School of Pharmacy

Development and Evaluation of a Pharmacist Diabetes Management Tool: A Mixed Method Study

Shamala Ayadurai

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Doctor of Philosophy

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DECLARATION

To the best of my knowledge and belief this thesis contains no material previously published by any other person except where due acknowledgment has been made.

This thesis contains no material which has been accepted for the award of any other degree or diploma in any university.

Human Ethics

The research presented and reported in this thesis was conducted in accordance with the National Health and Medical Research Council National Statement on Ethical Conduct in Human Research (2007) – updated March 2014. The proposed research study received human research ethics approvals from the Curtin University Human Research Ethics Committee (EC00262), Approval Numbers as follows:

1. PH-18-14 for Phase One
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PUBLICATIONS AND PRESENTATIONS

Publications arising from work in this thesis

1. Ayadurai, S., Hattingh HL, Tee LBG, Md Said SN (2016). A Narrative Review of Diabetes Intervention Studies to Explore Diabetes Care Opportunities for Pharmacists. Journal of Diabetes Research 2016: 11. A link to the paper is at https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4877480/

2. Ayadurai S, Sunderland VB, Tee LB, Hattingh HL. Consensus Validation of Simpler: A Tool to Improve Pharmacist Delivery of Quality, Evidence-Based Diabetes Care. *Curr Diabetes Rev* 2017. A link to the paper is at https://www.ncbi.nlm.nih.gov/pubmed/29243582

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3. *Evaluation of Simpler™: an evidence-based pharmacist diabetes intervention tool*. Poster presentation at Annual Conference of Australasian

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THESIS ABSTRACT

Introduction/Background: Pharmacists' contributions towards improving clinical outcomes of patients with diabetes are well documented. However, strategies used to deliver quality diabetes care are inconsistent. This research aimed to 1) develop and validate a structured pharmacist type 2 diabetes (T2DM) intervention tool, referred to as the Simpler™ tool; 2) explore the impact of targeted training addressing pharmacists' knowledge and ability to deliver evidence-based diabetes care and 3) determine the effectiveness of a multifactorial evidence-based diabetes intervention tool among T2DM patients.

Method: There were three phases for this research. In Phase One, the Delphi method was used to validate the Simpler™ tool by obtaining consensus from 12 diabetes experts from Australia and Malaysia. The experts consisted of endocrinologists from the community, hospital, pharmacy administration and academic practice, general practitioners, diabetes nurse, family medicine specialist and public health physician who was also the contributing author for the 2015 Malaysian diabetes guideline. In Phase Two, the Simpler™ training package was developed to train 12 pharmacists from community practice without formal diabetes training from Australia and Malaysia on diabetes management. Pharmacists' knowledge was assessed pre-and post-training and they were required to use the tool in practice for a one-month period. Subsequently, perception on the feasibility of the tool was obtained through semi-structured interviews. Participant feedback on the tool were applied to refine the tool and the training package. Phase Three consisted of a 6-month, parallel, randomised controlled trial (RCT) conducted in seven primary health clinics in Johor, Malaysia. Fourteen pharmacists were trained using the Simpler™ training package developed and validated in Phase Two. Pharmacists without formal diabetes training and with less than three years of providing diabetes management service were recruited. In Phase Three, the effectiveness of the tool was measured through the number of Simpler™ interventions conducted by pharmacists. Additionally, the

impact of the tool on the clinical outcomes such as glycated haemoglobin (HbA1c), blood glucose, blood pressure and lipid levels; changes to medication adherence, physical activity, waist circumference and body mass index was analysed. Consequently, the overall impact on patient's health related quality of life was assessed pre-and post-intervention for both arms.

Results: In Phase One, the Simpler™ indicators were categorised into seven broad treatment areas referred to as the seven diabetes factors presented in the figure below and are as follows:

1. the use of statin/lipid-regulation medicine
2. the use of insulin and glycaemic control
3. medication adherence and addressing medication-related problems (MRP)
4. addressing BP control
5. addressing lifestyle issues
6. providing education and
7. reducing CVD risk

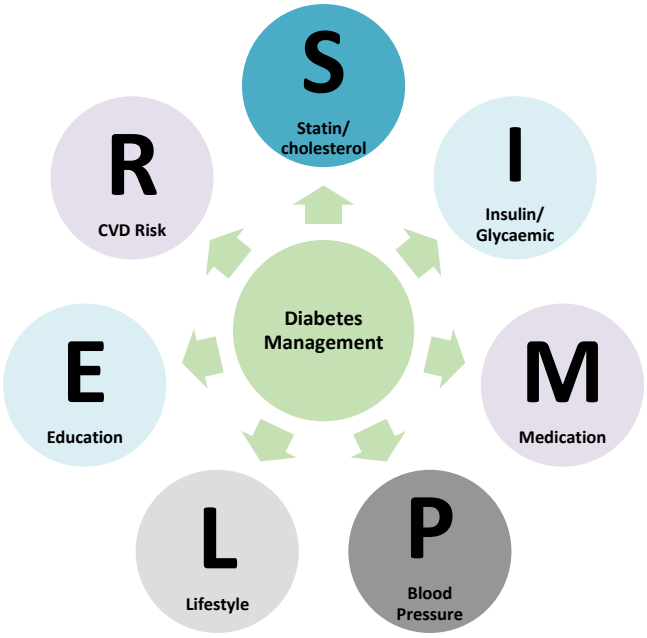

Figure: The seven diabetes factors in type 2 diabetes management

Of the 38 indicators presented to the panel, 36 (94.7%) achieved consensus level at 60% after a three round Delphi method. In Phase Two, pre-and post-training assessments showed significantly improved test scores (p=0.002). The median pre-test score was 6.5/27, IqR 1.4 (first assessor) and 5.3/27, IqR 2.0 (second assessor). The full marks being 27 marks. After attending the training program, the scores improved to 14.3/27, IqR 4.5 (first assessor) and 11.3/27, IqR 3.1 (second assessor). Interview analysis on the Simpler™ training revealed that the facilitating factors were 1) structured medication reviews, 2) improved knowledge and record keeping, 3) increased ability to detect problems in uncontrolled patients with diabetes and 4) focused on achieving diabetes targets. Five topics emerged from the interview regarding the tool. Those were:

1. it facilitated pharmacists' role,
2. it was specific for diabetes management,
3. it had wider usage,
4. it presented a competitive edge, and
5. it targeted glycaemic improvement

Participants' suggestions for improvements to the training modules were to:

1. include a template to record pharmacist's interventions,
2. retrieve patient's data first before application of the Simpler™ tool,
3. add more information on glucagon administration, MRPs, diet and lifestyle, and
4. include health information such as leaflets for patients

Improvements for the Simpler™ tool hand-out included:

1. visual prompts,
2. larger font for headings,
3. medication adherence assessment tool and plate model in the tool,
4. two versions of the tool to incorporate each country's (Australia and Malaysia) individual treatment goals,
5. Asian and Caucasian terms to differentiate the body mass index targets.

All suggestions were taken into consideration and subsequent improvements were made to the training modules content and to the tool.

Phase Three RCT recruited 77 patients in each arm. Of these, 49 intervention patients and 63 usual care patients were assessable for HbA1c measurement. The HbA1c levels significantly improved in the intervention arm; mean reduction of 1.59% (95%CI: -2.2, -0.9) compared with reduction of 0.25% (95%CI: -0.62, 0.11) in the usual care arm (n=63), (*p*=<0.001). In addition, there were significant improvements in systolic blood pressure: [-6.28 mmHg (95%CI: -10.5, 2.0), p=0.005] and health related quality of life [-1.75, (95%CI: -2.52, -0.97), p<0.001]. A total of 66 recommendations were made to prescribers and 51 interventions were predicated with doctors using the Simpler™ tool. The most common MRPs were patients' non-adherence (n=135, 44.9%) followed by sub therapeutic dosage (n=65, 21.6%) and needed additional therapy (n=52, 17.3%). The most frequent causes of non-adherence to medications was patients 'forget to take' (n=124, 68.1%) and 'prefers not to take' (n=42, 23.1%). A majority of pharmacist interventions included medication reminder chart (n=39, 59.1%) followed by reinitiating drug therapy (n=21, 31.8%). Pharmacists worked in collaboration with doctors to add medications (n=23, 45.1%) and change dosages (n=17, 33.3%).

Conclusions: Training involving the use of the Simpler™ tool developed by a structured process improved pharmacists' knowledge on diabetes management, facilitated delivery of evidence-based, individualised diabetes care, and consequently improved clinical and quality of life outcomes. It also provided an effective support for pharmacists with limited clinical experience in diabetes care to enhance quality of care provided.

ABBREVIATIONS

ACCORD	Action to control cardiovascular risk in diabetes trial
ACEI	Angiotensin converting enzyme inhibitor
ADDITION-Europe	Anglo-Danish-Dutch study of intensive treatment in people with screen detected diabetes in primary care
ADVANCE	Action in diabetes and vascular disease: preterax and diamicron MR controlled evaluation trial
ARB	Angiotensin receptor blocker
BGL	Blood glucose level
BMI	Body mass index
CONSORT	Consolidated standards for reporting trials.
CPG	Clinical practice guidelines
CDTM	Collaborative drug therapy management
CVD	Cardiovascular disease
DCCT	Diabetes control and complications trial
DESMOND	Diabetes education and self-management for ongoing and newly diagnosed for people with type 2 diabetes
DMAS	Diabetes medication assistance service
DPP-4 inhibitor	Dipeptidyl peptidase-4 inhibitor
ELIXA	Evaluation of lixisenatide in acute coronary syndrome trial
EMPA-REG OUTCOME	Empagliflozin-cardiovascular outcomes and mortality in type 2 diabetes trial
EXAMINE	Cardiovascular outcomes study of alogliptin in patients with type 2 diabetes and acute coronary syndrome
8-items MMMAS	Eight items modified Morisky medication adherence
FBG	Fasting blood glucose
FRS	Framingham risk score
GLP-1 agonist	Glucagon-like peptide-1 receptor agonist
GPs	General practitioners
HbA1c	Glycated haemoglobin
HCP	Healthcare professionals
KK	*Klinik kesihatan,*
LDL	Low density lipoprotein

LEADER	Liraglutide effect and action in diabetes: evaluation of cardiovascular outcome results trial
Look AHEAD	Look action for health in diabetes trial
MMS	Medication management service
MRP	Medication-related problem
NCD	Non-communicable disease
NICE	National Institute for Health and Care Excellence
OHA	Oral hypoglycaemic agents
PCC	Patient centred care
PDE-5 inhibitor	Phosphodiesterase-5 inhibitor
PMR	Patient medical record
PPG	Post prandial blood glucose
PROactive	Prospective pioglitazone clinical trial in macrovascular events
QOL	Quality of Life
RBG	Random blood glucose
RCT	Randomised controlled trial
RECORD	Rosiglitazone evaluated for cardiac outcomes and regulation of glycaemia in diabetes
SAVOR-TIMI 53	Saxagliptin assessment of vascular outcomes recorded in patients with diabetes mellitus
SC	Simpler™ care
SCR	Summary care record
SD	Standard deviation
SGLT-2	Sodium-glucose cotransporter-2
SMBG	Self-monitoring of blood glucose
SUSTAIN-6	Trial to evaluate cardiovascular and other long-term outcomes with semaglutide in subjects with type 2 diabetes
T2DM	Type 2 diabetes mellitus
TECOS	Trial to evaluate cardiovascular outcomes after treatment with sitagliptin
TG	Triglyceride
UC	Usual care
UK	United Kingdom

UKPDS	United Kingdom prospective diabetes study
USA	United States of America
VADT	Veterans affairs diabetes trial

DEFINITIONS

8-items MMMAS	This is a modified version of the Morisky medication adherence scale, which consists of eight questions.(1)
ACEI	Class of drugs that inhibit angiotensin-converting enzyme, which converts angiotensin 1 to angiotensin 2. Angiotensin 2 increases aldosterone synthesis and raises blood pressure through vasoconstriction.(2)
ARB	Class of drugs which blocks Angiotensin 1 receptor which reduces the effect of angiotensin 2 and subsequently reduces blood pressure.(2)
CONSORT	Consists of a checklist and a flow diagram which provides guidelines for authors to report the findings from randomised controlled trials.(3)
Diabetes MedsCheck	Diabetes medication management service provided by community pharmacy in Australia. This service includes a review of consumer's medications focusing on self-education and self-management. The program is funded under the fifth and sixth community pharmacy agreement under the Department of Health and Ageing.(4)
Education levels	In Malaysia, primary education starts at age seven to age 12. Secondary education begins at age 13 and ends at age 17. Pre-university/diploma courses are offered to students who have completed secondary education.
Ethnic Chinese	Refers to population from China who migrated to Malaysia in the 3rd and 19th century. (5)
Ethnic Indian	Refers to population from India, Sri Lanka, Pakistan and Bangladesh who migrated to Malaysia in the 3rd and 19th century.(5)
FBG	Blood glucose level taken in the morning before meals. Malaysian guideline recommends 4.4-7.0 mmol/L while Australia recommends 6-8 mmol/L.(6, 7)
FRS	Risk assessment tool used to predict patient's 10 year risk of developing cardiovascular disease.(8)
HbA1c	HbA1c is glycated haemoglobin. As HbA1c remains in blood circulation for 3 months, the amount of HbA1c present, expressed, as a percentage of haemoglobin A, is proportional to the glucose concentration over that time.(6) All HbA1c units in thesis report both % and mmol/ml. However,

	the conversion rate of HbA1c units from DCCT (%) to IFCC (mmol/mol) only allows from 4% to 24%. Therefore, HbA1c units below 4% are reported in % only.
KK	Primary health care clinics which are public funded, government managed institutions. Malaysian citizens pay a subsidised amount of RM1 (USD 0.23) for doctor's consultation and medicine cost for each visit.
Melayu	Also known as Malay. Refers to an ethnic in Malaysia whose origin dates to Indian, Chinese, Thai, Portuguese, Cambodian and Indonesian heritage(304) and includes indigenous population in Malaysia.(9)
MTAC Diabetes	Diabetes medication management service provided by pharmacists in government health institutions in Malaysia with no added cost to patients. The service includes a review of consumer's medicines focusing on clinical interventions, self-education, self-management and patient follow up for a maximum for eight visits.(10)
OHA	Drugs that are administered orally to treat Type 2 diabetes mellitus. They reduce elevated blood glucose.(6)
PPG	Blood glucose level taken two hours after meals. The recommended level according to Malaysian guidelines are 4.4-8.5 while Australian guidelines recommend 8-10 mmol/L.(6, 7)
Simpler™	The name of the diabetes intervention tool studied in this research. TM accompanying the word Simpler stands for the trademark symbol.
WHOQOL-BREF	World Health Organization Quality of Life Questionnaire is an abbreviated 26 item questionnaire to assess individuals' perceptions in relation to their goals, expectations, standards and concerns.(11) It consists of four domains namely physical health, psychological, social relationships and environment. Each of the four domains contains questions pertaining to facets of the specific domain. The facets are: 1.Physical health: daily activities, work ability, pain, sleep and energy 2.Psychological: body image, self-esteem, thinking and concentration, feelings 3.Social relationships: personal relationships, social support

	4.Environment: accessibility and quality to health and social care, opportunities for acquiring new information and skills, participation in leisure activities

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Chapter 1

Introduction

1.1 Introduction

Community pharmacists are easily accessed by patients, are increasingly seen as medicine experts and are expected to address clinical issues in patients with chronic diseases such as diabetes.(12) However, little is known of the processes followed by pharmacists to retrieve information and make pharmaceutical care interventions.(13) Hence, most diabetes studies evaluating pharmacists' intervention have reported varied clinical outcomes, ranging between some improvements to minimal difference.(14) Diabetes is a chronic condition with prevalence of diabetes continuing to rise, and hence there is an urgent need for a targeted and structured approach to diabetes care in order to prevent diabetes related complications such as CVD, nephropathy and neuropathy.

Diabetes Mellitus is a condition where there is lack of insulin to regulate the blood sugar level or when existing insulin is not utilised efficiently. The World Health Organization (WHO) classifies diabetes mellitus into Type 1 diabetes mellitus, Type 2 diabetes mellitus (T2DM) and Gestational diabetes.(15) Type 1 was formerly known as insulin-dependent, juvenile or childhood onset. Patients with Type 1 diabetes need insulin replacement as they are insulin deficient. T2DM used to be known as non-insulin dependent and is due to inefficient use of existing insulin in the body. Gestational diabetes occurs at first onset during pregnancy. Although the blood glucose level (BGL) is above normal in gestational diabetes it is below the level to be diagnosed as diabetes. This thesis will however only focus on the management of T2DM.

1.1.1 Type 2 diabetes mellitus

T2DM is typified by hyperglycaemia. The increase in blood glucose is caused by increased carbohydrate intake, increased synthesis of hepatic glucose, decreased

insulin secretion and consequently decreased peripheral glucose uptake. There are several factors involved in the pathogenesis of diabetes. Insulin resistance is associated with increase in intraabdominal adipose tissue, decrease in glucokinase action which increases the conversion of substrates to glucose. In addition, other factors postulated are a rise in free fatty acid levels which intensifies glucose production in the liver and enhanced gluconeogenesis process which increases glucose production in the kidney. The symptoms of T2DM include polyuria, polydipsia, polyphagia and weight loss, blurred vision and lower-extremity numbness. Current diabetes guidelines from Australia, Malaysia, the United Kingdom (UK) and the United States of America (USA) recommend diet and exercise as treatment and suggests pharmacological intervention if goals of therapy are not achieved within three months.(6, 7, 16, 17)

The guidelines also recommend glycated haemoglobin (HbA1c) to measure blood glucose concentrations among patients with diabetes.(6, 7, 16, 17) HbA1c gives an average measurement of blood glucose levels in the previous three months and therefore reflects a person's long term control of the disease. In addition, the guidelines require persons using insulin to monitor their blood glucose levels daily using the finger pricking method in order to optimise treatment.

The main aim of T2DM management is to improve clinical outcomes and subsequently prevent diabetes related complications.(16) Clinical outcomes in diabetes consists of body mass index (BMI), HbA1c, cholesterol, blood pressure, fasting blood glucose (FBG) and post prandial glucose (PPG). These outcomes are reported as therapeutic targets required to be achieved according to evidence-based practice. Often the therapeutic targets need to be individualised depending on the person's age, number of comorbidities and the person's risk of experiencing hypoglycaemia.(7) The health interventions conducted by healthcare professionals and consequent improved clinical outcomes may lead to enhanced quality of life (QOL).

The World Health Organization (WHO) defines QOL as a person's perception of their life in the culture and system where they live associated with their life's goals , expectations and concerns.(11) QOL scores reflect a person's self management of their disease.(16) A higher QOL score is associated with better clinical outcomes and less anxiety about the disease.(11) A lower score of diabetes QOL is presented among patients with multiple comorbidities.(18, 19) One determinant of increased QOL scores is patient education on diabetes self management.(16) The QOL questionnaire used in the thesis was the validated World Health Organization QOL abbreviated questionnaire (WHOQOL-BREF) assessment, the Bahasa Malaysia version. It consists of 26 questions which is grouped into four domains and its corresponding 24 facets. The 24 questions were derived from each of the 24 facets. The additional two questions asks a person's perception on their overall general health and QOL. The domains and their facets are as follows: (11)

1. Physical health: Activities of daily living, dependence on medication and medical aids, energy and fatigue, mobility, pain, sleep and work ability
2. Psychological: body image, negative and postive feelings, self esteem, religion, spirituality, personal belief, thinking, learning, memory and concentration.
3. Social relationships: personal relationships, social support and sexual activity
4. Environment: financial resources, freedom, physical safety, accessibility to health and social care, home environment, opportunities for acquiring new information and skills, participation in recreational and leisure activities, physical environment such as noise, pollution, transport.

1.1.2 Pharmacological treatment of T2DM

The different classes of medications involved in treating increased blood glucose levels (BGL) are oral hypoglycaemic agents (OHA) such as biguanides, sulphonylureas,

DPPIV inhibitors, thiazolidinedione, acarbose and the SGLT 2 inhibitors while the injectables consists of insulin and GLP1 agonists.

The standards of care, American diabetes association(16) recommends metformin as first choice to achieve HbA1c goals if non pharmacological interventions were ineffective. If goals are still not achieved after three months of metformin monotherapy then dual therapy is recommended such as metformin and sulphonylurea or other combinations with metformin. If after three months patients still fails to achieve the glycaemic target agreed, then triple drug combination shall be added such as metformin and sulphonlyurea and insulin or other combinations with metformin depending on patient factors. The patient factors include, weight issues, frequency of hypoglycaemia and CVD symptoms. Finally if three months of triple therapy which includes OHA does not produce the targeted outcome, then patients should be initiated on insulin specifically on basal insulin before addition of other insulin. Diabetes guidelines from Australia, Malaysia, the UK and the USA similarly recommend insulin initiation in patients whose HbA1c levels cannot be achieved despite being on two or three oral hypoglycaemic agents.(6, 7, 16, 17)

1.1.3 **Role of pharmacists in diabetes management**

Patients with diabetes often present themselves with multiple comorbidities and medications and therefore require complex care. Increased health burden costs due to diabetes has prompted countries like Australia, Malaysia and the UK to utilise pharmacists to promote medication adherence, reduce medication-related hospitalisations and medication wastage. Consequently, pharmacists in the community and primary health care settings provide medication management services (MMS) that include working with patients on non-compliance issues, managing patients with multiple chronic disease conditions and regularly educating patients to improve quality use of medications. MMS pharmacists work in

collaboration with other healthcare professionals with the aim to improve patients' clinical and QOL outcomes.

In Australia, the MMS service for patients with diabetes is known as diabetes MedsCheck and is provided in community pharmacies. Pharmacist conduct medication review, provide education and counselling and promote medication adherence. In Malaysia, the diabetes MMS is known as Medication Therapy Adherence Clinic (MTAC diabetes), but unlike Australia it is provided in primary health care clinics and at hospital outpatient departments. Similar to Australia, MTAC diabetes pharmacists conduct comprehensive medication review, provide education and counselling in order to increase patients' medication adherence and compliance to disease management. In addition, MMS pharmacists in both countries offer recommendations to prescribers to optimise treatments to achieve therapeutic targets and prepare a follow up care plan for patients. Diabetes guidelines from Australia, Malaysia, the UK and the USA outline seven diabetes factors required to reduce the complications mentioned above.(6, 7, 16, 17) To date, there is a lack of diabetes intervention studies evaluating a process followed by pharmacists that addresses all seven guideline discrete factors required to be monitored. This provided an opportunity to develop and evaluate a tool that was able to assist pharmacists deliver targeted diabetes care of consistent quality, and in accordance with evidence-based recommendations.

1.2 Overview of research

This research involved the development, evaluation and application of a tool that incorporated all seven factors and was conducted in Australia and Malaysia. While Australia's and Malaysia's healthcare systems differ, the diabetes practice guidelines and existing medication management services (MMS) are similar in both countries.

In addition, both countries have increasing prevalence of T2DM and similar concerns of the rising health and cost burdens.

The overall aim of this research was to:

i) develop and validate a structured pharmacist type 2 diabetes (T2DM) intervention tool, referred to as the Simpler™ tool;

ii) explore the impact of targeted training addressing pharmacists' knowledge and ability to deliver evidence-based diabetes care and

iii) determine the effectiveness of a multifactorial evidence-based diabetes intervention tool among T2DM patients.

The intention was for the tool to be incorporated into existing MMS, namely the Australian Diabetes MedsCheck services and the Malaysian MTAC Diabetes.(4, 10) The tool was expected to guide pharmacists with limited clinical experience to enhance the quality of diabetes care.

This thesis is composed of six chapters and the research comprised of three phases; Phases One, Two and Three. A mixed methods approach were selected during the development and evaluation process. Findings from each phase were used to inform the methodology of the next phase. Throughout this thesis, the term 'diabetes management' will referred to as T2DM management. Figure 1.1 summarises the phases of this research and the corresponding chapters.

