them for DM (Hasan, Ahmed, Bukhari, & Wei Loon, 2009). It is important for health care professionals to ensure medication safety and recognise potential drug-herb interaction.

A synthesis of qualitative studies on medicine taking revealed that patients do not take their medication as prescribed because of concerns about the medication (Pound et al., 2005). Some patients in this study self-modified treatment regimens without informing their physicians. Previous studies have shown that people make decisions that they believe to be rational, based on their values, beliefs, and knowledge about medicines, their conditions; and the need to perform daily activities (Benson & Britten, 2002; Gordon, et al., 2007; Pound, et al., 2005; Stack, 2009).Thus, health care professionals were recommended to find out patient's perception towards medication, that is, whether medication taking is uncomplicated or they have fears about it (Britten, 1994). Although other studies have cited that patients usually wish to discuss disease and personal therapy experiences with their physician and emphasise their intention to actively participate in the treatment process (Rohrbacher, Marx, Schaufler, & Schneider, 2009), only a few patients in this study emphasised the need to discuss medication-related issues with their physician. Similarly, physicians reported that patients do not usually complain about their medication-related problems to them and believed that they would have probably complained to the nurses as they provided DOT. On the other hand, patients might have felt that physicians knew better about their treatment and might not have raised their concerns unless they were asked about it. Some patients have been described as demonstrating a 'passive' expectation that health care professionals should be responsible for decisions about medication (Lawton, et al., 2008). Physicians are highly regarded and patient-physician relationships are generally based on the faith that patients have in their physicians and that the physicians know what is the best treatment for their patients. Within this continuum, either patients may limit themselves from expressing some of their medication-related problems or physicians may underestimate the patients' ability to communicate in greater depth with them.

Furthermore, patients in this study see their physicians by appointments and the out-patient clinic is usually crowded. Longer consultation period is required in order to provide patient centred-care (Beisecker & Beisecker, 1990). Lack of physician-patient communication due to time scarcity is often blamed to be the barrier to patient care. In order to provide more time per patient, more health care workers and team-based approaches are needed (Dunn, 2003). Although, patients were found to communicate better with nurses, there are possibilities of

patients' medication-related problems not being recognised by the nurses due to knowledge gaps. As such, pharmacist should be considered as part of the team to resolve medication-related problems. In fact, this study also provided evidence that pharmacist-led MTAC provided patients an opportunity to communicate their medication-related concerns more effectively due to longer consultation period and continuity of care.

Despite experiencing adverse drug reactions and having concerns about consuming multiple medication, most patients in this study appeared to be motivated to continue taking their medication especially TB medication. Almost all patients reported feeling better after taking their TB medication and this had encouraged them to adhere to the treatment. This finding is consistent with other research, which suggests that patients' adherence to medication is positively associated with the patient's beliefs about the benefits of taking the drugs (Benson & Britten, 2002; Gebremariam, et al., 2010; Munro, et al., 2007; Naidoo, et al., 2009; Noyes & Popay, 2007). Other studies have also shown how patients' adherence was compromised due to the believe that TB is incurable, or the treatment was not working, or preference for alternative treatment such as traditional medicine (Edginton, Sekatane, & Goldstein, 2002; Gebremariam, et al., 2010; Liefooghe, Baliddawa, Kipruto, Vermeire, & De Munynck, 1997; Munro, et al., 2007; Noyes & Popay, 2007; Rowe et al., 2005). The present study showed that patients who perceived the benefit of traditional medicines or remedies continued taking them in conjunction with TB and DM treatment. This indicates the importance of enquiring about the use of traditional medicines and documenting it in patients' medical record.

Conversely, except for some patients acknowledging that they sometimes forgot to take their DM medication, issues related to adherence to DM medication or the necessity of DM medication were not extensively expressed by patients. It is assumed that patients talked more about TB compared with DM due to the symptomatic nature of TB disease as compared to the silent disease of DM (Murphy & Kinmonth, 1995) and also due to the complex nature of TB management that involves DOT. Moreover, the patients were interviewed at the chest clinic.

Although DOT was perceived to be effective, flexible, provided the opportunity for better care and promoted peer support, some reported it to be inconvenient due to the need for daily attendance at the chest clinic. However, health care professionals in this study were in favour of DOT while some patients preferred self-supervision. Previous study have shown that self-supervision was the preferred option by most people (Noyes & Popay, 2007). A review of randomised controlled trials, comparing DOT with self administrations of therapy, provides no evidence that the routine use of DOT in low and middle income countries improves cure or treatment completions in people with TB (Volmink & Garner, 2006). Strategies based on self-treatment can be strengthened by support and supervision by an identified relative or neighbour, or through other social structures. TB control programmes that leave the choice of DOT supervisor to the patient have been shown to be successful (Adatu et al., 2003). As suggested by Noyes & Popay (2007), there is a need for patient-centred programmes rather than single world-wide intervention like DOT.

In fact, DOT may not be the gold standard in some conditions. For instance, in this study, a physician reported that DOT was not suitable for TB and DM patients who developed severe nausea and vomiting as different treatment strategy was recommended and the supervision of family members were required. Health care providers in other studies stated that patients found DOT to be the most burdensome aspect of the treatment, intrusive and an imposition on lifestyle (Hansel, et al., 2004). Health care professionals in this study acknowledged that patients may have the additional burden of attending multiple clinics besides DOT. Similarly, DOT was found to be particularly challenging for TB and HIV patients because of physical demands and economic constraints; and because further attendance to the clinic for anti-retroviral treatment were required (Gebremariam, et al., 2010). Therefore, it was recommended that TB and HIV clinics should work in collaboration (Gebremariam, et al., 2010). There is an identified need for an integrated management of TB and DM in order to reduce the burden of attending multiple clinics.

It was found that health care professionals from the respiratory department responded ambiguously on matters related to the treatment of DM in TB patients. They believed that they could handle patients with "simple DM" and the "difficult ones" were left to the DM experts. On the other hand, health care professionals from the endocrinology department confirmed that they only see TB patients occasionally upon referral. However, they believed that TB and DM patients should be receiving similar DM treatment and periodical evaluation that are scheduled for DM patients. There were some similarities between the perceptions of physicians from the chest and endocrine clinic concerning the poor acceptability of insulin injections among patients. However, the physician from the endocrine clinic argued that TB and DM patients could be persuaded to use insulin due to the possibility of poor glycaemic control. This indicates that TB patients with poorly controlled DM may benefit from insulin therapy but might not been receiving insulin due to the lack of confidence among chest physicians in managing 'difficult DM'. Furthermore, this issue could be further compounded due to the lack of communication between TB and DM care provider with regards to DM management in a health care system which is fragmented due to single disease management system.

Poor coordination between health care providers arises because of the common practice of single disease management across specialties (Elliott, et al., 2007; Struijs, Baan, Schellevis, Westert, & van de Bos, 2006). To overcome this problem, health care professionals from the chest and endocrinology department should work together to coordinate treatment and also to help early detection of TB in DM patients or vice versa. It has been recommended that DM care programmes should be integrated with other chronic diseases care programme to meet the complex health care demand of DM patients with other comorbidites (Struijs, et al., 2006). Some comorbidities such as cardiovascular diseases are known to be associated with DM due to their shared pathophysiological nature and therefore, it is incorporated into diabetes management programmes and clinical guidelines (Caughey et al., 2009). However, there are limited guidelines to facilitate the care of concomitant non-related diseases in DM patient (Caughey, et al., 2009), as in the case of TB and DM. Comorbidities interfered with patients' capacity to manage their medication and adhere to medication regimen (Jowsey, et al., 2009). Ongoing, regular discussion with patients about their medication is required, and for patients

with comorbidities, this requires integration and coordination of care across specialties (Bayliss, Edwards, Steiner, & Main, 2008; Elliott, et al., 2007; Gijsen, et al., 2001; Jowsey, et al., 2009; Smith & O'Dowd, 2007).

The fact that both TB and DM were diagnosed late in most of the patients in this study is a huge concern. Patients only presented to the hospitals when they could no longer tolerate symptoms, such as severe coughing. Almost all patients knew that something was wrong but none of the patients said that they suspected TB. Late treatment seeking behaviour corresponded to delayed diagnosis of TB. Some reported that they first sought treatment for cough from private clinics and pharmacies which also contributed to the delay in accurate diagnosis. This could have a potential impact to public health as TB and DM patients have worse clinical presentation as compared to TB only patients. Most of the patients also reported that they were diagnosed with DM when they presented to the hospital for some other problems and in some patients complications of DM had set in prior to being diagnosed. It has also been reported that late treatment seeking behaviour were commonly seen among TB (The Star, 2011) and DM patients in Malaysia (Rampal, et al., 2010). This indicated lack of awareness in patients with regards to symptom recognition as well as the importance of regular medical check-ups.

It was also found that some patients in this study associated the diagnosis of TB with risk factors such as smoking. Unfortunately, very few patients knew that DM was one of the contributing factors for TB infection. Lack of understanding could lead to lack of acceptance of the disease. In this study, one patient had put his family at risk by not referring them for TB screening. Denial about the illness could also lead to delayed diagnosis of TB. It is not clear whether some patients were not aware about the importance of TB treatment or they were worried about being stigmatised. The fact that some patients tended to be secretive about TB as reported by the nurses could be attributed to stigma. However, none of the patients in this study reported any issues about stigma as compared to the nurses. This issue was not explored as a main topic in the interviews and that could be one of the reason of why stigma was not reported.

This study provided an opportunity for pharmacists and other health care professionals to discuss their experience in relation to the existing pharmacist-led MTACs. MTACs were found to be strategically located and were able to overcome some barriers (e.g. long waiting time) in health care services by incorporating features of accessibility and timely delivery of care. Having MTAC beside the physician's clinic promoted convenient access to patients and eased communication between physicians and pharmacists. Innovations in access to care had been cited to be an important component in providing patient-centred care (Berry, Seiders, & Wilder, 2003). Pharmacist-led MTACs were well received by the health care professionals and pharmacists were able to provide pharmaceutical care services. Pharmacists suggested that MTAC could be adapted to provide pharmaceutical care service to TB and DM patients.

## 4.6 Strengths and limitations of the study

The strengths of this study lies in the unique nature of this investigation as it is the first to explore the experiences of both patients and health care professionals in managing TB and DM. Furthermore, it is also the first to highlight the views held about pharmacist-led MTAC in Malaysia.

The use of a qualitative methods in this study were also unique with regards to a pharmaceutical care study whereby pharmaceutical care needs were indirectly assessed based on patients' and providers' experiences. The findings of this study were beneficial in the sense that it assisted in developing the next phase of the study.

The use of focus group discussion with pharmacists allowed group interactions that facilitated and generated more discussion that may have not been possible if an interview was conducted. My supervisor who is an experienced qualitative researcher moderated the focus group. As she was not a local pharmacist, the questions raised were responded in-depth by the pharmacists, which may have not been attained if I was the moderator. This could be due to the perceived understanding that I already knew about the role of pharmacists in Malaysia. As such, it was a good strategy to have my supervisor to conduct the session. However, towards the end of the focus group discussion, the pharmacists were interested to find out about the role of pharmacists in the UK from my supervisor. As the main issues had been discussed, the slight diversion from the topic guide did not impact the data.

This study is limited by the participation of a small number of the health care professionals because they were the only ones involved with the care of the patients where this study was conducted. In addition, out of five physicians and five nurses approached, three physicians and three nurses participated. Two nurses and two physicians were unable to turn up for their interviews due to other work commitment. With regards to pharmacists, four pharmacists

who were actively involved in DM, HIV and in-patient management participated in this study. Although the number of health care professionals could have been increased by recruiting others from different hospitals, it was not done due to time limitation. Nevertheless, health care professionals in this study provided a rich description of their opinion which is the most important aspect in qualitative research as compared to sample sizes. Furthermore, this study provided the basis for the next phase of the study which is the development of a pharmaceutical care programme for TB and DM patients in the same hospital. Therefore, it is more logical to recruit health care professionals from the same hospital rather than multiple hospitals.

Conversely, patients were recruited from four government hospitals (the main hospital where the health care professionals were recruited and three other district hospitals) within the same state. The reasons for including patients from different locations were due to the recommendation by the nurses and the invitation from the chest physicians to participate in their weekly district hospital visits. The patient sampling strategy that was dependent on the nurses for identification of patients with TB and DM led to a limited number of patients identified in the main hospital. The nurses suggested that they knew their patients well and will be able to refer them for this study. However, in reflection, some patients may have been missed especially if nurses fail to enquire about the presence of DM in TB patients. Furthermore, newly diagnosed DM patients may not know that they have DM unless the nurses go through each TB patient's medical record to screen for DM from the laboratory investigations. Although the strategy of screening patient's medical record was proposed, it was considered a waste of time as the nurses informed me that not all patients were on DOT at that particular hospital as some patients go the nearest health clinic for DOT. As such, I relied upon the nurses to assist me in identifying and recruiting patients for this study. The first few interviews were all among older Chinese patients. However I wanted to interview patients from other ethnic group as well. According to the nurses, the population near the main hospital were predominantly Chinese and that the chances of recruiting Malay and Indian patients may be higher in the district hospitals. Therefore, I followed the physicians and nurses to those hospitals during their weekly visits and I managed to recruit Malay and Indian

patients. Nevertheless, Malay and Indian patients were also recruited from the main hospital at the later stages of the study.

This study may have been limited by the small number of female patients but the experiences shared were similar to male patients. On the other hand, patients were also largely middle-aged, married and teetotal men which could have impacted the generalisability of the findings to a certain extent. Although the study started with a purposive sampling strategy, it was converted to convenience sampling due to time constraint. Furthermore, it was a challenge to recruit patients with a specific cluster of comorbid condition as well as with different characteristics within a short period of time. Nevertheless, efforts were taken to include patients from different ethnic background as it was important to look at cultural differences in medicine-taking behaviour.

Having understood that there might be a possibility of missing some of the patients with TB and DM, the sampling strategy that relied on the nurses to identify patients were not used in the next phase of the study as I wanted to determine the prevalence of DM in TB patients. Instead, individual screening of all TB patients' medical records were performed.

The participants of the focus group discussion were all actively involved in pharmaceutical care activities and as such, they may have held stronger opinions on the subject matter. Nevertheless, having recruited a homogenous group of pharmacists allowed in-depth exploration with regards to pharmaceutical care issues.

As this was a cross-sectional study, the views presented were based on the participants' memory, knowledge, experience and feelings at that point of time. Whether similar accounts can be reproduced if they were to be interviewed again is unknown.

This study provided the experiences of patients presenting to government hospitals whereby TB and DM treatment were rendered free of charge and therefore the findings cannot be generalised to patients presenting to private hospitals or clinics as they may have different array of issues and concerns.

## 4.7 Reflection

Upon personal reflection, I believe that my background as a pharmacist could have impacted the way patients and health care professionals responded. Some of these aspects had been discussed in section 3.11.1.

The interviews were conducted in a hospital environment which might have led to more socially desirable answers as far as patients are concerned. Interviewing them at home might have been a better option, but considering the safety and the infectious nature of TB, this decision was not taken. In fact, I wore a mask when I conducted the interviews at the hospital. Initially, I felt awkward when I had to wear the mask and interview patients but after sometime I realised that patients did not find it as an issue as all health care professionals at the clinic were wearing masks. Some patients especially those who were newly diagnosed wore their masks while they were being interviewed. In one case, I had to reschedule the interview to a later date as the nurses advised me that the patient was highly infectious and it would be better to interview him after a month of treatment.

I had the chance to observe the clinic setting at the district hospital and found that it provided better environment for interviewing patients. It was less busy as compared to the main hospital and a counselling room was available at the clinic. I used the counselling room to conduct my interviews at the district hospitals. However, at the main hospital, I had to use any of the empty physician's or nurse's room to conduct the interviews. It was much easier to conduct the interviews at the district hospitals as compared to the main hospital.

None of the patients approached declined to be interviewed. Generally, patients in Malaysia have high regards about health care professionals and they might have felt that it was impolite to decline. Nevertheless, I gave patients the choice of when they wanted to have their interviews. Except for one, all the other patients preferred their interviews to be held on the

same day they were approached. In fact, one patient stated that he felt good that he could help me by agreeing for the interview. The patient believed that he was doing me a favour by participating in the study.

## 4.8 Connecting Phase 1 to Phase 2

Findings from this study were used to develop the research proposal for the following phase. It was concluded from this study that there was a need for a pharmaceutical care management for patients suffering with both TB and DM.

The pharmaceutical care needs of TB and DM patients were interpreted based on the patients' and health care professionals' experiences of managing TB and DM. The main themes that emerged centred on the concerns about medications and the management of TB and DM. It was then construed that there were needs to:

1. Monitor adverse effects of medications
2. Help patients manage multiple medications
3. Address patients' concerns about medications
4. Motivate and promote adherence to treatment
5. Advocate the importance of early treatment seeking behaviour
6. Conduct a thorough medication review and improve documentation of patients' medical and medication history
7. Create opportunities for patient and health providers for communication
8. Find ways to integrate the management of TB and DM
9. Enquire about self-management and the use of traditional remedies.

Therefore, phase 2 study would need to cover all the nine needs that have been identified. Pharmacist-led MTACs can be used as a model for designing a pharmaceutical care programme. The following chapter discusses the development of the phase 2 study.

# CHAPTER 5: METHODOLOGY AND METHODS (PHASE 2)

## 5.1 Introduction

This chapter describes how the phase 2 study was carried out. It begins with the description on the development of the phase 2 study. Then, it presents the research methodology, describes the data collection methods, explains how the data was analysed and discusses how validity and reliability of the phase 2 findings can be assessed.

## 5.2 Objective

The objective of the phase 2 study was to investigate the feasibility of providing a pharmaceutical care service for patients with TB and DM.

## 5.3 Development of Phase 2 study

### 5.3.1 Developing the study proposal for Phase 2

Based on the knowledge gained from the phase 1 study, a proposal for phase 2 was developed. The initial plan was to conduct a prospective pretest-posttest single group study. Each TB and DM patient would undergo an initial assessment which would include a medication use review and a structured interview with a pharmacist.

The pharmacist would cover all the relevant pharmaceutical care needs that have been identified in phase 1. Then an individualised pharmaceutical care plan would be prepared, peer-reviewed and then discussed with the clinicians for agreement. Patients would then be followed up by the pharmacist for a total of five visits (week 1, week 2, week 4, week 8, week 12).

A second assessment would be conducted 12 weeks from the initial interview to examine whether the pharmaceutical care issues that were identified had been resolved and to assess the outcome measures of the study. The outcome of the study includes the pharmaceutical care issues that were identified throughout the study period and the changes in the clinical parameters from initial to final assessment.

The changes in patient's beliefs about medicine would be assessed by using the beliefs about medicine questionnaire. Other assessments would include the changes in clinical measures such as the HbA1C, sputum conversion, chest-x-ray, blood pressure and total cholesterol.

