IMPACT OF A PHARMACIST-LED TYPE 2 DIABETES SELF-MANAGEMENT EDUCATION PROGRAMME AMONG THE COMMUNITY IN PENANG, MALAYSIA

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by

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AADE	American Association of Diabetes Educators
ACEi	Angiotensin converting enzyme inhibitor
ADA	American Diabetes Association
ADCM	Audit of Diabetes Control and Management
ARB	Angiotensin receptor blockers
BMI	body mass index
BP	blood pressure
CAM	complementary and alternative medicine
CCBs	Calcium channel blockers
CCM	Chronic Care Model
CHOs	carbohydrates
CI	confidence interval
CKD	Chronic kidney disease
CO	change objective
CORFIS	Community-based Cardiovascular Risk Factors Intervention Strategies
CTT	Cholesterol Treatment Trialists
CVDs	cardiovascular diseases
DASH	Dietary Approaches to Stop Hypertension
DAWN2^{TM}	Diabetes Attitudes, Wishes and Needs second study
DAWN	Diabetes Attitudes, Wishes and Needs
DBP	diastolic blood pressure
DESMOND	Diabetes Education and Self-Management for Ongoing and Newly Diagnosed
DM	Diabetes mellitus
DMSES	Diabetes Self-Management Self-efficacy Scale
DPP-4i	dipeptidyl peptidase 4 inhibitors
DQoL	Diabetes Quality of Life
DQoL-BCI	Diabetes Quality of Life Brief Clinical Inventory
DSME	diabetes self-management education
DSMES	diabetes self-management education and support
DSMS	diabetes self-management support

EQ VAS	EQ visual analogue scale
EQ-5D-3L	EuroQoL-5 Dimensions-3 Level
F	female
FBG	fasting blood glucose
FPG	fasting plasma glucose
GDM	gestational diabetes mellitus
GDP	gross domestic product
GLP-1 RA	glucagon-like peptide 1 receptor agonist
HbA_{1c}	glycated haemoglobin
HDL-C	high density lipoprotein cholesterol
HR	hazard ratio
HRQoL	health-related quality-of-life
ICCC	Innovate Care for Chronic Conditions
IM	intervention mapping
IQR	interquartile range
LDL-C	low density lipoprotein cholesterol
M	male
MANS	Malaysian Adult Nutrition Survey
MDKT	Michigan Diabetes Knowledge Tests
MoH	ministry of health
MRC	Medical Research Council
MTAC	medication therapy adherence clinic
MY-DEMO	Malaysia diabetes education module
NDR	national diabetes registry
NHMS	National and Health Morbidity Survey
NHS	National Health Service
NICE	National Institute for Health and Care Excellence
OHA	oral hypoglycaemic agent
OR	odds ratio
PFHDA	Penang Family Health Development Association
PO	performance objective
QoL	quality-of-life
RABB	Residents' Associations of Bayan Baru
RCTs	randomised controlled trials

REDEEM	Reducing Distress and Enhancing Effective Management
RR	relative risk
RRR	relative risk reduction
SBP	systolic blood pressure
SD	standard deviation
SDSCA	Summary of Diabetes Self-Care Activities
SGLT2	sodium-glucose cotransporter 2
SIDEP	South Korea Structure Intensive Diabetes Education Programme
SMBG	Self-monitoring of blood glucose
SMS	short message services
SU	sulphonylureas
T1DM	Type 1 Diabetes Mellitus
T2DM	Type 2 Diabetes Mellitus
TG	triglyceride
TZD	thiazolidinediones
UiTM	Universiti Teknologi MARA
UK	United Kingdom
UKPDS	United Kingdom Prospective Diabetes Study
US	United States of America
USM	Universiti Sains Malaysia
VADT	Veterans Affairs Diabetes Trial
WC	waist circumference
WHO	World Health Organisation

IMPAK PROGRAM PENDIDIKAN PENGURUSAN KENDIRI DIABETES JENIS 2 YANG DITERAJUI OLEH AHLI FARMASI DALAM KALANGAN KOMUNITI DI PULAU PINANG MALAYSIA

ABSTRAK

Pendidikan pengurusan kendiri diabetes (DSME) tidak dilaksanakan secara meluas dalam sistem kesihatan Malaysia. Memandangkan pesakit diabetes mellitus jenis 2 di Malaysia tidak mencapai kawalan glukosa yang baik, maka program DSME yang komprehensif perlu disediakan dan diuji. Kami menggunakan kaedah campuran untuk menilai impak program DSME yang berasaskan kumpulan. Pengukuran impak program adalah berdasarkan biomedikal (iaitu HbA_{1c}, glukosa darah puasa, tekanan darah, profil lipid, indeks jisim tubuh, lilitan pinggang, peratusan lemak badan dan otot), tingkah laku (iaitu pemakanan, senaman, pemantauan kendiri glukosa darah, penjagaan kaki dan pengambilan ubat) dan hasil psikososial (pengetahuan pengurusan diabetes, keberkesanan diri dan kualiti hidup) pesakit. Hasil kuantitatif para peserta diukur sebelum DSME, 2 bulan dan 6 bulan selepas DSME. Selepas DSME, kami mewawancarai peserta terpilih untuk mendapatkan perspektif yang mendalam terhadap kualiti dan keberkesanan program. Sebanyak 46 individu dengan T2DM menyertai kajian ini. Dua bulan selepas DSME, para peserta menunjukkan penambahbaikan ketara dalam kolesterol lipoprotein berkepekatan rendah [3.08±1.04 mmol/L *vs* 2.63±0.86 mmol/L ($p = 0.001$)] dan tingkah laku penjagaan diri tertentu termasuk pemantauan kendiri glukosa darah [0.92±1.73 *vs* 2.19±2.07 ($p < 0.001$)] dan penjagaan kaki [4.54±1.40 vs 5.17±1.17 ($p = 0.024$)]. Keputusan tersebut juga dikekalkan 6 bulan selepas program. Walau bagaimanapun, peserta tidak mengekalkan penurunan HbA_{1c} yang diperhatikan pada 2 bulan selepas program [6.85±1.84 % *vs*

