# EVALUATION OF PHARMACIST-LED HOME-BASED INTERVENTION AMONG TYPE 2 DIABETES PATIENTS FROM A PUBLIC PRIMARY CARE CENTRE AT BUKIT MINYAK, PENANG MALAYSIA

**CHOW EE PIN**

**UNIVERSITI SAINS MALAYSIA**

**2015**

# EVALUATION OF PHARMACIST-LED HOME-BASED INTERVENTION AMONG TYPE 2 DIABETES PATIENTS FROM A PUBLIC PRIMARY CARE CENTRE AT BUKIT MINYAK, PENANG MALAYSIA

**by**

**CHOW EE PIN**

**Thesis submitted in fulfilment of the requirements for the degree of Master of Science**

**September 2015**

## ACKNOWLEDGEMENT

First of all, I would like to express my utmost thanks and appreciations to my main supervisor Professor Dr. Mohamed Azmi Ahmad Hassali, my co-supervisors Associate Professor Dr. Asrul Akmal Shafie and Dr. Fahad Saleem for their tremendous support, guidance and encouragement throughout my candidature. Without their help and consistent encouragement, it would be impossible for me to complete this study.

Secondly, I would also like to thank the Ministry of Health Malaysia for their generous scholarship to enable me to further my postgraduate studies in Universiti Sains Malaysia. Without the scholarship I would not be able to pursue my dream in postgraduate study.

I would like to express my sincere appreciations to my head of department Mr. Nathiran Naidu, my colleagues in Bukit Minyak clinic Ms Wong Poei Feu and Mr. Tan Soo Leon and other colleagues in Discipline of Social and Administrative Pharmacy whom have given me support and help in this study.

I would also like to express my love and gratitude to my parents, parents' in-law, family and friends for their support and encouragement, especially to my husband, Tye Ching Foa who has constantly given me moral support and love that motivate me to pursue and accomplish my postgraduate study.

## TABLE OF CONTENTS

## LIST OF TABLES

## LIST OF FIGURES

## LIST OF APPENDICES

## LIST OF ABBREVIATIONS

| | |
|---|---|
| ACE | Angiotensin converting enzyme |
| ADA | American Diabetes Association |
| ADE | Adverse event |
| AE | Aerobic exercise |
| AHA | American Heart Association |
| ARB | Angiotensin II Receptor Blockers |
| BDA | British Diabetes Association |
| BMI | Body mass index |
| BP | Blood pressure |
| CCB | Calcium channel blockers |
| CDA | Canadian Diabetes Association |
| CG | Control group |
| CV | Cardiovascular |
| CVD | Cardiovascular disease |
| DBP | Diastolic blood pressure |
| DCCT | Diabetes Control and Complications Trial |
| DIF | Dose, indication and frequency |
| DM | Diabetes mellitus |
| DRP | Drug- related problems |
| DSME | Diabetes self-management education |
| EASD | European Association for the Study of Diabetes |
| FBS | Fasting blood sugar |
| GDM | Gestational diabetes mellitus |
| GI | Glycaemic index |

| | |
|---|---|
| HbA1c | Glycated haemoglobin A1c |
| HDL | High-density of lipoprotein |
| HMR | Home medicines review |
| IDF | International Diabetes Federation |
| IG | Intervention group |
| KA | Knowledge and awareness |
| LDL | Low-density of lipoprotein |
| MDKT | Michigan Diabetes Knowledge Test |
| MI | Myocardial infarction |
| MMAS-8 | 8-item Morisky Medication Adherence Score |
| MREC | Medical Research Ethic Committees |
| NCD | Non-communicable disease |
| NCEP | National Cholesterol Education Panel |
| NGO | Non-governmental organisations |
| NGSP | National Glycohemoglobin Standardization Program |
| NMRR | National Medical Research Register |
| NRGU | Not recommended for general use |
| NSA | No specific amount |
| NSAID | Non-steroidal anti-inflammatory drug |
| OGTT | Oral glucose tolerance test |
| OHA | Oral hypoglycaemic agents |
| OTC | Over the counter |
| PA | Physical Activity |
| R | Recommended |

| | |
|---|---|
| RCT | Randomised controlled trial |
| RM | Ringgit Malaysia |
| RT | Resistance training |
| SBP | Systolic blood pressure |
| SD | Standard deviation |
| SMBG | Self-monitoring blood glucose |
| SPSS | Statistical Package for the Social Sciences |
| T1DM | Type 1 diabetes mellitus |
| T2DM | Type 2 diabetes mellitus |
| TC | Total cholesterol |
| TG | Triglyceride |
| UK | United Kingdom |
| USD | United State dollar |
| WHO | World Health Organisation |

## LIST OF PUBLICATIONS

### Bulletin

1) Chow EP and Hassali MA. Social Pharmacy: Type II Diabetes Patient Education for Better Medical Adherence and Reduced Wastage. Advanced Research Initiatives Universiti Sains Malaysia Volume 1

### Newspaper

1) Chow EP, Hassali Ma, Fahad S. Use medicines correctly in the Star newspaper 7 July 2015

### Journal

1) Chow EP, Hassali MA, Fahad S. (2015) Effects of pharmacist-led patient education on diabetes-related knowledge and medication adherence: A home-based study. *Health Education Journal* 1-13

### Conferences

1) Chow EP, Hassali MA. A Pilot Analysis of A Pharmacist Initiated Home Medication Review Programme with Type 2 Diabetes Patients in The State of Penang, Malaysia. 8$^{th}$ National Pharmacy R&D Conference 2014: Shah Alam, Malaysia; 10-12 June 2014 (Oral presentation)

2) Chow EP, Hassali MA. Improving Patient Adherence and Minimizing Medication Wastage among Type 2 Diabetes Patients from Public Primary Centre in Penang. International Social Pharmacy Workshop 2014: Boston, Massachusetts; 5-8 August 2014 (Poster presentation)

3) Chow EP, Hassali MA. A Pilot Analysis of A Pharmacist Initiated Home Medication Review Programme with Type 2 Diabetes Patients in The State of Penang, Malaysia. National Conference on Pharmacy Practice, NCoPP 2014: Shah Alam, Malaysia; 9-10 April 2014 (Poster presentation)