### 5.3.2 Discussion with other health care professionals

A preliminary discussion regarding the findings of the phase 1 study and the proposal for phase 2 was held with a physician from the chest clinic. He suggested that feedback should also be obtained from a wider panel of experts, in particular other medical staff from the chest clinic, through an oral presentation.

He said that he would make arrangements to give continuous medical education (CME) points to the attendees in order to encourage the health care professionals to attend the presentation session. In addition to the health care professionals from the chest clinic, the pharmacists and the health care professionals from the endocrine clinic who participated in the phase 1 study were also invited to attend the session.

Subsequently, letters of invitation for the presentation were sent to all health care professionals who participated in the phase 1 study (see Appendix 9). The physician helped to inform the rest of the health care professionals from the chest clinic. The health care professionals were informed that the presentation was going to be held at the chest clinic during lunch break and that lunch was going to be provided to all the attendees after the presentation. A total of 30 health care professionals (physicians, pharmacists, nurses, pharmacy PhD students, medical assistants) attended the session but no one from the endocrine clinic attended.

The title of the oral presentation (power point) was 'Exploring the need for pharmaceutical care management of TB and DM: a qualitative study'. The findings of the Phase 1 study and a brief explanation on the proposed Phase 2 study were presented. The presentation was half an hour long and was followed by a 15 minute 'question and answer' session. Informed consent was obtained from all attendees in order to video the presentation and 'question and answer' session.

## Issues highlighted and discussed

Five main issues were raised and discussed during the 'question and answer session'.

1. **DM medications**

- Which antidiabetic drug (gliclazide or metformin) induced vomiting when administered concomitantly with TB medications?

- What was the cost-effectiveness of short-term insulin usage in TB and DM patients?

- Some chest physicians were unsatisfied with hospital guidelines imposed on insulin prescription. They reported that they did not have the authority to prescribe insulin pens as these were items restricted to prescription only by endocrine specialists. They argued for a shared authority in view of higher acceptability for insulin pen (versus needles) among patients.

- Some physicians perceived that patients disliked any form of injections.

**2. Language barriers**

- One physician requested for a pharmacist of Chinese ethnicity to provide the pharmaceutical care service. He informed that many patients were from the Chinese ethnicity, hence there could be language barrier if only non-Chinese speaking pharmacists were available.

- One pharmacist commented that non-Chinese pharmacists should also learn some key words in Chinese language to communicate.

- The variety of different dialects used among Chinese patients also caused difficulties for even the Chinese-speaking pharmacists who did not speak a particular dialect.

### 3. Stigma

- Physicians commented that TB is still a stigmatised disease. One physician reported an incident that happened on that day. "A 17-year-old Chinese girl was diagnosed with TB. She has to sit for her SPM exams next week. You know about the Chinese, the moment they know somebody has TB in school they will not send their children to school. So I spoke to the class teacher. I said look here there is one student in your class who has TB, the minute you see anybody coughing, please refer them to me. I don't want any chaos because I know that exams are going on." He emphasised that pharmacist should take note about stigma when providing pharmaceutical care.

- Another physician shared her experience of a lady who started crying when she was diagnosed with TB. Apparently, the lady was worried about how her family members would react and how she would be treated. She explained that it was important to counsel patients and their family members accordingly.

**4. Involvement of pharmacists**

- One pharmacist reported that the hospital pharmacists may not be able to fully participate in the study due to their high workload. Furthermore, pharmacists might be reluctant to go through the bureaucracy of securing permission from the chief pharmacist to participate in this study.

- Another physician suggested the researcher to conduct the study instead of relying on the hospital pharmacists.

**5. TB and DM education**

- One pharmacist suggested that a booklet aimed at providing TB and DM education could be designed and distributed to patients.

- Another physician suggested a video based group education programme where TB and DM patients could be invited to view the video.

The presentation and the 'question and answer' session allowed the researcher to interact with the health care professionals and provided an opportunity to discuss the plans for the phase 2 study.

Following the discussion, the protocol of the phase 2 study was refined. The researcher's participation in this study was inevitable. Another pharmacist of Chinese ethnicity was invited to be involved in the study.

Issues related to DM medications and stigma was considered during the provision of pharmaceutical care. However the recommendation to provide insulin pens was not appropriate since physicians in the chest clinic are not authorised to prescribe it. Instead, they could make recommendation to admit the patient and initiate insulin in the ward.

Although it was thought that the booklet and video based education were potentially good suggestions, these were not incorporated into the phase 2 study due to financial and time constraints.

## 5.4 The methodology of phase 2 study

Phase 1 study and the discussion held with the health care professionals helped to identify the components that need to be embedded in a pharmaceutical care service. However, there were other factors that need to be considered in order to determine the feasibility of providing the service. Further 'modelling' or fact finding as described in the UK MRC framework was required. Therefore, the revised phase 2 study focussed on the processes of developing a pharmaceutical care service.

The following were the research questions for phase 2 study.

- How can I estimate the number of patients who would require the service?
- How can I recruit patients with TB and DM?
- How can I follow-up patients?
- How can I collaborate with the hospital pharmacists?
- How can I obtain patients' clinical information?
- How can I provide the pharmaceutical care service?
- How can I identify medication-related problems?
- How can I classify and document medication-related problems?
- How can I assess adherence to medication?
- How can I assess whether patients have different sets of beliefs about medications with regards to TB and DM medication?
- How can I influence changes in patients' behaviour towards medicine-taking?
- How can I access physicians' response towards pharmacists' recommendation?

As the research questions take the form of 'How do I understand what I am doing? How do I improve it?', and place the emphasis on the researcher's intent to take action for personal and social improvement (McNiff & Whitehead, 2006), action research methodology was employed.

### 5.4.1 Action research

Action research is a style of research rather than a specific method (Meyer, 2000). It provides the flexibility needed in research that aimed to bring change (Tanna, 2005) and it has been used within pharmaceutical care research (Gilbert, Roughead, Beilby, Mott, & Barratt, 2002; Tanna, Pitkin, & Anderson, 2005). For example, Tanna, et. al. (2005) used action research methodology to develop the role of specialist menopause pharmacist in the UK. The approach allowed reflective practice, enabling the specialist menopause pharmacist to be both the service delivery provider (the intervention) and the researcher.

Action research is conducted in a systematic manner (McNiff & Whitehead, 2006), whereby the action plan is to

- take stock of what is going on
- identify a concern
- think of a possible way forward
- try it out
- monitor the action by gathering data to show what is happening
- evaluate progress by establishing procedures for making judgements about what is happening
- test the validity of accounts of learning
- modify practice in the light of the evaluation.

Action research implies that the nature of 'knowing' relies on the experience of doing and 'knowing' is seen to be embedded within the cycles of action and reflection (Ladkin, 2007). Knowledge is not derived from one theoretical proposition, but gained from an extended epistemology that includes multiple ways of knowing. The epistemology of action research include experiential knowledge, practical knowledge and presentational knowledge (Ladkin, 2007).

In short, action research involves the process of 'observe – reflect – act – evaluate – modify – move in new directions' which is generally known as the action-reflection cycle (McNiff & Whitehead, 2006).

**The application of action research methodology in phase 2 study**

The study would begin by taking stock of what was going on at the chest clinic and the subsequent process in the action research cycle would follow spontaneously.

For example, first, this study required the participation of the researcher and the need to collaborate with the hospital pharmacist. It was important to assess how the researcher who was an 'outsider pharmacist' could collaborate with the hospital pharmacist ('insider pharmacist') and other health care professionals to facilitate the provision of a new service. The researcher would need to experience 'working' in a new environment, find ways to initiate the service and improve service through experiential learning. There was also a need to assess the acceptability of pharmacists' recommendations by patients and physicians.

Second, the researcher would need to find out about other practical issues like patient recruitment, follow-up arrangement and the availability of space for patient education and counselling at the clinic. For example, it was important to know the prevalence of DM in TB patients at the chest clinic in order to make better prediction of the number of patients (sample size) who would attend the proposed pharmaceutical care service. This information would allow the estimation of additional practice hours required to provide the service.

Finally, pharmacists would need to address the nine pharmaceutical care needs that were identified in phase 1 study. For example, pharmacists would identify and resolve medication-related problems by assessing patients' adherence to medication, patients' beliefs about

medication, problems related to prescriptions and by addressing patients' concerns about medication. The researcher would then reflect on the process of service delivery and whether it was possible to improve the management of TB and DM.

## 5.5 Methods

### 5.5.1 Ethical Approval

This study received ethical approval from the Ministry of Health, Research and Ethics Committee, Malaysia (reference number: NMRR-09-463-4064) (See Appendix 10).

### 5.5.2 Study setting and duration

The study was conducted at a tertiary public hospital in the northern region of Peninsular Malaysia from November 2009 till February 2010.

### 5.5.3 Estimation of sample size

The sample size for this study was estimated based on the preliminary data (preliminary observational study) whereby nearly 23% (n=7) of TB patients had DM. Almost 50 patients were newly-diagnosed with TB at the chest clinic every month. Therefore, about 10 patients would be most likely to present with DM every month. Since the study was conducted for 3 months, a sample size of 30 patients was estimated.

### 5.5.4 Source of data

The source of data varied from medical registers, medical records, observations, interviews, questionnaire and informal discussions. Some of the data such as patients' clinical information were obtained from medical records prior to the provision of service, whilst other data were obtained during the consultation session.

The research process and procedures are summarised in Figure 5-1.

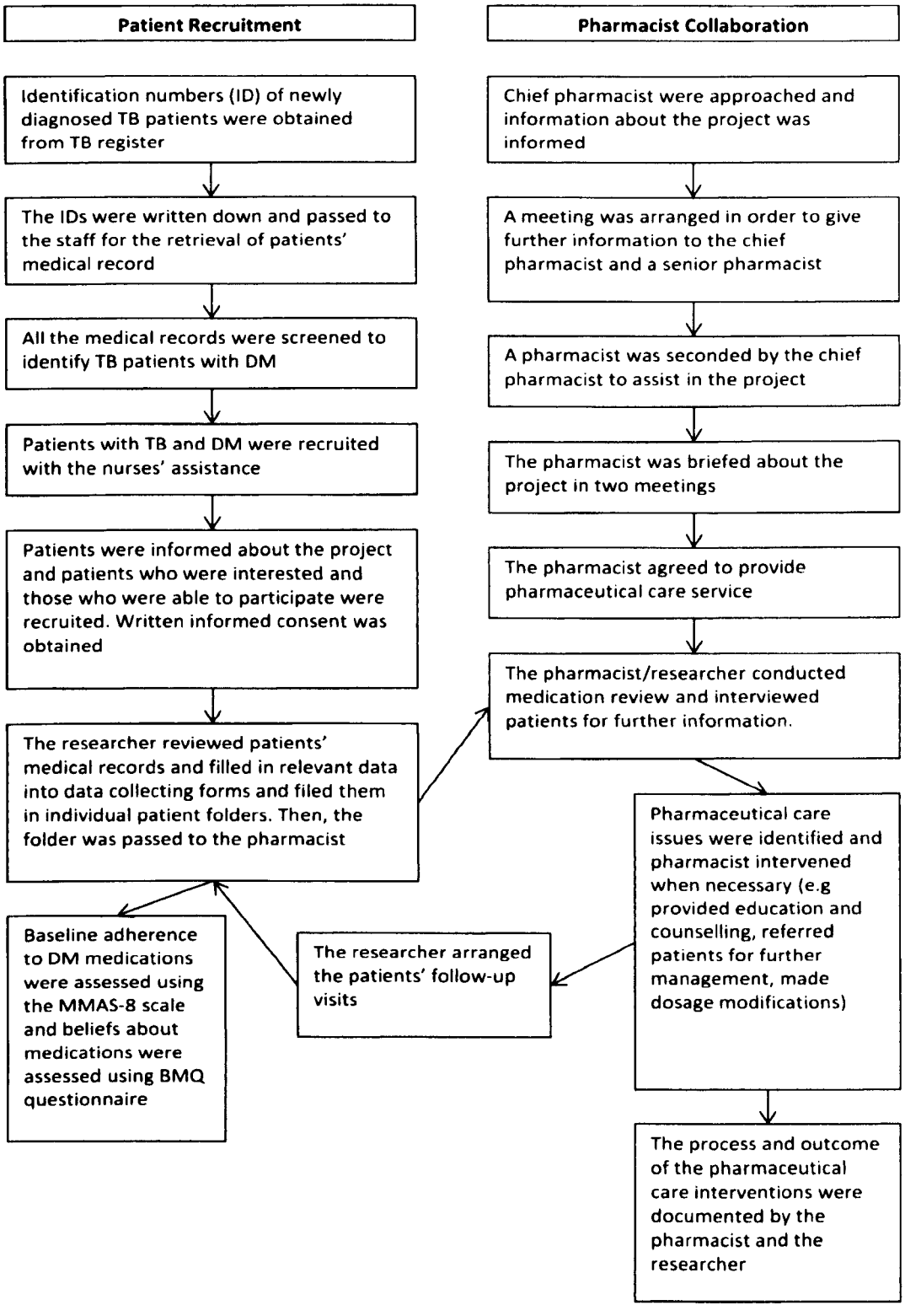


Figure 5-1 Research Process

### 5.5.5 Patient identification and recruitment

In order to identify potential patients for this study, all TB medical records from July 2009 till February 2010 were screened to identify patients with DM using the list of TB patients obtained from the TB register. The patients' identification number were noted and sent to the TB record office. The staff retrieved all the medical records, which were then reviewed to confirm eligibility. TB patients with a previous history or a new diagnosis of DM and who had been receiving diabetic medications were eligible to participate. Although the study began in November 2009, patients who had started their treatment as early as in July 2009 were included because they were still undergoing treatment during the study period hence considered eligible to participate.

After identifying the potential patients, patients were recruited by checking whether the patients were having their DOT at the hospital's chest clinic or in other health clinics. If they were not having DOT at the clinic, they would be recruited during their next follow-up clinic appointments. The follow-up dates were identified from patients' medical records. Patient's names were given to the nurses and they assisted the researcher in recruiting the patients. Then, the patients were approached by the researcher and were informed about the study. Those who were interested to participate were recruited. A patient information leaflet was given (see appendix 11) and written informed consent (see appendix 10) was taken.

### 5.5.6 Collaboration with a hospital pharmacist

The hospital's chief pharmacist was approached and informed about the proposed project. Subsequently, Alan (*pseudonym*) a hospital pharmacist, who is Chinese, was seconded by the chief pharmacist to assist with the project.

Then, Alan was briefed about the project in two meetings that lasted approximately two hours each. The pharmaceutical care needs of TB and DM patients which were identified in the previous study were explained. Recent literatures on TB and DM were provided for his own reference. Alan had been providing pharmaceutical care service to chronic obstructive pulmonary disease patients and he had pre-established working relationship with other health care professionals from the chest clinic. Alan requested the researcher to be present when he delivered the service especially during the initial stages of the service.

The pharmaceutical care project was meant to follow the seven practice steps suggested by Hepler and Strand (Hepler & Strand, 1990). The steps are (1) establishment of a pharmacist-patient relationship; (2) patient data collection, analysis and interpretation; (3) finding out medication-related problems; (4) establishing therapy outcomes and goals together with the patient; (5) setting possible pharmacotherapy alternatives and selecting the best plan, preparing a monitoring plan; (6) implementation of the individual pharmacotherapy regimen and monitoring plan; (7) follow-up.

### 5.5.7 Documentation of patients' clinical information

Upon obtaining patients' consent, the researcher documented all relevant patient information from the patients' medical records prior to the patients' appointments with Alan. The data was filled in a data collecting form (see Appendix 13). Information filled in the data collecting form included treatment centre, demographic data, social history, past medical history, past medication history, current medications (including TB treatment regimen), traditional medicine/herbal/supplement, current history of TB episode, TB classification, laboratory investigations, medication-related problems/pharmaceutical care issues, medication-therapy problems to be resolved and the pharmaceutical care plan.

### 5.5.8 Assessment of self reported adherence to medicine-taking

Patients' self-reported adherence to DM medications (at baseline) was assessed by using the translated version of Morisky 8-item medication adherence scale (MMAS-8) (Morisky, Ang, Krousel-Wood, & Ward, 2008). This tool was developed through modification of a previously validated four-item MMAS (MMAS-4) (Morisky, Green, & Levine, 1986) and was found to be more reliable and explored additional behavioural features than MMAS-4 (Morisky, et al., 2008). The MMAS-8 was used as this questionnaire is commonly used to assess adherence in Malaysia. Self-reported questionnaires are thought to give a good estimation of medication adherence (Shi et al., 2010).

The method for coding the scale is detailed in a copyrighted document which was obtained from the scale's developer.[2] The first seven items involves a *yes* or *no* response. The final survey item consists of 5-point Likert Scale. The total summary score ranges from 0-8. Patients were considered to be high adherers if the total score is 8, medium adherers if the total score is between 6 and less than 8, and low adherers if the total score is less than 6.

Besides using the translated version of MMAS-8, adherence to medication throughout the study period was also assessed through other methods like patient interviews and tablet counts (if patients brought their medicines with them).

Adherence to TB medications was not assessed using the translated MMAS-8 questionnaire as adherence could be assessed based on their daily attendance for DOT.

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[2] Coding Instructions for the © Morisky Medication Adherence Scale (8-item) was obtained from Prof Donald Morisky.

### 5.5.9 Assessment of patients' beliefs about medicines

Patients' beliefs about the necessity and concerns regarding TB and DM medications were measured using the translated version of Beliefs about Medicines questionnaire (BMQ) (Horne, Weinman, & Hankins, 1999). This questionnaire has been developed and validated in patients with chronic illness, and was found to have good psychometric properties.

The questionnaire consists of two 5-item scales assessing patients' beliefs about necessity of medications and their concerns about the potential outcomes of taking it (Horne & Weinman, 1999). Response options are provided as a 5-point Likert scale (1=strongly disagree to 5= strongly agree). The scores from the individual items within each scale are added to give a scale score. The total scores for necessity and concerns scales range from 5-25 points. The necessity-concerns differential is derived from deducting the concerns score from the necessity scores. The possible scores that can be achieved ranges from -20 to 20. A positive score indicates greater necessity or need for the medications, and a negative score indicates greater concerns about the medications. This differential can be regarded as a cost-benefit analysis. Patients' perceptions of cost (concerns) are weighed against the perceptions of benefit (necessity beliefs).

The BMQ and MMAS-8 were translated into Malay language because most patients did not understand written English. The translation was verified by one of my supervisors. In fact, there is a validated Malaysian version of the MMAS-8 which was also done in Malay language and was tested in Malay, Chinese and Indian patients (Al-Qazaz et al., 2010). However the validated Malaysian version of MMAS was not available for use when this study was conducted. Nevertheless, there was not much difference between the translated version of MMAS-8 that was used in this study and the validated Malaysian version of MMAS-8.