6.54±1.54 % (p = 0.661)] dengan peningkatan HbA_{1c} yang ketara dilaporkan 6 bulan selepas program [6.85±1.84 % *vs* 7.41±1.85 % (p <0.001)]. Pada 6 bulan selepas program, peningkatan yang ketara dalam kualiti hidup [32.97±9.79 *vs* 28.03±6.12 (p = 0.010)] juga didapati. Empat tema utama muncul daripada data kualitatif yang dikumpul, iaitu, kesan impak program DSME, model pembelajaran berkesan, mengekalkan pengurusan kendiri diabetes dan cara menjangkaui masyarakat yang lebih meluas. Peserta menikmati sesi pendidikan berasaskan kumpulan dengan analogi mudah dan aktiviti interaktif. Selepas DSME, peserta memahami bahawa penjagaan kendiri yang holistik diperlukan untuk mencapai kawalan penyakit yang optimum. Mereka menyatakan bahawa pengetahuan, keberkesanan diri dan motivasi yang diperoleh melalui DSME penting untuk pengurusan kendiri diabetes. Untuk mengekalkan pengurusan kendiri, para peserta memerlukan komunikasi berkesan dengan pegawai perubatan dan sokongan berterusan daripada DSME. Peserta mengakui manfaat DSME dan menggesa tawaran perkhidmatan tersebut untuk meagawal T2DM di Malaysia. Data kuantitatif dan kualitatif daripada kajian ini membuktikan bahawa DSME yang komprehensif dapat meningkatkan kesihatan pesakit T2DM dari segi biomedikal, tingkah laku dan psikososial. Walau bagaimanapun, kajian terkawal rawak berskala besar diperlukan untuk menentukan hubungan sebab-akibat dan kebolehmampuan DSME untuk masyarakat meluas di Malaysia.

IMPACT OF A PHARMACIST-LED TYPE 2 DIABETES SELF-MANAGEMENT EDUCATION PROGRAMME AMONG THE COMMUNITY IN PENANG, MALAYSIA

ABSTRACT

Diabetes self-management education (DSME) services are not widely implemented in the current Malaysia healthcare system. Considering substantial patients with type 2 diabetes mellitus (T2DM) in Malaysia do not achieve good glycaemic control, a comprehensive DSME programme was therefore developed and tested. We employed mixed-methods to evaluate the impact of a group-based, locally developed DSME programme on participants' biomedical (i.e. HbA_{1c}, fasting blood glucose, blood pressure, lipid profile, body mass index, waist circumference, percentage body fat and skeletal muscle), behavioural (i.e. diet, exercise, self-monitoring of blood glucose, foot care and medication taking) and psychosocial (i.e. diabetes management knowledge, self-efficacy and quality-of-life) outcomes. Using pre-post study design, participants' quantitative outcomes were measured at baseline, post 2-month and post 6-month of DSME. Post DSME, we interviewed selected participants to solicit in-depth perspectives towards the quality and effective components of the DSME programme. A total of 46 individuals with T2DM consented to the study. Post 2-month of DSME, participants demonstrated significant improvement in low-density lipoprotein cholesterol [3.08±1.04 mmol/L *vs* 2.63±0.86 mmol/L (p = 0.001)] and certain self-care behaviours including self-monitoring of blood glucose [0.92±1.73 *vs* 2.19±2.07 (p <0.001)] and foot care [4.54±1.40 vs 5.17±1.17 (p = 0.024)]. The aforementioned outcomes were also maintained at 6-month. Participants did not maintain the decreasing trend of HbA_{1c} observed at 2-

month [6.85±1.84 % *vs* 6.54±1.54 % (p = 0.661)] with significant HbA_{1c} increase reported at 6-month compared to baseline [6.85±1.84% *vs* 7.41±1.85% (p <0.001)]. At 6-month, significant improvement in quality-of-life [32.97±9.79 *vs* 28.03±6.12 (p = 0.010)] was observed. Four major themes emerged from the qualitative data, namely, perceived impact of DSME programme, self-perceived effective learning model, sustaining diabetes self-management and reaching out for wider community. Participants enjoyed group-based sessions with simplified analogies coupled with interactive hands-on activities. Following DSME, participants perceived holistic, self-directed multifactorial self-care strategies needed to achieve optimal disease control. They elicited that knowledge, self-efficacy and motivation gained from DSME participation engendering proactive diabetes self-management. To sustain T2DM self-management, participants expressed the need of effective healthcare professional-patient communication and continuous DSME support. Participants acknowledged the benefits of DSME and urged the widespread offer of the service to mitigate the current sub-optimal T2DM control in Malaysia. Both the quantitative and qualitative data corroborated that comprehensive DSME could improve some of the patients' biomedical, behavioural and psychosocial outcomes. Nonetheless, large scale randomised controlled study is needed to establish its cause-effect relationship and generalisability to wider population in Malaysia.

CHAPTER 1

INTRODUCTION

1.1 Background

Diabetes mellitus (DM) is a chronic metabolic disorder characterised by hyperglycaemia resulted from insulin deficiency and or insulin resistance. Although new β-cell centric DM classification is recently proposed (Schwartz et al., 2016), three main types of DM are widely accepted (International Diabetes Federation, 2017): Type 1 diabetes mellitus (T1DM), Type 2 diabetes mellitus (T2DM) and gestational diabetes mellitus (GDM). T1DM accounts for about 5-10% of cases and it is a result of immune-mediated depletion of pancreatic β-cells engendering life-long dependence on exogeneous insulin (Chiang, Kirkman, Laffel, & Peters, 2014). T2DM contributes most of the DM cases (i.e. 90-95%) due to the core pathophysiological defects of insulin secretion and actions (International Diabetes Federation, 2017). The prevalence of T2DM is expected to rise in the forthcoming years in parallel with increasing urbanisation, unhealthy diet, sedentary lifestyle, increasing obesity and aging population (Zheng, Ley, & Hu, 2017). GDM is often a temporary condition occurs during pregnancy, however, it carries long-term risk of T2DM (International Diabetes Federation, 2017). DM is currently the eighth leading cause of death globally and has been coined as a global health emergency where concerted effort is needed among countries to curb its rising prevalence (World Health Organisation, 2016).