4) Chow EP, Hassali MA. A Pilot Analysis of Pharmacist Initiated Home Medication Review Programme with Type 2 Diabetes Patients in Penang, Malaysia. International of Social Pharmacoepidemiology 2014: Taipei, Taiwan; 24-27 October 2014 (Poster presentation)

5) Chow EP, Hassali MA. Drug Related Problems Identified During Pharmacist-Initiated Home Medication Review in Type 2 Diabetes Patients. International Conference on Pharmaceutical, Medical & Environmental Health Sciences, IPharME 2014: 17-18 September 2014 (Poster presentation)

**PENILAIAN IMPAK INTERVENSI DI RUMAH OLEH AHLI FARMASI DALAM KALANGAN PENGHIDAP DIABETES JENIS 2 DI SATU PUSAT PENJAGAAN KESIHATAN AWAM DI BUKIT MINYAK, PULAU PINANG MALAYSIA**

## ABSTRAK

Kencing manis adalah salah satu penyakit tak berjangkit yang paling biasa di dunia. Kencing manis jenis 2 merangkumi 90-95% daripada populasi kencing manis. Kencing manis jenis 2 yang tidak terkawal akan menyebabkan komplikasi yang teruk. Di Malaysia, dalam masa 4 tahun terdapat peningkatan sebanyak 3.6% penyakit kencing manis di kalangan dewasa > 18 tahun. Penyakit kencing manis jenis 2 memerlukan penjagaan berterusan namun dalam kebanyakan kes terdapat kehilangan kesinambungan penjagaan pesakit-pesakit kencing manis jenis 2 sebaik sahaja mereka meninggalkan pusat penjagaan kesihatan. Oleh itu , kajian ini adalah untuk menilai kesan intervensi di rumah oleh pegawai farmasi di kalangan pesakit kencing manis jenis 2 di Bukit Minyak klinik di Pulau Pinang, Malaysia. Pesakit yang berumur 18 tahun ke atas dan disahkan menghidap kencing manis jenis 2 dengan HbA1c > 6.5 % yang mengambil tiga atau lebih ubat-ubatan jangka panjang untuk penyakit kencing manis, tekanan darah tinggi atau hyperlipidaemia, tinggal di rumah yang mempunyai alamat kediaman tetap serta nombor telefon, dapat memahami Bahasa Malaysia, Bahasa Inggeris atau Cina dan bersedia untuk mengambil bahagian telah diambil. Pesakit yang telah bersetuju untuk mengambil bahagian dalam kajian ini telah dibahagikan kepada kumpulan intervensi [(IG) yang terdiri dua lawatan rumah oleh pegawai farmasi] atau kumpulan kawalan [(CG) tiada lawatan ke rumah telah disediakan] menggunakan lambungan duit syiling. Pesakit dalam kumpulan intervensi menerima sesi pendidikan, kajian ubat-ubatan dan pemantauan tekanan darah dan gula semasa lawatan rumah. Tiada intervensi diberikan kepada kumpulan

kawalan. Pesakit dalam kedua-dua kumpulan telah dinilai pada kepatuhan ubat dan pengetahuan degan menggunakan MMAS-8 dan MDKT soal selidik semasa pendaftaran dan penilaian akhir bagi kumpulan kawalan dan lawatan rumah ke-2 bagi kumpulan intervensi. Secara umum, pesakit dalam kedua-dua kumpulan mempunyai kepatuhan ubat yang rendah dan kekurangan pengetahuan mengenai kencing manis. Walau bagaimanapun, selepas intervensi di rumah, pesakit dalam kumpulan intervensi menunjukkan peningkatan yang ketara dalam HbA1c (-0.73 ± 1.50), tekanan darah diastolik (-1.19 ± 9.96) , jumlah kolesterol (-0.45 ± 1.16), trigliserida (-0.14 ± 0.48), kepatuhan ubat (3.37 ± 1.67) dan pengetahuan (5.84 ± 1.90) berbanding dengan kumpulan kawalan, $p < 0.05$. Seramai 202 masalah berkaitan uabt yang dikenalpasti semasa lawatan pertama ke rumah pesakit dengan purata (3.37 ± 2.99) masalah  setiap pesakit yang dilawati. Empat puluh lapan daripada 60 pesakit (80%) mempunyai sekurang-kurangnya satu masalah berkaitan ubat. Daripada ubat-ubatan yang berlebihan dikumpul, sejumlah RM 2.805,50 (USD 770,38) dengan purata RM 47.55 (USD 13.06) setiap pesakit telah dikira daripada 59 pesakit. Metformin merupakan ubat yang paling banyak kuantiti yang berlebihan di rumah pesakit. Kajian ini telah menunjukkan bahawa intervensi di rumah oleh pegawai farmasi mampu meningkatkan hasil klinikal, pematuhan ubatan dan pengetahuan pesakit.

**EVALUATION OF PHARMACIST-LED HOME-BASED INTERVENTION AMONG TYPE 2 DIABETES PATIENTS FROM A PUBLIC PRIMARY CARE CENTRE AT BUKIT MINYAK, PENANG MALAYSIA**

## ABSTRACT

Diabetes mellitus is one of the most common non-communicable diseases in the world. Type 2 diabetes mellitus account for 90-95% of the diabetes population. Uncontrolled type 2 diabetes has severe complications. In Malaysia, within four years there was an increase of 3.6% of adults aged > 18 had diabetes mellitus. Type 2 diabetes mellitus required continuous care management, however in most cases there is a lost of continuity of care in type 2 diabetes mellitus patients once they left the healthcare facilities. Studies have shown a high incidence of drug-related problems among patients who had discharged from healthcare facilities. Thus, this study was to evaluate the impact of pharmacist-led home-based intervention among type 2 diabetes patients at Bukit Minyak clinic in Penang, Malaysia. This was a randomised controlled trial conducted in Bukit Minyak clinic. Patients aged 18 years and above and diagnosed with T2DM with the most recent HbA1c >6.5%, currently taking three or more long term medications for diabetes, hypertension or hyperlipidaemia, staying at house with permanent residential address and telephone number, able to understand Bahasa Malaysia, English or Chinese and willing to participate were recruited. Patients who were agreed to participate in the study were assigned to either the intervention group [(IG), which consisted a two home visits by the pharmacist] or control group [(CG) where no home visit was provided] using a coin tossing. Patients in the intervention group received educational sessions, medication review and point of care for blood pressure, cholesterol and sugar monitoring during the home visits. There was no intervention given to the control group. Patients in both groups were assessed on their medication adherence and knowledge using the validated MMAS-8