The translated Malay versions of the MMAS and BMQ were not self-administered by patients taking part in this study because some of them were not able to read. Therefore, in order to maintain consistency in how the tools were administered, the researcher read the items of the questionnaires in a face-to-face interview with all patients. This method was also used during the validation of the translated version of the eight-item MMAS in Malaysia (Al-Qazaz, et al., 2010).

## 5.5.10 Provision of pharmaceutical care

After collecting patients' clinical information, patients' appointments for the pharmaceutical care consultation with Alan were arranged. Patients were requested to bring along their medications to their first visit with Alan. Alan conducted the initial assessments which include medication reviews and interviews. Whenever, Alan was not around due to other important obligations, the researcher provided the service.

The medication-related problems were identified by assessing problems related to the prescriptions (e.g. adverse drug reactions, drug interactions), problems related to patient factors (e.g. patients' behaviour and attitude towards medications, beliefs and concerns about medications) and problems related to procedural/organisational factors (e.g. DOT). Details of the observation, assessment and interventions were recorded in the data collection form.

Following the initial assessment, a pharmaceutical care plan was designed by Alan, reviewed by the researcher and suggestions or recommendations were discussed with physicians treating these patients when necessary. If there was more than one patient at the same time, then the responsibility of providing the service was shared between the researcher and Alan in order to reduce the patient's waiting time.

Patients were educated and counselled on the management of TB and DM during their first visit. Some of the medication-related concerns were addressed during the consultation and some were communicated to their physicians. Subsequently, some of these patients were followed up for a total of four visits, in order to monitor safety and effectiveness of the treatment. In some occasions, telephone follow-up calls were made if they did not turn up for their follow-up visits.

Alan and the researcher met each week during the study period to reflect on the pharmaceutical care management of these patients (e.g. lessons learned and the barriers in providing optimal care).

## 5.6 Data management and analysis

Data was analysed using Statistical Packages for Social Sciences (SPSS) version 16.0; SPSS Inc, Chicago, IL, USA. Descriptive statistics were used to analyse patients' demographic, clinical characteristics and the scores for MMAS-8 and BMQ. Examination of the distributions of the necessity, concerns and necessity-concerns differential of total score of MMAS-8 and the BMQ revealed the data to be suitable for non-parametric analysis. Frequencies were used for categorical variables, while means and standard deviations were calculated for continuous variables. Wilcoxon Signed Rank Test was used to examine whether patients' beliefs about TB medications were different as compared to beliefs about DM medications. The internal consistencies of the scales were assessed using Cronbach's alpha. Some of the data (e.g. observational notes) were thematically analysed using the computer software package, NVivo qualitative data analysis software; QSR International Pty Ltd. Version 8, 2008.

## 5.7 Validity

Validity of action research based studies can be judged based on the following criteria:

- whether the work is participatory
- whether it is aimed at change
- whether it involves movement between reflection, action and evaluation

It is also argued that the inclusion of multiple ways of knowing should be a key criterion for validity assessment (Reason & Bradbury, 2001) and one of the most important arbiters of action research is the usefulness of the study (Ladkin, 2007).

Action research should feature both research and practice outcomes and it should give rise to theoretical insights as well as health care practice development that could be generalised to other settings (Waterman, Tillen, Dickson, & de Koning, 2001).

As action researchers are intensively involved in the research process at multiple levels and in multiple roles, it has been suggested that action researchers utilise critical friends (peers or colleagues) or a validation team to defend their ongoing findings (Herr & Anderson, 2005). Critical friends often encourage researchers to make explicit what they may understand on a more tacit level (Herr & Anderson, 2005). Due to the intensity of the research process, critical friends can help action researchers to step back in order to understand what they are seeing and doing(Herr & Anderson, 2005).

This strategy has been used in this study as weekly meetings were conducted with Alan (hospital pharmacist) to discuss and reflect upon the research activity and the findings. The

findings were also presented to the researcher's pharmacy colleagues and the feedback and questions posed challenged some of the opinions and allowed the researcher to look at the data in a different perspective.

## 5.8 Ethical issues

### 5.8.1 Anonymity and confidentiality

The names of all participants were removed, and pseudonyms were assigned. Due to the small number of health care professionals in the chest clinic, they stand a higher chance of being recognised. Therefore, the hospital's name is not mentioned in this study. All data were stored in a locked cabinet at the researcher's office.

### 5.8.2 Informed Consent

Written informed consent (see Appendix 12) for participating in this study was obtained from each patient prior to the start of any research activity.

The findings and discussion of phase 2 study are presented in Chapter 6.

# CHAPTER 6: PHARMACEUTICAL CARE SERVICE FOR PATIENTS WITH TB AND DM: A FEASIBILITY STUDY (PHASE 2)

## 6.1 Introduction

This chapter presents the findings and discussions of the phase 2 study. It begins with the prevalence of DM in TB patients in the hospital. Subsequently, it describes the patients' clinical characteristics followed by the pharmaceutical care issues and interventions. The chapter ends with the discussion of the feasibility of providing pharmaceutical care service to TB and DM patients.

## 6.2 Patient socio-demographic characteristics

Of the 356 TB patients' medical records screened, 53 patients were identified to have DM. The prevalence of DM among these TB patients was found to be 14.9%. Out of 53 patients identified, 35 patients participated in this study. The remaining 18 patients could not participate because:

1) two patients passed away
2) one patient declined to participate (he was not interested as he had received counselling from the diabetic clinic)
3) one patient had a diagnosis of schizophrenia and was unable to participate
4) two patients had end-stage renal disease and were admitted in other wards
5) eight patients failed to turn up for their appointments
6) four patients were not on DOT (Their TB medication was supplied weekly as they were older patients (>80 years) or too ill to come in for daily DOT and their medication was collected by a family member)

The characteristics of 35 patients with both TB and DM are provided in Table 6-1. The study patient's mean age was 52 years (range 29 -73 years) and the feasibility study involved 22 male and 13 female patients. The majority of the patients were Malays (n=13), followed by Chinese (n=11) and Indians (n=9). There was one patient each from Indonesia and Thailand. Twenty-nine patients were married. Out of the 17 patients who had ever smoked, 15 patients were current smokers and two patients were ex-smokers. Six patients consumed alcohol occasionally (e.g. during festive season). One patient was an intravenous drug abuser. Out of those employed, 10 of them did manual jobs (e.g. carpenter, construction worker, farmer). The remaining five were a policeman, factory manager, self-employed business man, clerk and chef.

Table 6-1 Socio-demographics of patients with TB and DM (n=35)

| Patient characteristics | Number of patients |
|---|---|
| ***Range of age, mean ± SD** | 29-73years, 52.2 ± 10.6 years |
| **Gender** | |
| Male | 22 |
| Female | 13 |
| **Ethnicity** | |
| Malay | 13 |
| Chinese | 11 |
| Indian | 9 |
| Others | 2 |
| **Social history** | |
| Ever smoked | 17 |
| Alcohol consumer | 6 |
| Intravenous drug abuser | 1 |
| **Marital status** | |
| Single | 6 |
| Married | 29 |
| **Occupational status** | |
| Employed | 15 |
| Unemployed | 17 |
| Retired | 3 |

*This is range of age and age (mean and standard deviation) rather than number of patients

## 6.3 Patient clinical characteristics

Patients' clinical characteristics include the classification of TB and DM, presence of concomitant diseases, past medical or surgical history and complications related to DM as detailed in Table 6-2.

The majority of patients (n=32) were diagnosed with pulmonary TB, of which two had a relapse of pulmonary TB and one patient had a recurrence of pulmonary TB due to previous history of defaulting TB treatment. The majority of patients had type 2 DM (n=34). In most cases, DM preceded TB. Twenty-nine patients had other concomitant diseases besides TB and DM. Six patients had undergone cataract surgery.

Table 6-2 Clinical characteristics

| Characteristics | Number of patients |
|---|---|
| **Classification of TB** | |
| Pulmonary TB | 32 |
| Extrapulmonary TB | 2 |
| Pulmonary TB and extrapulmonary TB | 1 |
| **Classification of DM** | |
| Type 1 DM | 1 |
| Type 2 DM | 34 |
| **Concomitant diseases*** | 29 |
| Hypertension | 13 |
| Hyperlipidemia | 5 |
| Ischemic heart disease | 3 |
| Gastritis | 2 |
| Hepatitis C | 2 |
| HIV positive | 2 |
| Chronic active hepatitis | 1 |
| Chronic renal failure | 1 |
| Chronic sinusitis | 1 |
| Deep vein thrombosis | 1 |
| Hyperthyroidism | 1 |
| Primary antiphospholipid syndrome | 1 |
| **Relevant past medical/surgical history** | |
| Cataract surgery | 6 |
| Previous pulmonary TB | 3 |
| Amputations due to DM | 2 |
| Stroke | 2 |
| Upper gastrointestinal bleed | 1 |

*Some patients had more than one disease

## 6.4 Patient's TB and DM treatment regimen

The number and types of medication prescribed for TB and DM are listed in Table 6-3. Most patients (n=26) were treated with the conventional single dose of TB medication. The remaining nine patients received fixed-dose combinations of TB medication. DM was mainly treated with oral hypoglycaemic agents. In addition, patients were taking an average of three medicines for concomitant problems.

Patients in this study were at risk of potential drug-drug interactions due to the use of multiple medicines. For example, rifampicin could reduce the glucose lowering effects of glibenclamide and gliclazide. Other drugs that had a potential to interact with rifampicin were warfarin, efavirenz, lovastatin and nifedipine.

Table 6-3 Number and types of medication

| Medication | N |
|---|---|
| **Number of medication for TB, range (mean ± SD)** | 2-6(4.1 ± 1.3) |
| **Number of patients on TB treatment**[a] | |
| EHRZ | 18 |
| *Akurit* (Fixed dose combination therapy) | 8 |
| HRZ | 6 |
| SEHRZ | 1 |
| H & Ofloxacin | 1 |
| **Number of medication for DM, range (mean ± SD)** | 1-4 (1.7 ± 0.9) |
| **Number of patients on DM treatment** | |
| Gliclazide and metformin | 12 |
| Gliclazide | 10 |
| Gliclazide, metformin and insulin | 4 |
| Metformin | 3 |
| Insulin | 2 |
| Acarbose, metformin and insulin | 1 |
| Glibenclamide | 1 |
| **Number of other medication for concomitant diseases, range (mean ± SD)** | 1-7 (3.4 ± 1.9) |
| **Number of patients on other medication**[b] | 14 |
| Lovastatin | 9 |
| Perindopril | 8 |
| Aspirin | 4 |
| Metoprolol | 3 |
| Frusemide | 3 |
| Nifedipine | 2 |
| Efavirenz | 2 |
| Isosorbide dinitrate | 2 |
| Lamivudine/Zidovudine (*Combivir*) | 2 |
| Ranitidine | 2 |
| Others[c] | 1 |

[a]All patients were given pyridoxine
[b]Some patients had more than one medication
[c] Amlodipine, Atenolol, Atorvastatin, Azathioprine, Chlorpheniramine, Clopidogrel, Diclofenac sodium, Enalapril, Glycine/aspirin(Cardiprin), Hydrochlorothiazide, L-Thyroxine, Magnesium trisilikat, Pottasium chloride, Prednisolone, Telmisartan, Terazosin, Ticlopidine, Tramadol and Warfarin
E ethambutol, H Isoniazid, R Rifampicin, Z Pyrazinamide, S Streptomycin

## 6.5 Pharmaceutical care issues and subsequent interventions by pharmacists

Patients with TB and DM presented with many medication-related problems. Five main issues identified were: (1) non-adherence, (2) uncontrolled DM, (3) adverse drug reactions, (4) absence of monitoring parameters, and (5) other medication-related problems. The information pertaining to the five main issues is summarised in Table 6-4. Although the findings are presented separately according to the five main issues, most patients had a combination of these issues.

Table 6-4 Pharmaceutical care issues

| Medication-related problems* | Normal range | Mean ± SD | N |
|---|---|---|---|
| **Non-adherence** | | | |
| Non-adherence to TB treatment | | | 3 |
| Non-adherence to non-TB treatment | | | 10 |
| **Uncontrolled DM** | | | 29 |
| Fasting plasma glucose | 3.5-6.7 mmol/l | 9.6 ± 3.5 mmol/l | 24 |
| Random blood glucose | 4.0-8.0 mmol/l | 13.2 ± 4.7 mmol/l | 12 |
| HbA1c | 4.0-6.0 % | 9.4 ± 2.7% | 12 |
| **Adverse drug reactions**** | | | 29 |
| Itchiness | | | 16 |
| Vomiting | | | 12 |
| Dizziness | | | 10 |
| Peripheral neuropathy | | | 8 |
| Gastrointestinal disturbances | | | 6 |
| Joint aches/gout | | | 3 |
| Vision disturbance | | | 3 |
| Nausea | | | 2 |
| Liver impairment | | | 2 |
| **Absence of monitoring parameters at baseline***** | | | |
| HbA1c | | | 23 |
| Blood pressure | | | 13 |
| Lipid profile | | | 12 |
| Hematology test | | | 10 |
| Renal function test | | | 1 |
| Liver function test | | | 1 |
| **Other medication-related problems** | | | 34 |

*Many patients had more than one medication-related problem
**Some patients experienced more than one reaction
***Some patients had a combination of unmonitored parameters

### 6.5.1 Non-adherence

**Baseline self-reported adherence to DM medication**

Baseline self-reported medication adherence behaviour of study participants to DM medication are presented in Table 6-5. Cronbach's alpha test of internal consistency was 0.794 for the translated version of MMAS-8.

Based on the translated version of the MMAS-8 for DM medication, 20 patients were low adherers, eight patients were medium adherers, and seven patients were high adherers. More than half of the patients (19/35) reported that they sometimes overlooked taking their DM medication, and 11 patients reported that they left behind their medication when they travelled (see Table 6-5). Fifteen patients reported that they did not take their medication on certain days within the last two weeks before the interview. However, 28 patients reported that they took their medication the day before the interview. Eleven patients reported discontinuing their medication when the treatment led to unwanted or adverse effects. Four patients discontinued treatment when they felt that their DM symptoms were under control. Twelve patients reported feeling hassled to stick to their treatment plans.

A study by Al- Qazaz et al. (2010), which had used the similar tool in measuring adherence to DM medication showed comparable findings whereby only the minority of DM patients in Malaysia were found to be high adherers. Nevertheless, self-reported medication adherence tools are not without limitations as it relies on patient's memory and the skills of the interviewer in eliciting patient's response.

Table 6-5 Self-reported medication adherence behaviour of study participants to DM medication as determined by the translated version of MMAS-8

| Item | Number of patients who answered yes (n=35) |
|---|---|
| 1. Do you sometimes forget to take your diabetes medicine? | 19 |
| 2. People sometimes miss taking their medicines for reasons other than forgetting. Thinking over the past two weeks, were there any days when you did not take your diabetes medicine? | 15 |
| 3. Have you ever cut back or stopped taking your diabetic medicine without telling your doctor because you felt worse when you took it? | 12 |
| 4. When you travel or leave home, do you sometimes forget to bring along your diabetic medicine? | 11 |
| 5. Did you take all your diabetic medicine yesterday? | 28 |
| 6. When you feel like your symptoms are under control, do you sometimes stop taking your diabetes medicine? | 4 |
| 7. Taking diabetes medicine everyday is a real inconvenience for some people. Do you ever feel hassled about sticking to your treatment plan? | 12 |
| 8. How often do you have difficulty remembering to take all of your diabetes medicine? | |
| a) Never/rarely | 19 |
| b) Once in a while | 6 |
| c) Sometimes | 8 |
| d) Usually | 1 |
| e) All the time | 1 |

Since patients were also taking other medication for comorbidities, adherence to those medication were assessed through patient interviews and tablet counts (for those who brought along their medication) during the consultation sessions. The translated version of MMAS-8 was not used to assess adherence for other comorbid condition as it was impractical to repeat the questionnaire for all their medication. In fact, patients were more comfortable to respond spontaneously in a casual discussion. Furthermore, patients were able to justify their reasons for non-adherence. For documentation purposes, patients who were found to be non-adherent to DM and other comorbid condition were categorised as non-adherent to non-TB medication.

Ten patients stopped taking their treatment for non-TB medication when they had started their TB treatment. The most common reason for non-adherence was the experience of adverse effects (e.g. giddiness and vomiting). Some patients were worried about consuming multiple medicines (e.g. HIV patients and patients with multi-morbidities). Forgetting to take medication and self reduction of the number of medication was also reported.

Below are some examples to illustrate the above.

- Saranya, a 58-year-old Indian woman asked 'Why should I inject insulin when I am not eating?' She highlighted that she had poor appetite and she had stopped taking all her medication except for her TB medication after experiencing giddiness.
- Rahman, a 68-year-old Malay man brought all his non-TB medication which was kept in a bag. Similar to Saranya, he also said that he experienced giddiness and therefore stopped taking his medicines. None of his non-TB medication was found to be consumed.
- Sivalinggam, a 40-year-old Indian man with multiple medicines believed that he had developed allergy (swelling of the face) and adverse effects (severe vomiting and headache) which led him to stop all his medication except for his TB medication.

None of these patients had informed their physicians that they had stopped taking their medication. We (Alan and I) provided education and counselling to address their concerns and to promote adherence to treatment. We emphasised the importance of taking all the other medication in addition to TB medication. We referred some of the patients to their physicians with some recommendations and treatment was modified according to the patients' needs (e.g. drug that was perceived to cause allergy was substituted with other drug; patients concerned about their giddiness were counselled and some of them who reported not taking their breakfast were advised to have their meals after taking their medication). We followed-up on some of these patients. They informed us that they had begun to take their medication. Furthermore, some even discussed problems or adverse effects that they had experienced with their medication.

**Non-adherence to TB treatment**

Two patients (Rosa, a 41-year-old Malay woman and Jamil, a 55-year-old Malay man) did not adhere to DOT prior to their participation in this study and one patient defaulted TB treatment during the study period due to adverse drug reaction. I identified the first two patients from their medical records and the nurses informed me that they have defaulted treatment. I contacted the patients and persuaded them to come to the clinic.

- The next day, Rosa came for treatment. She was wheelchair-bound as her toes were amputated due to DM complications. She had difficulties coming for daily intramuscular streptomycin injections. She explained that she was adherent to TB treatment prior to the addition of streptomycin. I informed the physician about Rosa's problem. As a result of this conversation with the physician, streptomycin was discontinued. She resumed treatment with the HRZ (isoniazid, rifampicin, and pyrazinamide) regime. Her medication was packed weekly for her as she was not a

suitable candidate for DOT. Changing her treatment from SHRZ (streptomycin, isoniazid, rifampicin and pyrazinamide) to HRZ and combined with a weekly supply of medication allowed her to continue her treatment.