Chronic uncontrolled DM is known to cause both micro- and macrovascular complications. The complications affect wide range of body organs including the eyes (retinopathy), kidney (nephropathy), nerves (neuropathy) and vascular system [cardiovascular diseases (CVDs), cerebrovascular and peripheral vascular diseases].

Of the complications, CVDs are the major cause of death and disability in individuals with DM (International Diabetes Federation, 2017), underlining the need of intensive management of CVD risk factors (i.e. lipids and blood pressure) beyond blood glucose control (Chatterjee, Khunti, & Davies, 2017).

Although sharing similar treatment goal (i.e. to maintain near to normal glycaemia), the pathophysiology and aetiology of the three DM types are distinct, and thus, the management strategies for each differ. For instance, individuals with T1DM are recommended to follow diet suitable for their body weight and to keep physically fit for cardiovascular health. In addition, they need to be adept in adjusting insulin doses based on their blood glucose levels, diet and physical activities to prevent hypo- and hyperglycaemia (Chiang et al., 2014). For individuals with T2DM to maintain optimal glycaemic control and to prevent disease complications, life-long commitment to complex multifactorial risk reduction self-management activities is needed on daily basis. These activities range from adopting healthy diet, taking medications, blood glucose monitoring, be physically active and foot inspection (American Diabetes Association, 2018). While for GDM, regular physical activity and individualised nutrition plan are needed to cater both foetal and maternal health (American Diabetes Association, 2018). Insulin therapy may be needed in later gestation stage to keep blood glucose level in range (American Diabetes Association, 2018).

Globally, the number of people with DM has quadrupled since 1980 (Zhou et al., 2016). In 2017, DM affects 425 million people (1 in 11 adults aged 20-75 years) and is projected to affect 629 million people worldwide by 2045 (International Diabetes Federation, 2017). Alarmingly, the largest increase in DM prevalence comes

from low and middle-income countries with Asia emerged as the epicentre of global T2DM epidemic (International Diabetes Federation, 2017).

DM is costly both to the affected person and healthcare system as a whole. The medical expenditures for individuals with DM are two to three-fold higher than general population without the disease (International Diabetes Federation, 2017). The high cost is mainly driven by the management of complications and the consequent loss of productivity (World Health Organisation, 2016). Bommer and colleagues reported that global DM cost amounting to USD 1.31 trillion for year-2015 [i.e. 1.8% of global gross domestic product (GDP)], with 34.7% contributed from indirect costs (Bommer et al., 2017). The authors highlighted that middle-income countries endure larger economic burden (1.8% of the GDP) compared to high income countries (1.2% of the GDP) (Bommer et al., 2017). In another review on DM medical expenditures within low and middle-income countries, individuals were estimated to spend USD 463 – 961 for out-patient care with an extra 5 to 10 times of expenditures needed to treat diabetes-related complications (Walker et al., 2018). The limited capacity of the public healthcare system in managing DM compounded by high out-of-pocket expenditures often cause catastrophic financial consequences among DM patients in the developing countries (Walker et al., 2018).

Whilst a plethora of drugs are available in the market, at least half of those diagnosed with T2DM still do not achieve satisfactory glycaemic control with millions of people at elevated risk of suffering from DM complications (Skovlund & Peyrot, 2005). T2DM is a patient-driven self-management disease as 98% of diabetes care is principally provided by the patients themselves (Anderson & Funnell, 2010; Jarvis, Skinner, Carey, & Davies, 2010). The complex nature of the disease requires not only

continuous medical care but also multifactorial risk reduction self-care activities performed outside of the clinic setting (American Diabetes Association, 2015). Accordinlgy, patients with T2DM are advocated to undertake seven self-care behaviours recommended by the American Association of Diabetes Educators (AADE): healthy diet, being active, medication-taking, self-monitoring, risk reduction, problem solving and healthy coping (American Association of Diabetes Educators, 2011a, 2014).

The episodic, fragmented medical management designed to treat acute diseases in the 19th century has been criticised by researchers to be irrelevant to patients suffering from chronic diseases such as T2DM (Russell E. Glasgow & Anderson, 1999; Sevick et al., 2007; Wagner et al., 2001). This is founded on the fact that chronic diseases are often without cure, multivariate causations with their characteristics unfold overtime (Holman & Lorig, 2004). Furthermore, chronic disease is not simply a physiological phenomenon but is heavily woven with patient's psychological, environmental, lifestyle and financial issues (Sevick et al., 2007). Patients often grappling with the desire to live normal life and obtaining appropriate medical care (Sevick et al., 2007). The undulating management course of chronic diseases therefore necessitates patients to be actively engaged in their own disease care process (Holman & Lorig, 2004).

Accordingly, a patient-centred collaborative care framework functions within the chronic diseases such as the Chronic Care Model (CCM), is advocated by researchers and international guidelines in the T2DM management (American Diabetes Association, 2018; Bodenheimer, Lorig, Holman, & Grumbach, 2002; Bodenheimer, Wagner, & Grambach, 2002; Clement et al., 2018). It has been

suggested that better chronic disease outcomes could be achieved when collaborative relationship established between motivated and empowered patients with proactive, well-coordinated healthcare team (Bodenheimer, Lorig, et al., 2002; Bodenheimer, Wagner, & Grumbach, 2005). According to Wagner, CCM consists of six inter-related key elements such as healthcare organisation, community resources, self-management support, delivery system design, decision support and clinical information system (Wagner et al., 2001). CCM model has been integrated within the primary care settings in developed countries such as Australia, UK and US, demonstrating improved health outcomes among patients with chronic diseases (Coleman, Austin, Brach, & Wagner, 2009; Dennis et al., 2008; Stellefson, Dipnarine, & Stopka, 2013).

Diabetes self-management education (DSME), in-line with CCM philosophy, is defined as "*ongoing process of facilitating the knowledge, skill and ability necessary for diabetes self-care, and incorporates patient-centred and collaborative decision making*" (Powers et al., 2015). It is a comprehensive patient-centred education that involves a multidisciplinary team to help patients with DM to achieve glycaemic control, improve health status and quality-of-life (QoL) (M. M. Funnell et al., 2011; Mensing & Eichorst, 2010). DSME plays an integral role in the diabetes care by empowering patients with the knowledge and skills required to make informed choices in managing their diabetes, and therefore, should be commenced from the first day the disease being diagnosed (American Diabetes Association, 2015; M. M. Funnell et al., 2011). Evidence shows that DSME improves glycaemic control (Chrvala, Sherr, & Lipman, 2015) coupled with four-fold lesser risks of developing complications (Nicolucci et al., 1996). Nevertheless, the uptake and utilisation of DSME remained poor globally (Powers, 2016).