and MDKT questionnaire during the enrolment and final assessment for the control group and 2nd home visit for the intervention group. In general, patients in both groups had low medication adherence and poor knowledge on diabetes. However, after the home-based intervention, patients in the intervention group had significant improvement in HbA1c (-0.73 ± 1.50), diastolic blood pressure (-1.19 ± 9.96), total cholesterol (-0.45 ± 1.16), triglyceride (-0.14 ± 0.48), medication adherence score (3.37 ± 1.67) and knowledge score (5.84 ± 1.90) compared to the control group, $p < 0.05$. A total of 202 drug related problems identified during the first visit with an average of (3.37 ± 2.99) DRP per visited patient. Forty eight out of 60 patients (80%) have at least one DRP. From the excessive medications collected, a total cost of RM 2805.50 (USD 770.38) with an average of RM 47.55 (USD 13.06) per patient was calculated from 59 patients. Metformin was the drug with most excess quantities in patient's house. This study had indicated that pharmacist-led home-based intervention is able to improve patients' medication adherence, knowledge and clinical outcomes.

# CHAPTER 1: GENERAL INTRODUCTION

## 1.1 Background of the study

Diabetes mellitus (DM) is one of the chronic non-communicable diseases around the world. It is the fourth leading cause of mortality in developed and developing countries. Recently, it was estimated that there were 382 million people around the world have DM and it is projected that the number will increase to 592 million in 2035 (International Diabetes Federation, 2013). Diabetes mellitus generally can be divided into type 1 DM (T1DM), type 2 DM (T2DM) and gestational DM (GDM) (International Diabetes Federation, 2013). Type 2 DM is the most common type of DM and it accounted about 90-95% of the cases around the world (World Health Organization, 2013a). It is estimated that T2DM will increase 55% more in 2035 (International Diabetes Federation, 2013). Changes in lifestyle, modernisation, obesity and changes in population demographic incidence have contributed to the increase of type 2 DM (T2DM) (Steiner, 2006).

Uncontrolled blood sugar level can lead to serious complications such as nephropathy, neuropathy, cardiovascular disease and early death (American Diabetes Association, 2008, International Diabetes Federation, 2013). Therefore, people with T2DM need multiple medications and lifestyle modifications to maintain blood sugar at the optimum level and reduce cardiovascular risk (Bailey and Kodack, 2011). Although multiple regimens might help to ameliorate the symptoms and improve quality of life, but the use of multiple medications can lead to non-adherence, drug interactions and others adverse events which the physicians might not be aware of (Steinman and Hanlon, 2010). Studies has indicated that inappropriate used of medications was one of the most common drug related problems in T2DM patients during a medication review and home interview (Ding et al., 2010). Another study on

the medication management at home has demonstrated that patients with higher number of medications at home were likely to have medication hoarding, duplication of therapy and severity of illness (Sorensen et al., 2005).

In Malaysia, the progression of T2DM has increased at an alarming rate. The overall prevalence of adults with diabetes aged > 18 years has increased from 11.6% to 15.2% within four years despite the existing treatment guidelines and the availability of the healthcare facilities (Institute for Public Health, 2011). There are many factors contributing to the increasing trend, one of them is the lack of awareness of the patients towards the disease and therapy. Studies conducted in one of the teaching hospital in Malaysia has shown that the majority of the T2DM with hypertension patients were lack of awareness on the disease, the medications they took and the complications of the disease (Letchuman et al., 2010).

### 1.2 Justification of the study

Type 2 DM is a chronic illness that requires continuity of medical care, self-management and support to prevent complication (American Diabetes Association, 2010, International Diabetes Federation, 2013). Lost in the transition of care, especially when patients leave the healthcare facilities could lead to major medication related problems such as non-adherence, stock piling at home, taking expired medications or taking herbal preparations which might interact with the prescribed medications (Cook et al., 2000). The risk of medication related problems or drug related problems are higher in patients taking multiple medications and discharged from the healthcare settings. Studies have shown that drug related problems were common among discharged patients. A study conducted at 112 community pharmacies in Europe identified a total of 451 drug related problems

among 277 patients (Paulino et al., 2004). Another study conducted in a tertiary care academic hospital found that a total of 66 patients had adverse events after discharged from hospital (Forster et al., 2003). Thus, there is higher risk of medication misadventures once patients leave the healthcare facilities back to their own house. These conditions become worse when the healthcare system enables patients to get their medication up to 6 months without further physician appointment (Eichenberger et al., 2011). Furthermore, healthcare providers have difficulties in managing T2DM patients that needed continuous follow-up, monitoring, education and counselling in a poorly designed healthcare system (Hayward et al., 2005). Besides that, long waiting time in the outpatient clinic and a long time lapse between the appointments could cause patients to miss their clinic appointments (McDonald et al., 2002). In order to obtain complete information on how patients manage their medications, it would be useful to visit patients at their homes rather than conducting the medication review at the healthcare settings.

From literature, home medication reviews conducted by pharmacists have demonstrated effectiveness in preventing, identifying and resolving drug-related problems encountered by the patients (Gilbert et al., 2002, Castelino et al., 2010). A retrospective study has shown that patients who received the Medication Management Program from pharmacist have lesser resource utilization (Flanagan et al., 2010). Similarly in another study conducted in elderly patients who received post-discharged home visits within five days had significant lesser drug-related problems and hospitalization after ninety days of discharged (Naunton and Peterson, 2003). However, majority of the studies were conducted in developed countries such as UK and Australia in a controlled environment (Lenaghan et al., 2007, Holland et al., 2005, Jackson et al., 2004). With the differences in social background and

cultural believes in Malaysia, the implementation of home-based intervention might have different outcomes from other developed countries. Furthermore, there is little local study on the impact of the home-based intervention conducted by pharmacist on patient's medication adherence, knowledge and clinical outcomes.

### 1.3 Study objectives

The objectives for this study were:

1) To evaluate the effectiveness of home-based intervention on patient's medication adherence and general diabetes knowledge among T2DM patients.
2) To assess the impact of home-based intervention on laboratory biomarkers and economic evaluation
3) To determine the drug related problems occurring among T2DM patients at their home during home visits.
4) To evaluate the patients' view on home-based intervention programme.