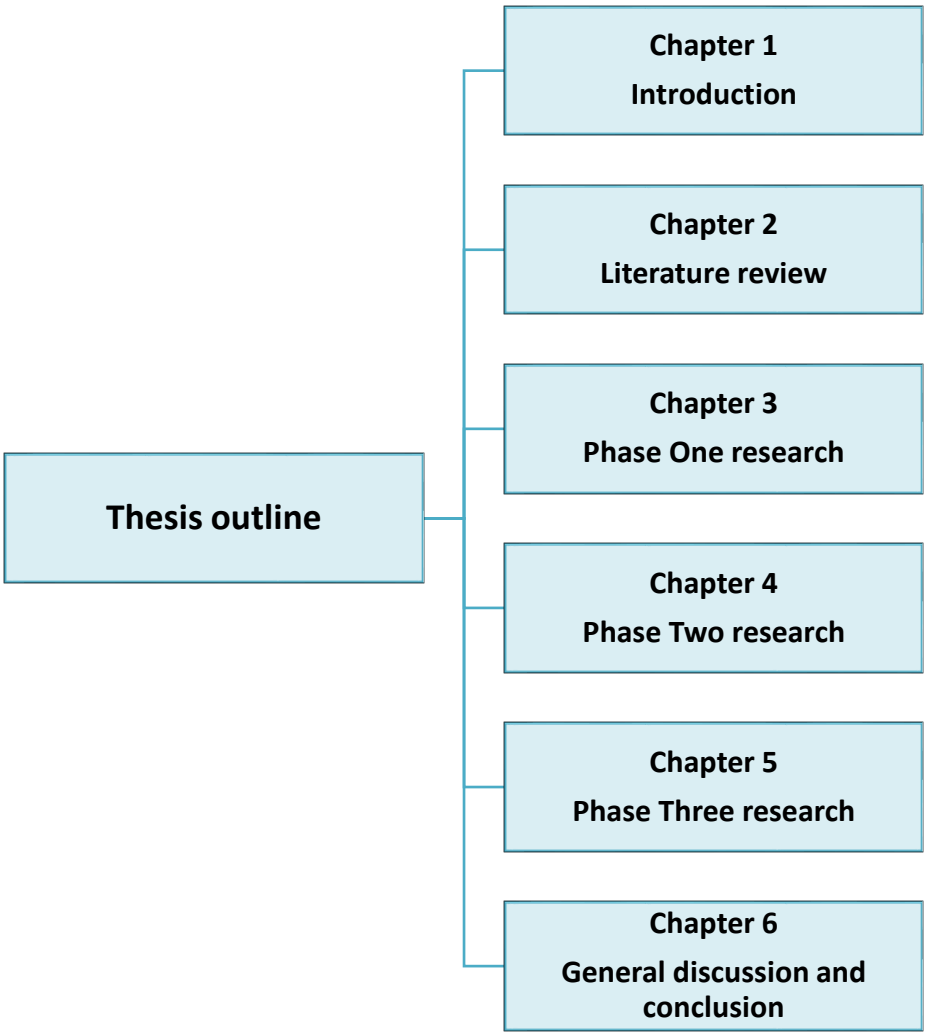

Figure 1.1: Overall thesis outline

Chapter 2 provides a comprehensive review of current literature on T2DM and the role of pharmacists in management of diabetes until August 2017. The chapter begins with the prevalence and complications of diabetes in Australia and Malaysia. This is followed by evidence-based management approach and the effectiveness of multifactorial interventions in the provision of diabetes care. The significance of patient centred care provided by pharmacists in diabetes management internationally is discussed. This is then followed by its relevance in the primary healthcare settings in Australia and in Malaysia. Finally, possible intervention strategies are reviewed. The chapter ends with the overall thesis research area.

The following chapter, Chapter 3 reports the findings of Phase One of the research. Phase One developed and validated a diabetes intervention tool. The development of the tool involved identifying and listing the seven factors of T2DM and the corresponding therapeutic recommendations. The validation of the contents and design input were obtained through the Delphi process. Chapter 3 begins with a brief introduction of the Delphi process and justification for use in this research. The methods and results sections follows, presenting findings from the Delphi questionnaire.

Chapter 4 presents Phase Two research. Phase Two research which pilots the tool, the Simpler™ tool, among community pharmacists in their practice settings in Australia and Malaysia and explores their views and perceptions of the tool. Prior to pharmacists using this tool in practice, a training package was developed to train pharmacists to make evidence-based recommendations incorporating the tool. Subsequently the tool and the training package were refined based on their recommendations. The chapter begins with an introduction followed by an explanation of Phase Two and the study design, participant recruitment from both Malaysia and Australia, development of the Simpler™ training modules and format of the training sessions. It then describes the interview guide, data collection process and analysis followed by a discussion.

Chapter 5 reports the methodology and findings of Phase Three research which comprised of a randomised controlled trial (RCT). The RCT was a parallel, six months study conducted at seven primary health clinics located as six districts in the state of Johor, Malaysia. Fourteen pharmacists without any formal diabetes training were trained to provide targeted diabetes interventions using the Simpler™ tool to T2DM patients. Patients were randomised to receiving care from pharmacists using the Simpler™ tool and to receiving the usual customary care. Chapter 5 begins with an introduction to the Phase Three research, followed by the research objectives and

method. The Simpler™ format is used to present results and discussion whereby each letter of the word represents one of the seven aforementioned diabetes factors.

The thesis ends with Chapter 6 which provides the overall discussion and conclusion. In addition, it outlines the overall significance of the research particularly the benefits of utilising the tool in practice settings.

1.3 Research questions

The framework of this thesis was guided by the research questions below:

1. Can an intervention tool that comprises all the seven required diabetes factors reduce glycated haemoglobin (HbA1c) by 1 or more%?

2. Can pharmacists without extensive formal diabetes management training using the tool improve clinical and quality of life (QOL) outcomes among T2DM patients?

3. Is the tool relevant and feasible for application in the community or primary care practice settings?

Chapter 2

A Review of Literature

2.1 Introduction

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Chapter 2 provides a comprehensive review of current literature on type 2 diabetes mellitus (T2DM) until September 2017. The chapter begins with the prevalence and complications of diabetes in Australia and Malaysia. This is followed by evidence-based management and the effectiveness of multifactorial interventions in the provision of diabetes care. The significance of patient centred care provided by pharmacists in diabetes management internationally is then discussed. This is then followed by its relevance in the primary healthcare setting in Australia and in Malaysia. The chapter then moves on to review possible intervention strategies. Finally, the chapter ends with the overall aims of the thesis.

2.1.1 Prevalence of diabetes and its complications

Globally 422 million people in 2014 had diabetes which is 8.5% of the adult population.(15) The reported prevalence of diabetes among Malaysian adults ($\geq$ 18 years) was 14.9% in 2006 and increased to 15.2% in 2011, according to a National Health and Morbidity Survey.(20) A more recent 2015 of the same survey found that the prevalence has further increased to 17.5%.(21) Although Australian diabetes prevalence statistics are lower, there has been an increase from 4.1% in 2008 to 5.1% reported in 2014-2015 among adults ($\geq$18 years).(22)

With the increasing prevalence of diabetes, health professionals are required to be knowledgeable about the need for appropriate glycaemic control and measures to prevent long-term diabetes complications. At an international level, 2012 data showed that non-communicable diseases (NCD), comprising cardiovascular diseases (CVD), diabetes, obesity, cancer and respiratory diseases, caused an estimated 38 million deaths per year. Diabetes alone caused 1.5 million deaths worldwide which was an increase from 1 million in 2000. It is the eighth leading cause of death with the number one being ischaemic heart disease.(23)

Australia seems to have a higher percentage of patients with macrovascular complications such as cardiovascular disease (CVD) compared to Malaysia. In the 2014-15 Australian Health Report, 63% of patients with diabetes reported having CVD(22) compared to the 2013 Malaysia Diabcare study, which showed that, of the 1688 patients studied, 15.7% had angina and 18.4% had suffered from a myocardial infarction. Malaysia had a higher percentage of patients suffering from microvascular complications. According to the Malaysia Diabcare study,(41%) had neuropathy and (31.5%) had cataracts.(24) In comparison, 37% of new cases of chronic kidney disease in Australia were caused by diabetes nephropathy while 5.9% of patients with diabetes hospitalised were owing to diseases of the eye.(22, 25)

2.1.2 Evidence-based diabetes care

There are several key landmark trials that have provided evidence to improve the outcome of T2DM management. These trials are as follows:

1. United Kingdom Prospective Diabetes Study (UKPDS)(26),
2. Action in Diabetes and Vascular Disease: Preterax and Diamicron MR Controlled Evaluation(ADVANCE)(27),

3. Veterans Affairs Diabetes Trial (VADT)(28),
4. Diabetes Control and Complications Trial (DCCT)(29), and
5. Action to Control Cardiovascular Risk in Diabetes (ACCORD)(30)

Table 2.1 provides a brief summary of these trials. The findings from these studies propose three main factors that need to be addressed in order to achieve treatment goals and prevent diabetes complications in clinical practice. These factors are glycemic control, blood pressure (BP), and cholesterol control. These factors are incorporated into diabetes practice guidelines in Australia, Malaysia, the UK and the USA.(6, 7, 16, 17) A 2011 concensus report by the American Diabetes Association indicated that diabetes management that follows these practice guidelines results in better disease control. The report noted a reduction in several diabetes complications, such as kidney failure and amputation, as more patients receive guideline-adherent therapy.(31)

Table 2.1: Landmark diabetes trials

Trial	n	Country	Measure	Outcome	Conclusion
UKPDS (26)	5102	UK-(White Caucasion, Afro-Caribbean, Asian-Indian)	Patients with T2DM. Intensive blood glucose control using metformin [to achieve HbA1c 7% (53mmol/mol] vs conventional treatment. Patient followed up for median of 10.7 years. Intensive BP control (less than 150/85 mm Hg). Efficacy of captopril or atenolol as antihypertensive and in controlling microvascular & macrovascular complications.	The trial managed to reduce mean difference of HbA1c to -1%. Therefore it produced significant risk reduction [12% (107.7mmol/mol)] for any diabetes related end point, 25% risk reduction for microvascular end points, 21% risk reduction for retinopathy and 33% risk reduction for albuminuria at 12 years, 16% risk reduction for myocardial infarction. Significant effect on microvascular and macrovascular complications. Captopril and atenolol were equally effective antihypertensive in preventing microvascular & macrovascular complications	• Intensive glycaemic control reduced microvascular complications, not mortality • Insulin and sulphonlyureas were effective. • Metformin was effective in obese patients • Intensive BP control reduced micro and macrovascular complications and mortality • Optimum targets: HbA1c<7% (53mmol/mol), BP< 140/80 mm Hg

Trial	n	Country	Measure	Outcome	Conclusion
ADVANCE (27)	10000	20 countries from Asia, Australia, Europe and North America	Patients with T2DM. Intensive lowering of blood glucose to HbA1c of 6.5% (47.5mmol/mol) (gliclazide MR in addition to other therapy) and BP (perindopril/indapamide combination) than UKPDS trial. Median follow up of 5 years	Trial stopped early at 4.3 years. Indapamide and perindopril combination reduced mortality, reduced weight gain, CVD events and nephropathy irrespective of baseline BP. Severe hypoglycaemia more frequent in intensive arm (2.7%) vs 1.7% in control group but this difference was not significant.	• Demonstrated that mean HbA1c=6.5% (47.5mmol/mol) can be achieved and remain at same level for 4.3 years using gliclazide MR, metformin and insulin. • No significant difference between European and Asian patients for glycaemic control. Severe hypoglycaemia and hospitalization • Current guidelines recommends HbA1c 6.5-7% (47.5-53mmol/mol) based on results from ADVANCE trial.
DCCT (32)	1441	29 medical centres in USA and Canada	Using three or more daily injections compared to conventional treatment (one or two insulin injections daily) among patients with Type 1 diabetes. Mean follow up of 6.5 years.	Intensive therapy reduced microalbuminuria by 39%, albuminuria by 54%, neuropathy by 60%, progression of retinopathy reduced by 54%, risk of retinopathy reduced by 76%. Significant weight gain and diabetes ketoacidosis were reported more on intensive arm	• Findings recommend intensive therapy for Type 1 DM but did not generalise to T2DM. • Risk of hypoglycaemia in elderly likely with intensive control with insulin. • Recommendations to intensify treatment for younger patients and

Trial	n	Country	Measure	Outcome	Conclusion
					individualise goals for older patients.
ACCORD (33-35)	1.10251 2. 4733 3. 5518	USA and Canada	1. Patients with T2DM. Intensive intervention to control hyperglycaemia to less than HbA1c of 6.0% (42.1mmol/mol). 2. Two targets for systolic levels in BP control (<120 vs <140) 3. Two regimens for plasma lipid levels. fenofibrate and simvastatin vs simvastatin alone Mean follow up of 3.4 years.	All-cause mortality was significantly greater in the intensive arm. No reduction in macrovascular, mortality or myocardial infarctions. No significant difference between the two arms	• Lowering BP and lipid levels to below recommended levels did not reduce CVD events significantly compared to the control group.
VADT (36)	1791	USA	Patients with T2DM, mean age 60.4 years followed up for 5.6 years. Comparison between intensive (metformin & rosiglitazone, glimepiride & rosiglitazone) and standard glucose control.	No significant difference in the rates of CVD events, death or microvascular complications between two groups. More hypoglycaemia (24.1%) in intensive group and 17.6% in standard therapy group.	• Intensive glucose control did not decrease the rate of CVD events. • Minimum effect on reduction of microvascular complications

ACCORD= Action to control cardiovascular risk in diabetes; ADVANCE: Action in diabetes and vascular disease: Preterax and diamicron MR controlled evaluation trial; BP=blood pressure; CVD=cardiovascular disease; DCT=Diabetes Control and Complications trial; HbA1c= glycated haemoglobin; n=sample size; UKPDS=The United Kingdom prospective diabetes study; VADT=Veteran affairs diabetes trial

However, there is evidence that guidelines are not always being followed in clinical practice. In a recent cross-sectional study, it was found that among 650 Malaysian outpatients, 32.1% of patients with T2DM and hypertension were not on antihypertensive such as an angiotensin converting enzyme inhibitors (ACEI) or angiotensin receptor blockers (ARB) as per guideline recommendation. Even though the patients had no contraindications to these antihypertensives.(37) A similar study conducted among 430 Australian patients with diabetes found evidence-based practice gaps especially in the prescribing of antihypertensive and lipid lowering medications.(38) Findings from another study in Sydney, Australia, indicated that among 118 patients with chronic disease including diabetes in eight general practices, less than 30% of patients received intervention relating to diet and exercise.(39)

2.1.3 Pathophysiology of T2DM

T2DM is typified by hyperglycaemia and is associated with resistance to insulin, insufficient insulin secretion and excessive glucagon secretion. An increase of blood glucose is caused by increased carbohydrate intake, increased synthesis of hepatic glucose, decreased insulin secretion and consequently decreased peripheral glucose uptake. In addition it is also characterized by declining β-cell function and ultimately to β-cell failure. Literature postulates the cause of declining β-cell function to be due to intraislet accumulation of glucose metabolites.(40)

Current studies have suggested insulin resistance to be the main factor in the pathogenesis of diabetes.(41) However, studies have found obesity can increase the intraabdominal adipose tissue associated with insulin resistance even though patient does not suffer from diabetes.(42) Furthermore, insulin resistance is found in

hypertension, hyperlipidemia, and heart disease.(43) These conditions are the main comorbidities of person with T2DM. In the case of hepatic insulin resistance, a decrease in glucokinase action increases the conversion of substrates to glucose even though insulin is present.(44) Additionally, free fatty acid levels identified in T2DM may lead to increased glucose production in the liver.(45) Recent studies have suggested increased action of gluconeogenesis in the kidney as the cause of further glucose production in the kidney.(46)

The symptoms of T2DM include polyuria, polydipsia, polyphagia and weight loss, blurred vision and lower-extremity numbness. Diet and exercise have been shown to improve weight especially in obese patients. Current diabetes guidelines from Australia, Malaysia, the UK and the USA recommend diet and exercise as treatment and suggests pharmacological intervention if goals of therapy are not achieved within three months.(6, 7, 16, 17)

2.1.4 Pharmacological treatment of T2DM

The different classes of medications involved in treating increased BGL are oral hypoglycaemic agents (OHA) such as biguanides, sulphonylureas, DPPIV inhibitors, thiazolidinedione, acarbose and the SGLT 2 inhibitors while the injectables consists of insulin and GLP1 agonists.

The standards of care, American diabetes association(16) recommends metformin as first choice to achieve HbA1c goals if non pharmacological interventions were ineffective. If goals are still not achieved after three months of metformin

monotherapy then dual therapy is recommended such as metformin and sulphonylurea or other combinations with metformin. If after three months patients still fails to achieve the glycaemic target agreed, then triple drug combination shall be added such as metformin and sulphonlyurea and insulin or other combinations with metformin depending on patient factors. The patient factors include, weight issues, frequency of hypoglycaemia and CVD symptoms. Finally if three months of triple therapy which include OHA does not produce the targeted outcome, then patient should be initiated on insulin specifically on basal insulin before addition of other insulin. The pharmacotherapy of each class of drug is summarised in Table 2.2. Diabetes guidelines from Australia, Malaysia, the UK and the USA similarly recommends insulin initiation in patients whose HbA1c levels cannot be achieved despite being on two or three oral hypoglycaemic agents.(6, 7, 16, 17)

Table 2.2: Pharmacotherapy of diabetes medications and its related trials on CVD risk reduction outcome

Diabetes medications Class (example)	(2) Mode of action	(6) HbA1c (1%) reduction	(6) Hypoglycaemia	(6) Weight change	(6) CVD risk reduction	(2) Side effects	(47) CVD outcome trials
Biguanides (Metformin)	Increase insulin sensitivity and glucose uptake into cells, inhibition of hepatic gluconeogenesis, delay in glucose absorption	1.0-1.5	Neutral	Possible benefit	Possible benefit	GI symptoms, absorption of vitamin B12 may be impaired.	UKPDS(26), ACCORD(30), VADT(28)
Sulphonylurea (Gliclazide)	Inhibition of hepatic glucose production and increased sensitivity to insulin	0.4-1.6	Increased risk	Increased risk	Neutral	GI disturbances and increased appetitie. Rashes may occur	ADVANCE(27), ACCORD(30), VADT(28)
Glinides/ Meglitinides (Repaglinide)	Increase insulin sensitivity	1.0-1.2	Minimal risk	Minimal risk	Neutral	GI symptoms, back and joint pain.	ACCORD(30)
Alfa glucosidase inhibitor (Acarbose)	Slows digestion and absorption of carbohydrates in the small intestine.	0.5-0.8	Neutral	Neutral	Neutral	GI symptoms, reversible increase in liver enzyme can occur	ACCORD(30)
Thiazolidinediones/TZD (Rosiglitazone)	Improves insulin sensitivity in adipose tissue, skeletal muscel and the liver	0.5-1.4	Neutral	Increased risk	Neutral	Increased apetitie, GI symptoms, headache,	ACCORD(30), VADT(28), PROactive(47), RECORD(47)

Diabetes medications Class (example)	(2) Mode of action	(6) HbA1c (1%) reduction	(6) Hypoglycaemia	(6) Weight change	(6) CVD risk reduction	(2) Side effects	(47) CVD outcome trials
						reductions in haemoglobin and haematocrit can occur.Increase bone fracture in women.	
Dipeptidyl peptidase-4 inhibitors/DPP4-I (Sitagliptin)	Inhibits DPP4, an enzyme involved in degradation of incretin homornes, GLP-1 and glucose-dependent insulinotropic polypeptide (GIP).	0.5-0.8	Neutral	Neutral	Neutral	Headache, dizziness and GI symptoms	SAVOR-TIMI53(47), EXAMINE(47), TECOS(47)
Sodium-Glucose co-transporter 2 inhibitors /SGLT2-I (Empagliflozin)	Enhances urinary excretion of glucose by suppressing renal glucose reabsorption.	0.2-0.8	Neutral	Beneficial	Posible benefit	Dysuria, polyuria, and genital and urinary-tract infections, dyslipidaemia and increased haematocrit. Fall in blood pressure.	EMPA-REG OUTCOME(47)

Diabetes medications Class (example)	(2) Mode of action	(6) HbA1c (1%) reduction	(6) Hypoglycaemia	(6) Weight change	(6) CVD risk reduction	(2) Side effects	(47) CVD outcome trials
Glucagon-like peptide-1 receptor agonists/GLP-1 RA (Liraglutide)	Stimulate insulin secretion, suppress glucagon secretion and slows gastric emptying, promote beta cell proliferation	0.5-1.4	Neutral	Beneficial	Neutral	GI symptoms, nausea but decrease with continued therapy. Rashes and hypersensitivity, acute pancreatitis.	ELIXA(47), SUSTAIN-6, LEADER(47), ACCORD(30)
Insulin (Glargine)	Inhibits hepatic glucose production and enhances peripheral glucose conversion. Inhibits lipolysis therefore prevents formation of ketone bodies. Consists of short acting, intermediate, basal and premix.	>1.5	Increased risk	Increased risk	Neutral	Excessive dose can cause hypokalaemia. Lipoatrophy. Blurred vision and oedema may occur in the first few weeks.	DCCT(29), ACCORD(30)

ACCORD= action to control cardiovascular risk in diabetes; ADVANCE: Action in diabetes and vascular disease: preterax and diamicron MR controlled evaluation trial; CVD=cardiovascular disease; DCCT=diabetes control and complications trial; ELIXA=evaluation of lixisenatide in acute coronary syndrome trial; EXAMINE=cardiovascular outcomes study of alogliptin in patients with type 2 diabetes and acute coronary syndrome; EMPA-REG outcome=empagliflozin, cardiovascular outcomes and mortality in type 2 diabetes trial GI=gastrointestinal symptoms; HbA1c=glycated haemoglobin A1c; PROactive= prospective pioglitazone clinical trial in macrovascular events; LEADER=liraglutide effect and action in diabetes: evaluation of cardiovascular outcome results trial; RECORD=rosiglitazone evaluated for cardiovascular outcomes in oral agent combination therapy for type 2

Diabetes medications Class (example)	(2) Mode of action	(6) HbA1c (1%) reduction	(6) Hypoglycaemia	(6) Weight change	(6) CVD risk reduction	(2) Side effects	(47) CVD outcome trials

diabetes; SAVOR-TIMI53= saxagliptin assessment of vascular outcomes recorded in patients with diabetes mellitus-Thrombolysis in myocardial infarction53; SUSTAIN-6=trial to evaluate cardiovascular and other long-term outcomes with semaglutide in subjects with type 2 diabetes; TECOS=trial to evaluate cardiovascular outcomes after treatment with sitagliptin; UKPDS=The United Kingdom prospective diabetes study; VADT=veteran affairs diabetes trial

2.2 Multifactorial intervention

Diabetes management aims to achieve a range of outcomes such as the reduction of microvascular and macrovascular complications, improvement in QOL and prevention of premature mortality.(6, 7, 16, 17) The main aim of treatment in diabetes management is to prevent short term and long term diabetes related complications which consists of macrovascular and microvascular diseases. The example of macrovascular complications are cardiovascular disease such as coronary artery disease which may cause heart attacks; peripheral artery disease leading to gangrene; carotid artery disease leading to strokes or dementia. The examples of microvascular complications are kidney, eye and nerve damage, which may result in erectile dysfunction.(48)

In order to achieve these outcomes, there is a need to address multiple factors in diabetes management, also known as multifactorial intervention. Guidelines from Malaysia, Australia, the UK and the USA outline seven important issues that need to be addressed inpatients with diabetes in order to achieve therapeutic goals.(6, 7, 16, 17) These are glycaemic, cholesterol, and blood pressure (BP) control, in conjunction with management of education, medication, lifestyle and CVD risk. These factors are summarised in Figure 2.1.