- The nurses informed me that Jamil was known to be a frequent defaulter. They said that he had the 'couldn't-be-bothered' attitude about his treatment and asked my help to counsel him. In 2007, Jamil defaulted treatment after 7 months of TB treatment. He had a relapse of TB in 2008 and he defaulted treatment again after 3 months. During the study period, he was found to be adherent for 3 months and he defaulted treatment for 3 days. He also admitted that he forgets to take his DM medication. I advised the importance of adherence to both TB and DM treatment and explained about the risk of developing MDR-TB given his previous history. He promised that he will continue his TB treatment.

**Beliefs about medications**

As adherence to treatment relates to patients' beliefs about medication, patients' beliefs about DM medicines and TB medicines were assessed using the translated Malays version of BMQ during their first visit. The internal consistency for Beliefs about Medication was tested for both beliefs for TB and DM medication. Cronbach's alpha was 0.566 when the questionnaire was tested for TB whilst a higher value was seen when the same questionnaire was tested for DM (Cronbach' s alpha = 0.732). Patients' mean scores on the individual item of the BMQ with regards to TB and DM are presented in Table 6-6.

Patients were more worried about taking TB medication as compared to DM medication and this was found to be statistically significant using the Wilcoxon signed-rank test ($P$= 0.01) (Table 6-6). Patients expressed more concerns about TB medication compared with DM medication and this was confirmed by the Wilcoxon-signed rank test ($P$= 0.01) (Table 6-7).

Necessity-concern differential was higher for DM medication as compared to TB medication (Table 6-7).

Table 6-6 Scores on the Beliefs about Medicine Questionnaire with regards to TB and DM medication

| Beliefs about medicine questionnaire | TB | DM |
|---|---|---|
| | Mean ± SD score | |
| 1. My health, at present, depends on my medicines | 4.1 ± 0.7 | 4.1 ± 0.8 |
| 2. Having to take medicines worries me* | 3.0 ± 1.2 | 2.2 ± 1.0 |
| 3. My life would be impossible without my medicines | 3.4 ± 1.1 | 3.4 ± 1.1 |
| 4. Without my medicines I would be very ill | 3.6 ± 1.0 | 3.3 ± 1.2 |
| 5. I sometimes worry about long-term effects of my medicines | 3.1 ± 1.1 | 2.9 ± 1.2 |
| 6. My medicines are a mystery to me | 3.1 ± 1.0 | 2.7 ± 0.9 |
| 7. My health in the future will depend on my medicines | 3.5 ± 1.0 | 3.5 ± 1.1 |
| 8. My medicines disrupts my life | 2.6 ± 1.0 | 2.2 ± 0.9 |
| 9. I sometimes worry about becoming too dependent on my medicines | 2.7 ± 1.0 | 2.9 ± 0.8 |
| 10. My medicines protect me from becoming worse | 4.1 ± 0.9 | 4.0 ± 0.8 |

*Wilcoxon signed-rank test (*P=0.01*)
Scores were based on 5-point Likert scale (1= strongly disagree, 5 = strongly agree)

Table 6-7 Necessity, concerns and necessity-concern differential for TB and DM medication

| Scores | TB | DM |
|---|---|---|
| | Mean ± SD | |
| **Necessity** | 18.6 ± 2.8 | 18.3 ± 3.9 |
| **Concerns*** | 14.5 ± 3.6 | 12.9 ± 3.7 |
| **Necessity-concerns differential** | 4.1 ± 4.4 | 5.4 ± 5.2 |

*Wilcoxon signed rank test (*P=0.01*)
Total necessity and concerns scores range from 5 to 25.

### 6.5.2 Uncontrolled DM

Despite receiving DM treatment, 29 patients had uncontrolled DM. Baseline fasting plasma glucose, random blood glucose and glycosylated haemoglobin (HbA1c) levels were all above the normal range (Table 6-4). Only 12 patients had baseline HbA1c test results. Not all patients had their fasting plasma glucose or random blood glucose test recorded in their medical records.

In order to optimise glycaemic control, the doses of oral hypoglycaemic agents were increased by their physicians. We influenced some of the decisions made by physicians which included alteration of the type of oral hypoglycaemic agents, dosage modifications of insulin and oral hypoglycaemic agents during the study. However, not many patients had regular blood glucose tests during their follow-up visits with their physicians at the chest clinic. What compounded the challenge in ensuring blood glucose tests were conducted was the expectation that this test would be done by any one of the other care providers involved in the treatment of these patients. Other health care providers for DM included practitioners from the private and public health clinics.

Although we made the recommendation to do regular finger-prick monitoring at the TB clinic, some physicians were in favour of fasting blood glucose tests. Waiting for fasting blood glucose test results led to a delay in making dosage adjustments in one patient and in initiating treatment for two newly diagnosed DM patients as these could not be done until a subsequent clinic visits.

Initially, Alan requested the nurses to do a finger-prick monitoring and the nurses did it. It helped us to get a quick picture of the patient's DM condition. For example:

- We requested a nurse to do a finger-prick monitoring for Malar, a 58-year-old Indian woman. The blood glucose level was so high that no reading was shown on the glucometer. We referred Malar to the physician immediately. She was then examined and was admitted in order to normalise her blood glucose and followed by further investigations.

However, after a couple of weeks the nurses reported that they will only consider doing the finger-prick monitoring if they were recommended by the physicians. That caused us some difficulties especially when patients who had seen us before had requested for finger-prick monitoring during their follow-up visit. For example:

- A patient's daughter requested for a finger-prick monitoring to check her mother's blood glucose. She said that her mother's appetite had increased and she had not been compliant to her diet restrictions. I told her to inform the physician so that the test can be done. However, her request was denied. She was disappointed and she informed me that the physician said "If you want to check blood glucose you have to go to the diabetic clinic." This problem was one of the barriers that we encountered in this study. Alan was not around at that time and I was not in a position to impose any action. I could only observe and take note of what was going on. Later, I discussed the matter with Alan. We were both disappointed with the physician's lack of consideration and we decided that we will not request for the test anymore but speak directly to the physicians if necessary.

- Zaman, a 52-year-old Malay, man informed me that he had checked his blood glucose in his DM clinic recently. He showed me a book and the result of fasting blood glucose was 31mmol/l. He did not bring along his medication with him and he did not know the name of his medication. However, he said that he was adherent to his treatment. Due to his high fasting blood glucose, I informed the staff nurse and suggested that this patient should be referred immediately. I followed the patients to the physician's

room. The physician's reaction surprised me. She blamed the patient for not being adherent to his medication without confirming with the patient whether he took his medication or not. She was confused about what to prescribe and she was unsure where the patient was being followed-up for DM (health clinic or hospital). In the end, she wrote a prescription and she asked me. "Are you the pharmacist managing this patient? Can you counsel him? Can you tell him to take his medication gliclazide 80mg bd and metformin 500mg bd for one week and then increase the dose of metformin to 1g bd." The patient and his wife sat quietly throughout this. I was not in a position to explain much to the physician as she was a stranger to me and I to her. The clinic was busy and there was another physician in the same clinic attending to another patient resulting in lack of privacy. I felt there was no proper communication between the physician and patient. She requested the nurse to do a finger prick monitoring test and the result was 23mmol/l. The nurse thanked me for helping the patient by making a timely referral. However, I was unhappy about the whole incident and the way the patient was treated. Despite my personal feelings, I explained to the patient about the importance of adherence to the medication and diet.

### 6.5.3 Adverse drug reactions

Twenty-nine patients experienced adverse drug reactions (Table 6-4). Many patients experienced a combination of adverse drug reactions. The most common ones were itchiness (n=16), vomiting (n=12), dizziness (n=10) and peripheral neuropathy (n=8). Some examples of the issues and interventions are presented below.

- In order to counteract the adverse effects of treatment such as vomiting, one patient Mei Ling, a 57-year-old Chinese woman resorted to stopping TB medication on some treatment days. She experienced vomiting and she believed that her TB medication was causing it. Alan not only counselled her, he also highlighted Mei Ling's problem to her physician. The physician advised her to stop metformin and continue with gliclazide and insulin. However, 3 days later, Mei Ling was admitted due to severe vomiting and she was rechallenged. Alan advised her regarding the process of rechallenge. Finally, rifampicin was identified as the culprit and the treatment administration time was modified. Ethambutol, isoniazid and pyrazinamide were prescribed in the morning and rifampicin was given at night.

- There was also a general concern that vomiting resulted in wastage of medication doses. Another patient Jamaludin, a 62-year-old Malay man said that he wanted to stop his TB treatment after two months as he questioned the effectiveness of his treatment as he kept on vomiting. I advised him to be patient and I also explained that he might end-up getting a relapse if he quits his treatment.

- Chan, a 35-year-old Chinese man who was a newly diagnosed DM patient reported that he felt sick and vomited when he was given metformin. Alan referred Chan to the physician with a suggestion to change metformin to gliclazide. The physician agreed to

the suggestion and Chan's problem was resolved as he did not complain about vomiting during his follow-up visits.

- Another patient, Mansur, a 49-year-old Malay man reported that he had severe episodes of vomiting which could not be controlled. He had tried to overcome it by taking breakfast. Mansur believed that he was 'charmed' and he sought help from a 'bomoh' (traditional Malay healer). He showed me photographs of needles that have been removed by the 'bomoh'. He believed that the number of needles that were removed reduced after a series of therapies which corresponded to improvement in his health. He said that he had gained weight after going to the 'bomoh'. I encouraged him to continue his TB treatment regardless of his beliefs. I told him to inform the physician regarding the vomiting and he was prescribed metochlopropamide.

- Eight patients reported symptoms that resembled peripheral neuropathy (pin-pricking sensation at the soles of the feet and numbness). Alan recommended increasing the dose of pyridoxine to 20mg in some patients and it was agreed by the physicians.

- Rajan, a 55-year-old Indian man who was on multiple medicines complained about developing gout after starting TB treatment. He reported blurring of vision and experienced swelling of the knee. His uric acid level was elevated. He experienced pyrazinamide induced hyperuricemia which contributed to the gouty arthritis. He was diagnosed with gouty arthritis after completing two months of EHRZ (ethambutol, isoniazid, rifampicin, pyrazinamide) treatment. If the problem was detected earlier, pyrazinamide could have been withheld. Rajan could also be experiencing ethambutol induced vision disturbances. I advised him to tell his physician regarding the blurring of his vision. I wanted to monitor his liver function as he had underlying hepatitis but the test was not done by the clinic.

### 6.5.4 Lack of monitoring

There were many parameters that lacked monitoring (see Table 6-4). Baseline HbA1C, blood pressure, lipid profile and haematology tests were absent in many patients' medical records. Lack of monitoring especially for DM and other multiple morbidities made it difficult to monitor the overall safety and effectiveness of the treatment at the chest clinic. Access to monitoring data was a challenge because laboratory investigation tests results were kept in different medical records and were not available at the chest clinic. For example, many patients were treated for hypertension and hyperlipidemia. However, blood pressure, lipid profile and liver function tests were not frequently checked or monitored at the chest clinic because the management was focused on TB. These data might be available at the DM or cardio clinic but there was no coordinated care between the TB and other health care providers.

### 6.5.5 Other medication-related problems

Besides the first four main issues discussed above, many patients had a myriad of additional concerns about medication or medication-related problems that required individualised pharmaceutical care management. Examples of issues and interventions are discussed below.

- Problems associated with the size of fixed-dose combination tablets

  Joanna, a 58-year-old Chinese woman reported that fixed-dose combination tablets were too big in size and she had stomach aches after taking them. She preferred to take the conventional single dose tablets even though she had to take a total of 13 tablets. We referred Joanna to the physician and suggested to change her treatment to conventional TB treatment. The physician agreed and her prescriptions were altered.

- Concerns about the effectiveness of medication

  Tan, a 51-year-old Chinese man sent me the following text message.
  "Hi, at certain days after taking TB medicines my urine does not turn as orange as compared with other days. Is this normal?" I contacted Tan and discussed his concern over the phone. I reassured him that the colour of the urine does not really matter and it is not an indicator for treatment success and encouraged him to continue taking his medication. He thanked me and informed that the explanation made him feel better.

- Preventing potential adverse drug reactions

  The examination of creatinine clearance revealed that three patients had low creatinine clearance. Of these, two were on metformin and we recommended reducing the dosage of metformin to prevent unwanted drug effects.

- Multiple medical and medication-related problems

  Matthew, a 46-year-old Indian man had DM for 10 years and presented with a relapse of pulmonary TB. He had a history of pulmonary TB and had completed his treatment in 2009. He had poorly controlled blood sugar and a diabetic foot ulcer. He was admitted in the ward in order to normalise his blood glucose. His random blood sugar level was very high and ranged from 14.4 to 23.6mmol/l. Insulin was initiated in the ward and the doses were increased to normalise his blood glucose. After a few days, insulin was stopped and he was prescribed with gliclazide 160mg bd and metformin 250mg bd. His past medication history showed that he was on glibenclamide 5mg bd and metformin 1g bd. He was treated with a fixed-dose combination of anti-TB medication combined with streptomycin injections. When Alan visited him for the first time, he complained about dizziness and said he was concerned about having Streptomycin injections on a daily basis. Alan discussed about the possibility of hypoglycaemia and explained what he should do if he experienced dizziness. Alan also found out that he had both gibenclamide and glicazide in his possession and he was taking both. Alan told him to stop taking glibenclamide. He also reassured him about the streptomycin injections by stressing that it would only be administered for two months and this treatment is important as he was having a relapse.

  During the second follow-up visit, Alan was not around and I visited Matthew in the ward. His wife was present and she complained that her husband was non-compliant to diet as well as his DM medication in the past. This had resulted in his diabetic foot ulcer. Matthew expressed regret for taking his health for granted and promised that he will take his medication accordingly. He said 'I'm worried that I might die'. He also complained that he was having abdominal pain, constipation and was unable to lift his hand. I advised him about the importance of adherence to diet and DM medication. I clarified that he had developed complications due to DM and his relapse could be due to poorly controlled DM. Matthew replied that he was not aware that his DM condition could have caused a relapse of his TB. I reassured him that TB can be cured provided that he takes his TB and DM medication accordingly. As the physician

treating Matthew was not at the ward at that time, I informed a nurse regarding his complaints.

Two weeks later, I made a telephone follow-up call and Matthew's wife informed that Matthew passed away due to cardiac arrest. Matthew was the only unfortunate patient in this study who passed way during the study period.

## 6.6 Discussion

The prevalence of DM in TB patients was 14.9% (n=53) in this study. A study that was conducted in another setting in Malaysia reported a similar prevalence of 14.6% (Nissapatorn, et al., 2005). A systematic review on bi-directional screening for TB and DM revealed that many countries had a wide range of DM prevalence in TB patients, ranging from 1.9% to 35% (Jeon et al., 2010). The wide range of DM prevalence in TB patients could be due to the varying degree of DM prevalence in different countries. One expert from the US Pacific Island reported that high prevalence of DM was seen in their setting and DM contributed to 42% of TB cases in the Northern Pacific (Brostrom, 2010). Increased prevalence of DM in urban areas in India was associated with a 15% greater smear positive TB incidence (Stevenson, et al., 2007). The Malaysian National Health Morbidity Survey III (NHMS III), conducted in 2006 showed that the prevalence of DM in the general population was 14.9% in people above the age of 30 and more than 20% in people who were between the age of 50 and 79 (Letchuman, et al., 2010). The survey indicated that the prevalence of DM in Malaysia almost doubled compared to its prevalence in 1996 which was at 8.6% in people above the age of 30. The increasing trend of DM prevalence in the general population could have a negative impact in TB control in Malaysia and a higher prevalence of DM in TB patients could be expected.

The mean age of TB and DM patients in this study was 52 ± 10 years and in terms of gender, male patients predominated. Another study from Malaysia also reported similar findings with regards to age and gender (Nissapatorn, et al., 2005). The present study did not compare the socio-demographic differences between TB patients with DM and those without. However, Nissapatorn et al. (2005) reported that TB and DM patients were older than TB patients without DM.

One of the key findings of this study was to highlight the change in medication taking behaviour with regards to consuming non-TB medication on commencing TB treatment. The fact that more than half of the patients did not adhere to their DM medication after starting

TB treatment suggests that patients may be giving priority to one class of medication over another. In a qualitative exploration of multiple medicines beliefs of patients with comorbid DM and cardiovascular disease showed that patients undervalued their cardiovascular medications as compared to DM medications (Stack, Elliott, Noyce, & Bundy, 2008). Conversely, the findings in this study showed that patients had prioritised their TB medication when compared with non-TB medication. These findings also suggest that when a patient presents with comorbidities, practitioners need to understand which group of medicines is likely to be omitted by the patient and once this has been identified extra vigilance and support for adherence is needed.

The fact that patients held different sets of beliefs for different diseases with the necessity-concern differential for DM medication being higher compared to TB medications indicate that patients' adherence level differs. It has been postulated that medication adherence is influenced by necessity-concern differential in which beliefs about the necessity of prescribed medication are weighed against concerns about the negative effects of taking it (Horne & Weinman, 1999). Based on this hypothesis, it could be assumed that patients might be low adherers to TB medication when compared with DM medication as they have more concerns about TB medication. However, this was not true in this study because patients were found to be low adherers to DM medication as compared to TB. One plausible explanation for this is that the majority of TB patients were treated through DOT whereby adherence was enforced. Alternatively, in agreement with the hypothesis, it could be interpreted that these patients might be low adherers to TB treatment if they were to be allowed for self-supervision. In fact, some of the patients in this study were allowed for self-supervision and of these, one patient was found to have defaulted TB treatment due to vomiting. This indicates that patients weigh the risk and benefit of taking their medication and decide whether to adhere to their treatment or not. As such, DOT is still important to ensure adherence and to monitor adverse effects of medication but alone, it may not be sufficient. It has been recommended that supplementing DOT with other strategies like patient education, individualised patient care and follow-up, effective communication, adherence aids, educational materials and incentives could strengthen DOT programmes (Cohen, 1997; Grange & Zumla, 1997; Morisky et al., 1990; Ormerod, 1999; WHO., 2003). Likewise, pharmacists in the present study helped to promote

adherence to TB treatment by addressing patients' concerns and persuaded patients who defaulted TB treatment to continue treatment.