### 1.4 Overview of thesis

Chapter 2, the literature review, commence with an overview of DM classification, the sign, symptoms and complication of T2DM as well as the screening and diagnosis of T2DM followed by the elaboration on the non-pharmacological and pharmacological treatment for T2DM, the prevalence and the burden of diabetes mellitus in Malaysia. The chapter continues with the drug-related problems that T2DM patients' encountered, the awareness and knowledge towards DM, the medication adherence in DM as well as the interventions to improve awareness and medication adherence. The chapter ends with the discussion on the role of pharmacist in diabetes management.

Chapter 3 is the general methodology of the study. It includes the study design and location, tools used for data collection, data analysis and randomization of the patients and implementation of the intervention.

Chapter 4 elaborates the results of pre-intervention analysis focusing on clinical outcomes, patients' medication adherence and diabetes knowledge among T2DM patients.

Chapter 5 discusses the development, implementation and evaluation of the home-based intervention.

Chapter 6 draws the thesis to a conclusion with the overall summary, the recommendations for future research and the study limitations.

# CHAPTER 2: LITERATURE REVIEW

## 2.1 Classification of diabetes mellitus

Diabetes mellitus (DM) can be classified by the underlying causes. There are three main types of DM which are: type 1 DM (T1DM), type 2 DM (T2DM) and gestational DM (GDM) (International Diabetes Federation, 2013). In T1DM, the insulin is absent due to the autoimmune pancreatic β-cell destruction which might be set off by the environmental factor of the genetic susceptible individual (International Diabetes Federation, 2013). Pancreatic β-cell destruction occurred over the years, however the symptoms developed over a short period of time (International Diabetes Federation, 2013). The incidence of T1DM often occurred in the early life, however it might appear at any age. Type 1 DM accounted about 5-10% of all diabetes cases (American Diabetes Association, 2014a). Patients with T1DM required insulin injection (Barceló and Rajpathak, 2001).

On the other hand, in T2DM, the high sugar level in the bloodstream is due to the combination of factors such as insulin resistance or insufficiency of insulin production (International Diabetes Federation, 2011). Type 2 DM accounted 90-95% of all diabetes in the world and it appears mainly in adults. The main risk factors for T2DM are obesity, sedentary lifestyle and over calories intake (International Diabetes Federation, 2011). Treatments for T2DM are many, ranging from lifestyle modification, oral hypoglycaemic agents (OHA), insulin or a combination of these (Barceló and Rajpathak, 2001). Gestational DM (GDM) occurred when high sugar level is diagnosed for the first time during pregnancy. It is estimated that nearly 4% of all pregnancy is GDM. Furthermore women with GDM have a higher risk of developing T2DM in later life (International Diabetes Federation, 2011). Other types

of DM could be due to genetic defect on the action of insulin, pancreas disease, infections, surgery or drugs (American Diabetes Association, 2014a).

### 2.2 Sign, symptoms and complication of type 2 diabetes mellitus

Hyperglycaemia often marked by symptoms such as polyuria, polydipsia, polyphagia, blur vision and weight loss (American Diabetes Association, 2014a). However, these symptoms are often asymptomatic for individuals with mild hyperglycaemia or early DM (The Merck Manual Professional Edition, 2014). Consequently, the diagnosis for these groups of patients is often delayed (International Diabetes Federation, 2011). Consistently high blood sugar level can lead to long term complications that can affect the heart, kidney, nerve and blood vessels however, individuals with T2DM often unaware of the long term complications caused by the disease (International Diabetes Federation, 2013, American Diabetes Association, 2014b).

### 2.3 Screening and diagnosis for type 2 diabetes mellitus

Diabetes mellitus is associated with serious morbidity and mortality. Early detection and treatment are crucial in helping to minimize the complications. However, early detection comes through screening procedures (International Diabetes Federation, 2012). Screening is important for high risk individuals to help identify them with impaired glucose tolerance or impaired fasting tolerance whom will be benefited from the intervention provided to delay the progression of the disease.

For decades, the diagnosis of diabetes has been based on the fasting blood sugar (FBS) with the cut point of ≥ 7mmol/L or the post 2 hours of the 75g of oral glucose tolerance test (OGTT) with the threshold of ≥ 11.1 mmol/L or a random plasma glucose of ≥ 11.1 mmol/L. Recently, the International Expert Committee had

suggested the use of HbA1c with the threshold of ≥ 6.5% as one of the ways to diagnose DM. There are advantages of using HbA1c as a diagnosis tool because it is more convenient (no fasting needed) and less perturbations during illness (American Diabetes Association, 2014a). Table 2.1 shows the criteria for diagnosing DM. Nevertheless, the HbA1c test should use a standardized method to execute and this might not be practical in all contexts.

**Table 2.1 Criteria for diagnosing DM**

| |
|---|
| HbA1c ≥ 6.5%. The test should be performed in a laboratory using a method that is NGSP certified and standardized to the DCCT assay |
| OR |
| FPG ≥ 126 mg/dL (7.0 mmol/L). Fasting is defined as no caloric intake for at least 8 hours |
| OR |
| 2-hours plasma glucose ≥ 200mg/dL (11.1 mmol/L) during an OGTT. The test should be performed as described by the WHO, using a glucose load containing equivalent of 75g anhydrous glucose dissolved in water |
| OR |
| In a patients with classic symptoms of hyperglycaemia or hyperglycaemic crisis, a random plasma glucose ≥ 200mg/dL (11.1 mmol/L) |

NGSP = National Glycohemoglobin Standardization Program, DCCT = Diabetes Control and Complications Trial, OGTT = Oral Glucose Tolerance Test
(Adopted from American Diabetes Association, 2014)

## 2.4 Non-pharmacological treatment for type 2 diabetes mellitus

### 2.4.1 Weight management

In treating T2DM, non-pharmacological treatment which include weight loss, diet and physical activity still remain the first line approach (Sigal et al., 2006). Overweight and obesity are strongly associated with the development of T2DM. In fact, there are studies that shown an increased risk in T2DM with increased of body mass index (BMI) (Narayan et al., 2007). Furthermore, overweight or obesity can increase the prevalence of hyperlipidaemia and hypertension (Crawford et al., 2010). Thus weight loss has additional benefit for T2DM because it helps to improve other risk factor such as cardiovascular disease by reducing blood pressure and improve

serum lipid (Look AHEAD Research Group, 2010). In order to reduce the risk of macrovascular and microvascular complication of T2DM, weight loss is recommended for individual who have or at risk of having T2DM and is overweight (BMI 25.0-29.9 kg/$m^2$) or obese (BMI $\geq$ 30 kg/$m^2$) (Klein et al., 2004). A moderate weight reduction of 5-10% have shown to improve cardiovascular risk in T2DM patients (Wing et al., 2011).