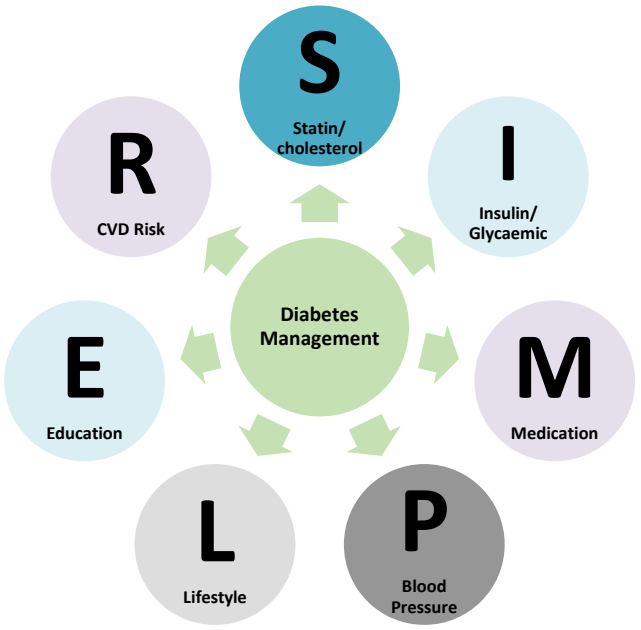


Figure 2.1: The multiple factors involved in providing diabetes care management

2.2.1 Cholesterol control

Patients with diabetes are at risk of developing CVD due to the macrovascular complications of the disease. Guidelines from Malaysia, the UK and the USA stress the importance for patients to be on a lipid-lowering medicine, namely a statin, unless contraindicated.(6, 7, 16, 17, 49-51)

In contrast, the Australian RACGP guidelines for T2DM updated their recommendation to use statins only in patients with known CVD regardless of their lipid levels based on evidence from two trials which reported increased fasting serum glucose and HbA1c with statin use.(52, 53) However a recent review in 2016 proposes a strong need to start or continue statin treatment as the benefits of statin in terms of cardiovascular risk reduction among patients with diabetes outweighs the rare risks of myopathy and muscle related symptoms.(54)

2.2.2 Glycaemic control

While patients on insulin and oral hypoglycemic agents may suffer from hypoglycaemia, it has been observed that reducing hypoglycaemia episodes is associated with increased patient adherence and satisfaction with medication.(55) The results from the landmark trials mentioned in section 2.1.2, highlight several factors that need to be addressed to prevent hypoglycaemia such as individualised glycemic targets, education of patients on hypoglycaemia awareness, self monitoring of blood glucose (SMBG), adjusting therapy and changing to treatment that causes low risk of hypoglycaemia.(56-59) WHO recommends glycated haemoglobin (HbA1c) to be measured twice a year in T2DM.(15) HbA1c is the chosen method to measure blood glucose level (BGL) as it gives an average value based on the past three months. However, due to its high cost, fasting or post prandial glucose levels are equally accepted methods to measure BGL.(15)

Previous studies have documented twice the risk of acquiring CVD complications among patients with diabetes compared to patients without the disease.(60) Glycemic control measures should aim to reduce glycated haemoglobin (HbA1c)by 1% or more for patients whose HbA1c is more than 7% (53mmol/mol) as this can produce significant reduction in macrovascular and microvascular complications, as shown in the UKPDS trial.(26) The UKPDS trial consisting of 4585 white, Asian Indian and Afro-Caribbean T2DM patients found that 1% reduction in HbA1c (glycated haemoglobin) was associated with reductions of:

1) 21% risk for a diabetes related death,
2) 14% risk of myocardial infarction
3) 37% risk for microvascular complications

The researchers in the same study found the lowest risk of complications were those with HbA1c less than 6% (42.1mmol/mol). However, results from the ADVANCE and ACCORD trial found that lowering HbA1c to less than 6% (42.1mmol/mol) and systolic blood pressure to less than 120 mmHg resulted in increased hospitalisations, hypoglycaemia and mortality in the intervention group.(27, 30) The results from these studies strongly suggest that blood glucose and BP targets should be individualised for each patient. The findings were incorporated into diabetes practice guidelines in Australia, Malaysia, the UK and the USA.(6, 7, 16, 17)

2.2.3 Medication management

Medication management requires that each patient's drug (medicine) related needs be addressed to achieve optimal therapeutic outcomes. The role of pharmacists has developed over the last few decades into the provision of medication management services, with pharmacists providing pharmaceutical care in addition to the management and dispensing of medications. Pharmaceutical care was originally defined by Hepler and Strand in 1990 as identifying, resolving and preventing MRPs.(61) Pharmaceutical care is also used interchangeably with patient centred care.(62) Patients taking medications often have MRPs, especially patients who are on multiple medicines. The types of MRPs are defined as below.(63):

1) Wrong medicine-contraindicated
2) Underdose/overdose
3) Medications not adjusted for renal failure
4) Non-adherence to medications
5) Adverse drug reaction
6) Drug-drug,food-drug, drug-herbal interaction
7) Unnecessary medicine use

Pharmacists ability to detect these MRPs mentioned above were documented in a 2012 study conducted in Malaysia. Of the 477 patients included in the study, 157 (33.3%) had MRPs, 74(15.6%) had developed adverse drug reactions, 45(9.5%) were not prescribed the most effective medicine and 16 (3.4%) had dosing problems.(64)

Several studies have suggested that patients with diabetes who are adherent with taking their medication can reduce the overall health care burden even though this could mean an increase in medication costs.(65-69) A randomised, prospective study of 107 patients with diabetes who were followed up for two years found adherence to medication was the strongest predictor of reaching the target HbA1c.(70) However, patient's reluctance to start or administer prescribed insulin remains a biggest hindrance to achieve glycaemic goals.

2.2.3.1 Psychological barriers to insulin adherence

In two recent studies conducted in Malaysia, patients perceived barriers were found to be religious purity of insulin, negative effects of insulin therapy such as fear, lifestyle restriction, hypoglycaemia and negative social stigma while healthcare professionals (HCP) barriers were lack of resources, language and communication skills.(71, 72) These perceived patients' barriers were similar to patients in other parts of the world as reported in a 2008 systematic review (73) and in a 2012 large scale survey conducted in China, France, Japan, Germany, Spain, Turkey, The UK and the USA.(74)

The results from the 2012 Diabetes, Attitudes, Wishes and Needs (DAWN) Japanese study on GP's barriers towards insulin initiation were concerns of using insulin among elderly patients and lack of support in providing insulin education to patients.(75)

Correspondingly, findings from a recent Australian primary care study conducted in 2016 reported only one in five patients reported 'very willing' to start insulin. The authors also found that reduced negative attitude towards insulin were related to higher socioeconomic status.(76) To overcome the perceived misconception that insulin is the "last resort" option or "punishment" for treatment failure, both GPs and patients should be educated about the requirement of insulin with increased disease duration.(77) Previous studies have shown that early intensive insulin in newly diagnosed T2DM patient can delay the need for OHA medications. Insulin initiation within two years of diagnosis was most efficient in these studies.(78, 79) In addition, pharmacists need to identify the risk factors associated with insulin non-adherences such as lifestyle burden, difficulty in insulin administration and adaptation to injection timing as shown in literature.(80)

2.2.4 Blood pressure (BP) control

BP that is less than 150/85 mmHg has been demonstrated to reduce microvascular and macrovascular complications, as noted in the UKPDS trial.(26) The 2016-2018 Royal Australian College of General Practitioners, the American diabetes association's standards of medical care in diabetes and the National Institute for Health and Care Excellence, United Kingdom guidelines recommends a target of less than 140/90 mmHg for all patients with diabetes and 130/80 mmHg for those with microalbuminuria or proteinuria.(7, 16, 17) In contrast, the 2015 Malaysian Ministry of Health diabetes clinical practice guideline recommends a standard target of 135/75 mmHg or less.(6) These guidelines strongly recommend prescribing, unless contraindicated, an Angiotensin Converting Enzyme inhibitor (ACEI) or an Angiotensin Receptor Blocker (ARB).(6, 7, 16, 17) However, there is evidence that guidelines are not always being followed in clinical practice. A 2013 cross sectional study found that

among 650 Malaysian outpatients, 32.1% of patients with diabetes with hypertension were not on any antihypertensive such as an ACEI or ARB, as per guideline recommendation, although these patients had no contraindications to these antihypertensives.(37) A similar study conducted among 430 Australian patients with diabetes in 2011 found evidence-based practice gaps, especially in the prescribing of antihypertensive and lipid lowering medications.(38)

2.2.5 Lifestyle management

In the Look AHEAD trial on obese T2DM patients, the intervention group had intensive lifestyle intervention on behaviour, nutrition and exercise while the control group only had education on diabetes management. The study significantly improved weight loss and fitness in the intervention group, subsequently increasing the number of participants achieving HbA1c<7% (53mmol/mol) from 46% at baseline to 73% at final study. In contrast, the education only group achieved 5% increase in the number of participants who achieved the targeted HbA1c.(81) Although evidence from numerous studies highlight the glycaemic lowering benefits of lifestyle management in diabetes, lifestyle intervention remains a problem. In a 2009 study conducted in Sydney, Australia, found that among 118 patients with chronic disease, including diabetes from eight general practices, less than 30% of patients received intervention on diet and exercise.(39) Of interest, a 2016 study conducted in the UK found patients with diabetes preferred demonstrating compliance to medications rather than to make lifestyle changes.(82)

2.2.6 Education provision

A systematic review study on 42 RCTs concluded that diabetes education on self-management could reduce the risk of diabetes related mortality.(83) The types of education provided included importance of medication adherence, lifestyle modification and monitoring of BGL. In Australia, the Diabetes Mellitus Education Programme (DMEP) conducted in 2006 showed significant improvement in glycaemic and blood pressure control, weight loss and understanding of diabetes management.(84) The DMEP was part of the Third Community Pharmacy Agreement under the Australian Government Department of Health & Ageing. In addition, the diabetes education and self-management for ongoing and newly diagnosed (DESMOND), is currently available for T2DM patients in Western Australia. DESMOND aims to provide education on weight loss, smoking cessation and instils positive beliefs about diabetes. The DESMOND education intervention for T2DM patients originally conducted in the UK was found to be more cost effective.(85) In Malaysia, home based diabetes education conducted by pharmacists significantly improved medication adherence among T2DM patients.(86)

Previous diabetes intervention studies on the self-management of foot care have shown improved foot care among patients with diabetes.(87) In 2012-13, Australia recorded 3570 amputations among patients with diabetes.(25) While in Malaysia, a 2013 study reported peripheral neuropathy among 41% of 1668 patients with diabetes.(24) Therefore, proper footwear, foot hygiene and regular assessment for neuropathy remain an important component of diabetes education to prevent complications that lead to amputation.(15) In addition, risk of lower limb amputation is increased by canagliflozin a SGLT2 inhibitor as advised by both the European Medicines Agency and the US Food and Drug Administration.(88) Therefore,

pharmacists need to be aware of this potential adverse reaction to prevent future complications.

2.2.7 CVD risk management

CVD risk can be estimated using risk prediction formulae. Several CVD risk prediction formulae are therefore used worldwide. The Framingham risk score (FRS) is the most commonly used tool, and has been adapted for use in diverse populations.(89) Other tools include the UKPDS tool for patients with diabetes.(90) In Australia, the absolute risk calculator was developed based on the Australian National Vascular Disease Prevention Alliance (NVDPA) guidelines.(91) Guidelines from Malaysia (for patients aged 65 years and above) and the USA suggest aspirin therapy (75mg-162mg/day) as primary prevention strategy for increased CVD risk (10 year risk>10%).(6, 16) Malaysian and USA guidelines recommend using the FRS. The UK National Institute for Health and Care Excellence (NICE) guidelines on Type 2 Diabetes Mellitus recommends the UKPDS risk engine for educating patients on CVD complications.(17)

2.2.8 Effectiveness of multifactorial interventions

Studies on multifactorial interventions have reported improved patient outcomes. For instance, the 2012 ADDITION-Europe study, which was a cluster-randomised study that involved interventions on glycaemia, BP and cholesterol control as well as lifestyle, reported reductions in cardiovascular events and death.(92) Another 2012 study conducted in China found that addressing multifactorial interventions according

to practice guidelines could delay diabetes related complications such as diabetes nephropathy.(93) The 2013 Multiple Intervention in type 2 diabetes Italy (MIND.IT), a cluster RCT study conducted in Italy, found significant improvements in patients' glycaemic, cholesterol and BP levels after following treat-to-target approaches which included lifestyle and pharmaceutical interventions.(94) In the Steno-2 study conducted in Denmark in 2003, showed the effect of a multifactorial intervention targeting hyperglycaemia, hypertension, dyslipidaemia, microalbuminuria and secondary prevention of CVD risks. The results showed reduction of CVD risk and microvascular events by 50%.(95)

2.2.8.1 Diabetes interventions conducted by healthcare professionals besides pharmacists

Despite the widely-documented evidence, recently conducted RCTs by healthcare professionals have failed to address all the seven diabetes factors in providing evidence-based diabetes care. Thus, diabetes interventions led by multidisciplinary teams which comprised of nurses, dieticians, psychologists and physiotherapists indicated improvements in some of the seven factors but not others.(96-102) This could be due to each member of the multidisciplinary team addressing the factors pertaining to their own expertise but not the others. For instance, certain diabetes interventions conducted by nurses emphasised self management.(96, 99, 103, 104) While others examined motivational interviewing to promote behavioural changes and attitudes among patients with diabetes, which consequently produced significant improvement in glycemic control, adherence and lifestyle changes (105-107) omiting other CVD risk factors. Interventions that focused on four factors, namely nutrition, blood glucose monitoring, medication taking and lifestyle resulted in significant improvement in HbA1c and health-related QOL values.(108, 109) However, there was no mention of improvement to other factors such as BP and cholesterol control.

In addition, the improvements in patients' outcomes were from studies conducted between three to 12 months. While there seems to be a short term improvement in clinical outcomes, long term outcomes, especially in delaying the progression of complications, could not be established. To address the limitations in these studies, a common, standardised multifactorial approach with common therapy goals for each member of the multidisciplinary team maybe beneficial.

Of interest is the effectiveness of cultural interventions documented in the diabetes intervention study conducted by HCPs besides pharmacists, which found improvements in problem solving skills and dietary intake but not for physical activity. These intervention comprised of self-management; acculturation from Latino to Mediterranean diet; stress management techniques; physical activity; smoking cessation and problem solving skills.(110) Other diabetes studies used 'local language' to discuss behaviour change in lifestyle issues thus utilising culturally relevant perspective to induce change in self-care management and this indicated a significant improvement in HbA1c compared to the usual care.(96, 98) Table 2.3 provides a summary of the diabetes intervention conducted by HCPs besides pharmacists.

Table 2.3: Types of diabetes intervention studies conducted by healthcare professionals besides pharmacists

Author, Year	Study Design	Study Duration	Country	Group Size		Intervention Strategy	Results
				*C	*I		
Barrera 2012**(110)**	RCT	12 months	USA	138	142	Culturally adapted diabetes intervention	Improvement in sources for dietary practice, problem solving, physical activity
Brennan 2012**(111)**	RCT	6 months	USA	24124	5123	Statin, ACEI/ARB initiation, total days of medication supply per month (adherence)	Increased adherence and GP initiation of ACEI/ARB and statin
Farmer 2012**(100)**	RCT	20 week	UK	81	114	Intervention on adherence, reinforcement of positive belief by nurse	Percentage of adherence days in intervention group was 77.4 and usual care group was 69%
Keogh 2011**(107)**	RCT	6 months	Ireland	61	60	Techniques from health psychology and motivational interviewing such as exchanging information, eliciting change talk, reducing resistance, building self-efficacy, problem solving, and goal setting/action planning.	Significant lower HbA1C levels (0.66%) , significant improvements in beliefs about diabetes, psychological well-being, diet, exercise, and family support
Nishita 2013**(112)**	RCT	7 months	Hawaii	62	128	Pharmacists and life coach counselling	Significant effect on QOL and BMI
DePue 2013**(96)**, Sinclair 2013**(103)**	RCT	3-12 months	American Samoa, Native	34-134	48-134	Culturally adapted community nurse intervention on self-	Significant reduction in HbA1c (0.5%-1.1%), understanding of diabetes self-management, performing diabetes self-management

Author, Year	Study Design	Study Duration	Country	Group Size		Intervention Strategy	Results
				*C	*I		
Spencer 2011**(99)**			Hawaiian and Pacific People			management among patients with diabetes	
Fischer 2012**(97)**	RCT	6 weeks	USA	381	381	Nurses independently initiated and titrated lipid therapy and promoted behavioural change through motivational interviewing and self-management techniques	Percentage of patients achieving target LDL increased in intervention group
Farmer 2012**(113)**	RCT	5 months	UK	85	126	Nurse led intervention to improve adherence to treatment	Significant increase in medication adherence days
Williams 2012**(114)** Quinn 2011**(108)**	RCT	6-12 months	Australia, USA	60-82	60-81	Diabetes care on nutrition, blood glucose monitoring, medication taking and lifestyle through telephone	Significant improvement in HbA1c (0.8%-1.9%) and health related QOL
Liu 2012**(115)**	RCT	12 months	Shanghai, China	89	119	Group visit model to support self-management	Increased duration of aerobic exercise, increase in self-management efficacy, decrease in systolic BP
Wu 2011**(101)**	quasi experimental	6 months	Taiwan	73	72	Self-management programmes by nurses	The scores for efficacy expectations, outcome expectations, and self-care activities had significantly increased in the intervention group at the 3 and 6month follow-ups
Kang 2010**(106)**	RCT	6 months	USA, Taiwan	28	28	Psychologically family intervention	Statistically significant

Author, Year	Study Design	Study Duration	Country	Group Size		Intervention Strategy	Results
				*C	*I		
							improvements in HbA1c (1.35%), psychological well-being, diet, exercise, and family support
Chen 2012**(105)**	RCT	3 months	Taiwan	111	104	Motivational interview using Miller and Rollnick's (2002) approach. Intervention based on readiness to change	Improvement in self-management, self-efficacy, QOL, and HbA1c (0.8%)

ACEI=angiotensin converting enzyme inhibitor; ARB= angiotensin receptor blocker; BP= blood pressure; C=control patients; HbA1c=glycated haemoglobin I=intervention patients; LDL=low density lipoprotein; RCT=randomised controlled trial; UK=United Kingdom; USA=United States of America; QOL=quality of life

2.2.8.2 Diabetes intervention studies conducted by pharmacists

Pharmacists' effectiveness in improving glycaemic control in RCTs have been well documented.(116-120) The reduced cost in hospital and emergency admissions due to pharmacist intervention has also been documented in several studies.(118, 121) Details of pharmacists led diabetes intervention studies are summarised in Table 2.4.

Similar to diabetes intervention studies conducted by other healthcare professionals discussed above, intervention methods in terms of addressing the multiple factors identified varied across RCT pharmacist studies. Patient education on medication management and lifestyle significantly improved body mass index (BMI), HbA1c, fasting blood glucose (FBG) and self-care management.(122-125) However, there was no evidence if BP or cholesterol control measures were addressed. RCTs which focused on pharmaceutical care interventions reported a reduction in HbA1c, cholesterol and blood pressure but there was no mention of CVDrisk prevention strategies.(84, 126-129) One study examined the impact of education, medicine management, pharmaceutical care and lifestyle counselling, HbA1c and cholesterol control, however there was no mention of BP control. There were also no mention of indicated medicines for reduction of CVD risks, such as aspirin or for BP such as antihypertensives, particularly ACEI, being prescribed.(130)

Table 2.4: Types of pharmacist led diabetes intervention studies

Study	Design	Duration (months)	Country	Group Size		Intervention Method	Pharmacist background	Results
				C	I			
Adibe 2013 (131)	RCT	12	Nigeria	110	110	Patient education on diabetes, SMBG, medications, lifestyle, effective interaction with health providers, identification of MRP	Experienced hospital pharmacists	Improved QOL
Ayadurai 2013(129)	Retrospective, cohort study	6	Malaysia	-	-	Experienced Pharmacists running intervention programme that looks at glycaemic control, BP, CVD risk factors, education, medication adherence and lifestyle factors.	Experienced pharmacists who are trained in diabetes management.	Significant reduction in HbA1c (1.33%), medication adherence and no. of hypoglycaemia events.

Study	Design	Duration (months)	Country	Group Size		Intervention Method	Pharmacist background	Results
				C	I			
Mitchell 2011(132)	Audit	2	Australia	-	-	Evaluation of pharmacist role in supporting DMAS	Experienced pharmacist	Community pharmacist is effective in supporting DMAS
Chan 2012(130)	RCT	9	Hong Kong	54	51	Pharmacist care on drug counselling, medication adherence, drug related problems, lifestyle counselling in addition to medical care	Experienced hospital pharmacists	Significant reduction in CVD risk, HbA1c levels (1.57%), LDL, increased level of medication understanding
Farsaei 2011(124)	RCT	3	Iran	87	87	Education on diabetes management, medication, adherence, medication taking during Muslim fasting month	Clinical pharmacist-led patient education program	Improvements in FBG, HbA1c (1.7%)
Hamarneh 2013(133)	Before and after	6	Canada	n=100		Independent prescribing of glargine and	Experienced Pharmacist	HbA1c reduced from 9.1% (76mmol/mol)-7.3% (56.3mmol/mol).

Study	Design	Duration (months)	Country	Group Size		Intervention Method	Pharmacist background	Results
				C	I			
						oral drugs for diabetes by Pharmacists		Improvement in fasting blood glucose
Jameson 2010(125)	RCT	12	United States	51	52	Pharmaceutical care intervention and education	Pharmacist is board-certified pharmacotherapy specialist trained in Diabetes	Improvements in HbA1c (1.0% reduction)
Jarab 2012(127)	RCT	6	Jordan	79	77	Pharmaceutical care by pharmacists	Pharmacist working in diabetes clinic	Improvements in FBG, BP, total cholesterol, LDL, medication adherence
Kumar 2011(128)	RCT	9	Malaysia	42	43	Experienced pharmacists running intervention programme that looks at glycaemic control, BP, CVD risk factors, education, medication adherence and lifestyle factors.	Experienced pharmacists who are trained as diabetes Pharmacists	Significant improvement in HbA1c (1.7% reduction), medication adherence levels and cost effective.