Adverse drug reactions either experienced or perceived were one of the reasons for non-adherence to treatment. This study not only identified patients who did not adhere to their treatment regimen but it also provided an opportunity to understand the reasons for non-adherence. Furthermore, pharmacists managed to help patients cope with their treatment by making timely recommendations and addressing their concerns. Problems that bothered patients were the experience of vomiting, itching and other sensations that resembled peripheral neuropathy. Regular telephone follow-up calls made by pharmacists allowed patients to communicate their problems and some of these were resolved by referring them to their physicians as soon as possible without the need to wait for their next follow-up visit. Other studies have also shown that pharmacists were able to reduce non-adherence in patients with chronic conditions and meet patients' needs for information and advice on medicines through telephone follow-up calls (Clifford, Barber, Elliott, Hartley, & Horne, 2006; Clifford, Garfield, Eliasson, & Barber, 2010; Elliott, Barber, Clifford, Horne, & Hartley, 2008; Kassam et al., 2001).

Uncontrolled DM was a concern in this study as tight glycaemic control is important to fight any infectious condition including TB. Besides non-adherence to treatment, drug-drug interactions, drug-induced hyperglycaemia and stress due TB could all contribute to poorly controlled DM. The majority of patients in this study were treated with oral hypoglycaemic agents. Despite the increase in the doses of DM medication in some of the patients, it was difficult to achieve the targeted blood glucose level. Even those who were on insulin had their doses increased by pharmacists in this study in order to optimise their blood glucose level. Concurring with this finding, a study from Turkey reported that 11.4% of the first-time TB patients and 27.5% of MDR-TB patients had poorly controlled DM and pharmacist's intervention resulted in the correction of hyperglycaemia in some patients (Clark, et al., 2007).

It is unclear whether the current measures that were taken to optimise blood sugar level were sufficient or insulin should have been given to all TB and DM patients. Although pharmacists felt that it was important to initiate insulin in patients with poorly controlled DM, chest physicians believed that patients would less likely to adhere to insulin (versus to oral medication) treatment especially in an out-patient setting. Moreover, hospital policy restricted chest physicians from prescribing insulin pens due to financial constraints. As such, pharmacists were reluctant to suggest the conversion from OHAs to insulin in this study despite some evidence supporting the use of insulin. It has been suggested that insulin might be beneficial to achieve tight glycaemic control in TB patients with DM (The Francis J. Curry National Tuberculosis Center, 2009). More research is being conducted in the area of TB and DM and more recommendations will be expected in the near future (World Diabetes Foundation, 2010, 2011). So far, the Brazilian Thoracic Association has considered replacing oral hypoglycaemic agents with insulin during TB treatment to keep fasting blood glucose below 160mg/dl (8.89 mmol/l) (Conde, et al., 2009).

The fact that patients' concerns were addressed and communicated using various means such as face-to-face verbal interactions, follow-up calls and text messages via mobile phone reinforces the importance of individualising patient care and using methods accessible to the patient. It has been recommended that health care professionals should utilise the frequent DOT visits with TB patients to help manage DM by encouraging lifestyle changes at every patient encounter and consider concurrent administration of both DM and TB medications, via DOT, for TB patients with DM (Brostrom, 2011; The Francis J. Curry National Tuberculosis Center, 2009). Piette & Kerr (2006) suggested that pharmacists can assist patients with comorbid conditions by managing patients' complex medication regimen. Based on the number of pharmaceutical interventions presented so far, it is evident that pharmacists could play a role in integrating TB and DM management by addressing medication-related concerns and by making relevant recommendations to patients and physicians. Besides, pharmacists also played a role in educating patients about the risk factors of TB such as advising patients to quit smoking as it is one of the risk factors that worsen TB infection. Furthermore, helping patients to understand the importance of adherence to DM medication by explaining the link between TB and DM was well appreciated by patients. For example, many patients in this

study reported that they did not know that DM is a risk factor for TB and therefore, did not recognise the importance of tight glycaemic control.

Another important observation suggests that patients' carers also played an important role by reporting patients' problems during follow-up visits or calls. During the counselling sessions, pharmacists provided relevant information to patients' carers. In fact, it has been recommended that families and carers should also have the opportunity to be involved in decisions concerning patients' treatment and care (Lewis & Newell, 2009; Nunes et al., 2009).

Another important finding is the absence of a comprehensive documentation of medical and medication history in TB patients' medical record. This finding was also found in the phase1 study. It was observed that physicians filled up a specific TB documentation form when patients were diagnosed with TB. The form has a number of prelisted medical problems that could be ticked as past or concurrent medical problems. Physicians may have overlooked the possibilities of enquiring about other medical problems not listed in that particular form or patients may not inform them about their problems if they were not asked specifically about it. Pharmacists identified a number of concurrent medical problems and past medical histories (e.g. chronic sinusitis, gastritis, history of cataract surgery) as well as past medication histories that were not documented in the patients' medical records. At times, pharmacists requested the patients to bring along all their medication during their next follow-up visits because most patients were unable to name their medication. This assisted in identifying other medical problems.

Despite being able to provide the pharmaceutical care service, there were some logistic barriers that need to be addressed. These barriers existed due to the inherent organisation of the health care system that was not adequately designed to accommodate patients with multiple disease profiles. Furthermore, the unavailability of shared electronic medical records restricted the access to obtain the results of the laboratory tests (e.g. HbA1c test, lipid profile test) that were done in other clinics. Lack of regular monitoring of certain clinical and

laboratory parameters (e.g. finger-prick blood glucose monitoring test, liver function test, renal function test) at the chest clinic was another barrier encountered. It has been recommended that monthly liver function test should be conducted as patients with TB and DM carry the risk of developing hepatotoxicity (The Francis J. Curry National Tuberculosis Center, 2009). Besides isoniazid, pyrazinamide and rifampicin, many patients in this study were on lovastatin which could increase the risk of developing hepatotoxicity and therefore needed to be monitored carefully (The Francis J. Curry National Tuberculosis Center, 2009). However, in the present study, there was a dilemma of whether to recommend certain monitoring tests or to wait and see whether a particular test was ordered by the physician or not. At times it was only feasible to take note of what was done and what was not. For example, despite the suggestion for finger prick monitoring of blood glucose, reluctance to conduct finger-prick monitoring by the nurses were observed in some occasions. It has been recommended that a glucometer should be available in every TB clinic and glucose should be checked at least weekly for the first four weeks of TB treatment and then less frequently thereafter if DM is well controlled (Brostrom, 2011).

Weekly meetings were held with Alan (hospital pharmacist) to reflect on the issues related to the provision of pharmaceutical care, to discuss the barriers encountered, and to come up with an action plan to improve the service. For example, one of the barriers encountered in this study was lack of space to provide counselling. Lack of privacy limited the depth of consultations with some patients. Nevertheless, action was taken to remedy the problem by using one of the nurse's rooms at the clinic. It was found that patients communicated better when they had more privacy.

## 6.7 Strengths and limitations

The action research methodology was the main strength of this study. It provided the flexibility that is needed to research a 'real world' environment by using multiple research methods. It allowed the researcher to participate, understand the local context and develop practical knowledge based on the experiences gained.

Nevertheless, this study has several limitations. The study was conducted in one public hospital in Malaysia which may restrict the generalisation of the findings. It was carried out in a relatively short period of time and only 15 patients were followed-up for a total of four visits. Nonetheless, recruitment of patients continued until the end of the study in order to have a larger sample size and the reason was to identify as many different problems as possible that were unique to patients with TB and DM.

Older bed-ridden patients above the age of 80 and those who were severely ill due to other complications did not participate in this study and as such the findings do not reflect the problems of those patients.

The prevalence of DM in TB patients in this study could have been underestimated as there was no standard strategy employed in screening for DM patients. The first step in the identification of DM was based on patients' self-report of DM. Secondly, baseline laboratory investigations which include fasting or random blood glucose were done and based on the results, some patients were newly-diagnosed with DM. In some instances, physicians repeated fasting blood glucose test to confirm the diagnosis of DM. However, a delay in diagnosis of DM in two patients was observed in this study as physicians waited for their next follow-up to initiate DM treatment. Screening of DM in TB patients with regards to when and how the screening should be performed is a current research agenda that has been put forward by the

experts (Harries, et al., 2010; Jeon, et al., 2010). Active screening may lead to the detection of more DM cases in TB patients and vice versa (Jeon, et al., 2010).

This study compared beliefs of two different diseases in the same patient. The translated Malays version of BMQ was tested for beliefs of TB and DM medication. With regards to the term used in the translated Malay version of BMQ, many patients reported that they could not understand the word 'mystery' in question 6 (*My medicines are a mystery to me*) in BMQ. Mystery is also known as *'misteri'* in Malay language. It seemed that the concept of mystery was not easily captured. Moreover, there were differences in the internal consistencies of the BMQ scale with regards to TB and DM. It is unclear whether the differences could be attributed to the different degree of beliefs on TB and DM medication respectively. BMQ questions were repeated twice, first for TB medication and subsequently for DM medication. It is not known whether repeated questioning could impact the way patients responded to the individual items of the questionnaire. Previous research has recommended the need to examine the impact of repeated questioning on the validity and reliability of responses to questionnaire items (Stack et al., 2010). Both the translated version of BMQ and MMAS-8 was not a validated instrument. Validation of a translated instrument is a huge project by itself and it was beyond the scope of this study. Although, the current availability of the validated Malaysian version of the MMAS can be used in future studies (Al-Qazaz, et al., 2010), this study signalled the need for the translated BMQ to be validated in Malaysia.

Feedback from the patients and health care professionals regarding the provision of pharmaceutical care service was not obtained. Their feedback would have helped to improve the service. With regards to the physicians, there were many physicians that managed patients and the researcher did not work with any particular physician. Therefore, it was not feasible to get the feedback from physicians. Furthermore, not all patients completed their follow-ups and therefore feedback was not attained. Nonetheless, feedback from the hospital pharmacist (Alan) was obtained (see appendix 15). Except for lack of space, language barriers (different dialects) and time limitation, Alan provided positive feedback and would like to continue providing the service.

## 6.8 Reflection

Reflection is an inseparable component in action research (Waterman, et al., 2001). The reflexivity in research includes reflection on self, the process, and representation. It is equally important to evaluate the power relations and the politics in the research process as well as the researcher's accountability in data collection and interpretation (Dickson-Swift, James, Kippen, & Liamputtong, 2006; Silverman, 2005; Thomas, 2008).

As compared to Phase 1 study, I was *emotionally* attached and felt responsible for the patients in Phase 2 study. The sense of *responsibility* was felt when I became part of the health care team and started to provide the service together with Alan. Coming from the clinical pharmacy background, I used to identify medication-related problems mainly through patient's medical record with limited interactions with patients and the problems were usually solved based on clinical knowledge. I provided recommendations according to evidence-based practice and I spent more time reviewing the literature to identify the best approach in managing a particular case. However, in this study, the way I approached patients changed from 'I know what is best for you' to 'I know that you can help me understand how best to solve your medication-related problems'. The approach taken was more patient-centred. The prospective nature of this study allowed me to provide a continuous service and follow-up on some of the patients. Although I wished that I had completed the follow-ups for all patients, action research is time consuming and I had to stop at a particular point for the purpose of completing this PhD study within the allocated time period.

The way I felt at the beginning changed when I compared with how I felt at the end of the research process. Initially, I was very theoretical in the sense that I believed that there was a standard way of managing a particular pharmaceutical care issue. However, as the study progressed, I scrutinised my own ability to execute the pharmaceutical care plan. I was able to appreciate the intricacies involved due to the complex nature of the intervention and how

different it would have been if I was just an observer. As an observer I would have been less attached to the patients and I would not have had the burden of deciding what I should do in a given situation. It would have been easier for me to say that 'Pharmacist A did a, b, c and not x, y, z'. But when I provided the service, I understood why such decisions were made.

The execution of a pharmaceutical care plan was not the same or identical in every patient even when there were similarities with regards to the pharmaceutical care issues. One of the reasons was related to the ease of communication between the physician treating the patients and me. For example, I was comfortable in communicating with the physicians that I have known when compared to those that I do not know. I had a pleasant experience working with physicians that I have known and my recommendations were usually acted upon. On the other hand, it was difficult for me to intrude a busy clinic and explain about the research and my role to a new physician. Besides, there were other issues like nurses who were initially cooperative in fulfilling our request in doing a finger-prick blood glucose monitoring, who later exhibited reluctance to do so. It was learnt that one of the nurses was ticked off by a physician who felt that the finger prick test should only be conducted after a physician's order was obtained. Such issues subconsciously affected me from making certain recommendations to physicians that I have not encountered before. As such, I limited my interactions with those physicians that I do not know. However, it was not a problem for Alan as he provided pharmaceutical care service for patients with chronic obstructive pulmonary disease at the same clinic and it was easier for him to provide recommendations and to communicate with the physicians and the nurses since a long term working relationship had already been established, compared to me who was new at the setting. Although, I had presented my research proposal to the medical audience prior to the start of the research and managed to develop rapport with some of the physicians, there were many new faces at the clinic when I started the study. I realised that there were many senior and junior house officers involved in managing TB and some of them were in rotation and were not permanent staff of the clinic. Lack of time to develop rapport with all the physicians created barriers in communication.

I observed Alan hesitating in writing the pharmaceutical care issues and plan in the patients' medical record despite having the permission for doing so. He felt that it was better to speak directly to the physicians if there were to be any recommendations. Although, it is better to communicate directly, documentation of such recommendations could serve as a reminder to other physicians during the next follow-up. Furthermore, documentation helped to acknowledge the contribution of a pharmacist to patient care. Reflecting on this issue, I understood that Alan found it simpler to communicate and solve the problem immediately but the hesitation to write could be due to the lack of practice or confidence. I did not write in the patients' medical record as I was not the hospital pharmacist.

In summary, action research allowed me to understand various pharmaceutical care issues of TB and DM patients and the organisational component that needed to be factored in when designing a pharmaceutical care service.

# CHAPTER 7: THESIS DISCUSSION

## 7.1 Introduction

This chapter aims to collate the key findings from the phase 1 and phase 2 studies to discuss how successful this research was in meeting its aim and objectives. Subsequently, it provides and overall discussion. Finally, it presents the implications of the findings for policy, practice and future research.

## 7.2 Summary of key findings

Firstly, a qualitative enquiry (phase 1) was carried out in order to explore the pharmaceutical care needs of TB and DM patients. The phase 1 study provided a snap shot of patients' and health care professionals' experiences in managing TB and DM. In addition, it also explored the health care professionals' perspectives on MTACs and the potential role of pharmacists in the management of TB and DM.

Concerns about medication and issues related to the management of TB and DM were the two main themes that emerged. Concerns about medication include the negative consequences of medicine taking (adverse effects of medication, burden of multiple medication, drug interactions and medication confusion) and the perceived positive effect of medication which were expressed in terms of necessity and efficacy of medication. Therefore, the pharmaceutical care needs of TB and DM patients include the need to monitor adverse effects of medication, help patients manage multiple medicines and address patients' concerns about medication. Issues related to the management of TB and DM patients include longer duration of TB treatment in DM patients, delayed initiation of TB and DM treatment, poor record keeping, communication barriers between patients and physicians, the ambiguity of DM management in TB patients, DOT and the burden of attending multiple clinics, and self-management and incorporation of traditional remedies. As such, the pharmaceutical care

aspects include the need to motivate and promote adherence to treatment, advocate the importance of early treatment seeking behaviour, conduct a thorough medication review and improve documentation of patients' medical and medication history, create opportunities to communicate with patients, find ways to integrate the management of TB and DM, and enquire about self-management and the use of traditional remedies.

Health care professionals believed that pharmacist-led MTAC programmes allowed the provision of pharmaceutical care, enhanced pharmacist-patient communication and encouraged pharmacist-physician interactions. Health care professionals proposed that pharmacists could play an important role in educating and counselling patients with TB and DM and that the MTAC model could be expanded to include management of patients with TB and DM.

Secondly, the findings of the phase 1 study and the proposed phase 2 study was presented to health care professionals at the chest clinic in order to incorporate their feedback into consideration. Then, the revised phase 2 study was conducted to determine the feasibility of providing a pharmaceutical care service. Phase 2 revealed more complex issues with regards to pharmaceutical care management of TB and DM. Due to the prospective nature of phase 2 and the study design that employed action research methodology, a variety of 'real-life' experiences were captured.

In spite of the need to address logistic barriers and the need for more collaborative practices between pharmacists and physicians, the provision of the pharmaceutical care service for TB and DM patients was a feasible conclusion. Pharmacists played an important role in managing DM in TB patients by: raising the awareness that DM is a risk factor for TB; emphasising the importance of adherence to DM medication as well as to dietary recommendations; advocating the importance of regular monitoring of blood sugar level; addressing patients' concerns about their medication; and referring patients to physicians and recommending treatment modifications. Nevertheless, there were other issues which could be regarded as

barriers to pharmaceutical care management such as communication barriers; delays in initiating DM treatment in newly-diagnosed DM patients; infrequent monitoring of blood glucose level; absence of certain clinical and laboratory data; and nurses' reluctance to conduct finger-prick blood glucose monitoring if it was not a physician's order at the chest clinic.

This study revealed the complex nature of pharmaceutical care interventions and provided various insights and experience that could be used for further development work prior to conducting a RCT to evaluate the effectiveness of the service.

The next section provides an overall discussion of findings.

## 7.3 Overall discussion

It has been reported that there is a need for quality research designs and a clear description of the pharmaceutical care process to evaluate the impact of pharmaceutical care (Kassam, et al., 2001; Kennie, et al., 1998; Roughead, Semple, & Vitry, 2005). Studies have also fshown that pharmaceutical care is a complex intervention and research in this area should reveal its complexity (Tulip & Campbell, 2001). In line with the pharmaceutical care theory, the present study has shown that pharmaceutical care interventions were indeed complex as it was not just about identifying, preventing and resolving medication- related problems in TB and DM patients but it also involved the need to establish a therapeutic relationship with the patients and their caregivers, develop a collaborative practice with other health care providers and follow-up the patients. The identification of these factors was possible with the application of the MRC framework for complex interventions which emphasised the importance of conducting qualitative and feasibility studies to identify the components of a particular intervention prior to developing a definitive trial.

Interest in using qualitative methodologies to investigate pharmaceutical care has been growing (Dupotey & de Oliveria, 2009; van Mil, et al., 2004). This study adds to the body of knowledge by demonstrating that qualitative methodologies are indeed valuable to assess the pharmaceutical care needs or issues from the patients' and providers' perspectives. Action research has also been suggested to be used in pharmaceutical care research (Tanna, 2005; Tulip & Campbell, 2001). The use of action research in the phase 2 study was helpful in identifying the intricacies of pharmaceutical care interventions by using multiple strategies of inquiries such as observation, interviews, medical chart/record reviews and participation of the researcher. The researcher played a dual role (researcher/practitioner) in the phase 2 study and this allowed the researcher to acquire experiential knowledge. Furthermore, action research allowed the researcher to identify various areas that needed to be strengthened prior to developing a full-fledged service such as the need for: more commitment and collaborative effort among health care professionals, access to medical records for comorbid

conditions and strategies to integrate or improve communication between different care providers/specialties.