### 2.4.2 Diet

Weight loss can only be achieved by reducing the dietary energy consumption or increasing the energy expenditure. By reducing the total amount of food consumed or selecting food with lower energy density is one of the way to reduce dietary energy consumption (Lindström et al., 2006). For T2DM patients, deciding what to eat is the most challenging task in their treatment plan (Evert et al., 2013). Even the American Diabetes Association (ADA), American Heart Association (AHA), British Diabetes Association (BDA), European Association for the Study of Diabetes (EASD), Canadian Diabetes Association (CDA), International College of Nutrition, group from South Africa and Japan and the National Cholesterol Education Panel (NCEP) have different recommendation for optimal diet for T2DM (summarized in Table 2.2). In a study that compared a low fat diet with a low carbohydrate Mediterranean-style diet in newly diagnosed T2DM patients has shown that patients taking low carbohydrate Mediterranean-style diet delay the initiation of OHA and have better glycaemic control (Esposito et al., 2009). A systematic meta-analysis on the different types of dietary approach have concluded that low carbohydrate, low glycaemic index (GI), Mediterranean diet and high-protein diet might be effective in improving several markers for cardiovascular disease and have better role in T2DM

management (Ajala et al., 2013). In Malaysia, a reduced calorie diet (20-25 kcal/kg body weight) consisted of 50-60% energy from carbohydrate, 15-20% energy from protein, 25-30% energy from fats and a high fibre diet of 20-30g/day are encouraged in T2DM patients (Ministry of Health Malaysia, 2009). However, there is no "one-size-fits-all" dietary pattern for T2DM patients. Individuals with T2DM have to play an active role in self-management, education and collaborate with healthcare providers for the development of their treatment plan (American Diabetes Association, 2010).

**Table 2.2 Recommendation for medical nutrition for diabetes patients**

| Variables | ADA | AHA | BDA | EASD | CDA | Japan | South Africa | India | NCEP |
|---|---|---|---|---|---|---|---|---|---|
| Carbohydrates (%) | 50-60 | 45-55 | 50-55 | 45-60 | 50-60 | 60 | 55-60 | > 65 | 50-60 |
| Fibre | NSA | ≥ 25 g/d | <30 g/d | Increase with low GI foods | 25-35 g/d | 1 fruit, 400g vegetables | 40 g/d | NSA | 20-30 g/d |
| Protein (%) | 15-20 | 15 | 10-15 | 10-20 | 11 | 15-20 | 12-20 | NSA | 15 |
| Fat (%) | 25-35 | < 30 | 30-35 | ≤ 35 | ≤ 30 | 20-25 | < 30 | <21 | 25-35 |
| GI (%) | NRGU | - | - | R | R | R | R | - | - |

ADA = American Diabetes Association, AHA = American Heart Association,
BDA= British Diabetes Association, CDA = Canadian Diabetes Association,
EASD = European Association for the Study of Diabetes,
NCEP = National Cholesterol Education Panel, NSA = No specific amount,
NRGU = Not recommended for general use, R = Recommended
(Adopted from Ajala, O., English, P. & Pinkney, J., 2013)

### 2.4.3 Physical activity

Physical activity is defined as bodily movement of the contraction of the skeletal muscle and subsequently increase the energy expenditure (Colberg et al., 2010). The term "exercise" is referred to the repetition of bodily movement to maintain or improve physical fitness such as aerobic capacity, muscle strength or endurance, flexibility of the body (Zanuso et al., 2010). There are numerous studies on the effect

of aerobic exercise (AE) on improving glycaemic control (Ibañez et al., 2005, Irvine and Taylor, 2009, Snowling and Hopkins, 2006, Zanuso et al., 2010). In a meta-analysis study that review regular AE at least eight weeks on T2DM patients has shown a significant reduction in HbA1c but not in the body weight (Boulé et al., 2003). In a more recent meta-analysis study on the effect of AE on lipids and lipoprotein in T2DM patients also shown improvement in HbA1c whereas no significant reduction in lipid profile was found (Kelley and Kelley, 2007). Besides AE, the American College of Sports Medicine has recently recommended resistance training (RT) as a well-rounded exercise for T2DM patients. In one study conducted in newly diagnosed old man on a twenty-weeks supervised RT twice a week are able to reduce abdominal fat, increase muscle strength and improve insulin sensitivity (Ibañez et al., 2005). Another meta-analysis study shown that either AE alone or RT alone or a combination exercise have moderate effect on glycaemic control and small effect on other diabetes complication risk factors (Snowling and Hopkins, 2006). With all the evidences, it is recommended that T2DM patients should accumulate a minimum of 210 minutes of moderate-intensity exercise or 125 minutes of vigorous exercise every week with a combination of AE and RT (Hordern et al., 2012). Although AE or RT or a combination exercise is able to improve glycaemic control however, the choice of the types of exercise is depending on the co-morbidity, personal preference in T2DM patients and the availability of the resources (Irvine and Taylor, 2009).

### 2.5 Pharmacological treatment

Pharmacological treatment will only be initiated when the lifestyle modification failed to achieve the targeted blood sugar level within 2-3 months (Canadian Diabetes Association Clinical Expert Committee, 2013). Currently, there are different types of pharmacological treatment available to treat T2DM. Table 2.3 shows the pharmacological treatment options available for T2DM. However, the selection of pharmacological treatment for T2DM need to be individualized according to their specific factors (such as age, gender, BMI, duration of DM, waist circumferences and cardiovascular disease risk factors) and also mechanism action of various drugs on the targeted organs (Charbonnel and Cariou, 2011).