Study	Design	Duration (months)	Country	Group Size		Intervention Method	Pharmacist background	Results
				C	I			
Maurao 2013(126)	RCT	6	Brazil	50	50	Care plan for each patient to meet therapeutic goals, patient education and pharmacotherapy change	Community pharmacists with minimum of four years of experience, trained in diabetes management	Significant reduction of HbA1c (0.6%), FBG, total cholesterol, LDL cholesterol, TG, BP and increase in HDL
Mehuys 2011(123)	RCT	6	Belgium	135	153	T2DM education and its complications, correct use of hypoglycaemic agents, adherence, lifestyle, reminders about annual eye and foot examination	Community pharmacist underwent training session on diabetes management	Significant reduction of HbA1c (1.05%), self-management and better knowledge of diabetes
Samtia 2013(122)	RCT	5	Pakistan	170	178	Education on short and long-term complications, medication adherence, timing of	Clinical pharmacist with minimum three years of experience in	Reduced BMI and waist circumference, fasting blood glucose, HbA1c (1.01%). Increase in

Study	Design	Duration (months)	Country	Group Size		Intervention Method	Pharmacist background	Results
				C	I			
						medication, before/after food, dietary restrictions, foot examination, exercise, SMBG, FBG and HbA1c, smoking cessation	hospital setting	compliance, foot care and SMBG.
Taveira 2010(134)	RCT	4	USA	28	28	Pharmacist intervention in community based primary care group	Clinical Pharmacists	Significant improvement in HbA1c (0.9%)

BMI= body mass index; BP=blood pressure; C=control patients; CVD= cardiovascular disease; DMAS= diabetes medication assistant service; FBG= Fasting blood glucose; HbA1c=glycated haemoglobin; HDL= high density lipoprotein; I=intervention patients; LDL=low density lipoprotein; n=sample size; RCT=randomised controlled trial; SMBG= self-monitoring blood glucose; T2DM= type 2 diabetes mellitus; TG=triglyceride; UK=United Kingdom; USA=United States of America; QOL=quality of life

Although extensive literature exists on effectiveness of pharmacists interventions in diabetes studies, the process used by pharmacists to retrieve information and make the interventions were rarely described as observed in a systematic review on diabetes intervention RCTs published in 2016.(13) Undoubtedly, pharmacists with varied experience and skills may have used their discretion when making an intervention as stipulated in a review study.(135)

The non uniformity in the number of diabetes factors addressed may have also contributed to the varied HbA1c reduction. For instance, RCTs which focused on education, lifestyle and medication significantly reduced HbA1c by 0.6% in the intervention group (n=50) vs an increase of 0.7% in the control group (n=50)](136). While another study which focused on the same three factors reduced HbA1c to a greater extent of 0.8% in intervention group(n=77) vs 0.1% in the control group(n=79)(127) Since most RCTs were led by hospital pharmacists with a minimum of three years of clinical experience (122-130, 137-142), it is uncertain if community pharmacists with limited clinical experience can provide a similar level of pharmaceutical care and patient outcomes. Similar views were discussed in two review studies.(13, 14)

The variation with reference to HbA1c reduction among RCTs could also be due to pharmacist dependence on prescriber to initiate or change medications. Previous research findings suggest not all pharmacists recommendations are accepted by GPs. Acceptance rate ranges from 82% to 94%.(64, 143-145) Comparatively, a review study conducted in 2016 showed more homogenity in studies where pharmacy had autonomy to add, change or modify dose of diabetes medications as part of agreed protocol. However, these studies were not associated with better therapeutic outcomes.(13)

2.2.8.3Quality of life (QOL) outcome

Diabetes guidelines strongly recommend using QOL to measure the effectiveness of healthcare interventions.(16) A 2017 review study have found that diabetes affects QOL domains such as the physical domain when patient presents with complications and comorbidities; the psychological domain when patient has depression or dementia and the social domain which affects family life and relationships.(18) A Taiwan study conducted in 2012 found that lower QOL ratings were scored by patients with dietary restriction, higher HbA1c, using insulin and with multiple comorbidities.(19) Thus, in providing individualised care it was deemed important to address patients' concerns in order for them to be compliant to treatment and continue self management for better diabetes control.(18) A recent 2016 study conducted in Malaysia found that existing diabetes complications, longer diabetes duration, insulin and glycaemic control were associated with patients' QOL. The authors further reported that patients who were prescribed insulin to achieve ideal glycaemic targets gave lower QOL scores.(146)

Although there was a lack of QOL studies conducted by pharmacists, yet almost all of the studies have reported that pharmacist interventions improved QOL scores.(147) Undoubtedly the education and counselling provided might have reduced patient concerns and worry about the disease as found in a 2013 study conducted in Nigeria.(137) Currently there are several health related QOL questionnaires utilised in diabetes intervention studies. Among them are WHOQOL-BREF, EuroQOL, SF36 and the recent ADDQOL 18 and DQOL.(18) The WHOQOL-BREF will be used in this research as it is a valid and reliable instrument which covers all health domains not covered in other established questionnaires such as European QOL measure (EuroQOL) and the 36-item short form health survey (SF36).(11) Furthermore, the WHOQOL-BREF (Bahasa Malaysia language version) has also been validated among the Malaysian population.(148)

2.3 Patient centred care (PCC)

Although disease guidelines stress the need to address specific issues in a particular disease, they rarely address all of the comorbidities that a patient may suffer from. For example, diabetes guidelines rarely mention treatment recommendations for dementia or rheumatoid arthritis. However, patients increasingly have multiple comorbidities and multiple medications(149) and therefore an individualised approach is required to prevent disease burden and associated complications.

The key attributes that defines PCC is holistic, individualised, respectful and empowering care.(150) In diabetes care, PCC is translated as having individualised therapeutic goals in terms of glycaemic, cholesterol and BP control based on a patient's comorbidities, hypoglycaemia episodes and age. In addition, patients' education on self care practice is vital to achieve therapeutic goals and consequently increase medication adherence.(6, 7) A recent review outlined seven step guideline when providing PCC to patients with multiple medications.(149) The steps are as follows:

1) Conduct patient assessment
2) Determine therapeutic goals
3) Identify medication that may cause potential harm
4) Risks and benefit assessment
5) Conduct intervention
6) Communicate to other healthcare providers
7) Provide patient monitoring

2.3.1 Role of pharmacists in diabetes management

As patients with multiple comorbidites continue to rise, the increasing pressure and workload on general practitioners (GPs) in Europe, the UK and the USA necessitate

collaboration with other HCPs in caring for patients with multiple comorbidites to reduce country's health and cost burdens.(151) For this reason, other healthcare professionals, specifically pharmacists, are in an ideal position to provide continuity of care, increase compliance to prevent emergency doctors' visits and hospitalisations, and thus reduce medical expenditure. Increased health burden costs due to chronic disease management has prompted countries like Australia, Malaysia and the UK to utilise primary care pharmacists to promote medication adherence, reduce medication-related hospitalisations and medication wastage.(152)

In Australia, between 2013 and 2014, GP services contributed to the majority(19.3%) of the primary healthcare expenditure.(22) To improve the management of patients with chronic disease, the Australian primary healthcare advisory group recommends to reform primary healthcare included enhanced role for pharmacists. This involves pharmacists and other HCP providing coordinated care in the primary healthcare system.(153) In Malaysia, public institutions mobilised pharmacist to provide diabetes medication management service (MMS) implemented in 2004. This was an iniatiative of the Pharmaceutical Services Division under the Ministry of Health.(10)

Although hospital pharmacists in the UK have been conducting patient medication reviews since the 1980's, the medication use review (MUR) service provided in the community sector was only implemented as part of community pharmacy contracts in 2005.(154) The reformation on the remuneration structure in healthcare in 2016 meant better payment for community pharmacists if they provided advanced specified services. The specified services included MUR for patients with long term illness and on multiple medications such as diabetes.(155)

2.3.2 Pharmacist-provided medication management service (MMS)

MMS is an intensive care that places emphasis on PCC provided by pharmacists in collaboration with other HCPs. It comprises of medication review, identification of MRPs, patient education and monitoring. In addition, pharmacists are able to address lifestyle issues such as diet and exercise which are pertinent to achieving appropriate therapeutic outcomes, particularly in diabetes management. Pharmacists provided MMS services in diabetes management have contributed significantly to the improvement to patients' clinical and humanistic QOL outcomes.(14, 147) Randomised controlled trials in diabetes management carried out in different parts of the world suggest that MMS pharmacists can make significant improvements in therapeutic outcomes.(125-127, 130, 137, 138) The diabetes MMS commonly provided by community pharmacists in Australia is known as Diabetes MedsCheck and the Malaysian one is known as MTAC Diabetes.

2.3.3 Australian provided diabetes MMS: Diabetes MedsCheck

In Australia, the Diabetes MedsCheck program was implemented in community pharmacies as part of the 5th and 6th Community Pharmacy Agreement (July 2010-June 2020).(156) The Diabetes MedsCheck program is a PCC service delivered by privately owned community pharmacists funded by the Department of Health and Ageing. It followed an initial trial study, DMAS that demonstrated effectiveness of trained community pharmacists in delivering self-management support to patients with diabetes that showed improvement in clinical and health outcomes.(132) Pharmacists providing Diabetes MedsCheck service conduct a MUR, educate patients on the quality use of medicines, develop a plan of action, follow up patients and document their interventions. The Diabetes MedsCheck guidelines require pharmacists to designate an appropriate private area in their pharmacy to faciliate

patient consultation. The process takes about 20 minutes to complete. Based on the number of patients with diabetes seen, pharmacists are reimbursed for their services.(157)

2.3.4 Malaysian provided diabetes MMS: MTAC diabetes

In Malaysia, the diabetes MMS provided by pharmacists is known as MTAC Diabetes. In comparison to Australia the Malaysian MTAC Diabetes services are provided as part of a comprehensive service in most government hospitals which act as tertiary referral centres and are catered to outpatients.(10) They are also provided at government-funded primary healthcare clinics at the community level. MTAC Diabetes involves pharmacists reviewing patients' medication (MUR), making recommendations to prescribers, developing a medication plan, educating patients and counselling them on lifestyle, documenting interventions and subsequent patient follow up for a minimum of eight visits.(10) Like Diabetes MedsCheck, MTAC Diabetes guidelines also stipulate the requirement for a private consultation area in close proximity with GPs when reviewing patients. Similarly, the consultation process takes about 20-30 minutes. Cross-sectional and RCTs in Malaysia suggest that MTAC Diabetes may improve clinical, humanistic and economic outcomes of patients with diabetes.(86, 128, 129, 158-161)

2.4 Diabetes intervention strategy for pharmacists

There is a growing body of literature that recognises the contribution of medication-related interventions made by pharmacist as mentioned in section 2.3.2. In addition, pharmacist ability to optimise medication therapy, refer patients for eye examination

and provide yearly immunisations and other screening tests according to diabetes practice guidelines are well recognised.(118) Yet pharmacists also express the need for further training to upskill their competency in providing advanced services such as medication management services.(162) The key elements identified in providing quality intervention include having access to patient medical information, good rapport between the general practitioners and pharmacist, written information as the form of communicating interventions conducted and medication review.(154)

2.4.1 Requirement for targeted training program

Despite the documented patient improvements made by pharmacist providing medication management services such as Diabetes MedsCheck and MTAC Diabetes, the number of diabetes related complications are still trending to increase.(22, 163) For instance, in the USA, these services were offered by 60% of community pharmacies from 2009 to 2014 (164) yet the number of patients with diabetes visiting doctor's clinic increased by 20% from 2005 to 2010.(165) Although the reasons for this increase have not been stipulated, several likely causes could be increased dispensing workloads, lack of staff and time for pharmacists to conduct medication reviews, as previously reported.(166, 167)

A recent study published in 2017 reviewed seven systematic review papers on pharmacist diabetes interventions. The authors recommended further training to address pharmacists' competency in managing patients with diabetes.(147) Diabetes credentialing programs offered in Australia, whilst addressing the competency issues required by other healthcare providers in diabetes management, are not specifically targeted to pharmacist.(168) Short term continuous professional education on the one hand while beneficial does not address experiential training through mentoring and supervision. A training program specifically targeted to diabetes intervention

competencies required by pharmacist in diabetes management would be advantageous. Unfortunately, such training programs are scarce.

2.4.2 Pharmacist access to patient medical records (PMR)

The benefits of pharmacist access to medical records are documented in several studies.(169-172) Pharmacist ability to conduct complete, efficient medication reviews has been shown in an exploratory study conducted in 2017.(173) In MMS provision, access to medical records enabled pharmacists to monitor patient adherence, identify MRPs and coordinate care given by other health care providers.(170) This is required to make evidence-based quality interventions in diabetes.(154)

Although hospital pharmacists may have greater access to medical records, most community pharmacists still face challenges in obtaining results of blood tests or current medical interventions. In a recent 2017 review on patient's perceptions on pharmacist prescribing, lack of pharmacists' access to medical records were a major concern, particularly in terms of safe prescribing.(174)

To address this issue, several countries such as the UK, USA and Australia have implemented electronic patient health records. In Australia, the My Health Record was introduced in 2012, but is still in the development phase, contains medical information such as allergies, medicine details, pathology details and current conditions.(175) Patients have control over which persons access their records. In the UK, the summary care record was implemented in 2015. Similar to Australia's My Health, the summary care records enables patients to have control over which

member of the healthcare providers are accessing their record.(176) Similar to Australia and the UK, the electronic personal health record is utilised in the USA.(171)

2.4.3 Diabetes intervention tool

In order for a tool be effective it has to first allow retrieval and organize information. Secondly, a healthcare professional should be able to apply his judgement based on the information to make his decision as suggested by Weed.(177) In a time constrained outpatient pharmacy, pharmacists should be able to retrieve information quickly and exercise judgement based on the information presented to make interventions.(177) Several studies have revealed that healthcare professionals utilise tools in making treatment choices and in providing patient counselling and education. A brief summary of intervention tools used in healthcare identified from a literature search is provided in Table 2.5.

Table 2.5: Evidence-based intervention tools

No.	Author, (year)	Name of Tool	Country	Function of Tool
1.	Anthierens 2012(178)	INTRO (internet training for antibiotic use)	Belgium, UK, Poland, Spain, Netherlands	Promote prudent antibiotic prescribing
2.	Barry 2007(179)	START (Screening Tool to Alert doctors to the Right Treatment)	Ireland	Evidence-based screening tool for indicated medicines in the elderly
3.	Basger 2008(180)	Prescribing indicators for elderly	Australia	List of medications indicated for elderly based on most frequently prescribed drugs for most frequent disease
4.	Joseph 2010(181)	CREDIT (cancer reduction education intervention tool)	USA	Computer-based learning to educate patients at risk of Hereditary Breast and Ovarian Cancer (HBOC)

No.	Author, (year)	Name of Tool	Country	Function of Tool
5.	Litvin 2013(182)	CDSS (clinical decision support system)	USA	A tool to improve antibiotic prescribing for acute respiratory infections
6.	Nelson 2011(183)	MyRxPad	USA	Prescribers make prescribing decisions based on personal medication records contributed by patients
7.	Paxton 2011 (184)	STC (Starting the conversation)	USA	Eight-item simplified food frequency instrument designed for non-dieticians
8.	Santo-Novak 2001(185)	MSHAKE (Mary Starke Harper Aging Knowledge Exam)	USA	A 25-item tool for measuring knowledge related to geriatric mental health of staff caring for elderly
9.	Stein 2013(186)	CommonGround	USA	Shared decision-making tool on psychotropic medicine adherence
10.	Murphy 2012(187)	Signposting, Inhaler technique, Medication review, Peak Flow Expiratory, Lifestyle advice & health promotion and Education (SIMPLE)	UK	Each letter represents a component of intervention for asthma patients as recommended by national guidelines.
11.	Morisky 2008(188)	The 8-items MMMAS	USA	Tool to assess patients' adherence to their medication
12.	Miller 1994(189)	Responsibility for change, Advice to change, Menu of treatment options, Empathic style, Self-efficacy of participant (FRAMES)	USA	A tool used as intervention method to reduce harm in substance abuse
13.	Cameron 2002(190)	Subjective, objective, assessment, plan (SOAP)	USA	Format for documentation of patient's continuity of care

UK= United Kingdom; USA= United States of America

A tool used by physicians and healthcare professionals for record keeping is SOAP, an acronymn for subjective, objective, assessment and plan where each letter of the

word represents a section that is included in the case notes(190). An eight item intervention tool used to assess dietary patterns entitled starting the conversation (STC) is a brief validated tool used by non-dieticians in outpatient settings.(184)

Literature search on tools used by pharmacists in the community and primary health care settings revealed specialised tools for specific population. One tool to detect potentially inappropriate prescribing for the elderly is the Ghent older people's prescriptions community-pharmacy screening (GheOP^{3}S) tool. This tool was found feasible among community pharmacists in Belgium.(191) Pharmacist successfully detected inappropriate medications among 987 patients. A nine-item questionnaire measured patients' perception of their medication by categorising their concerns using a five-point Likert scale. This tool was found beneficial for pharmacists to conduct interventions based on patients' medications concern.(192) In heart failure, community pharmacists successfully detected patients with worsening heart failure utilising a six item screening tool for heart failure symptoms named The One Minute Clinic for heart failure.(193) A simple tool, DOCUMENT, to identify and conduct clinical interventions among community pharmacists in Australia recorded 5948 MRPs. The tool was found advantageous and was therefore implemented nationwide.(194) In Australia, a tool to assess risk of T2DM, the AUSDRISK tool, was found acceptable among pharmacists in the community setting.(195)

Literature searche on available diabetes intervention tools revealed a checklist for pharmacist to use when conducting diabetes management reviews. It consisted of 88 questions that effectively identified potential drug related problems.(196) However, there was a lack of published evidence of pharmacists using this checklist in practice. Nevertheless, a tool to manage T2DM patients with complications which prompts about their management is lacking and little evidence is offered in the processes followed by pharmacists to retrieve necessary information in published diabetes studies. A targeted training incorporating a diabetes intervention tool that delivers structured and consistent method of intervention will be valuable.

2.5 Overall thesis research area

The review of the literature over the last decade has revealed numerous pharmacist intervention studies on diabetes management. Although most studies showed improved clinical outcomes, the results were inconsistent, even though the same factors were addressed, little is known about the process followed by pharmacists to make diabetes care interventions. This research therefore was aimed to prioritise, rank and construct validate evidence-based indicators utilised in the management of T2DM. In addition, it developed a targeted training package on the application of the tool and explored pharmacists' perceptions of the tool's relevance and usefulness in delivering quality diabetes care. Finally, the research trialed the clinical and QOL outcomes of patients managed with the tool.

The research has important clinical significance for management of diabetes. The intention of the tool is to assist pharmacists to provide targeted intervention in a structured and consistent way. In addition, it is hoped that the research findings of the tool's effectiveness will increase the uptake of this tool in MMS services such as Diabetes MedsCheck in Australia, MTAC Diabetes in Malaysia and MMS service worldwide.

Specific objectives of each of the three phases are presented in specific chapter sections: the objectives of Phase One are located in Section 3.2. Objectives of Phases Two and Three are provided in Sections 4.2 and 5.2 accordingly.

Chapter 3

Development and Validation of the Tool

3.1 Introduction

Sections of this chapter were published in: Ayadurai S, Sunderland VB, Tee LB, Hattingh HL. Consensus Validation of Simpler: A Tool to Improve Pharmacist Delivery of Quality, Evidence-Based Diabetes Care. *Curr Diabetes Rev* 2017. A link to the paper is at https://www.ncbi.nlm.nih.gov/pubmed/29243582

The development of the diabetes intervention tool incorporated the validation of the content and obtaining design input through the Delphi process. The Delphi process constituted Phase One of this research. The purpose of this chapter is to present the Delphi process followed by the Delphi process results. The overview provides a brief introduction of the Delphi process and justification for use in this research. This is followed by the methods and results sections, presenting findings from the Delphi questionnaire. Further analysis and limitations are also discussed.

3.1.1 The Delphi process

The Delphi process has been well tested and used to obtain opinions from a group of experts on particular issues.(197) It includes a series of rounds of written questionnaires with the purpose of achieving group consensus.(198) The researcher sets the consensus level or level of agreement in the beginning. Delphi participants remain anonymous to each other but each participant knows what the other participants' scores are as the researcher sends each participant the group's median scores. Participants have the option to either keep or revise their answers in light of the collated responses from the rest of the participants to each question in each round. The Delphi process is reiterated and the rounds stop once the set level consensus has been achieved.(199)

The stages of the Delphi process(200) can be summarised as below:

1. Selection of panel (respondents) and allocation of identification numbers.
2. Construction and distribution of the first questionnaire (Round 1). Completion and return of the Round 1 questionnaire.
3. Collation of individual and group scores and categorisation of suggestions. Construction of second questionnaire (Round 2).
4. Distribution of the second questionnaire (Round 2). Completion and return of the Round 2 questionnaire.
5. Collation of individual and group scores and categorisation of suggestions. Construction of the third questionnaire (Round 3) which is similar to the Round 2 questionnaire but with individual and group scores for each suggestion from Round 2 incorporated.
6. Distribution of the third questionnaire (Round 3). Completion and return of the Round 3 questionnaire.
7. Recollation of individual and group scores for each suggestion.
8. Possible further rounds of voting and possible request for rationale and comments for more extreme scores.
9. Achievement of group consensus with calculation of summary statistics: maximum, minimum, and range of scores for each suggestion.
10. Distribution and use of findings.

3.1.2 Advantages of using the Delphi process

The Delphi process allows people with different opinions to either conform to the group's view or keep their views. It can also guide a group to achieve consensus.(198, 200) Several health care studies have used the Delphi process to develop and validate processes of care (201-203), develop protocols to reduce inappropriate prescribing (204-206) or to reduce medication errors.(207-209) There have also been instances where the Delphi process was used to obtain opinions of experts on specific issues

like drug addiction problems (210) or food safety hazards.(211) Details of these studies are summarised in Table 3.1.

Table 3.1: Intervention studies using the Delphi process

Study site	No. of participants	No. of Rounds	% set for level of agreement	Type of Intervention
Malta, UK, Ireland (207-209)	12-20	2	70%->80%	Identify and develop prescribing indicator to reduce prescribing and medication errors
Taiwan, Northern Ireland, France (179, 204-206)	8-21	2	55% >75%	Develop a tool to detect potentially inappropriate medicine among patients
European countries, Australia (201-203, 212)	20	2	>50%	Develop guidance to facilitate process of care
Finland, UK (210, 211)	7-86	3	>75%	Find out experts' opinion on food safety hazards and changes to the drug addiction problems

A literature search found the Delphi process to be a more suitable approach rather than traditional surveys in studies that involve a need to obtain opinions from experts.(213) The Delphi process was therefore considered relevant and appropriate for the validation of the Simpler™ tool based on the following reasons:

1. In comparison to traditional surveys that targets the general population who may or may not be knowledgeable in the subject matter, Delphi process participants include experts who are knowledgeable and experienced in their field.(213) This was important as the Simpler™ tool included indicators such as complementary therapies which contained insufficient data to support their effectiveness in diabetes treatment. Nevertheless, these treatments were still used in diabetes management and thus required diabetes experts' viewpoints.(214-216)
2. The Delphi process enabled sharing of experts' opinions without meeting face-to-face. In this case, it was impractical for participants to meet due to geographical reasons as participants were from both Australia and Malaysia.
3. The Delphi process could also be used to rank, prioritize and construct validate the researcher's interpretation of indicators in the Simpler™ tool during the Delphi rounds.(213)
4. Delphi participants were anonymous to each other but not to the researcher. Therefore, the researcher had the opportunity to privately clarify responses that were different from the group's responses.
5. In traditional surveys, statistical calculations do not include data from participants who have missing answers. In contrast, the Delphi process allows researchers to contact participants regarding the missing answers, as the participant is not anonymous to the researcher.
6. A study on group opinion found it was beneficial for participants to remain anonymous to each other.(198) Advantages included eliminating influence of dominant individuals and avoiding situations where an individual may change his/her opinions due to group pressure. This is particularly useful as participants in the Simpler™ validation tool consisted of various healthcare professionals who provided different types of care. These included pharmaceutical care, nursing and medical care.

An evaluation of the Delphi process and the literature reporting on its use found it to be a suitable method to obtain input in the development phase of the Simpler™ tool.

3.2 Objectives

Phase One, the Delphi process, involved collating opinions from a panel of diabetes experts. This phase of the research aimed to prioritize, rank and construct validate evidence-based indicators utilised in the management of diabetes. These indicators involved evidence-based recommendations from the literature and existing diabetes guidelines. Phase One was conducted between September and December 2014 and had three objectives:

- The first was to determine, using the Delphi process, the order in which the indicators would appear in the Simpler™ tool hand-out;
- Secondly, to determine additional indicators to be included and
- Thirdly to determine the layout of the Simpler™ tool.

3.3 Method

A detailed account of the steps involved in Phase One of the research are discussed below. This involved a description of the strategies followed to select potential participants, the construction of questionnaires, the duration and stability of Delphi rounds and the justification for setting the level of agreement or consensus.