Given the higher prevalence of T2DM and the different management and education objectives among the three types of DM, the research focus of this thesis limits only to T2DM. Limiting our research to a single type of DM allows less population heterogeneity, and therefore, reducing the risk of selection bias (Delgado-Rodríguez & Llorca, 2004). Once thought to be an elderly disease, T2DM is also currently affecting the younger generation (Nadeau et al., 2016). The different disease pathogenesis and early onset of complications have posed unique challenges on the disease management among the younger population (Nadeau et al., 2016). The diabetes care among the younger generation warrants in-depth exploration in other studies. This thesis, therefore, addresses only T2DM management among adults.

In Malaysia, T2DM affects one in five Malaysians aged 30-year-old and above (Hussein, Wahyu Taher, Gilcharan Singh, & Siew Swee, 2016). Alarmingly, only 12.2% of patients with T2DM achieved recommended glycaemic control (i.e. HbA_{1c} < 6.5%) with serious complications abound (Mafauzy, Hussein, Nazeri, & Chan, 2016). The healthcare system in Malaysia is still fall short of addressing the complex needs of individuals with T2DM. Although initiatives have been made to transform the Malaysian healthcare system by integrating innovative strategies in managing chronic diseases as delineated in CCM and WHO Innovate Care for Chronic Conditions (ICCC) framework, the transformation is still at the infancy stage (Hussein et al., 2016). The majority of T2DM patients in Malaysia have yet to benefit from comprehensive diabetes care compared to the other Western counterparts (Hussein et al., 2016). Currently, diabetes educational resources such as dietary counselling, individualised patient-centred diabetes education and pharmacist-led medication adherence clinic are mostly constrained to state level hospitals in Malaysia (Hussein et al., 2016). With an estimated 80% of patients attending general primary care clinics

in Malaysia (Hussein et al., 2016), a large proportions of T2DM patients do not have access to holistic diabetes care. Hence, there remains a huge disparity of diabetes care in the community setting.

1.2 Problem Statement

Currently, patients with T2DM in Malaysia have limited accessibility to comprehensive diabetes care and resources. Collaboration between local non-governmental organisations in empowering community dwellers with diabetes self-management knowledge and skills *via* structured DSME programme may be a holistic approach in curbing the deteriorating states of T2DM in the country. Although DSME programmes from other countries are available, the positive findings and benefits of these programmes cannot be directly extrapolated to the Malaysian setting due to different culture and health beliefs, knowledge level, social and ethnic structures. Hence, the development and evaluation of a comprehensive DSME programme is imperative.

1.3 Justification and Significance of Study

The poor glycaemic control and high complications among patients with T2DM in the Malaysian healthcare system warrants immediate attention. Since Ministry of Health (MoH), Malaysia is currently working towards optimising the healthcare system by embracing the CCM and WHO ICCC framework to better management of people with chronic diseases (Hussein et al., 2016); the development and implementation of DSME and support, an essential component of the CCM, is therefore deemed timely. DSME may contribute significant benefits not only in the diabetes care but also towards a holistic and sustainable healthcare system which

addresses the complex needs of patients with T2DM, leading to good glycaemic control and reduced complications.

1.4 Aim and Specific Objectives

This PhD study aimed to develop and evaluate the impact of a structured, group-based DSME programme on biomedical, behavioural and psychosocial outcomes among community-dwelling T2DM patients in Malaysia. Specific objectives of the project are:

1. To develop a structured DSME programme underpinned by evidence-based behaviour change theory and practical applications.

2. To determine the feasibility of DSME programme at community setting and participant's comprehension towards programme materials.

3. To evaluate the effectiveness of the DSME programme on participant's biomedical outcomes [i.e. glycated haemoglobin (HbA_{1c}), fasting blood glucose (FBG), lipid profile, blood pressure (BP), body weight, body mass index (BMI), waist circumference (WC), percentage body fat and percentage skeletal muscle].

4. To determine the effectiveness of the DSME programme on participant's diabetes-related behavioural outcomes [i.e. diet, exercise, medication taking, foot-care and self-monitoring of blood glucose (SMBG)]

5. To assess the impact of the DSME programme on participants' psychosocial outcomes [i.e. knowledge of diabetes management, diabetes management self-efficacy and quality-of-life (QoL)].

6. To explore participants' perspectives on the quality and effective components of the DSME programme.

1.5 Overview of The Thesis

Chapter 2 kick-starts with an overview on the aetiology and pathophysiology of T2DM. It then followed by a concise introduction to the current management of T2DM. The complex needs of patients in daily self-management of T2DM is then highlighted which directs reader's focus to detailed discussion of the benefits and needs of DSME in empowering patient's self-management. The chapter is then followed by a concise review of T2DM in the Malaysian setting. The knowledge gaps in literature and justifications of this PhD study are presented at the end of the chapter.

Chapter 3 provides an overview for the conceptual framework of the PhD study. The justifications for employment of mixed quantitative and qualitative research approaches are presented. In each research approach, the selection of methods is described and justified. The chapter ends with the descriptions of management for both quantitative and qualitative data analysis.

Chapter 4 illustrates the systematic approaches of designing and developing the DSME programme. The process involved selecting relevant behaviour change theory and portraying the approaches used to translate the underpinning theory into practical interventional strategies at real-world community setting. The findings from pilot modelling study are then presented to guide the direction and refinement of programme materials.

Chapter 5 presents the detailed analysis of biomedical, behavioural and psychosocial outcomes of the DSME programme conducted at three different communities in the state of Penang, Malaysia.

Chapter 6 explores participants' perceptions towards the impact and effective components of DSME programme, the needs and challenges of rolling out the programme to wider communities at large.

The summary of findings, conclusions and recommendations for future research are in Chapter 7.