Several studies that have been conducted in patients with multiple diseases had identified numerous medication-related problems (Elliott, et al., 2007; Krska et al., 2001; Townsend, et al., 2003). However, identification of pharmaceutical care issues of patients with specific comorbid conditions was difficult due to heterogenous sampling of patients in those studies. In contrast, this study identified medication-related problems of a homogenous group of patients. As such, some common medication-related problems associated with TB and DM had been identified. Nevertheless, many of these patients had other comorbidities besides TB and DM which shows that despite some similarities among the patients, each individual was unique and had their own concerns about medication that requires individualised pharmaceutical care management. Hence, despite the need for 'specialised knowledge' on pharmaceutical care issues in a specific comorbid condition, there is also a need to have 'generalised knowledge' in order to provide individualised or holistic pharmaceutical care management. Therefore, it can be implied that pharmacist could play a generalist role by bridging the care for TB, DM and other comorbid conditions which is currently separated due to the single disease management system. Although there have been calls to move from single disease management system to a more integrated disease management system, radical changes are unlikely to happen overnight. However, integrating pharmacists into a multidisciplinary health care team might be a feasible option.

Harries et al. (2010) reported that there is a need for research in four key priority areas in TB and DM management which include: 1) the need to screen DM in TB patients and vice versa, 2) the impact of DM on TB treatment outcome, 3) the implementation of the TB DOTS strategy for managing and monitoring DM, and 4) the development of diagnostic and monitoring test including HbA1C for DM patients. Interestingly, the findings of the present study were in agreement with the key research area that has been put forward by Harries, et. al. (2010) and could be considered as preliminary evidence. Firstly, this study has shown that there is a need for thorough screening of DM in TB patients as the prevalence of DM in TB patients could have

been underestimated in this study due to lack of standard screening mechanisms. Secondly, poorly controlled DM and non-adherence to DM medications may have a detrimental effect to TB treatment outcome although it has to be further investigated in a longitudinal study. Thirdly, it is possible to implement the TB DOTS strategy to incorporate DM monitoring through finger-prick monitoring test at the chest clinic, although lack of support from the other health care professionals with regards to finger-prick monitoring was observed in this study. This indicates the lack of awareness on the importance of monitoring DM at the chest clinic. Fourthly, there was either lack of monitoring of HbA1c at the chest clinic or lack of amalgamation of this data into TB patients' medical records if the HbA1c test had been carried out at the DM clinic. Therefore, it is important to improve communication between TB and DM care providers with regards to access to monitoring data.

Some of the findings in this study (e.g. pharmaceutical care issues, barriers to provision of service) might be transferable to other public health care settings in Malaysia. As with other qualitative research, the degree of generalisability or transferability to other settings could only be determined by the reader as it is context specific. The researcher has provided a thick description about the setting and it is up to the reader to decide on the components that are relevant to their setting. This study could be taken as an example for investigating the role of pharmacists in other clusters of comorbid conditions. Despite the fact that each patient may have different pharmaceutical care needs, it might be worthwhile to investigate the pharmaceutical care issues in other specific clusters of comorbid conditions because general problems pertinent to those conditions could be unveiled.

The following three sections provide the implications of the findings in relation to policy, practice and future research.

## 7.4 Policy implications

Based on a myriad of pharmaceutical issues identified and intervened, this study has established evidence that pharmacists have a role to play in integrating the management of TB and DM. Although this study targeted TB patients with comorbid DM, it was found that other non-DM comorbid conditions also required individualised pharmaceutical care management. Based on this finding, it can be argued that pharmacist's service is not only relevant to TB and DM patients per se but could be extended to all TB patients. As such, it is recommended that pharmacists should become one of the participating health professionals for the National TB programme. In order to have an impact on practice, it is imperative to first have a policy that supports the integration of pharmacist in the National TB programme. Having such policies in place may ensure the integration of pharmacist in the management of TB at a larger scale. Recently, the WHO and FIP have signed a joint statement at the World Pharmacy Congress in Hyderabad in September 2011 on the role of pharmacists in the management of TB (FIP, 2011b) and this may bring positive changes in many National TB programmes in the near future. The present study could provide good political support for pharmacists to be part of the National TB programme.

It was observed that there was an association between non-adherence to DM medication and suboptimal blood glucose control. As it is important to maintain tight glycaemic control while on TB treatment, this finding indicates a need for policies to support co-management of TB and DM. At the moment, TB and DM patients receive treatment from various care providers and there is a lack of coordination between TB and DM care providers. It is suggested that health care professionals at the chest clinic integrate the management of TB and DM by utilising the opportunity of meeting patients during DOT to provide DM education. It might be the most ideal if DM medications can be dispensed at the same time in order to reduce the need to attend multiple clinics. There is a lack of effective communication between both TB and DM care providers. Innovative approaches such as using shared electronic medical records or any other means of communication should also be considered. Development of guidelines with regards to the management of TB and DM will be beneficial to health care

providers. Lately, the WHO have published a collaborative framework for care and control of TB and DM (WHO, 2011) and some of its recommendations are in agreement with the proposed suggestions derived from this study .

## 7.5 Practice implications

Factors that could have affected the pharmaceutical care service in this study include logistic barriers, communication barriers due to lack of inter-professional relationships and pharmacist's hesitation in documenting pharmaceutical care plans in a patient's medical record. In order to enhance practice in the future, it is suggested to:

a) Enhance collaboration between pharmacists, physicians and nurses

b) Access to patients' other medical records for comorbid conditions

c) Provide patient education and counselling in a separate consultation space

d) Encourage pharmacists to document pharmaceutical care plans in patients' medical records

The following is a summary of recommendations that were drawn from the experience of providing the pharmaceutical care service. These recommendations could be used as a guide to enhance practice.

- **Communicate with patients and patients' carers**

It is important to listen, empathise, develop rapport and communicate with patients in a private consultation area. Therefore, health care professionals should encourage patients to voice their concerns and provide assurance that TB can be cured. Patients' carers play an important role in supporting patients' treatment. As such, health care professionals should also communicate with patients' carers.

- **Monitor**

Firstly, patients need to be informed about the potential adverse drug reactions of their medication and how they should respond if adverse drug reactions occur. Patients need to be monitored for adverse effects like vomiting, itching, joint pain, visual disturbances, hypoglycaemia and sensations that resembled peripheral neuropathy. Parameters that need to be monitored for adverse drug reactions include liver enzymes, serum creatinine, uric acid and visual acuity. Patients might have additional risk of developing liver impairment especially when lovastatin is added. Regular monitoring (e.g. monthly monitoring of liver and renal function test) should be recommended. It is suggested that health care professionals should also ask patients whether they have cataract or have a history of cataract surgery as ethambutol may not be suitable for these patients or they may need to have their visual acuity assessed prior to the administration of the drug. Similarly, patients should also be asked about history of gout as their uric acid level will require monitoring.

Secondly, adherence to both TB and DM treatment need to be assessed and monitored. It is also important to encourage patients to adhere to all the other medications that have been prescribed for comorbidities. Patients may need to be provided with strategies to cope with multiple medicines and at the same time monitored for polypharmacy. Patients who have other comorbidities like hypertension will need blood pressure monitoring. Due to the consumption of multiple medicines as well as the use of traditional and herbal remedies, drug-drug interactions and drug-herb interactions need to be checked. Some patients in this study also highlighted that they had difficulties in consuming medication on an empty stomach. In such cases, patients should be advised to take their medication with light food.

- **Optimise blood glucose level**

It is very important to keep blood sugar level within the targeted range. Fasting blood sugar should be checked monthly and HbA1c should be checked every three months. Health care professionals should take note of blood glucose levels and advocate regular finger-prick monitoring. Nurses should conduct regular finger prick monitoring at the chest clinic. Nurses have plenty of opportunity to reinforce DM education due to their frequent contact with patients during DOT. Health care professionals should explain to patients that DM is a risk factor for TB and that it is important to keep their blood glucose under control. Health care professionals should look out for drugs that could induce hyperglycaemia (e.g. prednisolone, atypical antipsychotics). It is important to check whether patients adhere to DM treatment and whether they are being followed-up. Health care professionals at the chest clinic may have to contact the DM care provider if there is a need for further information. Patients with poorly controlled DM may benefit from insulin therapy.

- **Educate, counsel and address patients' concerns**

It was found that patients had various concerns about medication, misconceptions, and knowledge gaps which required individualised pharmaceutical care management. Pharmacists could play an important role in providing drug information, communicating patients' problems to their physicians, making timely referrals and recommending early initiation of treatment for adverse effects (e.g. antihistamines for itchiness and metoclopramide for vomiting). Educating and helping patients understand the link between TB and DM may encourage adherence to treatment.

- **Empower patients**

In order to optimise medication use, health care professionals should empower patients to make decisions about goals, therapeutic options, self-care behaviors and to assume responsibility for TB and DM care in order to help patients care for themselves. Although health care professionals are experts in disease management, this study showed that patients are the experts on their own lives and that they have their own strategies to manage their medicines. As such, knowing about the disease is not the same as knowing about a patient's life, beliefs, culture and medicine-taking behavior. Therefore, patients are the primary decision-makers with regards to their daily self-management of their diseases. Health care professionals should help patients assume responsibility for their care and encourage patients to participate actively during consultations.

## 7.6 Implications for patients

Patients will benefit from a pharmaceutical care service because it provides an opportunity for them to discuss their concerns about medication and receive education and counselling for both TB and DM. They will have an opportunity to have their medication reviewed by the pharmacists before they see their physicians and at the same time their waiting time will be utilised effectively. Furthermore, they may not have to wait for their next appointment at their DM clinic to monitor their blood glucose or to optimise the dosage of their medication since their daily attendance for DOT can also be utilised for DM management. Pharmacists will be able to make a timely referral as well as recommendations to physicians should there be any medication-related problems.

## 7.7 Research implications and future work

- Lack of time to develop rapport with other health care professionals was a barrier in the phase 2 study. Future work should consider the involvement of a multidisciplinary research team. A collaborative agreement should be made prior to the start of the study so that the research team members are aware of their responsibility and their expected contribution to the study. Regular meetings should be held with health care professionals participating in the study and their feedback should be obtained. Researchers could also discuss and have an agreement with physicians on the following:
    - issues related to monitoring parameters for TB and DM
    - access to medical records
    - the role of nurses in supporting patient care activities such as conducting regular finger-prick monitoring.

- The present study showed that patient's beliefs about medications and adherence can be assessed by using the BMQ and MMAS-8. However, there is a need to validate the translated Malay version of the BMQ in a larger sample in Malaysia.

- As there is a need for more evidence for the use of insulin in the management of DM in TB patients, future research should investigate the benefit and cost effectiveness of intensifying DM treatment with insulin therapy to control blood glucose in TB and DM patients through a RCT.

- The phase 2 study demonstrated that it was relatively feasible to provide pharmaceutical care to TB and DM patients. However, future research should

evaluate the effectiveness of the pharmaceutical care service using a prospective, longitudinal study design. Based on the findings, a RCT could be designed to evaluate the clinical, humanistic and economic outcomes of the pharmaceutical care study. A qualitative study should also be conducted to examine patients' and health care professionals' perceptions with regards to the provision of service.

## 7.8 Thesis conclusion

This study applied the first three phases of the MRC framework for complex intervention as a theoretical guide to develop a pharmaceutical care service for TB and DM patients in a public hospital in Malaysia. The use of qualitative approaches in phase 1 and action research in phase 2 helped to identify various medication-related problems in patients with TB and DM. Despite the need to address the barriers encountered during the provision of pharmaceutical care, this study demonstrated that pharmacists could play a generalist role by integrating care for TB and DM in a health care system which is fragmented due to the single disease management system. In short, this study has laid the foundation for future work to be carried out in improving the current pharmaceutical care service through thorough analysis of the challenges faced in the developmental phase prior to evaluating its effectiveness in a RCT.

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# APPENDICES

## Contents

# Appendix 1: Literature review search terms and strategy

# Literature review search terms and strategy

The initial literature search was conducted in 2007-2008. The search was updated during data analysis in 2010-2011.The search used the terms below.

***Search term***

Comorbidity (comorbid, co-morbid, comorbidities)

Complex intervention (Complex intervention AND Pharmaceutical care)

Diabetes (Type 2 diabetes, Diabetes mellitus, DM)

Directly observed therapy (Directly observed treatment, DOT, DOTS)

Malaysia (TB AND Malaysia, Diabetes AND Malaysia)

Pharmaceutical care (Pharmaceutical care AND diabetes, Pharmaceutical care AND tuberculosis)

Pharmacist (Pharmacist AND tuberculosis, Pharmacist AND diabetes, Pharmacist AND Malaysia)

Qualitative (Qualitative AND TB, Qualitative AND diabetes, Qualitative AND comorbidities)

Tuberculosis (TB, Tuberculosis AND diabetes)

***Databases used***

Medline, Embase, Ovid, Pubmed, Google Scholar, Scopus.

A hand search of the references cited in some of the key journals on TB and DM was also conducted.

## Appendix 2: Ethical approval letter for Phase 1 study

**PEJABAT TIMBALAN KETUA PENGARAH KESIHATAN**
***OFFICE OF THE DEPUTY DIRECTOR-GENERAL OF HEALTH***
**(PENYELIDIKAN & SOKONGAN TEKNIKAL)**
***(RESEARCH & TECHNICAL SUPPORT)***
**KEMENTERIAN KESIHATAN MALAYSIA**
***MINISTRY OF HEALTH MALAYSIA***
Aras 12, Blok E7, Parsel E, Presint 1
*Level 12, Block E7, Parcel E, Precinct 1*
Pusat Pentadbiran Kerajaan Persekutuan
*Federal Government Administrative Centre*
62590 PUTRAJAYA

Tel 03 88832543
Faks 03 88895184

**JAWATANKUASA ETIKA & PENYELIDIKAN PERUBATAN**
**KEMENTERIAN KESIHATAN MALAYSIA**
**d/a Institut Pengurusan Kesihatan**
**Jalan Rumah Sakit, Bangsar**
**59000 Kuala Lumpur**

Ruj. Kami : (2) KKM/NIHSEC/08/0804/P08-62

Tarikh : 5 Mac 2008

Cik Shubashini a/p Gnanasan
Division of Social Research in Medicines & Health
School of Pharmacy
The University of Nottingham

Puan,

**NMRR-08-10-1165**
**Complex intervention to initiate pharmaceutical care in patients with tuberculosis and diabetes mellitus in Malaysia**
**Phase 1 ; The need for pharmaceutical care in the management of tuberculosis and diabetes mellitus : an exploratory study**

**Lokasi projek : Hospital Pulau Pinang**

Dengan hormatnya perkara di atas adalah dirujuk.

2. Jawatankuasa Etika & Penyelidikan Perubatan (JEPP), Kementerian Kesihatan Malaysia (KKM) mengambil maklum bahawa projek tersebut merupakan syarat akademik program ijazah kedokoran dan telah diluluskan oleh pihak The University of Nottingham.

3. Sehubungan dengan ini, dimaklumkan juga bahawa pihak JEPP KKM tiada halangan, dari segi etika, ke atas pelaksanaan projek tersebut.

4. Laporan tamat kajian dan sebarang penerbitan dari kajian ini hendaklah dikemukakan kepada Jawatankuasa Etika & Penyelidikan Perubatan selepas tamatnya kajian ini.

Sekian terima kasih.

**BERKHIDMAT UNTUK NEGARA**

Saya yang menurut perintah,

Shahnaz

**(DR SHAHNAZ MURAD)**
b.p. Pengerusi
Jawatankuasa Etika & Penyelidikan Perubatan
Kementerian Kesihatan Malaysia

s.k. Urusetia NIH, KKM

## Appendix 3: Patient information sheet for phase 1 study

The University of Nottingham

# The need for pharmaceutical care in the management of tuberculosis and diabetes mellitus: an exploratory study (Phase1 )

## PATIENT INFORMATION SHEET

You are invited to take part in a research study. However, before you decide whether you want to be involved in the study, it is important that you understand what the study is about and what taking part will mean to you. Please take time to read the information carefully.

The information is presented in two parts. Part 1 explains the purpose of the study and describes what will happen to you if you agree to participate in the study. After you have finished reading part 1, and you feel that this study is of interest to you and you are thinking of taking part then continue to read part 2. Part 2 provides you with additional information about how the project will be managed.

**PART 1**

**What is the purpose of the study?**

This study aims to understand patients' experiences of living with tuberculosis and diabetes mellitus. We are interested to learn how you manage your medicines. We are also interested to find out what things make it easier or harder for you to follow your treatment.

**Do I have to take part in this study?**

Taking part in this study is entirely your choice. Only make a decision once you have had the chance to read the information provided and have asked us any questions you might have. Whatever your decision is, please contact Shubashini Gnanasan at 012-2877774 or email paxsg2@nottingham.ac.uk . If you have decided to take part in the study, we will ask you to sign an informed consent form to show your agreement. You will be given a copy of the signed informed consent form to keep for your records.

**Will my decision affect the care I receive?**

Please be assured that the standard of care you to receive will not be affected in anyway.

**Can I change my mind once I have signed the consent form?**

If you agreed to take part in the study, and for whatever reason you are unable to, that is absolutely fine. If you have initially decided not to take part and would now like to be involved, that is fine too. All you need to do is contact us. This will not affect the standard of care you receive

**What will happen to me if I take part in the study?**

You will be invited to take part in an interview. We will ask you about your experiences of managing tuberculosis and diabetes mellitus. The interview will take place in the hospital and it will be expected to last between 30 to 45 minutes. You will be contacted for an interview appointment. If you are unable to make your interview appointment for whatever reason, don't worry. Please contact us and we will have this arranged for a more suitable time.

**What are the risks of taking part in the study?**

As this project involves you in an interview, we believe that the risks of taking part in this project are minimal.

**What are the benefits of taking part in the study?**

This project is not expected to directly benefit you. However, the information you provide us may help in the future development of services designed to help patients affected with both tuberculosis and diabetes mellitus.

**What happens if something goes wrong?**

Any complaint you have resulting from taking part in the study will be addressed accordingly. For more details, see Part 2.

**Will the information provided be kept confidential?**

Confidentiality will be maintained at all times. For more details, see Part 2.

If the information in Part 1 has been of interest and you are considering taking part in the study, please read the additional information given in Part 2 before you make a decision.

**PART 2**

If you have any complaints or concerns regarding an aspect of this study, please contact me (Ms. Shubashini Gnanasan) at 012-2877774 or e-mail paxsg2@nottingham.ac.uk and I will try to resolve any issues to the best of my ability.