3.3.1 Ethical approval

This study received low-risk Curtin University Human Research Ethics Committee approval (PH-18-14) shown in Appendix 3.1.

3.3.2 Recruitment of participants

The Delphi process does not require a statistical sample that represents a population. Rather a group of experts is required to provide input that leads to a decision.(213) The Delphi process participants were therefore purposively selected as participants who had to be experts in the care of patients with diabetes with advanced knowledge on diabetes management (217).

In both primary healthcare settings and hospitals, the healthcare professionals with expertise in medication are mainly endocrinologists, general practitioners, diabetes nurse educators and pharmacists. These health professionals are involved in the medication management of patients with diabetes. (4, 10) and were targeted to take part in the process. Apart from these healthcare professionals, individuals targeted also included doctors specialising in public health who were involved in developing health policies from academic, government and private sectors. Participants approached were through personal contacts of researchers. These experts then nominated other experts and a snowball technique was used to recruit more participants. The recommended number of participants in a Delphi study ranges between 10 to 15 members (218) and the recruitment process continued until a sufficient number of participants were recruited.

Potential participants from Malaysia and Australia were targeted as the intention was to use the Simpler™ tool as a diabetes intervention tool in both countries. An electronic mail (email) was used to personally invite each participant. This followed the suggestion of Turoff and Hiltz who found that invitation by name rather than a blank invitation increased the likelihood of participation.(219) In addition, participants were provided with a brief introduction of the research. The information sheet (Appendix 3.2) and introductory letter (Appendix 3.3) were sent to participants who agreed to participate.

3.3.3 Development of Simpler™

As previously mentioned in Chapter 2, paragraph 2.2, there are seven factors involved in the management of T2DM. The factors and indicators for goals of treatment were outlined particularly in the 2009 Malaysian diabetes guidelines and the more recent 2015 guidelines; 2014/2015 and the recent 2016/2018 Australian diabetes guidelines; the 2014 and later the 2016 American Diabetes Association (ADA) [ADA position statements].(6, 7, 16, 49, 220, 221) The seven factors are:

1. the use of statin/lipid-regulation medicine
2. the use of insulin and glycaemic control
3. medication adherence and addressing MRPs
4. addressing BP control
5. addressing lifestyle issues
6. providing education and
7. reducing CVD risk

By incorporating the first letter of each intervention mentioned above, the acronym SIMPLER was derived. For the purpose of this and the following chapters, the diabetes intervention tool developed and evaluated in this research will be referred to as the Simpler™ tool. Figure 3.1 gives an illustration of the Simpler™ tool derivation.

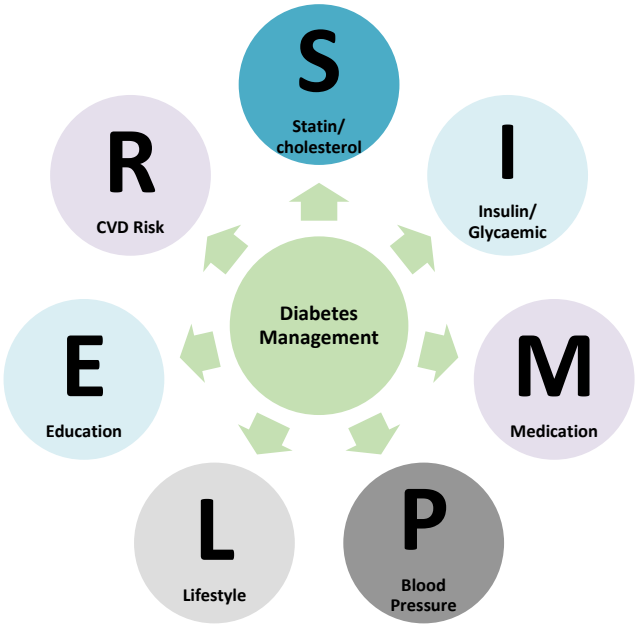


Figure 3.1: The Simpler acronym derived from letters in the seven diabetes factors

3.3.4 Development of the Delphi questionnaire

The Delphi questionnaire consisted of two sections: Parts 1 and 2 as shown in Appendix 3.4. Each questionnaire was labelled with a unique code linked to an individual participant. Participants were asked to provide feedback and suggestions through questionnaires sent through email.

3.3.4.1 Part 1 Delphi Questionnaire

There were seven factors and 29 indicators in Part 1 of the Delphi questionnaire. The sources for Part 1 indicators in the questionnaire are shown in Table 3.2

Table 3.2: Reference justification for each indicator of Part 1 questionnaire

Factors and Indicators	Excerpts from 2016/2018 Australian, 2015 Malaysian and 2016 American Guidelines(6, 7, 16)
Statin • Statin initiation in patients over age 40 years without CVD Malaysian CPG 2015, Australian CPG 2016/2018	Australian guideline recommends statins as the first-line choice. Results from literature reviews shows that treatment with statin significantly decreases morbidity and mortality in patients with T2DM and have high cardiovascular risk. The guideline also suggests nicotinic acid, bile-acid resins, ezetimibe and fibrates (fenofibrate, gemfibrozil) as alternatives for people who cannot tolerate statin. Fenofibrate should be considered in patients with diabetes with retinopathy. The goals to reach in cholesterol levels are total cholesterol < 4.0 mmol/L, HDL ≥ 1.0mmol/L, LDL < 2.0mmol/L, TG < 2.0mmol/L.
• Statin initiation in patients with CVD • Achieve targets: LDL, Malaysia (LDL<2.6mmol/L, TG<1.7mmol/L) Australia (LDL<2.5mmol/L), TG (<1.5mmol/L).	Malaysian guideline recommends all patients without CVD over the age of 40 years to be treated with statin regardless of baseline LDL cholesterol levels. The target LDL is 2.6mmol/L. Target triglyceride level is <1.7mmol/L. In individuals with overt CVD, statin is also strongly recommended. The target of LDL cholesterol in this population is 1.8mmol/L. The main objective of treatment is to lower LDL. Nicotinic acid is recommended for patients with pancreatitis with TG level more than 10 mmol/L. Combination therapy using simvastatin and ezetimibe has helped to achieve lipid targets.

Factors and Indicators	Excerpts from 2016/2018 Australian, 2015 Malaysian and 2016 American Guidelines(6, 7, 16)
Insulin • Insulin initiation if glycaemic control not achieved despite being on two or more oral hypoglycaemic agents • Management of hypoglycaemia • Self-monitoring of blood glucose • Target of HbA1c ≤ 7% (53mmol/mol) if no other complications • Aim 1% reduction of HbA1c • Initiation/continuation of metformin if no other contraindications	Australian guidelines recommendations for goals of therapy are 6-8 mmol/L fasting and 6-10mmol/L 2 hours postprandial, recommends ongoing self-monitoring blood glucose for those on insulin. However, routine self-monitoring of blood glucose in low risk patients who are using oral anti diabetes medication (except sulphonylureas) is not recommended. HbA1c needs to be individualised but generally should be ≤7% (53 mmol/mol) [range 6.5-7.5 (48-58 mmol/mol)]. Patients with severe hypoglycaemia should raise their glycaemic targets to avoid further hypoglycaemia. Metformin is the first choice if lifestyle modification does not achieve glycaemic control unless contraindicated. While stepwise approach is recommended for the management of T2DM, it however does not match individualised patient needs. Therefore, patients are given a choice on the treatment depending on efficacy, risk of hypoglycaemia, major side effects, weight gain and costs. Insulin should be initiated in patients who are taking maximum doses of oral hypoglycaemic agents such as metformin and sulphonylureas who have suboptimal glycaemic control or above individualised target of HbA1c either with symptoms or without symptoms of hyperglycaemia. Before starting insulin, ensure that all possible causes of hypoglycaemia such as lifestyle, noncompliance to medications or other medical conditions have been addressed. HbA1c is recommended to assess long-term blood glucose control. Adjustments to diabetes treatment should be considered if HbA1c target is above 7% (53mmol/mol). Measurement error with HbA1c means a target range of 6.5-8% (48-64 mmol/mol) is acceptable to allow for measurement variation and for individualised approach. Target should be individualised to as low as possible without side effects. HbA1c should be maintained at no lower than 7.5% (59 mmol/mol) depending on life expectancy. Malaysian guideline outlines the target for glycaemic control is fasting 4.4-6.1mmol/L, and non-fasting is 4.4-8.0 mmol/L. The target HbA1c for newly diagnosed, younger age, patients with low risk of hypoglycaemia is 6.0-6.5% (42-48 mmol/mol), 7.1-8.0% (54-64 mmol/mol) for patients with co-morbidities which is also in line with ADA recommendation, short life expectancy and prone to hypoglycaemia and 6.6-7.0% (49-53 mmol/mol) for the rest.

Factors and Indicators	Excerpts from 2016/2018 Australian, 2015 Malaysian and 2016 American Guidelines(6, 7, 16)
	Metformin is the preferred choice as first line therapy. If targets are not met after optimal oral anti diabetes therapy, consider adding basal insulin or GLP-1 RA. For patients on insulin, metformin is strongly recommended to be continued indefinitely unless patients develop CKD stage 4 and 5.

Factors and Indicators	Excerpts from 2016/2018 Australian, 2015 Malaysian and 2016 American Guidelines(6, 7, 16)
Medication • Review medication adherence using 8-item MMMAS.(1) • Assess medicine related problems (pharmacotherapy)	Australian guideline recommends asking about hypoglycaemia or other side effects of medications especially for patient on insulin or sulphonylureas. Complementary and alternative medicines are not recommended for glycaemic control for patients with diabetes according to Malaysian guideline. The latter also strongly suggests health education, diet therapy, exercise and compliance to medicines to be reinforced at follow up which later outlines the role pharmacist play in ensuring adherence and giving information about medication mode of action and side effects. Also, it includes administration and adjustment of insulin dosing. To increase medication adherence, the medication therapy management service (MMS) as suggested by Strand and Cipolle is adopted (62). In MMS, each patient's medications including supplements, traditional, alternative, non-prescription are reviewed. This is to ensure the medicine is appropriate, effective, safe and convenient for the patient to take. If there is medicine related problem, it will be resolved by changing product, doses or by educating the patient effective use of medication. The care plan is developed to achieve goals of therapy and the patient is followed up. Both MTAC Diabetes and Diabetes MedsCheck recommend using the 8-item MMMAS to assess the medication adherence.

Factors and Indicators	Excerpts from 2016/2018 Australian, 2015 Malaysian and 2016 American Guidelines(6, 7, 16)
BP • BP Target: 130/80 or less • Reduce sodium • ACEI/ARB for patients without microalbuminuria/proteinuria • ACEI/ARB for patients with microalbuminuria/proteinuria	Australian guideline recommends reaching target blood pressure (BP) of 130/80 mmHg and for people with microalbuminuria or macro albuminuria. Target BP≤140/90 mmHg in general or people with CKD. Treatment to lower BP in people with diabetes must include angiotensin converting enzyme inhibitor (ACEI) or angiotensin receptor blocker (ARB). If monotherapy does not reduce BP, calcium channel blocker or low-dose thiazide or thiazide-like diuretic is recommended. The Malaysian guideline recommends a reduced sodium intake for normotensive and hypertensive patients. It recommends <2400mg sodium/day or 6g of salt a day or 1 teaspoon). Sodium restriction can be achieved through avoiding high sodium foods, reducing the number of times to eat out and limit salt in cooking to ¼ to ½ teaspoonful of salt per person per day. Further sodium restriction is necessary if patient has nephropathy and BP is not controlled. ACEI or ARB is recommended first line for patients with diabetes and microalbuminuria or proteinuria. Multiple drug therapy such diuretics, calcium channel blockers (CCBs), beta blockers and peripheral alpha blockers are generally required to achieve blood pressure targets. Target BP in patients with diabetes with proteinuria should be ≤130/80 and ≤125/75 in patients with proteinuria. Pharmacological treatment should be initiated in patients with diabetes when the BP is >140mmHg and or >90mmHg and to treat if SBP lower than 135mmHg and DBP lower than 75mmHg.

Factors and Indicators	Excerpts from 2016/2018 Australian, 2015 Malaysian and 2016 American Guidelines(6, 7, 16)
Lifestyle • Alcohol intake ≤2 standard drinks (20g)/day for men and women • Exercise -30 mins walking (or equivalent) 5 or more days/week • Smoking Cessation • Advice on foot care • Weight loss, BMI<25kg/m2(Australia), BMI <23kg/m2 (Malaysia); • Achieve waist circumference targets • Erectile dysfunction- PDE-5 inhibitor as first line therapy • Management of stress & diabetes related distress	Australian guideline recommends loss of body weight as it can lead to improved glycaemic control, BP and lipid profiles. Weight reduction of approximately 5 kg is associated with an approximate reduction of HbA1c of 0.5-1%. Weight loss of 2-3 kg is associated with a reduction with 4.5mmHg systolic and 3-3.5mmHg diastolic. BMI is different for different ethnic groups. For European descent, BMI is 18.5-24.9, while people of Asian origin, BMI is lower and higher BMI for people with Torres Straits Islander and Maori people. The therapeutic goal is 5-10% loss for people overweight or obese. For patients with diabetes with BMI>35 and comorbidities or BMI>40, should consider more weight loss. People with moderate (Framingham risk= 10-15%) and high-risk CVD, (Framingham risk>15%), advice and support regarding diet and physical activity 30 minutes or more on most days of the week (total ≥150minutes/week), smoking cessation as well as education on BP and lipid lowering therapy is recommended. It also recommends assessing patients at risk of developing foot complications. Full eye review to be conducted every 2 years. The Malaysian guideline recommends normal range for BMI as 18.5-22.9 kg/m2. Achieve weight loss of between 5 to 10% in 6 months to improve glycaemic control, blood pressure, lipid profile and QOL. Physical activity consisting 250 to 300 minutes per week of exercise. For erectile dysfunction in men the recommended first line treatment is Phosphodiesterase-5 (PDE-5) inhibitors e.g. sildenafil. The problems and concerns that cause distress to the patient need to be addressed as this may affect management of diabetes.

Factors and Indicators	Excerpts from 2016/2018 Australian, 2015 Malaysian and 2016 American Guidelines(6, 7, 16)
Education • Structured education programme include knowledge and understanding of medicine • Medicine taking and storage during travel • Medication optimisation during fasting month for Muslims	T2DM patients should be given structured diabetes education either in groups or delivered individually. It should target different cultures and socioeconomically disadvantaged population. This is the recommendation from the Malaysian guideline. In addition, it recommends diabetes education to all patients with T2DM regardless of treatment mode. The more the duration of contact time between the educator and the patient, the better the A1c reduction. A face to face delivery, reinforcement of education using monthly telephone calls improves glycaemic control and compliance. Malaysian CPG suggests that contents of education should include diet, food exchanges, exercise, medication including timing and dosing, complications, self-care, SMBG, foot care, smoking cessation, problem solving skills e.g. management of hypoglycaemia, sick days and psychosocial adaptation to diabetes. The benefits of achieving glycaemic control for period of time presents benefit in terms of prevention of diabetes complications and this known as legacy effects should be emphasised to all newly diagnosed patients with diabetes. Adjustment of the diet and medication protocol for Ramadan fasting is required. Diabetes treatment should be individualised during fasting. Education on hypoglycaemia, hyperglycaemia and dehydration is emphasised. Patient need to check the blood glucose level before, during and after prolonged physical activity. This is also stressed by the standards of medical care published by American Diabetes Association who recommends to ask individuals at risk for hypoglycaemia about hypoglycaemia like symptoms at every visit.

Factors and Indicators	Excerpts from 2016/2018 Australian, 2015 Malaysian and 2016 American Guidelines(6, 7, 16)
CVD risk • Aspirin therapy (75mg-162mg/day) as primary prevention strategy at increased CVD risk (10-year risk>10%, Framingham) • Aspirin therapy as secondary prevention in those with diabetes with history of CVD • Use of Framingham risk calculator to calculate CVD risk and educate patient	Australian guideline does not recommend aspirin for primary prevention. Intensive antithrombotic therapy is recommended for secondary prevention. Patients with high risk of CVD must be simultaneously treated with lipid and BP lowering treatment and given lifestyle advice. Malaysian guideline recommends CVD risk calculator such as Framingham risk score (FRS) or Systematic coronary risk evaluation (SCORE) to calculate the CVD risk score. Aspirin is recommended as secondary prevention and primary prevention of CVD with low dose aspirin (100mg) is not recommended in patients unless they are above 65 years. This differs from the previous 2009 Malaysian CPG which recommended aspirin for primary prevention only if they are at high risk using the Framingham risk score. The USA guidelines recommend aspirin therapy (75-162mg) as a primary prevention strategy among patients at increased cardiovascular risk (10-year risk >10%). This includes men aged >50 years and women aged ≥50years who have at least one additional major risk factor for e.g. family history of CVD, hypertension, smoking, dyslipidaemia, or albuminuria. However, the level of evidence for this recommendation is low.

ADA= American Diabetes Association; ACEI= angiotensin converting enzyme inhibitor; ARB=angiotensin receptor blocker; BMI= body mass index; BP=blood pressure; CCB= calcium channel blocker; CKD= chronic kidney disease; CVD= cardiovascular disease; CPG= clinical practice guideline; DBP=diastolic blood pressure; GLP-1RA= glucagon like peptide 1 receptor agonist; HDL= high density lipoprotein; HbA1c=glycated haemoglobin; LDL= low density lipoprotein; MMMAS= modified Morisky medication adherence scale; MTAC diabetes= medication therapy adherence clinic diabetes; PDE-5 inhibitor=phosphodiesterase-5 inhibitor; T2DM= Type 2 diabetes mellitus; TG=triglyceride;

An informed decision was made to include all the 29 indicators in the hand-out as these indicators were evidence-based factors emphasized in diabetes guidelines from Australia, Malaysia, Europe, the USA and the UK.(6, 7, 16, 17) However, opinions were required on the order of importance the indicators should appear in the hand-out. A score = 1 was ranked as most important and would appear as the first subheading, 2 as the second subheading which is the second most important indicator, 3 as the third subheading and so on. Participants were instructed to choose only one number per subheading. A space was allocated in the questionnaire for the participants to enter their comments or suggestions. Table 3.3 and Figure 3.2 below gives a clearer illustration of this procedure.

Several articles from the literature regard pilot testing of Delphi questionnaires as optional.(222, 223) In this study, test and retest reliability were not conducted as the questionnaires were validated by three members of the research team who were knowledgeable in diabetes.

Table 3.3: Part 1 questionnaire instructions

Code	Indicator Name and Description		Appearance of indicator in hand-out in order of importance. Please choose one number for each indicator. The same number cannot be picked more than once for each of the indicator.			Order of appearance in hand-out
1	1.1	Statin initiation in patients with CVD	□1	☒2	□ 3	This will be the second bullet point to appear in the hand-out
	1.2	Statin initiation in patients over age 40 years without CVD	☒1	□2	□ 3	This will be the first bullet point.
	1.3	Achieve targets: LDL, Malaysia (LDL<2.6mmol/L, TG<1.7mmol/L) Australia (LDL<2.5mmol/L), TG (<1.5mmol/L).	□1	□2	☒ 3	This will be the third bullet point.

Based on the numbers chosen in the table above, the order of appearance in the hand-out is as below (Figure 3.2)

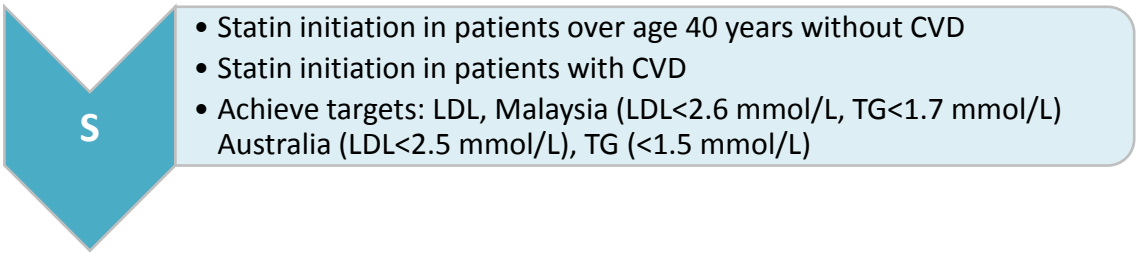


Figure 3.2*:* Order of appearance in hand-out

3.3.4.2 Part 2 Delphi Questionnaire

Part 2 consisted of two indicators on the layout of Simpler™ hand-out and seven additional indicators on prevention of diabetes complications and treatment recommendations not included in the 2009 Malaysian guideline.(49) Some of the recommendations from these additional evidence-based indicators were sourced from 2014 EASD/ADA position statement and 2014/2015 Australian guidelines.(220, 221) While others were from randomised controlled studies carried out on small cohort population. As such, a consensus was required for these seven indicators to be included in the Simpler™ hand-out. Of interest, the recent 2015 diabetes guidelines from Malaysia (6) included two out of seven of Part 2 indicators of the questionnaire constructed prior to 2015.

Participants were asked to rate each indicator in terms of its importance in making diabetes interventions. The score was rated according to a five point Likert-scale where 1 = least important or redundant and 5 =most important, as suggested in Delphi literature references.(200)

In addition, participants were asked to provide their rationale for choosing a certain score as well as additional suggestions or interventions apart from that already provided in the questionnaire. An excerpt of that follows:

> *A space is provided for you to briefly explain the reason for your rating if you wish to. This additional information is optional and could help us understand the reasons some indicators received a more important ranking than others. The space could also be used for additional suggestions or interventions that should be included according to indicators mentioned.*

The indicators in Part 2 consisted of two questions on Simpler™ hand-out layout and seven indicators on medication management, lifestyle issues such as diet and sleep hygiene and annual eye assessment.

There were two choices for the layout. Figure 3.3 and Figure 3.4 shows these choices. Participants were required to rank using the Likert scale their preferred choice. A score of 1 denoted least preferred and a score of 5 denoted most preferred.

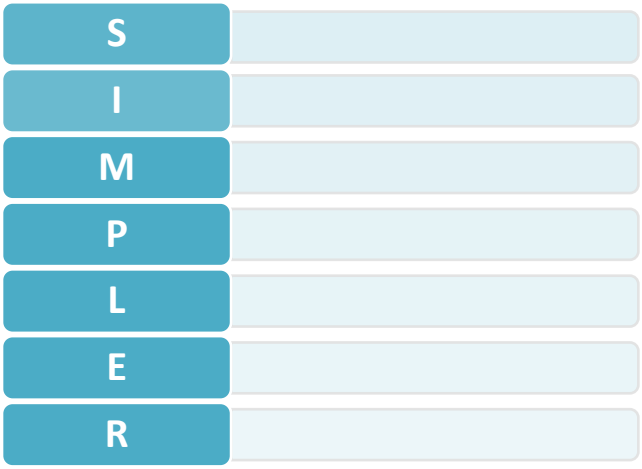


Figure 3.3: Hand-out of the Simpler™ tool (Bookmark design)

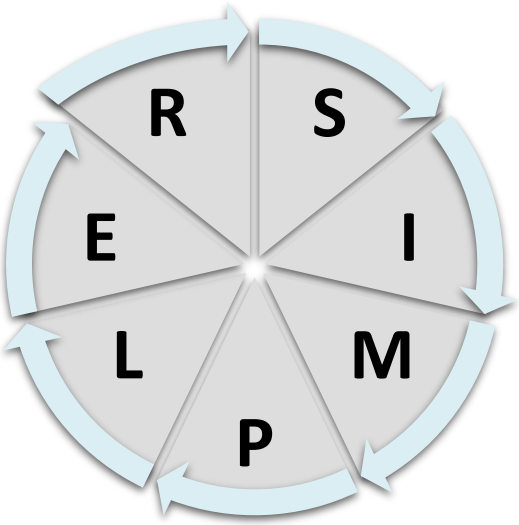


Figure 3.4: Hand-out of the Simpler™ tool (Wheel design)

Table 3.4 provides the seven indicators, the excerpts and the sources of reference for each of these indicators.