**Table 2.3 Pharmacological treatment options for type 2 diabetes mellitus**

| Groups | Example of drugs | Mode of action | Advantages | Disadvantages |
|---|---|---|---|---|
| Biguanide | Metformin | Reduce hepatic glucose production and insulin resistance | No weight gain and hypoglycaemia, Decrease in CVD events | Gastrointestinal side effects (diarrhoea, abdominal discomfort), Vitamin B12 deficiency |
| Sulphonylurea | Gliclazide, Glibenclamide, Glimepiride, Glipizide, Glyburide | Stimulate insulin release from pancreas β-cell | Decrease in microvascular risk | Hypoglycaemia, weight gain, possible blunt myocardial ischemic preconditioning, Low durability |
| Alpha-Glucosidase Inhibitors | Acarbose, Miglitol | Slow intestinal carbohydrate digestion/absorption | No hypoglycaemia, decrease in post-prandial glucose excursions, possible decrease in CVD event, non-systemic | Modest reduction in HbA1c, Gastrointestinal side effects, need frequent dosing |
| Thiazolidinediones | Pioglitazone Rosiglitazone | Increase insulin sensitivity | No hypoglycaemia events, increase in HDL, | Weight gain, oedema, bone fractures, increase in LDL, |

| | | | | |
|---|---|---|---|---|
| | | | decrease TG (Pioglitazone), possible to reduce CVD events | possible to increase MI |
| Meglitinides | Repaglinide, Glinides, Nateglinide | Stimulate insulin release from pancreas β-cell | Decrease post-prandial excursions, flexible dosing | Hypoglycaemia, weight gain, possible blunts myocardial ischemic preconditioning, need frequent dosing |
| Dipeptidyl peptidase four (DPP-4) inhibitors | Sitagliptin, Linagliptin, Saxagliptin | Increase insulin secretion (glucose-dependent) Increase glucagon secretion (glucose-dependent) | No hypoglycaemia, well tolerated | Modest reduction in HbA1c, urticarial / angioedema, possible pancreatitis |
| Dopamine-2 agonists | Bromocriptine | Modulates hypothalamic regulation of metabolism, Increase insulin sensitivity | No hypoglycaemia. Decrease in CVD events | Modest in HbA1c reduction, dizziness/ syncope, nausea, fatigue, rhinitis |
| Glucagon-like peptide-1 (GLP-1) receptor agonists | Exenatide, Liraglutide | Insulin secretion (glucose-dependent), Reduce glucagon secretion (glucose-dependent), Slows gastric emptying, Increase satiety | No hypoglycaemia, weight reduction, possible for improved β-cell mass/function, possible CV protective actions | Gastrointestinal side effects, possible acute pancreatitis, injectable, training requirements |
| Amylin mimetics | Praminitide | Reduce glucagon secretion Slow gastric emptying, Increase satiety | Decrease in post-prandial glucose excursions, weight reduction | Modest reduction in HbA1c, Gastrointestinal side effects need frequent dosing, injectable, hypoglycaemia unless insulin dose also reduced |

| | | | | |
|---|---|---|---|---|
| Insulin | Aspart, Detemir, Glargine, Glulisine, Human (NPH or regular), Lispro, Premixed | Increase glucose disposal, Reduce hepatic glucose production | Universally effective, Decrease in microvascular risk | Hypoglycaemia, weight gain, possible mutagenic effects, injectable, training requirement, "Stigma" (for patients) |

(Adopted from Inzucchi et al., 2012)

### 2.6 Prevalence of diabetes mellitus in Malaysia

Malaysia is undergoing a transformation in the cause of morbidity from communicable diseases to non-communicable diseases (World Health Organization, 2013b). In Malaysia, the prevalence of diabetes mellitus of adults aged > 30 years has increased from 6.3% to 14.9% within twenty years (Institute for Public Health, 2011). The high prevalence of diabetes was mainly due to the population growth, urbanisation, changes in lifestyle, increased in physical inactivity and obesity (Wild et al., 2004). As shown in the Malaysian National Health Morbidity Survey III, higher prevalence was found in urban area compared to rural area. In the similar study, Indian ethnic group was found to have the highest prevalence were compared with other races (Institute for Public Health, 2011).

### 2.7 Burden of diabetes mellitus in Malaysia

Diabetes mellitus imposed a huge economic burden to the national healthcare system. Globally, a total of 490 billion will be expected to spend in healthcare in 2030 (Zhang et al., 2010). Non-communicable diseases are one of the major health burdens in Malaysia (Disease Control Division, 2010). According to the statistic of causes of death in Malaysia, DM is one of the top ten leading causes of morbidity and mortality in the country (Department of Statistic Malaysia, 2010). The total burden for disease in 2000 was 2.8 million with more than two third was due to non-

communicable diseases (Zainudin et al.). The complication of DM is one of the causes for disability and loss of life (Zhang et al., 2010). Because of its involvement in multiple organs, diabetes has significant impact to the individual, families and the society (International Diabetes Federation, 2013) .

Malaysia is one of the few countries that offer a minimum charge for medical care for the people (World Health Organization, 2013b). However, the changes in the lifestyle have rapidly raised the healthcare cost in this country. Since 1990, Ministry of Health Malaysia has spent RM1.27 billion in healthcare and within 10 years the amount has increased to RM4.21 billion (Merican et al., 2004). Diabetes mellitus imposed financial burden to the individual with the disease, the family members, the society as well as the healthcare system (International Diabetes Federation, 2013). . For the year of 2000, the total burden of disease was accounted for 2.8 million disability adjusted life with 69% was contributed by non-communicable disease (NCD) (World Health Organization, 2013b). The increased in the disease has caused a vast increased in expenditure for anti-diabetes medications in Malaysia. As in 2008, the total cost spent in diabetes medications in the public sectors was RM 86,423,000 compared to RM 84,489,000 in 2007 (Lian et al., 2013). Another study conducted in an outpatient clinic of a teaching hospital in Kelantan has demonstrated that the estimated average of direct treatment cost for T2DM was RM 861.35 (USD 572.7) per patient per year (Ibrahim et al., 2010).