You may also contact the academic supervisors of this project.

| Academic Supervisors | Email | Contact number |
|---|---|---|
| Professor Claire Anderson | Claire.Anderson@nottingham.ac.uk | 0115 951 5389 |
| Dr. Ting Kang Nee | Kang-Nee.Ting@nottingham.edu.my | 03-89248209 |
| Assoc. Prof. Dr. Salmiah Mohd A | drsalmiah@salam.uitm.edu.my | 03-55442761 |

**Will the information I give be kept confidential?**

Any information you provide will be kept strictly confidential. However, if you tell us information that indicates that you or your health might be endangered we might need to inform somebody else. However, we will discuss this with you first and ask you permission to do so.

**Will you be contacting my doctor?**

If you agree to take part in the study, we will inform your doctor. However, we will NOT discuss anything you tell us, without your permission. What you tell us is confidential and will not be repeated back to your doctor. Please feel free to talk to your doctor about taking part in this study.

**Will the information I give be handled and stored safely?**

The overall responsibility for handling any information you provide during the course of the study lies with Shubashini Gnanasan. The information you provide us will be held on secure protected computers and/or in a locked and secure drawer or filing cabinet.

**Who will have the access to the data collected during the study?**

Only the research team involved in this project will have access to the data collected. The data collected will be stored at the University of Nottingham for 5 years following the completion of the study.

**What will happen to the results of the study?**

We will share the information with you if you wish. We can send you a short communication about our findings. We will also present results at conference and write journal articles so that other people can learn from our study. None will have any of you personal information. Nobody will know that the results are yours.

**Who is organising this research?**

This study is being organised by Shubashini Gnanasan as a part of a requirement for the completion of an educational qualification (PhD). This research study is conducted under the supervision of Professor Claire Anderson and Dr. Ting Kang Nee from University of Nottingham as well as Dr. Salmiah Mohd Ali from Universiti Teknologi MARA.

**Who has reviewed the study?**

Before any research project is allowed to go ahead, it has to be checked by a Medical Research Ethics Committee. They make sure that the research is fair and pose minimal risks to study participants. This project has been registered in the National Medical Research Register (Research ID: 1165).

**Whom should I contact for further information?**

If you need further information on this study, please feel free to contact me on the details provided below:

Ms. Shubashini Gnanasan, BPharm (Hons), MPharm (Clinical)

PhD research student

University of Nottingham.

Tel. number: 012-2877774

Email address: paxsg2@nottingham.ac.uk

**Thank you for reading this document.**

**Please ask any questions if you need to.**

# Appendix 4: Patient Informed consent form for phase 1 study

The University of Nottingham

## INFORMED CONSENT FORM

**Title of Project: The need for pharmaceutical care in the management of tuberculosis and diabetes: an exploratory study**

Name of Investigator: Shubashini Gnanasan

Please initial the box at the end of each statement:

1. I confirm that I have read and understood the information sheet for the above study. I have had the opportunity to consider the information, ask questions and have had these answered satisfactorily. ☐
2. I understand that my participation is voluntary and that I am free to withdraw at any time, without giving any reason, without my legal rights being affected. ☐
3. I understand that relevant data collected during the study, may be looked at by responsible individuals from The University of Nottingham and Universiti Teknologi MARA. I give permission for these individuals to have access to this data. ☐
4. I give my informed consent for the audio-taping of the interview. ☐
5. I give my informed consent for anonymised direct quotes to be used in reports and publications. ☐
6. I agree to take part in the above study. ☐

Name of Participant: Date: Signature:

Investigator: Date: Signature:

# Appendix 5: Interview schedule

**Interview Schedule**

**The need for pharmaceutical care in patients with tuberculosis and diabetes: an exploratory study (Phase 1)**

General Themes:

1. Experiences of managing TBDM and issues related to medication
2. Health-system barriers
3. Potential role of pharmacists in a multidisciplinary team
4. DOTS

**Patients:**

Medication issues

1. What medication are you currently taking?
2. How long have you been on this medication for?
3. How do you take your medication?
4. How many medicines do you have to take?
5. Has your medication changed over time?
6. Are you taking any supplements or traditional medicines? If yes, what do you take?
7. Are there times when you feel you need to take more or less of your medication?
8. Do you experience any side effects from your medication?
9. What are your concerns about your medication?
10. How do you feel about DOTS?

Patient understanding of TBDM and experiences

1. Can you share your experiences when you found out that you had TB and DM?
2. What do you think caused you to get TB and DM?
3. What effect has your disease had on your life? Has having TB and DM changed your life?
4. How do you cope when you have more than one illness?
5. What kind of support do you receive from your family?

Health system

1. Since your diagnosis, whom within the hospital have you seen?
2. When did you see them?
3. What information and advice have you received?
4. What other sorts of support have you had or want?
5. Would you like to see a pharmacist?

**Doctors (Chest clinic):**

1. Can you share with me how TBDM patients are managed?
2. How do patients prioritize treatment and self management when faced with multiple, complex diseases/conditions?
3. How does that affect their medication-taking behavior?
4. What measures do you take to improve glycemic control in TBDM patients?
5. How do the health systems create barriers to patient care?
6. What are the common drug-related problems that occur in TBDM patients?
7. How can collaborative practice improve TBDM care?
8. What kind of contribution will you expect from a pharmacist?
9. What is your opinion on patient-centered care?
10. What is your opinion on DOTS?

**Doctors (Endocrine clinic):**

1. How do you manage diabetes patients in your clinic?
2. How do you manage diabetes patients with comorbidities?
3. Do you manage the co-morbid condition of the diabetic patients as well or do you refer them to other specialties?
4. Have you encountered TBDM patients in your practice? For eg. Patient coming in with chronic cough?
5. Can you share with me how TBDM patients are being managed?
6. How will you treat TBDM patients?
7. What are the common drug related problems that occur in TBDM patients?
8. Would you prescribe Insulin for TBDM patients?
9. Do TBDM patients get the same treatment as the other DM patients?
10. How do the health systems create barriers to patient care?
11. How can collaborative practice improve TBDM care?

12. How do you feel about the MTAC run by the pharmacist?

**Nurses (Chest clinic):**

1. Can you share your experiences of caring for TBDM patients?
2. What measures do you take to improve glycemic control in TBDM patients?
3. What are your experiences of working in a multi-disciplinary team?
4. What are the common drug-related problems that occur in TBDM patients?
5. How do the health systems create barriers to patient care?
6. How can collaborative practice improve TBDM care?
7. What kind of contribution will you expect from a pharmacist?
8. What is your opinion on patient-centered care?
9. What are the usual complaints of TBDM patients?
10. What is your opinion on DOTS?

**Nurses (Endocrine clinic):**

1. How do you manage diabetes patients in your clinic?
2. How do you manage diabetes patients with comorbidities?
3. Can you share your experiences of caring for DM patients with comorbidities?
4. Have you encountered TBDM patients in your practice?
5. Can you share with me how TBDM patients are being managed?
6. What are the common drug related problems that occur in TBDM patients?
7. How do the health systems create barriers to patient care?
8. How can collaborative practice improve TBDM care?
9. What is your opinion on patient-centered care?
10. What kind of contribution will you expect from a pharmacist?
11. How do you feel about the MTAC run by the pharmacist?

# Appendix 6: Focus group schedule

**Focus group schedule**

**The need for pharmaceutical care in patients with tuberculosis and diabetes: an exploratory study (Phase 1)**

**Pharmacists**:

1. Can you share your experiences of providing pharmaceutical care?
2. How do you assist patients with comorbidities?
3. What are the common drug-related problems that occur in patients with comorbidities?
4. What are your experiences in managing TBDM patients?
5. What kind of service will you be able to provide to TBDM patients?
6. What are your experiences of working in a multi-disciplinary team?
7. How can a pharmacist provide pharmaceutical care services by collaborating with other health care professionals?
8. What is your opinion on DOTS?

# Appendix 7: Data collecting form for phase 1 study

## DATA COLLECTING FORM-PHASE 1

**The need for pharmaceutical care in patients with tuberculosis and diabetes: an exploratory study (Phase 1)**

**A. Demographic Data**

| Patient's Name | R/N | Age | Gender |
|---|---|---|---|
| | | | M/F |

| Race | Marital Status |
|---|---|
| Malay/Chinese/Indian/Others | Single/Married |

| Contact Number | Occupation |
|---|---|
| | |

**B. Medical History**

| Past medical history of DM | Newly diagnosed DM |
|---|---|
| | |
| FPG/ RBS | |
| HbA1c | |

| Other past medical history |
|---|
| |

| Past medication history |
|---|
| |
| |

A. TB Classification

| | | |
|---|---|---|
| Pulmonary tuberculosis | Yes | No |
| Extrapulmonary tuberculosis | Yes | No |
| Pulmonary with extrapulmonary tuberculosis | Yes | No |
| If extrapulmonary | | |
| Tuberculous Meningitis | Yes | No |
| Miliary TB | Yes | No |
| Others | | |

B. Participation

| | |
|---|---|
| Patient willing to participate in the study | Yes / No |
| Patient's command of English language | Good/ Moderate/Poor |
| Patient's command of Malay language | Good/ Moderate/Poor |
| Interview Date | |

# Appendix 8: Background information of participants (phase 1)

## Background information of patients

| Patient's name (pseudonym) | Age (years) | Sex | Ethnicity | Duration of DM | Other comorbidities/ complications | Tobacco use | Alcohol use | Occupation | Language used |
|---|---|---|---|---|---|---|---|---|---|
| R1: Yong | 50 | Male | Chinese | Newly diagnosed | Nil | Nil | Nil | Carpenter | Malay |
| R2: Yuen[c] | 64 | Male | Chinese | 5 years | Nil | Nil | Nil | Carpenter | Malay |
| R3: Ooi[a,b] | 63 | Male | Chinese | 30 years | Nil | Nil | Regular consumption | Ex-lorry driver | Malay |
| R4: Mydeen | 72 | Male | Indian | 16 years | Nil | Nil | Nil | Retired government officer | Tamil |
| R5: Imran[a] | 69 | Male | Malay | 9 years | Hypertension | Ex-smoker | Nil | Ex-driving instructor | Malay |
| R6: Najib | 54 | Male | Malay | 8 years | Nil | Smoker | Nil | Ex- factory worker | Malay |
| R7: Pavithran | 49 | Male | Indian | 1 year | Gout | Nil | Nil | School lab assistant | English |
| R8: Badrul | 55 | Male | Malay | 5 years | Cholelithiasis | Nil | Nil | Medical assistant | Malay |
| R9: Zaman | 50 | Male | Malay | 12 years | Nil | Ex-smoker | Nil | Policeman | Malay |
| R10: Eliass | 64 | Male | Malay | 18 years | Nil | Nil | Nil | Retired postman | Malay |
| R11: Tim[a,c] | 78 | Male | Chinese | 20 years | Hypertension | Ex-smoker | Nil | Retired businessman | Malay |
| R12: Long[c] | 63 | Male | Chinese | 10 years | Hypertension/ Osteoarthritis | Smoker | Nil | Retired businessman | Malay |
| R13: Veeramuthu | 50 | Male | Indian | 7 years | Hypertension/ Heart disease | Ex-smoker | Nil | Ex-security guard | Tamil |
| R14: Sharon | 42 | Female | Chinese | 1 year | Nil | Nil | Nil | Ex-nursery worker | Malay |
| R15: Ramamany | 56 | Female | Indian | 2 years | Nil | Nil | Nil | Ex-factory worker | Tamil |
| R16: Jeyaraj | 52 | Male | Indian | Newly diagnosed | Diabetic foot/ Pneumonia | Nil | Nil | Ex-factory worker | Tamil |
| R17: Hakim | 55 | Male | Malay | 10 years | Hyper-cholesterolemia | Ex-smoker | Nil | Retired enforcement officer | Malay |
| R18: Goh | 51 | Male | Chinese | 4 years | Nil | Nil | Nil | Ex-restaurant worker | Malay |
| R19: Choo[c] | 53 | Male | Chinese | 15 years | Gout | Nil | Regular consumption | Salesman | Malay |
| R20: Nusa[c] | 53 | Male | Malay | 8 years | Nil | Smoker | Nil | Ex-quarry factory worker | Malay |

[a]These patients had a relapse of TB

# Appendix 9: Invitation letter for phase1 research presentation

**Example of invitation letter for Phase 1 research presentation**

Dato' Dr. Haji Abdul Razak Mutallif

Head of Respiratory Department

1 June 2009

Dear Dato'

**Invitation to a research presentation and discussion**

We are glad to inform that we have successfully conducted the first phase of our research which aimed to explore the pharmaceutical care need of tuberculosis patients' with co-morbid diabetes mellitus (TBDM). Hence, we would like to present the findings of our research. We take this opportunity to thank all healthcare professionals who participated in the interviews and focus group discussion which was held last year. We would like to cordially invite you to attend a presentation and discussion followed by lunch.

| | |
|---|---|
| Title: | Managing tuberculosis with co-morbid diabetes mellitus (TBDM) |
| Venue: | Chest Clinic, Hospital Pulau Pinang |
| Date: | 29th June 2009 |
| Time: | 1.00 pm |

Thank you.

Yours sincerely,

Shubashini Gnanasan

PhD Research Student

Division of Social Research of Medicine and Health

School of Pharmacy, University of Nottingham

Email: paxsg2@nottingham.ac.uk

Tel: 012-2877774

# Appendix 10: Ethical approval letter for Phase 2 study

PEJABAT TIMBALAN KETUA PENGARAH KESIHATAN
*OFFICE OF THE DEPUTY DIRECTOR-GENERAL OF HEALTH*
(PENYELIDIKAN & SOKONGAN TEKNIKAL)
*(RESEARCH & TECHNICAL SUPPORT)*
KEMENTERIAN KESIHATAN MALAYSIA
*MINISTRY OF HEALTH MALAYSIA*
Aras 12, Blok E7, Parsel E, Presint 1
*Level 12, Block E7, Parcel E, Precinct 1*
Pusat Pentadbiran Kerajaan Persekutuan
*Federal Government Administrative Centre*
62590 PUTRAJAYA

Tel : 03 88832543
Faks : 03 88895184

**JAWATANKUASA ETIKA & PENYELIDIKAN PERUBATAN**
**KEMENTERIAN KESIHATAN MALAYSIA**
**d/a Institut Pengurusan Kesihatan**
**Jalan Rumah Sakit, Bangsar**
**59000 Kuala Lumpur**

Ruj. Kami : (2) KKM/NIHSEC/08/0804/P09-313

Tarikh : 1 September 2009

Ms Shubashini Gnanasan
Division of Social Research in Medicines and Health
School of Pharmacy
University Nottingham

Puan,

**NMRR-09-463-4064**
**Pharmaceutical care management for patients with tuberculosis and diabetes mellitus : a feasibility study**

**Lokasi projek : Hospital Pulau Pinang**

Dengan hormatnya perkara di atas adalah dirujuk.

2. Jawatankuasa Etika & Penyelidikan Perubatan (JEPP), Kementerian Kesihatan Malaysia (KKM) mengambil maklum bahawa projek tersebut merupakan syarat akademik program Falsafah Kedoktoran dan telah diluluskan oleh the University Nottingham.

3. Sehubungan dengan ini, dimaklumkan juga bahawa pihak JEPP KKM tiada halangan, dari segi etika, ke atas pelaksanaan projek tersebut. JEPP mengambil maklum bahawa projek tersebut tidak melibatkan intervensi klinikal dan hanya melibatkan pengumpulan data kajian melalui temuramah dan pemerhatian ke atas plan farmaseutikal subjek kajian. Segala rekod dan data subjek adalah SULIT dan hanya digunakan untuk tujuan kajian dan semua isu serta prosedur mengenai *data confidentiality* mesti dipatuhi. Kebenaran daripada Pengarah hospital di mana kajian akan dijalankan mesti diperolehi terlebih sebelum kajian dimulakan. Puan perlu akur dengan keputusan yang diberikan.

4. Laporan tamat kajian dan sebarang penerbitan dari kajian ini hendaklah dikemukakan kepada Jawatankuasa Etika & Penyelidikan Perubatan selepas tamatnya kajian ini.

Sekian terima kasih.

**BERKHIDMAT UNTUK NEGARA**

Saya yang menurut perintah,

**DATO' DR CHANG KIAN MENG**
Pengerusi
Jawatankuasa Etika & Penyelidikan Perubatan
Kementerian Kesihatan Malaysia

# Appendix 11: Patient information sheet for phase 2 study

The University of Nottingham

## Patient Information Sheet

**Pharmaceutical Care Management for Patients with Tuberculosis and Diabetes Mellitus (TBDM): A Feasibility Study**

Dear Sir/Madam,

This letter is to inquire whether you would be willing to participate in a pharmaceutical care project for patients with TBDM. The study is being conducted to evaluate the impact and feasibility of having a pharmacist to run a pharmaceutical care programme for TBDM patients. This study will be useful to enhance the current health management of TBDM patients. We hope to identify and resolve medication related problems in TBDM patients.

We are asking if you would allow the pharmacists to interview you; ask specific questions regarding your medications; conduct a thorough medication used review and provide health education and counselling. Upon the first meeting with the pharmacist, subsequent appointments for the next visits will be given. You will only be seeing the pharmacist when you come to the clinic for your TB treatment. No additional trip to the hospital will be required. The pharmacist will be seeing you while you wait to see your doctor or while you wait to take your medications. You will be followed up for five visits which will take a total of 3 months to complete. Each visit will take about 15 minutes and will only be conducted after your consent. Even if you agree to participate in this project, you may stop your involvement at any time during the study if you wish.

Your privacy will be maintained and your details will be held in the strictest of confidence. Your name and any other identifying information will not be revealed.

The outcome of the study will help us to understand the benefits of having a pharmacist in a multi-disciplinary health care team in enhancing the current management of TBDM patients. The results will be provided to the government and published in relevant journals to show the

impact and the feasibility to provide pharmaceutical care to TBDM patients. If you are willing to participate in this pharmaceutical care project, please sign the consent form and return it to the researcher.

Thank you for considering this request to participate in this study.

Sincerely,

Shubashini Gnanasan

PhD Research Student
Division of Social Research in Medicines and Health
School of Pharmacy, University of Nottingham, United Kingdom.

Note:

1. If you have any complaints or concerns regarding an aspect of this study, please contact me (Ms. Shubashini Gnanasan) at 012-2877774 or e-mail paxsg2@nottingham.ac.uk and I will try to resolve any issues to the best of my ability. You may also contact the academic supervisors of this project.

| **Academic Supervisors** | **Email** | **Contact number** |
|---|---|---|
| Professor Claire Anderson | Claire.Anderson@nottingham.ac.uk | 01159515389 |
| Dr. Ting Kang Nee | Kang-Nee.Ting@nottingham.edu.my | 03-89248209 |
| Assoc. Prof. Dr. Salmiah Mohd Ali | drsalmiah@salam.uitm.edu.my | 03-55442761 |

2. This study has been reviewed and approved by the Medical Research & Ethics Committee, Ministry of Health Malaysia. This committee is responsible for reviewing and approving any research project that involves patients or public.