Table 3.4: Reference justification for seven indicators in Part 2 of the questionnaire

Factors and Indicators	Sources of References
Administer once daily antihypertensive at bedtime	Both the 2016 Malaysian and the 2016 ADA guidelines recommend the administration of one or more antihypertensive medications at bedtime. (6, 16)
Diet advice using plate model	Plate model was introduced as a simple way to eat small portions as well as an education tool. Dieticians from Canada, Finland, France, Sweden and now the USA found it to be a better alternative carbohydrate exchange-based method. (224-226)
Annual eye assessment	The Australian guidelines recommend eye examination to be carried out once every two years. The Malaysian and the American guidelines recommend annual eye assessment.(6, 16)
Address sleep hygiene	The Australian and Malaysian guidelines suggests management of sleep deprivation which can aggravate insulin resistance, hypertension and hyperglycaemia.(6, 7)
1g-3g cinnamon intake per day	Several randomised controlled studies conducted have found the benefits in taking cinnamon especially in the improvement in glycaemic control. The range of dose used in these studies were 1g to 3g in the capsule form.(227-231)
Vitamin B12 supplement in patients on long term metfomin	Although both the current, 2016 Malaysian and the American guidelines acknowledge Vitamin B12 deficiency when on long-term treatment with metformin, clear guidance on taking vitamin B12 was not mentioned.(6, 16)
Encourage daily Intake of tree nuts (almonds, brazil nuts, cashews, hazelnuts, macadamia, pecans, pine nuts, pistachios and walnuts)	Systematic review done found 12 randomised controlled studies on tree nut consumption led to improved glycaemic control.(232) However, consuming tree nuts to improve glycaemic control were not recommended in the Malaysian, Australian, European, the UK or American guidelines.

3.3.5 The Delphi rounds

3.3.5.1 Delphi round 1

In this round, Part 1 and Part 2 questionnaire were sent to 12 participants recruited earlier. They were asked to rank Part 1 indicators in the order they should appear in the Simpler™ hand-out and chose the indicators in Part 2 questionnaire which should be included in the hand-out.

3.3.5.2 Delphi round 2

At the conclusion of Round 1, three (27%) participants in Part 1 of the questionnaire chose the same number for more than one sub-indicator for a specific indicator multiple times despite the detailed instructions provided as indicated in paragraph 3.2.3. Therefore, in Delphi Round 2, these three participants were sent the same questions as was in Round 1 but the instructions for questions in Part 1 were rephrased to:

> *1. In Part 1 of the questionnaire, the same number cannot be picked more than once for each of the indicators, however you have chosen the same numbers multiple times for some of the questions. You are given the opportunity in this round to revise your rankings. The table provides comparison between your score and median score for the rest of the participants.*

The rest of the participants also received a similar questionnaire to Round 1 and similar to the questions received by the three participants mentioned above but with separate instructions as below:

1. *In Part 1 of the questionnaire, the same number cannot be picked more than once for each of the indicators, however some of the participants have chosen the same numbers multiple times for some of the questions. In this round, you can either retain or revise your scores.*
2. *In Part 2 of the questionnaire, you are asked to either retain your score or revise it up or down. The table provides a comparison between your score and the median score for the rest of the participants.*

An excerpt of the Round 2 questionnaire is presented in Appendix 3.5.

During Round 2 the second questionnaire was distributed which was similar to the Round 1 questionnaire but in addition it contained scores of individual participants and the group median scores. The group median scores represented statistically analysed results of collected opinions from each of the 12 participants. This allowed participants to view his/her result in relation to the group scores. Participants however did not know other participants' individual scores as each participant was only provided with his/her scores thereby maintaining individual anonymity. A similar process was repeated in Round 3.

Returned Round 2 questionnaires were scrutinised for missing answers and whether the same answer was chosen multiple times in Part 1 of the questionnaire. Such questionnaires were sent back to the participants in order for them to complete the questionnaire.

3.3.5.3 Delphi round 3

Completed Round 2 questionnaires were analysed and group median scores and the frequency of the answers were calculated using IBM Statistical Package for Social Sciences (SPSS) software version 22.(233) An excerpt of the dataset in SPSS is shown in Appendix 3.6. The format of the Round 3 questionnaire was the same as the Round 2 questionnaire (Appendix 3.7). However, it contained an additional instruction, shown below:

1. *In this round, your score and the group median score is revealed. The indicators highlighted in yellow shows where your score differs from that of the group score (median score). The aim of the Delphi process is to achieve consensus on an indicator and this can only be achieved if more than 60% of participants give the same answer for each indicator.*
2. *Participants do not have to revise indicators where consensus was achieved. This will be indicated in the table below.*
3. *Participants have the option to revise or retain indicators where their scores are similar to that of the group score. Bearing in mind, consensus would be harder to achieve if your scores are not the same as the group score.*

3.3.6 Duration of the Delphi rounds

Participants were given two weeks to complete the questionnaire during Rounds 1 and 2 and one week for Round 3. The overall duration of the Delphi process was three months. Questionnaires were sent to participants through emails with reminders three days before due dates. Ongoing reminder emails were sent to participants who were

overdue in their responses. The data analysis for each round commenced once all responses were received. Figure 3.5 represents the flow of the Delphi process.

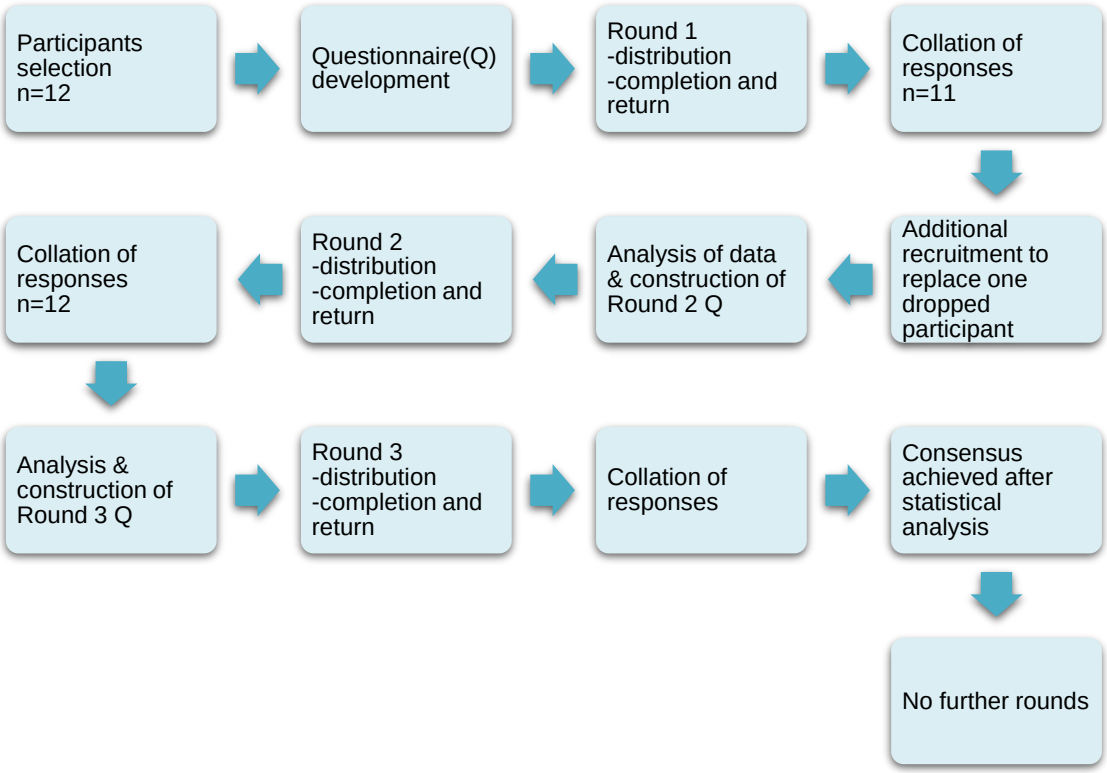


Figure 3.5*:* Flow of the Delphi process

3.3.7 Achieving consensus

The goal of the Delphi process is to achieve consensus; that is when participants unanimously agree on a criteria or issue. In this research, consensus is achieved when participants agreed on the order the indicators should appear in the Simpler™ hand-out (Part 1) and on indicators that should be included in the hand-out (Part 2). However, the literature search indicated lack of guidelines on consensus levels with levels from previous studies varying between more than 50% (201-203, 212) to more than 80%.

(209) However, this is in agreement with a review study which states that more than a 50% level of agreement constitutes a majority and successive rounds should cease at this point.(199) For the purpose of this research, a consensus level of more than 60% was set, as suggested by Stitt-Gohdes,W.(234) This meant, consensus was reached if more than 60% of participants ranked the indicators with the same score. Median rather than mean was chosen to represent the group scores as median can be used to establish the central tendency in the Delphi process.(235)

In Part 2 of the questionnaire, consensus agreement criteria was when more than 60% of the participants rated each indicator's score = 4 or 5. In one study the author defined a score of = 4 or more in a 7-point rating scale as a high level of agreement.(200) The justification for this is that a score of 4 or more falls in the upper quartile range in a 7-point Likert scale. In a 5-point Likert scale the upper quartile range includes scores of 4 and 5. For the purpose of this research, an indicator in Part 2 of the questionnaire had to receive a score of 4 or 5 from more than 60% of participants in order to be included in the hand-out.

3.3.8 Stability of the rounds

Stability is described as consistency in responses between two rounds.(199) However, Delphi studies do not define a definite method to measure stability. This resulted in some studies using both stability and agreement criteria as necessary to determine if further rounds should continue (199, 213, 236), while others concluded that either stability or consensus should be the determining factor in continuing the rounds.(235) The majority of the Delphi studies done recently suggested achieving consensus as the sole reason for terminating the rounds.(179, 201, 203-212) In the absence of a standard

method to measure stability, it was decided that the criteria to stop further rounds should depend solely on achieving the predetermined consensus level.

3.4 Results

In the following section, the results of the Round 1 questionnaire are presented followed by construction of the Round 2 questionnaire based on the Round 1 results. The findings from Round 2 and construction of Round 3 questionnaire are subsequently presented. The final section provides the results of the changes in rankings between Rounds 2 and 3 and between and the consensus level for each of the questions in Round 3.

3.4.1 Participants

Twelve participants agreed to take part in Round 1, however only 11 responded. In Round 2, an additional participant was recruited to account for the Round 1 non-respondent. Hence, the total number of Round 2 participants was 12. Both Rounds 2 and 3 produced 100% response rates. Table 3.5 is a summary of the participants' areas of expertise and workplace.

Table 3.5: Breakdown of Delphi process participants (n=13)

Practitioner	Country		Practice	
	Malaysia	Australia	Public	Private
Primary health care pharmacist, (Klinik Kesihatan Mahmoodiah), Johor	✓		✓	
Clinical pharmacist (hospital) Hospital Pulau Pinang	✓		✓	
Clinical pharmacist (Administration) Pharmaceutical Services Division, Malaysia	✓		✓	
Consultant endocrinologist Hospital Sultanah Aminah, Johor	✓		✓	
Public health physician, Disease Control Division, Department of Public Health, Malaysia	✓		✓	
Family medicine specialist, Johor	✓		✓	
General practitioner, Johor	✓			✓
Academic pharmacist, Perth		✓		✓
Community pharmacist (diabetes educator), Perth		✓		✓
Community pharmacist (multiple chain stores), Perth *(dropped out in Round 1)*		✓		✓
Endocrinologist, Hollywood Hospital, Perth		✓		✓
General practitioner, Perth		✓		✓
Diabetes nurse educator, Hollywood Hospital, Perth		✓		✓
Total	7	5	6	6

3.4.2 Delphi round 1

In round 1, 11 of the 12 participants responded. In addition, not all questions received a 100% response rates. Although the percentage of participants who answered the questions were high (80%), this however, had the potential to influence the consensus

level as documented in a previous study(218). Therefore a 100% response rate was aimed for all questions. Table 3.6 shows the number and percentages of participants who answered those questions.

Table 3.6: Indicators which participants missed answering

Questions	No. answered	Total participants	% participants responded
Part 1			
Lifestyle 5.7	10	11	90.9
Part 2			
Additional 9.5	10	11	90.9
Additional 9.7	9	11	81.8

One participant pointed out that *medication optimisation during fasting month for Muslims* also applies to other religious groups (Part 1, question 6.3). Another participant required more information on addressing sleep hygiene (Part 2, question 6.3). The results of Round 1 Part 1 of the questionnaire are shown in Table 3.7. The results are presented in the same format as reported in Delphi literature.(200, 234) Similarly, results for Part 2 of the questionnaire are presented in Table 3.8.

Table 3.7: Results of Round 1 Part 1

No	Part 1 Indicators	Round 1 (n=11)		
		#Median	*Mode	No.participants (% Consensus)
Statin				
1.	Statin initiation in patients over age 40 years without CVD	1	1	8 (72.7)
2.	Statin initiation in patients with CVD	3	3	11 (100)
3.	Achieve targets: LDL, Malaysia (LDL<2.6mmol/L, TG<1.7mmol/L) Australia (LDL<2.0mmol/L), TG (<2.0mmol/L)	2	1	9 (81.8)
Insulin/Glycaemic Control				
4.	Insulin initiation if glycaemic control not achieved despite being on two or more oral hypoglycaemic agents	4	1	7 (63.64)
5.	Management of hypoglycaemia	3	6	6 (54.6)
6.	Self-monitoring of blood glucose to achieve targets	3	5	7 (63.6)
7.	Target of HbA1c ≤ 7% (53mmol/mol) if no other complications	2	1,2	6 (54.6)
8.	Aim 1% reduction of HbA1c	4	6	6 (54.6)
9.	Initiation of metformin if no other contraindications	3	1	6 (54.6)
Medication				
10.	Review medication adherence	2	2	11 (100)
11.	Assess medication-related problems (pharmacotherapy)	1	1	9 (81.8)
Blood Pressure				
12.	BP Target: 130/80 or less	1	1	8 (72.7)
13.	Reduce sodium	3	4	6 (54.6)
14.	ACEI/ARB initiation in patients without microalbuminuria/proteinuria	3	3	8 (72.7)
15.	ACEI/ARB initiation in patients with microalbuminuria/proteinuria	2	2	7 (63.6)
Lifestyle				
16.	Moderate alcohol intake ≤2 standard drinks (20g) per day for men and women	5	5	9 (81.8)
17.	Exercise-30 mins walking (or equivalent) 5 or more days/week (total ≥150 min/week)	2	1,2	8 (72.7)
18.	Smoking cessation	2	1	6 (54.6)
19.	Advice on foot care	6	6	9 (81.8)

No	Part 1 Indicators	Round 1 (n=11)		
		#Median	*Mode	No.participants (% Consensus)
20.	Weight loss targets	3	4	6 (54.6)
21.	Waist circumference targets	4	1,2,5	6 (54.6)
22.	Erectile dysfunction-recommend PDE-5 inhibitor as first line therapy for male patients	6	8	5 (50)
23.	Management of stress & diabetes related distress	7	7	9 (81.8)
Education				
24.	Structured education program include knowledge and understanding of medicine	1	1	8 (72.7)
25.	Medicine storage	2	2	9 (81.8)
26.	Medication optimisation during fasting month for muslims and other religious groups	3	3	11 (100)
CVD Risk				
27.	Aspirin therapy (75mg-162mg/day) as primary prevention strategy at increased CVD risk (10 year risk>10%, Framingham)	2	2	6 (54.5)
28.	Aspirin therapy as secondary prevention in those with diabetes with history of CVD	1	1	6 (54.6)
29.	Use of Framingham risk calculatorto calculate CVD risk and educate patient	2	1	7 (63.6)

#Median denotes the score lying at midpoint of scores chosen by participants
*Mode denotes the score that was chosen most frequently
ACEI= angiotensin converting enzyme inhibitor; ARB=angiotensin receptor blocker; BP=blood pressure; CVD=cardiovascular disease; FRS=Framingham risk score; HbA1c=glycated haemoglobin; LDL=low density lipoprotein; PDE-5 inhibitor=phosphodiesterase-5 inhibitor; TG=triglyceride;

The following comments were provided for those indicators that were ranked the least important in Part 1 of the questionnaire:

Indicator 27: Aspirin therapy (75mg-162mg/day) as primary prevention strategy at increased CVD risk (10 year risk>10%, Framingham):

> 'This is controversial in primary care' (P7)

Indicator 8: Aim 1% reduction of HbA1c:

> 'If very high on insulin initiation' (P12)

Indicator 9: Initiation of metformin if no other contraindications:

> 'If considering metformin when initiating insulin…it should be done well before initiating insulin' (P12)

Table 3.8: Results of Round 1 Part 2

No	Part 2 Indicators	Round 1 Results (n=11)				
		#Median	*Mode	+Min	^Max	No.participants (% Consensus)
30	Appendix 3a (bookmark design)	4	5	1	5	7 (58.3)
31	Appendix 3b (wheel design)	3	3	1	5	7 (63.6)
32	Administer once daily antihypertensive at bedtime	3	3	2	5	8 (72.7)
33	Diet advice using plate model	4	5	1	5	6 (54.6)
34	Annual eye assessment	4	4	1	5	7 (63.6)
35	Address sleep hygiene	4	4	1	5	9 (81.8)
36	1g-3g cinnamon intake per day	2.5	1	1	5	5 (50)
37	Vitamin B12 supplement with metfomin	3	1,4	1	5	6 (54.6)
38	Encourage daily intake of tree nuts	3	3	1	5	8 (88.9)

#Median denotes the score lying at midpoint of scores chosen by participants
*Mode denotes the score that is chosen most frequently
+Min denotes the lowest score chosen by participants
^Max denotes the highest score chosen by participants

The following comments were provided for those indicators that were ranked the least important in Part 2 of the questionnaire:

Indicator 32: Administer once daily antihypertensive at bedtime:

> 'Sometimes multiple drugs needed' (P12)

Indicator 36:1 g-3 g cinnamon intake per day:

> 'Some proof' (P12)
>
> 'I see that you have references to show/support the use of cinnamon, however I have not personally seen that being recommended in practice for this purpose' (P2)

Indicator 37:Vitamin B12 supplement with metfomin:

> 'Although long term use of metformin may be associated with B12 deficiency, it is not a routine recommendation in Australia to supplement patients who are on metformin (most of them will be on long term) with B12 unless lab results show low B12 levels or if patient also has other risk factors for example on long term PPIs [proton pump inhibitors] or have macrocytic anaemia' (P2)

Indicator 38: Encourage daily Intake of tree nuts (almonds, brazil nuts, cashews, hazelnuts, macadamia, pecans, pine nuts, pistachios and walnuts):

> 'Some proof' (P12)

3.4.3 Delphi round 2

Findings from Round 2 Part 1 of the questionnaire is presented in Table 3.9 and Part 2 in Table 3.10.

Table 3.9: Results of Round 2 Part 1

No	Part 1 Indicators	Round 2 (n=12)		
		#Median	*Mode	No.participants (% Consensus)
Statin				
1.	Statin initiation in patients over age 40 years without CVD	1	1	7 (58.3)
2.	Statin initiation in patients with CVD	3	3	12 (100)
3.	Achieve targets: LDL, Malaysia (LDL<2.6mmol/L, TG<1.7mmol/L) Australia (LDL<2.0mmol/L), TG (<2.0mmol/L)	2	2	11 (91.7)
Insulin/Glycaemic control				
4.	Insulin initiation if glycaemic control not achieved despite being on two or more oral hypoglycaemic agents	2	1	6 (54.6)
5.	Management of hypoglycaemia	3	3	7 (58.3)
6.	Self-monitoring of blood glucose to achieve targets	4	4	7 (58.3)
7.	Target of HbA1c ≤ 7% (53mmol/mol) if no other complications	2.5	2	6 (50)
8.	Aim 1% reduction of HbA1c	5	6	7 (58.3)
9.	Initiation of metformin if no other contraindications	2.5	1,2,6	6 (50)
Medication				
10.	Review medication adherence	2	2	11 (100)
11.	Assess medication-related problems (pharmacotherapy)	1	1	11 (91.7)
Blood Pressure				
12.	BP target: 130/80 or less	1.5	1	6 (50)
13.	Reduce sodium	4	4	12 (100)
14.	ACEI/ARB initiation in patients without microalbuminuria/ proteinuria	3	4	7 (58.3)

No	Part 1 Indicators	Round 2 (n=12)		
		#Median	*Mode	No.participants (% Consensus)
15.	ACEI/ARB initiation in patients with microalbuminuria/ proteinuria	2	1	9 (75)
Lifestyle				
16.	Moderate alcohol intake ≤2 standard drinks (20g) per day for men and women	5	5	8 (66.7)
17.	Exercise:30 mins walking (or equivalent) 5 or more days/week (total ≥150 min/week)	2	2	7 (58.3)
18.	Smoking cessation	3	2,3	8 (66.7)
19.	Advice on foot care	5.5	3	6 (50)
20.	Weight loss targets	2.5	1,4	6 (50)
21.	Waist circumference targets	4	1,4	7 (58.3)
22.	Erectile dysfunction-recommend PDE-5 inhibitor as first line therapy for male patients	7.5	8	6 (50)
23.	Management of stress& diabetes related distress	6	7	7 (58.3)
Education				
24.	Structured education programme include knowledge and understanding of medicine	1	1	10 (83.3)
25.	Medicine storage	2	2	10 (83.3)
26.	Medication optimisation during fasting month for muslims and other religious groups	3	3	11 (100)
CVD Risk				
27.	Aspirin therapy (75mg-162mg/day) as primary prevention strategy at increased CVD risk (10 year risk>10%, Framingham)	2.5	2,3	6 (50)
28.	Aspirin therapy as secondary prevention in those with diabetes with history of CVD	1	1	7 (58.3)
29.	Use of FRS calculator to calculate CVD risk and educate patient	2	1	8 (66.7)

#Median denotes the score lying at midpoint of scores chosen by participants

*Mode denotes the score that was chosen most frequently

ACEI= angiotensin converting enzyme inhibitor; ARB=angiotensin receptor blocker; BP=blood pressure; CVD=cardiovascular disease; FRS=Framingham risk score; HbA1c=glycated haemoglobin; LDL=low density lipoprotein; PDE-5 inhibitor=phosphodiesterase-5 inhibitor; TG=triglyceride;

Table 3.10: Results of Round 2 Part 2

No	Part 2 Indicators	Round 2 Results (n=12)				
		#Median	*Mode	+Min	^Max	No.participants (% Consensus)
30.	Appendix 3a (bookmark design)	3.5	5	1	5	6 (50)
31.	Appendix 3b (wheel design)	3	3,5	1	5	7 (58.3)
32.	Administer once daily antihypertensive at bedtime	3	3	1	5	8 (66.7)
33.	Diet advice using plate model	4	5	1	5	7 (58.3)
34.	Annual eye assessment	4	4,5	2	5	8 (66.7)
35.	Address sleep hygiene	4	5	1	5	8 (66.7)
36.	1g-3g cinnamon intake per day	1.5	1	1	5	6 (50)
37.	Vitamin B12 supplement with metfomin	2.5	1	1	5	6 (50)
38.	Encourage daily intake of tree nuts	3	3	1	5	11 (91.7)

#Median denotes the score lying at midpoint of scores chosen by participants
*Mode denotes the score that is chosen most frequently
+Min denotes the lowest score chosen by participants
^Max denotes the highest score chosen by participants

3.4.4 Delphi round 3

All 12 participants completed the Round 3 questionnaire. Incomplete questionnaire were returned to participant concerned to obtain missing answers. Table 3.11 presents the results of Round 3 Part 1 of the questionnaire.