### 2.8 Current healthcare system approach in managing diabetes mellitus

In Malaysia, the healthcare system mainly can be divided into public, private sectors and non-government organisations (Merican et al., 2004). The public sectors are the main provider for the healthcare system in Malaysia and it is operated according to

the WHO model for district health system. In each typical district, there would be a district hospital with a few number of public primary care clinics. These public primary care clinics provide mainly ambulatory care services such as acute medical care, antenatal and postnatal care and non-communicable diseases management such as diabetes mellitus (Yasin et al., 2012). In 2002, the Innovative Care for Chronic Conditions (ICCC) Framework has been adapted from the Chronic Care Model (CCM) to improve the ambulatory care in the public primary care clinics in treating long term chronic diseases. Realizing the increased in the epidemic of the chronic diseases such as diabetes mellitus, Malaysian government have incorporated different professionals such as dietitians, pharmacists, physiotherapists and diabetic educators in the public primary care clinics to manage chronic diseases (Coleman et al., 2009). Thus, in the recently year, there was multiple disciplinary in the public primary care clinics to cater for the needs in chronic disease management.

The public primary care clinics are heavily subsidised by the government and are delivered almost free of charge with a minimal charge of RM 1 for outpatients clinics and RM 5 for specialist consultations.

### 2.9 Medication adherence in diabetes mellitus

Type 2 DM is a complex metabolic disease that required multiple medications and lifestyle changes to reduce the blood sugar, cardiovascular risk and other comorbidities (Bailey and Kodack, 2011). Thus, polypharmacy is common among these groups of people (Grant et al., 2003). Studies have indicated that multiple doses, increased number of tablets and concurrent used of other medications are associated with low level of adherence (Melikian, 2002, Vanderpoel et al., 2004). There is no consensus on the adherence rate for chronic diseases to be considered as adequate

adherence. Some trials considered the adherence rate to be > 80% , whereas others considered 95% to be considered as adequate adherence (Osterberg and Blaschke, 2005). The adherence rate for prescribed medication for diabetes mellitus vary from 36-93% in worldwide (Wabe et al., 2011). According to WHO, non-adherence to medication is accounted for 50% of the chronically ill patients (World Health Organization, 2003). Recently, a systematic review has shown that the average adherence rate for oral anti-hyperglycaemia (OHA) was 36-93% (Cramer, 2004). Non-adherence to medications often led to suboptimal of glycaemic control (Rozenfeld et al., 2008). Addition to that, inadequate adherence to medications has imposed not only significant poor clinical outcomes but also the economic burden to the healthcare system (Cramer, 2004). Many studies in diabetes mellitus have proved that lower level of medication adherence associated with poor clinical outcomes (Ho et al., 2006, Howteerakul et al., 2007, van Bruggen et al., 2009, Pladevall et al., 2004) and higher cost of medical care (Sokol et al., 2005).

### 2.10 Awareness and knowledge about diabetes mellitus

Patients with chronic diseases such as T2DM required long term and sustainable disease management and prevention. Type 2 DM is a self-managed disease which required the patients to make decision on their daily dietary intake, medication adherence, physical activity and blood sugar monitoring. It is not easy to make decision without self-efficacy from the patients (Atak et al., 2008). In order for patients to be self-managed, patients must be well equipped with the knowledge of the disease, the importance of the management of the disease and the ability to solve problems (Murata et al., 2003). However, not many T2DM patients were aware of the disease itself and the management (Mohan et al., 2005). One of the study

conducted in Southern India has shown that patients with diabetes were not aware of the cause of the disease and the importance of healthy lifestyle (Murugesan et al., 2007). Similarly in a study conducted at a tertiary hospital in Malaysia has shown that 26% of the problem encountered was due to insufficient awareness on disease (Huri and Wee, 2013) .

Adequate knowledge and awareness on the disease can prevent patients from diabetes comorbidities (Moodley and Rambiritch, 2007). Thus, diabetes self-management education (DSME) is important in helping patients to optimize the blood sugar control, prevent acute and chronic complications, improve quality of life and reduce unnecessary healthcare cost (Norris et al., 2002). A study conducted to assess the effectiveness of diabetes education in T2DM using the knowledge and awareness (KA) questionnaire has indicated that patients who have undergone a proper diabetes education have significant lower HbA1c and BMI compared to those who did not attended the education session (Ozcelik et al., 2010).

## 2.11 Intervention to improve awareness and medication adherence in diabetes mellitus

Polypharmacy and complexity of regimens are one of the contributing factors to non-adherence. Interventions of simplifying the regimens such as once daily dosing instead of twice daily dosing (Christopher M.D. et al., 2002) and fixed dose regimens (Melikian, 2002) have shown improvement in patients medication adherence. In one meta-analysis of the comparison between the fixed dose combination and free-drug regimens has indicated that fixed dose combination regimen has reduced non-adherence of medications by 24-26% (Bangalore et al., 2007). In another study to evaluate the effectiveness of a simple and brief integrated approach has indicated that

there was a significant improvement in adherence in OHA and anti-depression agents in the intervention group (Bogner et al., 2012).

In addition to that, patients' awareness and knowledge on the disease and treatment have association with medication adherence (Al-Qazaz et al., 2011). A focus group study has explored T2DM patients' perception on the problems they faced with non-adherence to medications. Insufficient information provided by the doctors and the lack of knowledge on the disease were part of the reasons that they did not adhere to the prescribed regimens in that study (Vermeire et al., 2003). Studies on patients' education and telephone follow-up (Piette et al., 2000) or short message services have shown improvement in patients' knowledge and thus promote medication adherence (Zolfaghari et al., 2012). However, the ability of the patients to comprehend to treatment regimens was often overestimated as well. Studies have demonstrated that less than 50% of what the patients were told by the doctors was unable to recall and comprehend by the patients (Schillinger et al., 2002). Assessing patients' recall and comprehension by the physicians is one of the strategies to enhance adherence (Rubin, 2005).

Several interventions have been tested on the impact towards the improvement of medication adherence in T2DM. However, McDonald et al. have conducted a systematic review on all RCT interventions that intended to improve patients medication adherence has shown that strategies to improve medication adherence in chronically ill patients were complex, expensive and unable to predict the effectiveness (McDonald et al., 2002). It is complicated to perform an accurate adherence measurement, furthermore adherence varied over time (Vermeire et al., 2001). Up to now, there is no standard method to enhance medication adherence.