CHAPTER 2

LITERATURE REVIEW

2.1 Type 2 Diabetes Mellitus

T2DM, is a complex metabolic disorder resulted from two core defects (i.e. insulin resistance and or insulin deficiency), causes eight pathophysiological abnormalities which contribute to glucose intolerance among individuals with T2DM (Defronzo, 2009). The eight abnormalities are summarised and presented in Figure 2.1. Whilst advancing age and genetics could influence the development of T2DM (DeFronzo, 2004); sedentary lifestyle, physical inactivity and energy-dense diet leading to overweight and obesity are the paramount drivers of global T2DM pandemic (DeFronzo, Eldor, & Abdul-Ghani, 2013; International Diabetes Federation, 2017; Zheng et al., 2017).

Obesity and physical inactivity are known as insulin resistance states which pose substantial stress on pancreatic β-cells to compensate defect insulin action by increasing insulin secretion (Defronzo, 2009). The long-term exhaustion on pancreatic β-cells leads to cell failure and therefore overt DM (Defronzo, 2009). At the point of T2DM diagnosis, individuals are reported to have loss nearly half of the β-cell mass coupled with 80% loss of its functions (Defronzo, 2009). This bleak picture, however, could largely be mitigated. Clinical trials such as the United States Diabetes Prevention Programme, the Finnish Diabetes Prevention Study and the Da Qing Impaired Glucose Tolerance and Diabetes Study in China have demonstrated that up to 58% of T2DM can be prevented by lifestyle interventions focusing on increasing physical activities and adopting healthy diet (Li et al., 2008; Lindstrom et al., 2003; Schellenberg,

Dryden, Vandermeer, Ha, & Korownyk, 2013; The Diabetes Prevention Program Research Group, 2002).

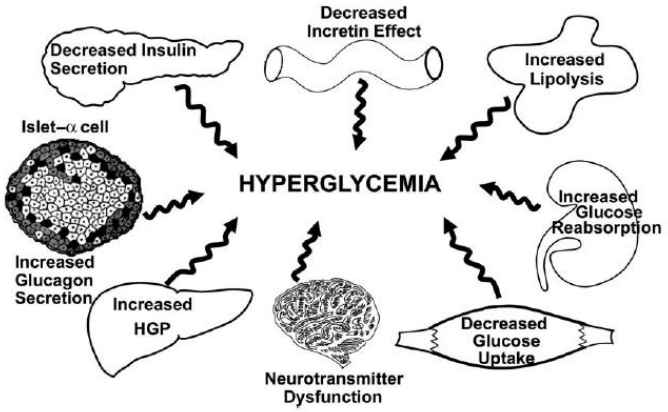

Figure 2.1 Eight pathophysiological abnormalities which contribute to glucose intolerance in T2DM (Defronzo, 2009)

2.2 Current Management of Type 2 Diabetes Mellitus

The current optimal management of T2DM consists of a combination of lifestyle modifications such as healthy diet, increased physical activity, weight loss, smoking cessation, moderation of alcohol consumption and glucose lowering therapies to achieve recommended glycaemic targets (American Diabetes Association, 2018; Chatterjee et al., 2017). These interventions should be supported by structured patient self-management education programmes right from the disease diagnosis (American Diabetes Association, 2018; Chatterjee et al., 2018; Powers, 2016). Beyond glycaemic control, multifactorial risk reduction strategies to address CVD risk factors (i.e. hypertension, dyslipidaemia) are essential given the higher risk of T2DM patients in developing CVDs (American Diabetes Association, 2018; Stone, Houlden, Lin, Udell, & Verma, 2018).

In this section, the discussion on clinical management of T2DM is presented in accordance to ABCDES acronym of diabetes care employed by Diabetes Canada (Diabetes Canada, 2019). The ABCDES (stands for Hb**A**$_{1c}$, **b**lood pressure, **c**holesterol, **d**rugs, **e**xercise, **e**ating and **s**elf-management) acronym signifies key diabetes care components, warrant further discussion in the subsequent sections of this chapter. The essence and treatment goal of T2DM management, as highlighted in the international clinical practice guidelines [i.e. American Diabetes Association (ADA) Standards of Medical Care in Diabetes-2018 or National Institute for Health and Care Excellence (NICE)-2015] and the local clinical practice guideline by the MoH Malaysia (Ministry of Health Malaysia, 2015) are either summarised or juxtaposed in tables and presented according to relevant diabetes care components as below.

2.2.1 A – Glycated Haemoglobin (HbA_{1c})

Glycated haemoglobin (HbA_{1c}) is a reliable indicator of mean plasma glucose levels for the past 8-12 weeks (American Diabetes Association, 2018) with HbA_{1c} > 7% is associated with significant risks of developing micro- and macrovascular complications (Stratton et al., 2000). Optimal glycaemic control is therefore fundamental to the management of T2DM (American Diabetes Association, 2018; Imran, Agarwal, Bajaj, & Ross, 2018). The recommended HbA_{1c} targets among published guidelines are shown in Table 2.1.

Table 2.1 Summary of key messages from current clinical practice guidelines on glycated haemoglobin (HbA_{1c})

	ADA, 2018 (US)	NICE, 2015 (UK)	Malaysia, 2015
A = HbA_{1c} and glycaemic control	• HbA_{1c} < 7%* • Fasting capillary plasma glucose: 4.4 – 7.2 mmol/L* • Peak postprandial capillary plasma glucose: < 10 mmol/L* • Postprandial glucose measurements should be made 1 – 2 hours after meal. *glycaemic goals should be individualised based on duration of diabetes, life expectancy, comorbid conditions, known CVD or advanced microvascular complications and hypoglycaemia unawareness.	• Involve patient in decision making on HbA_{1c} target. • HbA_{1c} ≤ 6.5% (for patients managed by either lifestyle and diet or lifestyle and diet combined with single drug not associated with hypoglycaemia). • HbA_{1c} < 7% (for patients treated with a drug associated with hypoglycaemia). • Less strict HbA_{1c} target for older or frail individual, people with reduced life expectancy, high risk of hypoglycaemia, people who drive or operate machinery as part of their job, individual with significant comorbidities.	• HbA_{1c}: 6% - 6.5% (for newly diagnosed, no significant CVD, long life expectancy and have minimal risk of hypoglycaemia) • HbA_{1c}: 6.6% - 7% (most patients) • HbA_{1c}: 7.1% -8% [for patients with comorbidities (e.g. coronary disease, heart failure, renal failure, liver dysfunction), short life expectancy and prone to hypoglycaemia] • Fasting: 4.4 – 6.1 mmol/L • Random: 4.4 – 8 mmol/L • Glycaemic target should be individualised to minimise risk of hypoglycaemia.