## Appendix 12: Patient informed consent form for phase 2 study

The University of Nottingham

# Patient Consent Form

**Consent to Participate in a Pharmaceutical Care Management Project for Patients with Tuberculosis and Diabetes Mellitus (TBDM)**

I have been asked to take part in a pharmaceutical care project for patients with Tuberculosis and Diabetes Mellitus (TBDM). I have read the informed consent document for this project. I have received an explanation of the nature, purpose and duration of this

project. My questions have been answered satisfactorily.

I, _____(name of participant)

hereby consent to participate in the pharmaceutical care project.

I understand that:

a. My participation is voluntary. I can stop participating in this project at any time and I

am free to not answer any particular question(s).

b. While information gained in this study may be used in a conference presentation, and may also be published in a journal article, I will not be identified. Information concerning me will remain strictly confidential.

c. I can ask the investigator, at any time for any additional information.

Investigator's name: _____

Participant's name: _____

Date: _____

Date: _____

Investigator's signature:

Participant's signature:

# Appendix 13: Data collecting form for phase 2 study

| | | | |
|---|---|---|---|
| | | | |

**Pharmaceutical Care Management for Patients with Tuberculosis and Diabetes Mellitus (TBDM): A feasibility study**

**(Phase 2)**

**A. Treatment Centre**

| Treatment Initiation Centre | Treatment Continuation Centre | Treatment Start date | Daily DOTS/ Weekly packing | Admitted in TB ward |
|---|---|---|---|---|
| | | | | |

**B. Demographic Data**

| Patient's Name | IC | R/N | Contact number | Age | Gender | Race | Marital Status |
|---|---|---|---|---|---|---|---|
| | | | | | M/F | Malay/ Chinese/ Indian/ Others | Single/ Married |

| Tobacco Use | Alcohol Use | Occupation |
|---|---|---|
| | | |

| C. Past Medical History | D. Past Medication History |
|---|---|
| | |
| | |
| | |
| | |
| | |

**E. Current medication history**

| Drug | Dosage Regimen |
|---|---|
| | |
| | |
| | |
| | |

**Non-prescribed drugs (Traditional/Herbal/Supplements)**

| |
|---|
| |
| |

**F. Laboratory Test**

| **Sputum AFB** | **Other Specimen** |
|---|---|
| **Positive/Negative** | **Positive/Negative** |

**G. Chest X-Ray**

| **Date** | | | | |
|---|---|---|---|---|
| **X-ray presentation** | | | | |

F. Current History of TB episode

**Main symptoms:**

| | Tick |
|---|---|
| Cough more than 2 weeks | |
| Cough with blood stained sputum | |
| Loss of weight | |
| Loss of appetite | |
| Fever | |
| Night sweats | |
| Others | |

G. TB Classification

| | | |
|---|---|---|
| Pulmonary tuberculosis | Yes | No |
| Extrapulmonary tuberculosis | Yes | No |
| Pulmonary with extrapulmonary tuberculosis | Yes | No |
| If extrapulmonary | | |
| Tuberculous Meningitis | Yes | No |
| Miliary TB | Yes | No |
| Others | | |

J. TB treatment regimen

| Initial Body Weight | | | | |
|---|---|---|---|---|
| Treatment Start Date | | Treatment Change Date | | Tick |
| Intensive Phase Regimen | Dosage | Change of Regimen(if there is) | Dosage | Reason for Change |
| Streptomycin | | Streptomycin | | Resistant TB |
| Isoniazid | | Isoniazid | | ADR |
| Rifampicin | | Rifampicin | | OTHERS: |
| Pyrazinamide | | Pyrazinamide | | |
| Ethambutol | | Ethambutol | | |
| AKURIT 4 | | | | |

| | | | | |
|---|---|---|---|---|
| **Body Weight at Continuation Phase** | | | | |
| **Treatment Start Date** | | **Treatment Change Date** | | **Tick** |
| **Maintenance Phase Regimen** | **Dosage** | **Change of Regimen(if there is)** | **Dosage** | **Reason for Change** |
| **Streptomycin** | | **Streptomycin** | | **Resistant TB** |
| **Isoniazid** | | **Isoniazid** | | **ADR** |
| **Rifampicin** | | **Rifampicin** | | **OTHERS:** |
| **Pyrazinamide** | | **Pyrazinamide** | | |
| **Ethambutol** | | **Ethambutol** | | |

**K. LABORATORY INVESTIGATION**

| | **Normal Range** | **Baseline** | | | |
|---|---|---|---|---|---|
| **Random blood glucose** | **>5.5-doFBG** | | | | |
| **Fasting blood glucose** | **3.5-6.7** | | | | |
| **HbA1C** | **4.0-6.0** | | | | |

| LIVER FUNCTION TEST | Normal Range | Baseline | | | |
|---|---|---|---|---|---|
| Total Protein | 66-87 g/L | | | | |
| Albumin | 35-50 g/L | | | | |
| Globulin | 20-36 g/L | | | | |
| A/G Ratio | 0.9 -1.8 | | | | |
| Total Bilirubin | 3- 21 µmol/L | | | | |
| Alanine Transaminase | 0-55 µ/L | | | | |
| Alkaline Phosphatase | 40-150 µ/L (>15yrs) <500 (1-12 yrs) | | | | |

| RENAL PROFILE | Normal Range | Baseline | | | |
|---|---|---|---|---|---|
| Sodium | 136-145 mmol/L | | | | |
| Pottasium | 3.5 -5.0 mmol/L | | | | |
| Urea | 3.5-7.2 (>50yrs) mmol/L | | | | |
| Creatinine | 53-115 µmol/L | | | | |
| Chloride | 98-107 mmol/L | | | | |

| ESR | Normal Range | Baseline | | | |
|---|---|---|---|---|---|
| ESR (Men) | 3-10mm/hr | | | | |
| ESR (Women) | 4-15mm/hr | | | | |

| HEMATOLOGY | Normal Range | Baseline | | | |
|---|---|---|---|---|---|
| WBC | 5.2-12.4 | | | | |
| RBC | 4.2-5.4 | | | | |
| HGB | 12.0-16.0 | | | | |
| HCT | 37-47 | | | | |
| MCV | 81-99 | | | | |
| MCH | 27-31 | | | | |
| MCHC | 33-37 | | | | |
| RDW-CV | 11.5-14.5 | | | | |
| PLT | 130-400 | | | | |
| NE% | 40-74 | | | | |
| LY% | 19-48 | | | | |
| MO% | 3.4-9.0 | | | | |
| EO% | 0.0-7.0 | | | | |
| BA% | 0.0-1.5 | | | | |
| NE# | 1.5-8.0 | | | | |
| LY# | 0.9-5.2 | | | | |

| | | | | | |
|---|---|---|---|---|---|
| MO# | 0.16-1.00 | | | | |
| EO# | 0.0-0.8 | | | | |
| BA# | 0.0-0.2 | | | | |

| FASTING LIPID PROFILE | Normal Range | Baseline | |
|---|---|---|---|
| Total Cholesterol | <5.2 desirable<br>5.2-6.2 borderline<br>>6.2<br>high | | |
| Triglcerides | <1.7 normal<br>1.7-2.3 borderline high<br>>2.3-5.6 high | | |
| LDL Cholesterol | 3.3-4.9<br><3.3 low risk<br>> 4.9 high risk | | |
| HDL Cholesterol | >1 negative risk factor<br><1 major risk factor | | |
| % HDL Cholesterol | 15-25 low risk<br><15 high risk | | |

| | | | |
|---|---|---|---|
| Visual acuity for patient on ethambutol | | | |

## L. DRUG RELATED PROBLEMS

a) (i) Adverse drug reaction related to TB drugs (Symptom based approach)

**Minor side- effects**

| Tick | Side- effects | Drug(s) probably responsible | Tick | Recommended WHO Management |
|---|---|---|---|---|
| | Anorexia | Pyrazinamide, Rifampicin | | Give drugs with small meals or last thing at night |
| | Nausea | Pyrazinamide, Rifampicin | | Give drugs with small meals or last thing at night |
| | Abdominal pain | Pyrazinamide, Rifampicin | | Give drugs with small meals or last thing at night |
| | Joint pains | Pyrazinamide | | Aspirin |
| | Burning sensation in the feet | Isoniazid | | Pyridoxin 100 mg daily |
| | Orange/red urine | Rifampicin | | Reassurance |

**Major Side-effects**

| Tick | Side- effects | Drug(s) probably responsible | Tick | Recommended WHO Management |
|---|---|---|---|---|
| | Itching, skin rash | S,H, R, Z | | Stop anti-TB drugs |
| | Deafness | Streptomycin | | Stop streptomycin, Use ethambutol |
| | Dizziness(vertigo and nystagmus) | Streptomycin | | Stop streptomycin, Use ethambutol |
| | Jaundice | Isoniazid<br>Pyrazinamide<br>Rifampicin | | Stop anti -TB drugs |
| | Hepatitis | Isoniazid<br>Pyrazinamide<br>Rifampicin | | Stop anti -TB drugs |
| | Confusion<br>(suspect drug-induced acute liver failure if jaundice present) | Most anti-TB drugs | | Stop anti-TB drugs.<br>Urgent liver function tests and prothrombin time |
| | Visual Impairment | Ethambutol | | Stop ethambutol |
| | Shock | Rifampicin | | Stop rifampicin |
| | Purpura | Rifampicin | | Stop rifampicin |
| | Acute renal failure | Rifampicin | | Stop rifampicin |

**ii) Adverse drug reaction to non-TB drugs**

| ADR | Offending Drug |
|---|---|
| | |
| | |

**b) Drug Interactions**

| Isoniazid | Rifampicin | Streptomycin | Others |
|---|---|---|---|
| Phenytoin | Cyclosporine | Aminoglycoside | Aminoglycoside |
| Carbamazepine | Corticosteroids | Amphotericin B | Amphotericin B |
| Aluminium Hydroxide | Protease Inhibitors | Cephalosporine | Cephalosporine |
| | Oral Contraceptive pill | Ethacrynic acid | Ethacrynic acid |
| | Oral hypoglycaemic agents | Cyclosporine | |
| | Oral anticoagulants | Frusemide | |
| | Phenytoin | Cisplatin | |
| | Cimetidine | Vancomycin | |
| | Theophylline | | |
| | Digoxin | | |

| Follow-up progress notes |
| --- |
| |
| |
| |

| | | |
|---|---|---|
| **DRUG THERAPY PROBLEMS** | **Medical condition and drug therapy involved** | **INDICATION** |
| | | ***Unnecessary Drug Therapy***<br>----- No medical indication<br>----- Duplicate therapy<br>----- Non drug therapy indicated<br>----- Treating avoidable ADR<br>----- Addictive / recreational<br>***Needs Additional Drug Therapy***<br>----- Untreated condition<br>----- Preventive/prophylactic<br>----- Synergistic/potentiating |
| | **Medical condition and drug therapy involved** | **EFFECTIVENESS** |
| | | ***Needs different drug product***<br>----- More effective drug available<br>----- Condition refractory to drug<br>----- Dosage form inappropriate<br>----- Not effective for condition<br>***Dosage Too Low*** |

| | | |
|---|---|---|
| | | ----- Wrong dose<br>----- Frequency inappropriate<br>----- Drug interaction<br>----- Duration inappropriate |
| | **Medical condition and drug therapy involved** | **SAFETY** |
| | | ***Adverse Drug Reaction***<br>----- Undesirable effect<br>----- Unsafe drug for patient<br>----- Drug interaction<br>----- Duration inappropriate<br>***Dosage Too High***<br>----- Wrong dose<br>----- Frequency inappropriate<br>----- Duration inappropriate<br>----- Drug Interaction<br>----- Incorrect administration |
| | **Medical condition and drug therapy involved** | **COMPLIANCE** |
| | | ***Noncompliance***<br>----- Directions not understood |

| | | |
|---|---|---|
| | | ----- Patient prefers not to take<br>----- Patient forgets to take<br>----- Patient cannot afford<br>----- Cannot swallow/administer<br>----- Drug product not available |

**DRUG THERAPY PROBLEMS TO BE RESOLVED**

---------- No Drug Therapy Problem(s) at this time

**PHARMACEUTICAL CARE PLAN**

**Indication:**

(Description and history of the present illness or medical condition including previous approaches to treatment and responses)

**Goals of Therapy** (improvement or normalisation of signs /symptoms/laboratory tests or reduction of risk)

1.

2.

**Drug Therapy Problems**- to be resolved

_ None at this time

Therapeutic Alternatives (to resolve the drug therapy problem)

1.

2.

**Pharmacotherapy plan** (Includes current drug therapies and changes)

| Medications<br><br>(Drug products) | Dosage Instructions<br><br>(Dose, Route, Frequency, Duration) | Note Changes |
|---|---|---|
| | | |
| | | |
| | | |
| | | |

Other intervention to optimize drug therapy:

**Schedule for next follow-up evaluation**:

# Appendix 14: Follow-up schedules

**Follow-up schedule**

| Patients | 1st visit | 2nd visit/call | 3rd visit/call | 4th visit/call |
|---|---|---|---|---|
| P1 | √ | √ | √ | √ |
| P2 | √ | √ | √ | √ |
| P3 | √ | √ | √ | √ |
| P4 | √ | √ | √ | √ |
| P5 | √ | √ | √ | √ |
| P6 | √ | √ | √ | √ |
| P7 | √ | √ | √ | √ |
| P8 | √ | √ | √ | √ |
| P9 | √ | √ | √ | √ |
| P10 | √ | √ | √ | √ |
| P11 | √ | √ | √ | √ |
| P12 | √ | √ | √ | √ |
| P13 | √ | √ | √ | √ |
| P14 | √ | √ | √ | √ |
| P15 | √ | √ | √ | √ |
| P16 | √ | √ | Passed away | |
| P17 | √ | √ | √ | |
| P18 | √ | couldn't contact | | |
| P19 | √ | √ | √ | |
| P20 | √ | √ | | |
| P21 | √ | √ | | |
| P22 | √ | √ | | |
| P23 | √ | √ | | |
| P24 | √ | | | |
| P25 | √ | | | |
| P26 | √ | | | |
| P27 | √ | | | |
| P28 | √ | | | |
| P29 | √ | | | |
| P30 | √ | | | |
| P31 | √ | | | |
| P32 | √ | | | |
| P33 | √ | | | |
| P34 | √ | | | |
| P35 | √ | | | |

**Follow-up dates**

| Patients | Treatment start date | 1st visit date | 2nd visit/call date | 3rd visit/call date | 4th visit/call date |
|---|---|---|---|---|---|
| P1 | 03/11/2009 | 04/11/2009 | 19/11/2009 | 23/11/2009 | 03/12/2009 |
| P2 | 08/10/2009 | 05/11/2009 | 19/11/2009 | 03/12/2009 | 31/12/2009 |
| P3 | 20/10/2009 | 05/11/2009 | 19/11/2009 | 14/12/2009 | 18/01/2010 |
| P4 | 23/10/2009 | 05/11/2009 | 19/11/2009 | 31/12/2009 | 25/02/2010 |
| P5 | 03/11/2009 | 09/11/2009 | 23/11/2009 | 07/12/2009 | 31/12/2009 |
| P6 | 26/10/2009 | 09/11/2009 | 23/11/2009 | 07/12/2009 | 27/01/2010 |
| P7 | 16/10/2009 | 16/11/2009 | 19/11/2009 | 10/12/2009 | 11/02/2010 |
| P8 | 05/11/2009 | 16/11/2009 | 30/11/2009 | 14/12/2009 | 26/01/2009 |
| P9 | 19/08/2009 | 16/11/2009 | 30/11/2009 | 14/12/2009 | 12/01/2010 |
| P10 | 04/11/2009 | 16/11/2009 | 19/11/2009 | 31/12/2009 | 21/01/2010 |
| P11 | 05/11/2009 | 19/11/2009 | 03/12/2009 | 31/12/2009 | 28/01/2010 |
| P12 | 24/09/2009 | 19/11/2009 | 03/12/2009 | 17/12/2009 | 12/01/2010 |
| P13 | 18/11/2009 | 30/11/2009 | 14/12/2009 | 28/12/2009 | 25/01/2010 |
| P14 | 11/11/2009 | 30/11/2009 | 14/12/2009 | 28/12/2009 | 07/01/2010 |
| P15 | 23/09/2009 | 03/12/2009 | 21/12/2009 | 09/02/2010 | 22/02/2010 |
| P16 | 30/11/2009 | 08/12/2009 | 22/12/2009 | 15/01/2010 | |
| P17 | 30/09/2009 | 10/12/2009 | 26/11/2009 | 21/01/2010 | |
| P18 | 04/08/2009 | 24/12/2009 | | | |
| P19 | 13/07/2009 | 31/12/2009 | 09/02/2010 | 25/02/2010 | |
| P20 | 10/07/2009 | 07/01/2010 | 09/02/2010 | | |
| P21 | 27/08/2009 | 11/01/2010 | 21/01/2010 | | |
| P22 | 05/10/2009 | 11/01/2010 | 09/02/2010 | | |
| P23 | 10/11/2009 | 14/01/2010 | 09/02/2010 | | |
| P24 | 10/12/2009 | 14/01/2010 | | | |
| P25 | 14/06/2009 | 28/01/2010 | | | |
| P26 | 12/10/2009 | 28/01/2010 | | | |
| P27 | 14/08/2009 | 08/02/2010 | | | |
| P28 | 06/07/2009 | 11/02/2010 | | | |
| P29 | 19/11/2009 | 11/02/2010 | | | |
| P30 | 27/08/2009 | 11/02/2010 | | | |
| P31 | 13/01/2009 | 11/02/2010 | | | |
| P32 | 20/08/2009 | 22/02/2010 | | | |
| P33 | 17/07/2009 | 22/02/2010 | | | |
| P34 | 15/10/2009 | 25/02/2010 | | | |
| P35 | 26/01/2010 | 25/02/2010 | | | |

# Appendix 15: Pharmacist's feedback

The following was the hospital pharmacist's (Alan)feedback regarding the provision of pharmaceutical care service for TB and DM patients that I received via email on the 30 October 2010.

1. *Practicality of the project*

- *Can be done and pharmacist have a role in helping patients to identifying drug- related problems in patients as patients are having lots of medications due to different disease condition*

2. *Barriers*

- *Space (no proper place to counsel patient and no privacy)*
- *Time (have several work commitments)*
- *Language (dialect)*

3. *Physicians and pharmacist collaboration*

- *Definitely will improve patient's benefit (increase understanding about their condition, medication and compliance)*
- *Enhance understanding and collaboration between pharmacist and doctors*
- *Physician's implementation of therapy recommended by pharmacist will increase pharmacist's confidence and satisfaction*

4. *Continue with the service?*

- *Yes, it is very satisfying to see patients condition improving and to build patient-pharmacist rapport*

## Appendix 16: Research publication