## 2.12 Drug-related problems in diabetes mellitus

Drug related problem or medication-related problem is the broadest scope of addressing the vitality problems in the medicine use (Ackroyd-Stolarz et al., 2006). According to the Pharmaceutical Care Network Europe, drug related problem is defined as "*an event or circumstance involving drug therapy that actually or potentially interferes with desired health outcomes"* (Pharmaceutical Care Network Europe Foundation, 2006). In order to consider an event as DRP, the patient must either experiencing or about to experiencing the undesirable outcomes and the conditions have to be related to drug therapy (Strand et al., 1990). Drug related problems can be occurred during medications prescribing phase, medications dispensing phase or medications use phase by patients (van Mil, 2005).

In patients with T2DM, often complex medications were prescribed to achieve optimal blood pressure, sugar and lipid level. Multiple regimens used have been linked to the high risk of the occurrence of drug related problems (DRP) (Viktil et al., 2007). Although the prescribed medications are clinically justified, patients often seek alternative treatment (Stawicki and Gerlach, 2009). There are over the counter medications, supplements and traditional products sold in numerous palaces such as pharmacies and groceries shops which patients can easily buy without a prescription (Glintborg et al., 2004). Many patients with chronic disease such as T2DM often have more than one healthcare provider to treat their disease and received multiple prescriptions. Little or lacking of patients information sharing between the healthcare providers can lead to drug related problems (Stawicki and Gerlach, 2009).

In Malaysia, there is an increasing trend of adverse reactions cases reported every year. In 2012, there were 10102 cases of adverse drug reactions reported compared to 2011 there were 9385 cases reported (National Pharmaceutical Control Bureau

Ministry of Health Malaysia, 2012). Not only the prescribed medications that can lead to adverse drug reactions, there were 151 cases reported on traditional products used in 2012 (National Pharmaceutical Control Bureau Ministry of Health Malaysia, 2013). The increased trend of the cases of adverse drug reactions has led to higher healthcare cost.

Studies have conducted to identify drug-related problems in T2DM patients. In Switzerland, the authors found out that 26 (48.1%) of DM patients had encountered with ADE since they started the regimens (Eichenberger et al., 2011). In Brazil, a study to evaluate the effectiveness of pharmaceutical care program on T2DM patients has identified an average of 6.7 drug-related problems at baseline with majority was due to ineffective drugs (Mourão et al., 2012). Another study conducted in a tertiary hospital in Malaysia has indicated that majority of the T2DM with dyslipidaemia patients have potential interaction on the medications, non-adherence and lack of awareness (Huri and Ling, 2013).

## 2.13 Pharmacist role in diabetes management

The dramatic increase in new diabetes mellitus cases have put physician in a straining position to treat the patients. More time is required for the physician to manage chronic cases. However, primary care physicians have little time to spend with patients with chronic diseases rather than patients with acute conditions (Campbell, 2002). As shown in one study to estimate the time required for the primary healthcare providers to provide high quality healthcare services for chronic cases has indicated that physicians need to spend at least 3.5 hours of every working day to provide the service (Østbye et al., 2005). Thus, pharmacists who are well-trained and able to spend time with patients can help in solving the problem.

Pharmacists have been actively playing an important role in identifying, educating, assessing, referring and monitoring in diabetes management (Campbell, 2002). Many studies have supported the effectiveness of adding pharmacist in diabetes management in hospital, clinics and community settings. In one of the randomised controlled studies on pharmaceutical care model conducted by pharmacists has shown improvement in patients' medication adherence and glycaemic control (Chung et al., 2014). In the Asheville Project, pharmacists provided education, self-monitoring blood glucose (SMBG) training, monitoring and follow-up to diabetes patients has reduced patients' HbA1c and all diagnosis costs (Cranor and Christensen, 2003). Another study that aimed to evaluate the effectiveness of the collaboration between the physicians and pharmacists on uncontrolled diabetes patients has improved lipid and glycaemic control (Ramser et al., 2008). Similarly in the study conducted in Sioux City, Iowa, pharmacists have group sessions appointment with the patients, medication reviews and telephone follow-up have shown a significant reduction by 1.7% of HbA1c within 9 months (Scott et al., 2006).

# CHAPTER 3: GENERAL METHODOLOGY

## 3.1 Introduction

This chapter briefly described the overview of general quantitative study design and further outline the types of non-experimental, experimental designs, randomisation procedures and finally the summary of the method used in this study.

## 3.2 Quantitative study design

A quantitative study approach is one of the ways the researchers used post-positivist claims to develop information, employed strategies in seeking truth such as experiments and surveys, and collects information that yield statistical data (Creswell, 2003). A quantitative method is on interest to maximize the objectivity, the generalizability and the replicability of the results (Harwell, 2011). Basically, a quantitative study can be categorised into two categories: non-experimental study and experimental study.

### 3.2.1 Non-experimental

Non-experimental study design has no randomisation process, manipulation of the study variables and comparison group. The researchers observe what happened naturally without any intervention imposed. Thus, non-experimental design is similar to post-test only experiment (Sousa et al., 2007). With that, non-experimental design can be classified into:

(i) Cohort study design: This study determines the incidence, causes and prognosis of a natural condition. It measures the event in a temporal time that enables it to distinguish between causes and effects.

(ii) Cross-sectional study design: This study mainly determines the prevalence of a population at a single point of time.

(iii) Case-control study design: This study normally conducted retrospectively and determines the factors that can contribute to the condition by comparing the group of people with the condition with the group of people without the condition (Mann, 2003).

### 3.2.2 Experimental

An experimental study design follows a randomisation process, manipulation of the study variables and presents comparison of groups. It examines the cause-relationships effect of the study variables (Sousa et al., 2007). An experimental design can be further divided into:

(i) True-experimental design: In this design, the process of randomisation must take place with the presence of comparison group and manipulation of the study variables. The design is useful in addressing the evaluation on the effectiveness and impact of a program. The most common true-experimental design are post-test only comparison group, pre-test post-test comparison group, Soloman four groups and cross-over designs (Pamela J. Brink).

(ii) Quasi-experimental design: In this design, anyone of the key elements in the true-experimental design is absent, especially the random assignment of the groups. The design is useful as well in evaluating the effectiveness or the impact of a program. However, there are lack of confidence and generalizability in the findings. Example of commonly used quasi-experimental designs are non-equivalent group pre-test post-test group