ADA = American Diabetes Association; NICE = National Institute for Health and Care Excellence
HbA_{1c} = Glycated haemoglobin; CVD = Cardiovascular disease

In T2DM management, evidence supports the use of multifactorial risk-reduction strategies to achieve blood pressure control and lipid targets, in addition to glycaemic control. The Steno-2 study enrolled 160 T2DM patients with microalbuminuria demonstrates that step-wise implementation of lifestyle modification coupled with target-driven polypharmacy approach can reduce approximately 50% each of the CVD and microvascular complications following a 8-year of intervention (Gaede et al., 2003). Apart from microvascular and CVD benefits, the recent 21-year follow-up of the Steno-2 study further revealed that such multifactorial intervention can increase T2DM patients' median survival (i.e. 7.9

years) and median time before first CVD event (i.e. 8.1 years) (Gæde et al., 2016). Beyond glycaemic control, the aggressive management of other CVD risk factors (i.e. blood pressure and dyslipidaemia) is therefore warranted.

2.2.2 B – Blood Pressure

Hypertension, defined as sustained blood pressure ≥ 140/90 mmHg, is the major risk factor for CVDs and microvascular complications among T2DM patients (de Boer et al., 2017). Given that CVDs are the leading cause of morbidity and mortality for individuals with T2DM and impose the largest economic burden to T2DM patients, treatment of hypertension is therefore paramount (de Boer et al., 2017).

The UKPDS has established the need of treating hypertension among T2DM patients which reported that tight BP control significantly reduces 32% ($p = 0.019$) diabetes-related deaths, 44% ($p = 0.013$) stroke and 37% ($p = 0.0092$) microvascular complications (UK Prospective Diabetes Study Group, 1998). Several recent systematic reviews and meta-analyses provide unequivocal evidence that anti-hypertensive therapy reduces atherosclerotic CVDs, heart failure, stroke and microvascular complications among T2DM patients (Bangalore, Kumar, Lobach, & Messerli, 2011; Brunström & Carlberg, 2016; Emdin et al., 2015; Reboldi et al., 2011). Prompt initiation and timely titration of anti-hypertensive agents with CVDs benefits are advocated in T2DM patients with hypertension (de Boer et al., 2017). The BP targets and treatment approach recommended in the published clinical guidelines are summarised in Table 2.2.

Table 2.2 Summary of key messages from current clinical practice guidelines on blood pressure management

	ADA, 2018 (US)	NICE, 2015 (UK)	Malaysia, 2015
B = Blood pressure	• BP < 140/90 mmHg for most patients with T2DM and hypertension. • BP < 130/80 mmHg appropriate for patients with high risk of CVDs. • BP management include lifestyle modifications and timely pharmacological initiation. • Use anti-hypertensive drugs with evidence of CVD benefits (i.e. ACEi, ARBs, thiazide diuretics, dihydropyridine CCBs). • BP ≥ 140/90 mmHg, use single drug • BP ≥ 160/100 mmHg, use two drugs or single pill with combination of drugs. • ACEi or ARBs first-line choice for T2DM patients with microalbuminuria or proteinuria.	• BP < 140/80 mmHg for most patients. • BP < 130/80 mmHg for patients with kidney, eye or cerebrovascular damage. • Blood pressure management include lifestyle advice and anti-hypertensive therapy. • ACEi or ARB (if intolerant to ACEi) as first-line. If target not achieve then add-on therapy CCB, thiazide diuretic, alpha-blocker, beta-blocker or potassium-sparing diuretic.	• BP ≤ 135/75 mmHg • Dietary management to achieve optimal body weight and sodium restriction. • ACEi or ARB as first-line. • Add-on therapy may include CCB, beta-blockers or peripheral alpha blockers.

ADA = American Diabetes Association; NICE = National Institute for Health and Care Excellence; *BP = Blood pressure; CVD = Cardiovascular disease; ACEi = Angiotensin converting enzyme inhibitor; ARB = Angiotensin receptor blocker; CCBs = Calcium channel blockers; T2DM = Type 2 diabetes mellitus*

2.2.3 C – Cholesterols

Compared to individuals without diabetes, T2DM patients are 2- to 4-fold greater risk of developing CVDs (Mancini, Hegele, & Leiter, 2018). Aggressive management of all CVDs risk factors such as BP (as described in previous section) and dyslipidaemia are therefore essential in the diabetes care (American Diabetes Association, 2018; Chatterjee, Khunti, & Davies, 2016; Mancini et al., 2018; Ministry of Health Malaysia, 2015).

Clinical trials in patients with T2DM (Coulhoun et al, 2004; Knopp et al, 2006) and subgroup analysis of patients with DM from larger trials (Goldberg et al., 1998; Sever et al., 2005; Shepherd et al., 2006) collectively showed beneficial effects of statin therapy in primary and secondary prevention of CVDs. Moreover, the Cholesterol Treatment Trialists' (CTT) meta-analysis involving 18,686 patients with DM from 14 randomised trials of statin therapy demonstrated that every 1 mmol/L low density lipoprotein cholesterol (LDL-C) decrement is associated with 9% reduction in all-cause mortality (RR 0.91, 99% CI 0.82 – 1.01; p = 0.02) and 13% reduction in vascular mortality (RR 0.87, 99% CI 0.76 – 1.00; p = 0.008) (Cholesterol Treatment Trialists' Collaborators, 2008). Accordingly, statins are the drugs of choice for lowering LDL-C and providing cardio-protection among patients with T2DM (American Diabetes Association, 2018; Mancini et al., 2018). The recommended treatment targets and strategies for cholesterols management are summarised in Table 2.3.