Table 3.11: Results of Round 3 Part 1

No	Part 1 Indicators	Round 3 (n=12)		
		#Median	*Mode	Number (%Consensus)
Statin				
1.	Statin initiation in patients with CVD	1	1	12 (100)
2.	Statin initiation in patients over age 40 years without CVD	3	3	12 (100)
3.	Achieve targets: LDL, Malaysia (LDL<2.6mmol/L, TG<1.7mmol/L) Australia (LDL<2.0mmol/L), TG (<2.0mmol/L)	2	2	12 (100)
Insulin/Glycaemic Control				
4.	Insulin initiation if glycaemic control not achieved despite being on two or more oral hypoglycaemic agents	1	1	10 (83.3)
5.	Management of hypoglycaemia	3	3	10 (83.3)
6.	Self-monitoring of blood glucose to achieve targets	4	4	10 (83.3)
7.	Target of HbA1c ≤ 7% (53mmol/mol) if no other complications	2	2	10 (83.3)
8.	Aim 1% reduction of HbA1c	5	5	8 (66.7)
9.	Initiation of metformin if no other contraindications	5.5	6	6 (50)
Medication				
10.	Review medication adherence	2	2	11 (91.7)
11.	Assess medicine related problems (pharmacotherapy)	1	1	11 (91.7)
Blood Pressure				
12.	BP Target: 130/80 or less	1	1	10 (83.3)
13.	Reduce sodium (<2400mg sodium/day (6g salt/day)	4	4	11 (91.7)
14.	ACEI/ARB initiation in patients without microalbuminuria/proteinuria	3	3	10 (83.3)
15.	ACEI/ARB initiation in patients with microalbuminuria/proteinuria	2	2	8 (66.7)
Lifestyle				
16.	Moderate alcohol intake ≤2 standard drinks (20g) per day for men and women	5	5	9 (75)
17.	Exercise-30 mins walking (or equivalent) 5 or more days/week (total ≥150 min/week)	1	1	9 (75)
18.	Smoking Cessation	3	3	10 (83.3)
19.	Advice on foot care	8	8	7 (58.3)
20.	Weight loss targets	2	2	9 (75)
21.	Waist circumference targets	4	4	11 (91.7)

No	Part 1 Indicators	Round 3 (n=12)		
		#Median	*Mode	Number (%Consensus)
22.	Erectile dysfunction-recommend PDE-5 inhibitor as first line therapy for male patients	7	7	9 (75)
23.	Management of stress & diabetes related distress	6	6	10 (83.3)
Education				
24.	Knowledge and understanding of medicine	1	1	12 (100)
25.	Medicine storage	2	2	12 (100)
26.	Medication optimisation during fasting month for muslims and other religious groups	3	3	12 (100)
Cardiovascular Risk				
27.	Aspirin therapy (75mg-162mg/day) as primary prevention strategy at increased CVD risk (10 year risk>10%, Framingham)	3	3	11 (91.7)
28.	Aspirin therapy as secondary prevention in those with diabetes with history of CVD	1	1	10 (83.3)
29.	Use of Framingham risk calculator to calculate CVD risk and educate patient	2	2	10 (83.3)

#Median denotes the score lying at midpoint of scores chosen by participants

*Mode denotes the score that was chosen most frequently

ACEI= angiotensin converting enzyme inhibitor; ARB=angiotensin receptor blocker; BP=blood pressure; CVD=cardiovascular disease; FRS=Framingham risk score; HbA1c=glycated haemoglobin; LDL=low density lipoprotein; PDE-5 inhibitor=phosphodiesterase-5 inhibitor; TG=triglyceride;

In Part 1 of the questionnaire, two indicators (highlighted in red at Table 3.11) namely indicator number 9 *Initiation/continuation of metformin if no other contraindications* under glycaemic control/insulin factor and indicator number 19 *Advice on Foot care* under lifestyle factor had consensus levels of less than 60%. As explained in the methods section, participants were asked to choose a number (depending on the number of indicators) to appear in the Simpler™ tool in order of importance with number one being the most important and two being the second most important and henceforth. As the rest of the indicators under insulin/glycaemic control factor and lifestyle factor have achieved consensus on the numbers selected ranked in the order of importance by the participants, the last remaining numbers not chosen was therefore allocated to these questions. These process is clarified in the following paragraphs.

Under glycaemic control/insulin factor, there were six indicators thus participants were asked to rank the order of importance from one to six, one being the most important and six being the least important. Indicator 9 only received a 50% consensus whereas indicators 4, 5 to 8 achieved more than 60% consensus on the order of importance they should appear in the hand-out. There were each ranked one, two, three, four and five. The only number left out by most participants to rank the indicators under insulin was number six. Therefore, this number was allocated to indicator 9. Figure 3.6 further illustrates this process.

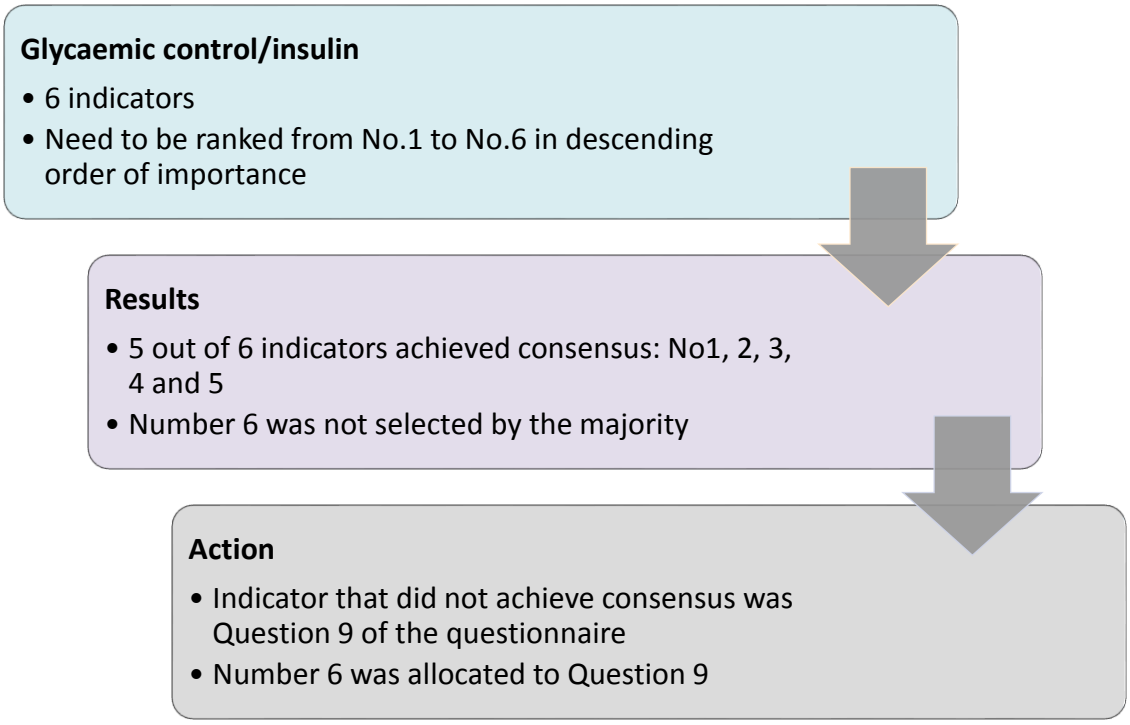


Figure 3.6: Clarification of allocation of numbers for indicator 9 under glycaemic control/insulin factors

Under the lifestyle factor, there were eight indicators thus; participants were asked to rank the order of importance from numbers one to eight. One being most important and eight being least important. Indicator number 19 only achieved a consensus level of 58.3% less than the 60% consensus level set at the beginning of the study. The rest of the indicators, namely indicators 16, 17, 18, 20-23, all achieved more than 60% consensus and they were ranked with numbers 1, 2, 3,4,5,6 and 7. The only number not selected by majority of participants to rank the indicators under the lifestyle factor was number 8, thus this number was allocated to question 19. This process is presented in Figure 3.7.

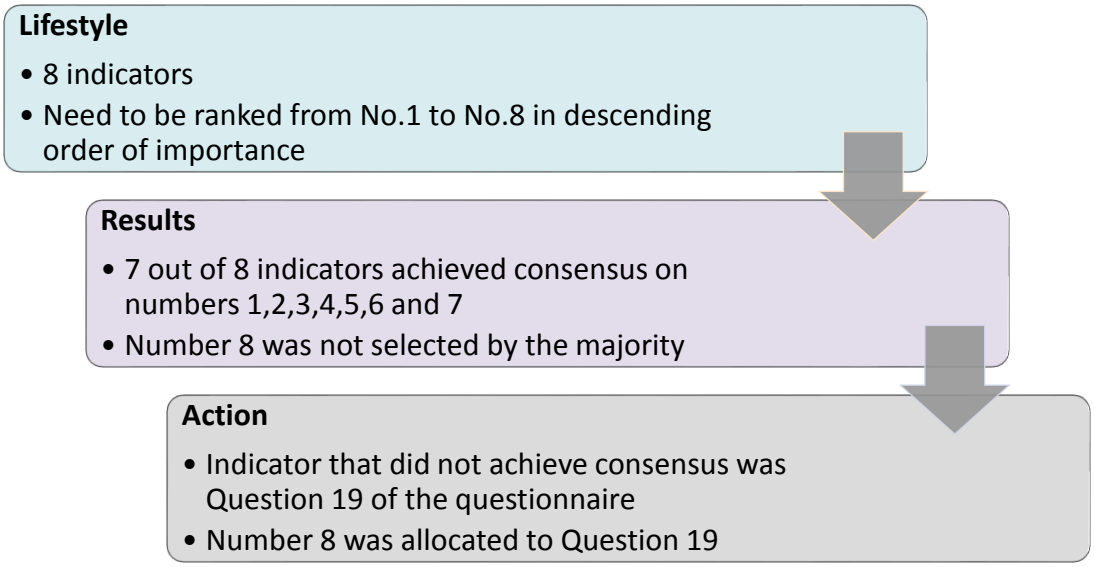


Figure 3.7: Clarification of allocation of numbers for indicator 19 under lifestyle factors

Table 3.12 presents the results of Part 2 of the questionnaire. Only questions with a median of 4 or 5 were selected to be included in the hand-out. These questions were grouped together under 'lifestyle'. Regarding the format of the hand-out the consensus was the bookmark design, as represented in Figure 3.3 rather than the Figure 3.4 wheel design. The bookmark design obtained a median score of 4 compared to the wheel design which received a median score of 3. Three out of seven indicators obtained consensus on the highest level of the Likert scale (4 or 5). The three indicators are as follows:

1. Diet advice using plate model
2. Annual eye assessment
3. Address sleep hygiene

There was a need for a detailed explanation on sleep hygiene during Round 1. Therefore, users were signposted to information on sleep hygiene. However, there were four indicators which received low rankings. Those indicators are as follows:

1. Administer once daily antihypertensive at bedtime
2. 1g-3g cinnamon intake per day
3. Vitamin B12 supplement with metfomin
4. Encourage daily intake of tree nuts

Table 3.12: Results of Round 3 Part 2

No	Part 2 Indicators	Round 3 Results (n=12)				
		#Median	*Mode	+Min	^Max	No.participants (% Consensus)
30	Appendix 3a (bookmark design)	4	4	3	5	9 (75)
31	Appendix 3b (wheel design)	3	3	1	5	9 (75)
32	Administer once daily antihypertensive at bedtime	3	3	3	4	11 (91.7)
33	Diet advice using plate model	4	4	4	5	12 (100)
34	Annual eye assessment	4	4	4	5	12 (100)
35	Address sleep hygiene	4	4	1	5	11 (91.7)
36	1g-3g cinnamon intake per day	1	1	1	3	9 (75)
37	Vitamin B12 supplement with metfomin	2	2	1	4	8 (66.7)
38	Encourage daily intake of tree nuts	3	3	2	3	11 (91.7)

#Median denotes the score lying at midpoint of scores chosen by participants
*Mode denotes the score that is chosen most frequently
+Min denotes the lowest score chosen by participants
^Max denotes the highest score chosen by participants

Based on the findings from the Delphi process, the final order of Parts 1 and 2 indicators is shown in Table 3.13. Each indicator appears in the same order as chosen by the Delphi participants. The predetermined consensus level for this research was set at 60% and 36/38 (94.7%) indicators achieved consensus at this level.

Table 3.13: The order of appearance of indicators in Simpler™ hand-out based on outcomes from the Delphi interview

Factors	Indicator
Statin	• Statin initiation in patients with CVD • Achieve targets: LDL, Malaysia (LDL<2.6mmol/L, TG<1.7mmol/L) Australia (LDL<2.0mmol/L), TG (<2.0mmol/L) • Statin initiation in patients over age 40 years without CVD and has one or more CVD risk factors
Insulin/Glycaemic control	• Insulin initiation if glycemic control not achieved despite being on two or more oral hypoglycemic agents • Target of HbA1c ≤ 7% (53mmol/mol) if no other complications • Management of hypoglycaemia • Self-monitoring of blood glucose Australia (4.0-6.0mmol/L fasting); Malaysia (4.4-7.0mmol/L fasting); ; Australia (8-10mmol/L, 2h postprandial). Malaysia (6-8mmol/L-2h postprandial) • Aim a reduction of 1% HbA1c • Initiate/continue metformin if not contraindicated
Medication	• Assess medication-related problems • Review medication adherence using 8-item MMMAS
Blood Pressure	• BP target: ≤130/80 • ACEI/ARB initiation in patients with or without microalbuminuria/proteinuria • Reduce sodium intake
Lifestyle	• Exercise: 30 mins walking (or equivalent) 5 or more days/week (total ≥150 min/week) • Weight loss: Australia (BMI<25kg/m^2) • Malaysia (BMI <23kg/m^2) • Smoking cessation • Waist circumference Australia (<94cm in men,<80cm in women, waist circumference), Malaysia (≤90cm in men,≤80cm in women) • Moderate alcohol intake: ≤2 standard drinks (20g) per day for men and women with max 4 standard drinks on any occasion • Management of stress& diabetes related distress • Erectile dysfunction: recommend PDE-5 inhibitor as first line therapy for male patients • Foot care • Diet advice using plate model • Annual eye assessment • Address sleep hygiene
Education	• Knowledge and understanding of medicine • Medicine storage • Medication optimisation during fasting month for Muslims and other religious groups

Factors	Indicator
CVD risk	• Aspirin therapy as secondary prevention in those with diabetes with history of CVD • Use of Framingham risk calculator to calculate CVD risk and educate patient • Aspirin therapy (75mg-162mg/day) as primary prevention to decrease CVD risk (10 year risk>10%, Framingham)

ACEI= angiotensin converting enzyme inhibitor; ARB=angiotensin receptor blocker; BP=blood pressure; CVD=cardiovascular disease; FRS=Framingham risk score; HbA1c=glycated haemoglobin; LDL=low density lipoprotein; PDE-5 inhibitor=phosphodiesterase-5 inhibitor; TG=triglyceride;

This section presented the results and briefly examined some of the reasons why an indicator was ranked a certain score. The following section will discuss possible explanations on the difference of opinions and potential reasons why certain indicators were not ranked as important as initially predicted.

3.5 Discussion

Phase One of the study was designed to construct and validate the contents of the Simpler™ tool as a management tool for diabetes mellitus. Phase One also aimed to determine the layout of the Simpler™ tool. The validation process followed has also been used in similar published studies.(179, 204-209) However, this will be the first published research to use the Delphi process involving diabetes experts from both Malaysia and Australia in the development of a diabetes intervention tool.

The effectiveness of using letters from an acronym to represent an intervention has been utilised in healthcare delivery for disease management such as:

- Asthma management through the SIMPLE tool that represents signposting, inhaler technique, Medication Review, Peak expiratory flow reading, lifestyle advice and health promotion and education.(187),
- Reducing harm in substance abuse through the FRAMES tool, which stands for feedback, responsibility, advice, menu, empathic, self-efficacy.(189) and
- In first aid treatment for injury through the RICE tool, which represents rest, icepacks, compression bandages and elevate.(237)

The decision to develop the Simpler™ tool was based on the premise that diabetes is a complicated disease and there are multiple factors involved in the management of diabetes. The Simpler™ tool aims to prompt health professionals to retrieve information quickly through a structured process that assists with organising of the information to formulate an intervention. The Simpler™ tool summarises seven fields of evidence-based factors from diabetes guidelines in delivering diabetes care namely cholesterol, glycaemic and BP control, medication, lifestyle, CVD risk management and provision of

education. Each letter of the Simpler™ tool acronym represents those seven individual factors. Although the indicators in the Simpler™ tool were based on widely published evidence, yet in terms of importance, the expert participants ranked certain indicators more important in diabetes management than others. The paragraphs below will postulate on the possible reasons under the separate factors.

3.5.1 Cholesterol control

Participants ranked statin initiation in patients with CVD as the most important, and this indicator was also strongly recommended in CPG from both Australia and Malaysia. Statin initiation in patients over age 40 years without CVD was ranked least important. This could be due to different recommendations from different CPG. While the Malaysian CPG recommends statin to be initiated in patients with diabetes over the age of 40 years regardless of baseline lipid levels, the Australian and American guidelines have slightly different recommendations. Recent Australian guidelines suggest initiation of a statin only on cardiovascular risk assessment regardless of age.(7) The 2016 American Diabetes Association Standards of Care recommendations, however, are to add statin therapy for patients with diabetes who are over the age of 40 years and have one or more CVD risk factors such as hypertension or a family history of CVD.(16) Both the Australian and American guidelines were published after concerns of poor glycaemic control with statin use.

3.5.2 Insulin/glycaemic control

The majority of the participants ranked the indicator: *aim a reduction of HbA1c* the least important. This could be because insulin targets are individualised and patients suffering from frequent hypoglycaemia or with multiple comorbidities would be at risk of further complications if aiming for a stringent target. This is in agreement with the ACCORD, ADVANCE, DCCT and VADT trials.(27-30)

There was uncertainty among the participants in ranking the indicator: *Initiation of metformin if no other contraindications*. The phrase *initiation of metformin…* caused some participants to rank it the least important as they indicated that metformin should be started first before initiating insulin. This is in agreement with diabetes CPG from Australia, Malaysia, the UK and the USA which emphasis metformin as first line agent for T2DM and strongly recommends continuing metformin even though the patient is on insulin.(6, 7, 16, 17) Therefore, the phrase *Initiation of metformin if no other contraindications* is changed to *Initiate/continue metformin if not contraindicated*.

3.5.3 Medication management

The indicator: *Assess medication-related problems* was ranked more important than the indicator: *Review medication adherence using 8-items MMMAS*. One reason could be that medication non-adherence is a MRP. This is also clarified in the Pharmaceutical Care Network Europe classification system and in previous studies where non-adherence is categorised as a MRP.(62, 238)

3.5.4 BP control

The observed importance on BP target: ≤130/80 mmHg as more important than other indicators could be attributed to overwhelming evidence that achieving the BP target can reduce morbidity. This evidence originates from both the UKPDS and the ACCORD trials.(26, 30) However, the target level for BP varies between the guidelines. The 2016/2018 Australian guidelines recommend target of ≤130/80 mmHg while the recent 2015 Malaysian CPG recommends <135/75 mmHg.(6, 7) The 2016 ADA Standards of Medical Care in Diabetes recommends <140/90 mmHg.(16) Due to changes in BP goals, the targets in the Simpler™ were ammended to follow the recent Malaysian CPG. In addition, Malaysian CPG recommends salt restriction in normotensive and hypertensive patients with diabetes to <2400 mg sodium/day or 6g of salt a day or 1 teaspoon. Salt in cooking is limited to a daily of ¼ to ½ teaspoonful for each person.(6)

3.5.5 Lifestyle

Exercise was rated more important than the other indicators in the lifestyle factor. A possible explanation for this might be due to compelling evidence on benefits of exercise in diabetes management.(239-244)

While most of the lifestyle indicators from Part 1 of the questionnaire were based on CPG from both Australia and Malaysia, the indicators from Part 2 were from published clinical trials. Surprisingly, the majority of participants did not rank the indicators as being important. Comments from participants suggest insufficient studies to support the safety and efficacy of these recommendations. The participants' comments seemed to

be consistent with studies indicating a need for trials that are larger and of longer duration.(227, 245)

For instance, the first indicator that did not score well on the Likert scale was indicator: *Administer once daily antihypertensive at bedtime* despite graded as the highest level of evidence in ADA standards of medical care which suggests to "administer one or more antihypertensives at bedtime".(16, 246) This bedtime recommendation is based on studies which found dosing of antihypertensives reduced CVD events and achieved better BP control.(247, 248). Six trials were conducted among hypertensive patients who had diabetes or Chronic Kidney Disease. However, the number of trials do not reflect a diverse population. Additionally, the class of antihypertensive medicine that should be taken at bedtime were not studied. However, the more recent 2015 Malaysia Guidelines and 2016 ADA Standards of medical Care in diabetes recommend one or more antihypertensive medicine to be taken at bedtime. Both these guidelines grade this recommendations with the highest level of evidence.(6, 16) Based on this, the research team decided to include the indicator, *one or more antihypertensive medicine to be taken at bedtime* into the Simpler™ tool.

The second indicator that the panel of experts did not chose to be included in Simpler™ tool was indicator: *1g-3g cinnamon intake per day* to improve glycaemic control. This seem to be consistent with data obtained from a few randomised clinical trials which, although they have shown cinnamon to be effective in improving fasting blood glucose levels, the limitations in the these studies do not warrant the use of cinnamon in practice settings.(227-231) This is mainly because cinnamon doses and the formulations used in the trials varied and long-term effects are not known.

The third indicator which did not achieve concensus was the need to take *Vitamin B12 supplement in patients on long term metfomin*. Studies conducted in the Netherlands,

India, and the USA found evidence of vitamin B12 deficiency among patients on long term metformin.(245, 249, 250). Although these studies strongly suggest Vitamin B12 supplementation, long term large trials on the effectiveness of Vitamin B supplements in these patients are lacking.

The final indicator not selected was the *daily intake of tree nuts (almonds, brazil nuts, cashews, hazelnuts, macadamia, pecans, pine nuts, pistachios and walnuts).* A systematic review and meta analysis of 12 RCTs showed an association of tree nuts with significant improvement of HbA1c.(232) However the authors found inconsistencies in the studies and concluded that there was a need for larger trials that show evidence of long term effects.