Table 2.3 Summary of key messages from current clinical practice guidelines on cholesterols management

C = Cholesterol

ADA, 2018 (US)

Statin classification:

Statin	Reduction in LDL-C and examples
High-intensity	Lowers LDL-C by 50% e.g. Atorvastatin 40 – 80 mg Rosuvastatin 20 – 40 mg
Moderate-intensity	Lowers LDL-C by 30 - 50% e.g. Atorvastatin 10 -20 mg Rosuvastatin 5 – 10 mg Simvastatin 20 – 40 mg

Treatment target and approaches:

Age	CVD	Management
<40	No	– None – High risk CVD† consider moderate intensity statin
	Yes	– Lifestyle modification* – High-intensity statin – If LDL ≥ 1.8 mmol/L despite maximal dose statin, add additional LDL lowering agent (e.g. ezetimibe)

NICE, 2015 (UK)

Statin classification:

Statin	Reduction in LDL-C and examples
High-intensity	Lowers LDL-C > 40% e.g. Atorvastatin 20 – 80 mg Rosuvastatin 10 – 40 mg Simvastatin 80 mg
Moderate-intensity	Lowers LDL-C 31 - 40% e.g. Atorvastatin 10 mg Rosuvastatin 5 mg Simvastatin 20 – 40 mg
Low-intensity	Lowers LDL-C by 20 - 30% e.g. Simvastatin 10 mg Pravastatin 10 – 40 mg Fluvastatin 20 – 40 mg

Primary prevention:

- Support lifestyle modification.
- Offer atorvastatin 20 mg for primary prevention of CVD among people who have 10-year CVD risk of ≥ 10%.

Secondary prevention:

- Support lifestyle modification.
- Initiate atorvastatin 80 mg in people with CVD. Lower dose of atorvastatin if:

Malaysia, 2015

Overall treatment targets:

- TG ≤ 1.7 mmol/L
- HDL-C ≥ 1.1 mmol/L
- LDL-C ≤ 2.6 mmol/L (≤ 1.8 mmol/L for individuals with overt CVD)

Treatment approaches:

- Main aim is to lower LDL-C

Age	CVD	Management
>40	No	– Lifestyle modification* – Initiate statin regardless of baseline LDL – Target LDL ≤ 2.6 mmol/L
	Yes	– Lifestyle modification* – Initiate statin – Target LDL ≤ 1.8 mmol/L

*Lifestyle modification includes reduction of saturated fat, trans fat and cholesterol intake; increased physical activity and weight loss if overweight or obese.

>40	No	– Lifestyle modification* – Moderate-intensity statin	– Potential drug-drug interaction. – High risk of adverse drug effects. – Patient preference.
	Yes	– Lifestyle modification* – High-intensity statin If LDL ≥ 1.8 mmol/L despite maximal dose statin, add additional LDL lowering agent (e.g. ezetimibe)	

†High CVD risk factors include LDL-C ≥ 2.6 mmol/L, high BP, smoking, CKD, albuminuria and family history of premature CVD

*Lifestyle modification includes reduction of saturated fat, trans fat and cholesterol intake; increase dietary fibre and plant sterols; increase physical activity and weight loss if overweight or obese.

ADA = American Diabetes Association; NICE = National Institute for Health and Care Excellence; LDL-C = Low density lipoprotein cholesterol; HDL-C = High density lipoprotein cholesterol; TG = Triglyceride; CVD = Cardiovascular disease; CKD = Chronic kidney disease

2.2.4 D – Drugs

Currently there are eleven classes of drugs available to treat T2DM, namely, biguanides, sodium-glucose cotransporter 2 (SGLT2), glucagon-like peptide 1 receptor agonist (GLP-1 RA), dipeptidyl peptidase 4 inhibitors (DPP-4i), thiazolidinediones (TZD), glinides, sulphonylureas (SU), amylin mimetics, insulins, bile acid sequestrants and dopamine-2 agonists. The efficacy and pharmacological properties of these drugs have been comprehensively reviewed by other authors (Tran et al., 2015b, 2015a; White, 2014) and updated in the latest ADA guideline on the pharmacological management of T2DM (American Diabetes Association, 2019).

Previous published guidelines (American Diabetes Association, 2018; Ministry of Health Malaysia, 2015; National Institute for Health and Care Excellence, 2015) have consistently recommended step-wise pharmacological management approach for T2DM in which metformin and lifestyle modifications should be the first-line treatment for T2DM; addition of drugs is then guided by patient's HbA_{1c}. In addition, the updated ADA guideline has advocated the selection of drug choices to take into considerations both the drug efficacy and patient's factors (i.e. comorbidities such as CVDs and chronic kidney disease, risk of hypoglycaemia, impact on weight, risk of side effects and patient's preferences) (American Diabetes Association, 2019). The latest T2DM treatment algorithm is shown in Figure 2.2.

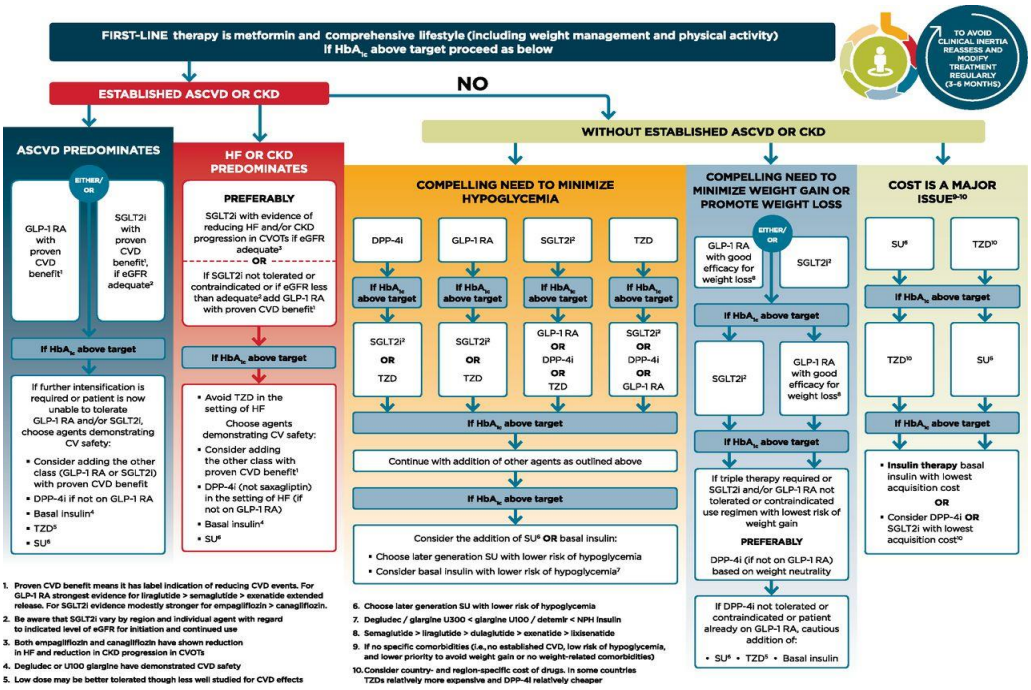

Figure 2.2 T2DM treatment algorithm adapted from ADA Standards of Medical Care in Diabetes 2019 (American Diabetes Association, 2019)

2.2.5 E – Eating and Exercise

Sedentary lifestyle and unhealthy diet are the known risk factors of T2DM and drivers of poor prognosis in T2DM leading to various complications (Zheng et al., 2017). Previous systematic reviews and meta-analysis demonstrated that multifaceted lifestyle management improve cardiometabolic outcomes in T2DM (Chen et al., 2015; Schellenberg et al., 2013). Lifestyle modifications including healthy diet, increase physical activities and smoking cessation remain fundamental in diabetes care (American Diabetes Association, 2018).

Evidence for ideal amalgam of calories from carbohydrates (CHOs), proteins and fats is currently inconclusive for T2DM patients (Forouhi, Misra, Mohan, Taylor, & Yancy, 2018). Whilst several dietary patterns such as Mediterranean diet and Dietary Approaches to Stop Hypertension (DASH) have shown positive results, guidelines recommend meal planning individualised to patient's preferences and

metabolic goal (American Diabetes Association, 2018; Ministry of Health Malaysia, 2015; National Institute for Health and Care Excellence, 2015).

Published literature suggested that the most challenging part of T2DM management among patients is to determine what to eat and adhere to meal plan (Buchmann, Wermeling, Lucius-Hoene, & Himmel, 2016; Carolan, Holman, & Ferrari, 2015; Forouhi et al., 2018). Information processing burden has been suggested as one of the contributing factors particularly among elderly with cognitive deficits (DiMatteo, 2004; Sevick et al., 2007). T2DM individuals opting for healthy diet require to identify CHOs from food sources and space out CHOs intake per meal within daily allowance (American Diabetes Association, 2018). Such planning could be complicated by protein and salt-intake limitations if suffering from other co-morbidities. Providing patients with vague information such as cut down sugar-intake or expecting patients to wade through cumbersome reading materials is impractical and not realistic. Individuals with T2DM warrants practical guidance from dietitian to achieve treatment goals given that such counselling can lower HbA_{1c} by 0.3% - 2% (American Diabetes Association, 2018).

Physical activity is defined as any bodily movement due to skeletal muscle contraction that requires energy expenditure above basal level (American Association of Diabetes Educators, 2012; Sigal et al., 2018; U.S Department of Health and Human Services (HHS), 2008). Exercise, on the other hand, is a planned, structured and repetitive physical activity designed to improve physical fitness (American Association of Diabetes Educators, 2012; Sigal et al., 2018). Both types of activities are essential in the T2DM management (American Association of Diabetes Educators, 2012; Colberg et al., 2016). Previous meta-analysis and Cochrane review concluded

that exercise interventions reduce HbA_{1c} by 0.6 – 0.66% despite no changes in BMI (Boulé, Haddad, Kenny, Wells, & Sigal, 2001; Thomas et al., 2006). Habitual participation in active lifestyle has also been shown to increase cardiorespiratory fitness and therefore reduces risk of CVDs by 35% – 55% in patients with DM (American Association of Diabetes Educators, 2012; Sigal et al., 2018). For glycaemic control and general health benefits, all published guidelines (American Diabetes Association, 2018; Ministry of Health Malaysia, 2015; National Institute for Health and Care Excellence, 2015) collectively recommend T2DM patients to:

1. engage in moderate-intensity aerobic activity for at least 150 minutes per week with no more than 2 consecutive days without activity.
2. decrease daily sedentary behaviour by interrupting prolonged sitting time (i.e. every 30 minutes) with brief standing, walking or other physical activity.
3. perform resistance training for 2 to 3 times per week.

2.2.6 S – Self-management

Self-management is first proposed in the 1960s by Thomas Creer and colleagues who posited that patients need to engage actively in the management of their own chronic diseases (Lorig & Holman, 2003). Since then, self-management has been widely used but with variety of definitions and conceptualisation causing a lack of clarity in the literature (Grady & Gough, 2014). Self-management is often used interchangeably with self-care in the literature. Although sharing similar concepts, self-care is interpreted by many researchers as tasks performed by healthy people to prevent rather than managing illnesses (Jones, MacGillivray, Kroll, Zohoor, &

Connaghan, 2011; Richard & Shea, 2011). Self-management, on the other hand, involves tasks that an individual must undertake to live with one or more chronic conditions (Adams, Greiner, & Corrigan, 2005). Such tasks require individuals' confidence in the medical management, role management and emotional management (Captieux et al., 2018; Lorig & Holman, 2003).

To avoid confusion, the term "self-management" will be consistently used in this thesis, referring to the process patients perform to manage their T2DM outside of the clinic setting. The term "self-care behaviours" used in this thesis refers to the specific tasks that patients with T2DM performed to achieve recommended glycaemic control. A total of seven self-care behaviours are recommended by AADE: healthy diet, be active, self-monitoring, medication-taking, problem-solving, healthy coping and risk reduction (American Association of Diabetes Educators, 2014).

To cruise through life with a chronic illness, Lorig and Holman advocated five core self-management skills (i.e. problem solving, decision making, resource utilisation, forming a patient-provider partnership and action taking) (Lorig & Holman, 2003). Each core self-management skill is further described as following:

a) Problem solving

   This includes problem definition, generation of possible solutions such as solicitation of suggestions from friends and healthcare professionals, solution implementation, and evaluation of results.

b) Decision making

   This is part of problem-solving. The rationale is founded on the fact that persons with chronic illness must make day-to-day decisions in response to the changes in disease condition. To adapt to the changes