3.5.6 Education

Patients with diabetes ranked "knowledge and understanding of medicine" to be most important. Several RCTs have shown that education alone can decrease HbA1c by 1% and simultaneously improve medication adherence.(124, 251-256) The need to have a structured education process to create awareness patients are, to some extent, addressed by diabetes nurse educators in Australia and in Malaysia. In comparison to pharmacists, they are not easily accessible as there is a need to be referred by a GP in both countries in the primary healthcare setting. Community pharmacists, on the other hand, are easily accessible with extended opening hours, therefore provision of diabetes services through pharmacies could enable more patients to be able to receive education. In the DMAS program conducted among 90 community pharmacies in Australia, it found pharmacists were equally competent to educate patients to self-manage and consequently contribute to better health outcomes.(257)

Education is also important in self-management of patients with diabetes during the fasting month for Muslims, Ramadan, and in other religious groups. Patients who were given education on disease management and their medications were found to have less weight gain and hypoglycaemia episodes.(258) Education tailored to these patient demographics has shown to clarify certain issues believed by some that drawing blood and insulin injections would nullify the fast.(259)

3.5.7 CVD risk factors

"Aspirin therapy (75mg-162mg/day) as a primary prevention strategy at increased CVD risk (10 year risk>10%, Framingham)" was ranked the least important. One participant wrote this as "controversial in primary care". This comment is consistent with the recent Australian guidelines in which aspirin is not recommended for the management of cardiovascular risk. Although, aspirin was strongly suggested in 2009 Malaysian CPG and currently the 2016 ADA standards of care, the 2015 Malaysian CPG recommends aspirin for primary care only if patients are above 65 years old.(6, 16, 49) Based on this recent high level evidence the research team felt it was important to add the words, *patients > 65 years old* to *Aspirin therapy (75mg-162mg/day) as primary prevention to decrease CVD risk (10 year risk>10%, Framingham).*

The majority of participants indicated that the Framingham risk calculator should be used to calculate CVD risk and educate patients as more important over other indicators. The most likely explanation could be due to data by World Health Organization showing that 50%-80% of mortality cases among patients with diabetes were due to CVD.(260)

The Simpler™ tool incorporated the results of the Delphi study and the recent 2015 Malaysian and 2016 ADA Standards of medical care.(6, 16)

3.5.8 Strengths of Phase One

The strengths of Phase One were the participation of a team of multidisciplinary professionals involved in diabetes care. Both in Malaysia and Australia, pharmacists, endocrinologists, diabetes nurse educators, dietitians and primary health care physicians (GPs) are part of diabetes teams. Diabetes guidelines from Malaysia, Australia, the UK and the USA stress the need for a multidisciplinary team in order to achieve clinical and health related QOL outcomes.(6, 7, 16, 17, 49, 51) Participants were chosen from the community, hospital, and academia and health administration covering both public and private sectors. The panel of experts were actively involved in the design of the Simpler™ tool in terms of the order of indicators, content and layout. Participants were purposively selected from a range of health professionals as the intention was for the Simpler™ tool to be used among healthcare practitioners from both countries and among a wide range of healthcare professionals. It is hoped that if these healthcare professionals are involved in the development of the Simpler™ tool, then there may be increased use of this tool in their respective professions. This distinction can be seen in several studies where tools developed by a wide range of professionals from different countries have found to be effective for their purpose.(205, 207, 209, 212)

Most participants provided positive comments on the tool and were supportive during the Simpler™ tool development phase. There were no dropouts during Rounds 2 and 3 which highlighted the second strength of this study.

Thirdly, the Delphi process took only three months to complete. In addition, consensus was achieved on 36 out of 38 indicators, which further suggests the importance of preselecting indicators rather than asking the participants for suggestions. Having a selection of indicators in the questionnaire meant that more indicators had a higher chance of achieving consensus. Similar results were also achieved in studies that preselected indicators before presenting them to the panel of experts, as indicated in Table 3.14.

Table 3.14: Response rate from participants and number of indicators that achieved consensus

Study	Type of study	Response rate from participants (%)	No. of indicators where consensus was achieved
Chang AM et al 2010 **(202)**	Validate a tool to measure competency standards for advance practice nursing role	93.8	37/42
Thomas SK et al 2013 **(209)**	Develop list of hospital prescribing indicators in order to standardize types of high risk errors to facilitate data collection	100	80/109
Parsons C et al 2014 (**(205)**	Categorize appropriate medications for patients with advance dementia	100	87/97
Spencer R et al 2014 **(208)**	Identify and update prescribing safety indicators for GP	100	23/56
Prot-Labarthe S et al 2014 **(206)**	Develop a screening tool to identify inappropriate prescribing and omissions for paediatrics	71.4	104/108

3.5.9 Limitations of Phase One

Although both Malaysia and Australia had similar diabetes practice guidelines, the guidelines did differ on aspirin therapy for cardiovascular risk prevention strategies. However, experts from both countries managed to arrive at a consensus despite this difference. The limitation of Simpler™ is that the validation method involved experts from only two countries namely Australia and Malaysia which means validation of the tool is needed in other countries. Nevertheless, due to similar practice guidelines in some countries, it is envisaged that the validation would not be a lengthy process.

All indicators in Part 1 and Part 2 of the Simpler™ tool were provided to the Delphi participants as done in previous research(179). This could have introduced bias in the participants' responses, as they were only required to give their opinions on pre-existing indicators. There was no requirement for them to contribute an indicator which may or may not have been important to be included in Simpler™. In addition, participants in the Delphi method gave their opinion based on their existing knowledge and experience.(217) Although, the indicators were from published RCTs, some still chose to base their opinion on current practice trends which may not be the best approach. Nevertheless, the Simpler™ questionnaire consisted of a combination of indicators required to be included in the hand-out and indicators which required consensus from the majority. Thus, not depending entirely on participants' opinions.(261)

Delphi rounds required much of participants' time and commitment. As the rounds, would have been repeated until consensus is achieved, some participants may have felt the need to conform to group's consensus in order to shorten the process. Despite that, the number of rounds to achieve consensus in studies mentioned in Table 3.1 were similar to number of rounds in this research.

3.5.10 The next stage

Diabetes is a complex disease and there are many factors involved in achieving appropriate glycaemic control and to prevent diabetes related complications. This phase of the research has construct validated these factors. Pharmacists can utilise the Simpler™ tool to facilitate targeted, consistent care and structured interventions in enhancing the quality of diabetes care. Ideally, the clinical benefit as well as health related QOL outcomes of the Simpler™ tool need to be evaluated. Phase Two of this research tested the tool in terms of feasibility, adaptability and reliability and further refined the Simpler™ tool. In Phase Three of the research, a randomised controlled trial were conducted to show the effectiveness of the tool in measuring evidence-based recommendations in addition to clinical and QOL outcomes.

Chapter 4
Pharmacists' Experience and Perceptions on Using the Simpler™ Tool

This chapter describes and discusses Phase Two of the study which was conducted between May and August 2015. This phase consisted of a pilot study evaluating the feasibility and adaptability of the Simpler™ tool in pharmacy practice settings. The contents of the Simpler™ tool were previously developed and validated in Phase One of the study. Phase Two involved the development of the Simpler™ training package and evaluation of pharmacists' knowledge before and after the training, their views on the training content and experiences and perceptions on using the tool in their daily practice. The chapter begins with an introduction on literature reviews followed by an explanation of Phase Two and the study design, participant recruitment from both Malaysia and Australia, development of the Simpler™ training modules and format of the training sessions. It then moves on to describe the interview guide, data collection and analysis.

4.1 Introduction

Increasingly, pharmacists in primary health care settings are expected to provide medication management services (MMS) that include working with patients on non-compliance issues, managing patients with multiple chronic disease conditions and regularly educating patients to improve quality use of medications.(118) As part of patient-centred care, emphasis is placed on effective use of medications through identification of MRPs, interviewing patients to explore reasons for non-compliance and documenting the care given to patients.(61) Patients with multiple comorbidities require complex care and are often on many medications.

Diabetes management, for instance, require pharmacists to address patient-centred issues that may prevent patients from achieving targeted therapeutic outcomes. These issues may include cultural eating patterns, inability to self-manage blood sugar levels,

unfavourable job conditions and emotional stress.(262, 263) Pharmacists who have practised in traditional roles such as dispensing medications might lack the confidence, skills and experience to address these patient-specific issues.(264, 265) Although continuous professional education or development (CPE/CPD) may address the need to increase pharmacists' knowledge, there is lack of studies documenting its effectiveness in improving pharmacists' competence in medication management. Studies that do are mostly subjective data based on participants' perception of its effectiveness rather than measured objective data.(266, 267)

There is evidence indicating that effective learning is enhanced by a cycle that includes observation, application, reflection and experience sharing.(268) Learning through experience also known as experiential learning is used in both the medical and nursing professions for continuing education.(269)

4.1.1 Credentialed diabetes pharmacist

Accreditation programs for pharmacists wishing to specialise in diabetes care such as the credentialed diabetes pharmacist incorporates experiential learning which involves supervised practice hours in MMS and an evaluation post completion.

Training and credentialing pharmacists in diabetes management equips them with the required knowledge to provide specialised diabetes services such as the provision of MMS. MMS were first introduced in the United States of America (USA) which enabled pharmacists to implement pharmaceutical care to solve medicine related issues and

achieve therapeutic outcome goals.(62) Since then, MMS have been adopted and practised in many countries.

4.1.1.1 Diabetes MMS in Malaysia

The process to become a credentialed MMS diabetes pharmacist in government funded hospitals and primary healthcare clinics in Malaysia includes a requirement to spend 38 hours of supervised practice hours in a diabetes medication management clinic, conducting inpatient ward rounds and clinical case assessments. The pharmacists are then required to undertake a written assessment on diabetes management according to local diabetes practice guidelines.(270)

4.1.1.2 Diabetes MMS in Australia

In comparison, MMS pharmacists from both public and private institutions wishing to be credentialed with the Australian Diabetes Educators Association (ADEA) are required to complete a post graduate certificate in diabetes education and a minimum of 1000 hours spent in practice to educate patients on self-management. In addition to practising pharmacists, other healthcare professionals such as nurses, medical practitioners, podiatrists, physiotherapists and dietitians are eligible to apply. As well as meeting the criteria of the national core competencies for credentialed diabetes educators, they are also required to complete a six-month mentoring program.(168) In order to be a credentialed diabetes educator, a candidate must have obtained a graduate certificate in diabetes education and management which is provided by various universities in Australia.

4.1.2 Short term diabetes management training program

Pharmacists however are not required to be credentialed to conduct MMS and therefore not all pharmacists undergo targeted diabetes management training to provide MMS to patients. Nevertheless, pharmacists' perceived lack of time was found to be a continued barrier for pharmacists' participation in short term training activities as reported in several studies.(166, 266, 271)

Various short-term diabetes management training programs targeted towards pharmacists have previously been developed and tested in the USA and in Australia. For instance, in 2010, pharmacists in the USA obtained diabetes management accreditation on completing 25 hours of a diabetes education program with the National Community Pharmacists Association (NCPA).(272) In Australia, the Pharmacy Diabetes Care Program (PDCP) under the DMAS pilot study was carried out under the Third and Fourth Community Pharmacy Agreements, funded by the Australian Government Department of Health and Ageing.(273) The PDCP was conducted between 2005 and 2010. It focused on the ongoing management and review of T2DM patients to facilitate quality use of medication. Pharmacists involved in the pilot had to complete a workshop of 14 hours which incorporated diabetes management, motivational interviewing and goal setting.(274, 275)

Both the training programs mentioned above focused more on patient education and self-care aspects of diabetes management and less on the clinical aspects of the disease such as evidence-based medication management. Thus, there was a lack of a diabetes training program that emphasised on evidence-based best practice and the clinical skills, which include patient case assessment, provision of monitoring plans and documenting interventions.

A 2010 study identified the need for training programs which integrate theory into practice to boost pharmacists' confidence in MMS.(264) Therefore, a short-term diabetes management training program focused on clinical aspects of diabetes and which incorporated application of theory into practice were taken into consideration during the Simpler™ training modules design phase.

Australia and Malaysia were chosen as study sites based on their similarities. Firstly, community pharmacists from Australia and primary health care pharmacists from Malaysia provided diabetes MMS to ambulatory patients.(4, 10) Secondly, both countries had similar diabetes management guidelines.(6, 7) In addition, the research teams had strong connections in both countries which facilitated the recruitment process. While both countries shared some similarities, they did differ on income per capita. Malaysia is a developing country with much lower income per capita than Australia.(276) Thus, the piloting of the tool in both countries provided a unique opportunity to compare the tool's applicability and adaptability in different countries.

4.2 Objectives

The aim of this phase of the research was to develop a clinical training program on diabetes management incorporating the application of the Simpler™ tool. In addition, this phase of the research explored pharmacists' perceptions of the tool's relevance and usefulness in delivering quality diabetes care.

The specific objectives were to:

1. Describe the development and validation of the Simpler™ training modules,
2. Present the findings of the pre- and post-training questionnaire,

3. Report pharmacists' views on the Simpler™ training package and recommendations for further improvement, and
4. Explore pharmacists' perceptions on the utilisation of the Simpler™ tool as well as suggestions to improve the tool.

4.3 Method

This section describes the development of the Simpler™ training package, participant selection and recruitment, delivery and evaluation of the training content, development of the interview guide and finally the data analysis process.

4.3.1 Ethics approval

This study received ethics approval from the Curtin University Human Research Ethics Committee on 18 December 2014 (Approval number: RDHS-06-14). Ethics approval was also obtained from the Malaysian Medical Research & Ethics Committee, Ministry of Health on 15 May 2015 (Approval number: NMRR-15-339-24167 (IIR) (See Appendix 4.1&4.2). Throughout the study, the researcher respected all rights, cultures and beliefs of participants. Participants signed a consent form and were assured that their identity would remain confidential and extracts from their comments would be anonymous. They were also given the option to withdraw at any time. Participants were reimbursed for their time and effort. There were no ethical issues raised during this phase of the research. Data from audio recorders were erased once they were transcribed verbatim.

4.3.2 Study design

The development of the training package and the training sessions were conducted between January and June 2015 followed by participant interviews between July and August 2015. Prior to the interviews, participants had the opportunity to apply the tool in practice for a four-week trial period.

Pharmacists from both countries were trained to use the tool for skill uniformity before utilising the tool in practice. This phase of the study explored the views of pharmacists from both countries on the tool usage in their practice setting and whether their views were different. The sample of participants from both countries were conveniently selected based on the following criteria:

1. Being a full time registered pharmacist
2. Involved in the provision of diabetes MMS;
3. Have not undergone formal diabetes training;
4. Willing and available to participate in the research.

A recent systematic review on 11 studies conducted from 2001 to 2012 concluded that on-line learning or e-learning improved pharmacists' knowledge immediately following training.(277) Given that the same review showed e-learning to be equally as effective as face-to-face learning provided that sufficient support is administered, a decision was made to conduct e-learning (on-line, self-directed learning) in addition to face-to-face training. Since the student researcher was in Australia at time of the study, face-to-face training sessions were conducted on the Australian participants first, followed by e-learning sessions for the Malaysian participants.

The Simpler™ training content incorporated patient case studies to enhance pharmacists' knowledge. Simulation exercises using virtual patients, live actors or patient case studies similar to patients in real practice settings have been used before to train medical and nursing students.(269) Similar formats utilising case studies in medication management training programs for pharmacy students have also been reported.(278, 279) The examples used in the case studies were based on the student's experience conducting diabetes medication reviews and as a preceptor supervising registered pharmacists to become credentialed diabetes pharmacists.

The Simpler™ training package also incorporated pre- and post-training questionnaires which tested pharmacists' knowledge, attitudes and practice before and after the training. Several studies have used a similar process in assessing pharmacists' knowledge, attitudes and practice through the completion of a questionnaire before and after being given training on disease management.(280-284) Studies suggest that statistically significant improvement in the scores before and after training demonstrates the effectiveness of the training program.

To investigate the feasibility and adaptability of using the Simpler™ tool in practice, participating pharmacists were given a four-week trial period on completion of the training session to use the tool before an in-depth interview was conducted. To develop an overall framework for the interview process, Kvale's seven stages for conducting interviews was utilised followed by the requirements of consolidated criteria for reporting qualitative research guidelines (COREQ).(285) The seven stages are as follows.(286):

1. Thematising: Determining the purpose of the interview
2. Designing: The design of the qualitative study took account of the contracted knowledge

3. Interviewing: Interview conducted in accordance with the interview guide
4. Transcribing: Verbal interview to be transcribed into written form for analysis
5. Analysing: Analysing interview using an appropriate method. In this case, the framework method for qualitative data analysis was applied.(287, 288)
6. Verifying: to establish the reliability of the results in terms of consistency and the validity which refers to what needs to be investigated
7. Reporting: Reveal the findings of the study

Taking into consideration the research aim and objectives, this phase of the study used mixed methodology that consisted of qualitative and quantitative data collection. Quantitative data were used to analyse the difference between pre- and post-training responses while qualitative analysis was used to gain insight into pharmacists' opinions, views and perceptions of the Simpler™ tool.

Qualitative methodology was suggested by Strauss and Corbin to be the appropriate choice when more in-depth research was required about a phenomenon or experience.(289) The qualitative component consisted of interviews which allowed an understanding of experiences through participants' perspective and beliefs.(290, 291) The ability of qualitative study to explore the abstract side of behaviour such as frustration, achievement and difficulty was considered more helpful than capturing the magnitude of usefulness using a Likert scale as suggested in previous literature.(292)

The following sections will describe the development of the Simpler™ training package including the development of training objectives, the pre-and post-training questionnaire and the training modules. This is followed by pharmacist criteria involved in the recruitment process. The duration of training sessions and the steps involved are further described. Following the training, pharmacist experience utilising the Simpler™ tool is explored through semi structured interviews. Data obtained from the pre- and

post-training assessment were analysed quantitatively for differences in performance. Recurring topics from the interview data were investigated using qualitative framework method as suggested by Boyatzis.(287) Phase Two research outline is illustrated in Figure 4.1.

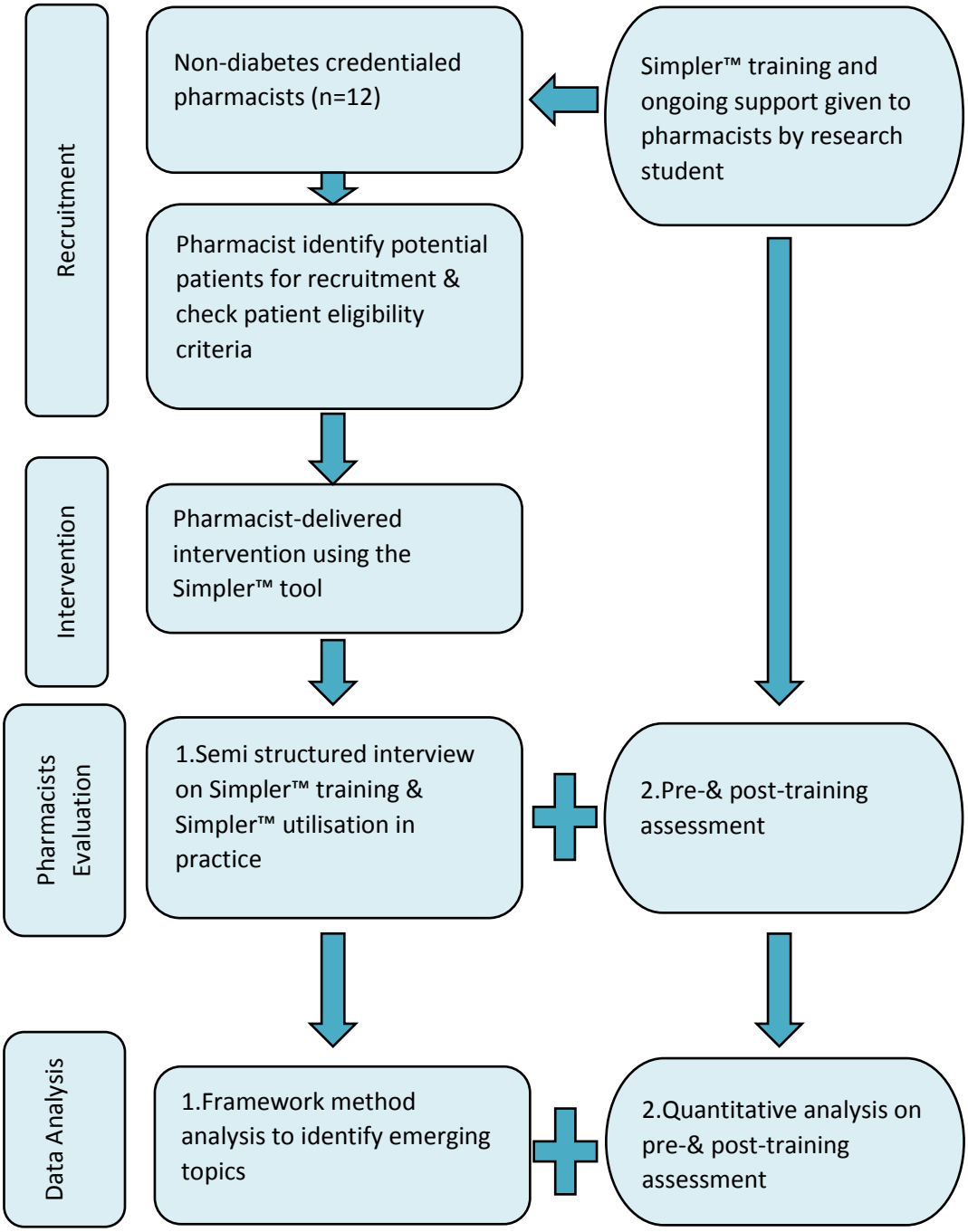


Figure 4.1*:* Phase 2 research workflow

4.3.3 Development of the Simpler™ training package

The objectives of the Simpler™ training were constructed using Bloom's taxonomy for knowledge-based goals, skills-based goals and affective goals.(293) On completion, participants should have demonstrated an understanding of a pharmacist's role in providing diabetes care and how the Simpler™ tool facilitates the provision of structured diabetes care. In practice, they should have been able to apply the tool to identify reasons for therapeutic failure and solve the issues by providing evidence-based suggestions using a systematic approach. The following factors informed the design of the modules:

1. Relevance to practising pharmacists
2. Based on evidence-based practices, as per local diabetes practice guidelines
3. Easily accessible via on-line modules
4. Comprised of clinical scenarios that simulate real practice to facilitate knowledge application
5. Short, concise and incorporated a practice session
6. Included pre- and post-training assessments

The topics selected were based on another study on a pharmacists' training program that aimed to cover patient-centred care. That study demonstrated an improvement in pharmacists' skills and knowledge.(280) In addition, an overview of local diabetes practice guidelines such as the Australian general practice management of type 2 diabetes (7) and the Malaysian diabetes clinical practice guideline (6) were considered important to be included.

The training programme outline, pre- and post-training questions, and presentation slides were peer-reviewed by three academics from the School of Pharmacy, Curtin University. The accuracy, typographical, grammatical and formatting errors were rectified before the pilot testing by two Malaysian and two Australian pharmacists

who were experienced in the management of patients with diabetes. The pharmacists provided feedback on the accuracy, content validity and appropriateness of the training modules.

4.3.3.1 The Simpler™ training modules

The Simpler™ training package included four modules, Modules 1, 2, 3 and 4. The content of each module was informed by the results of the Australian government department of health and ageing pharmacists' diabetes pilot program.(275) In the final report, the pharmacists found the content useful, although they described the training being more theoretical than practical and requested for more concise information. This feedback was taken into consideration in designing the Phase Two training package.

Participants had to complete module 1 first before starting on the next module in ascending order. The learning objectives and goals are shown in Table 4.1. The duration of the training session were two hours and twenty minutes to complete pre- and post-training questionnaire. The two-hour time frame was chosen given pharmacists time constraints for participation in training as mentioned in section 4.1.2.

Table 4.1: Simpler™ modules contents and goals

Module no.	Module title	Module content	Module goals
1.	Introduction	1. Describe the pharmacist's role in management of type 2 Diabetes Mellitus 2. Explain the research objectives and significance 3. Outline the research plan and present results of the Phase 1 study	To provide an overview and understanding of pharmacists' role in diabetes management.
2.	Simpler™ tool validation	1. Outline and describe the seven indicators incorporated into Simpler™ 2. Explain the benefits of Simpler™ using evidence-based information	To help pharmacists understand the Simpler™ tool development and evaluation process to increase confidence in its usage
3.	Case study discussion	1. Outline the information gathering process 2. Practise effective intervention using the Simpler™ tool	To analyse the causes of therapeutic failure in case study example. To demonstrate and apply the Simpler™ tool to solve the issues. To justify each suggestion with evidence-based information using the Simpler™ tool
4.	Writing intervention Notes	Writing case notes/*GuildCare using Simpler™	To compose patient notes using a systematic approach for writing

*GuildCare refers to the software used by Australian pharmacists to record and report patient information.

Module 1 consisted of a 15-minute slide presentation. It provided an introduction to the prevalence of diabetes in Australia and Malaysia and highlighted the urgency in preventing complications among patients. It also described the methods used to rank, prioritize and construct validate the content of the Simpler™ tool.

Module 2 consisted of a 30-minute slide presentation. It outlined the seven indicators incorporated into the Simpler™ tool. It also explained the benefits of using the tool as an evidence-based source as per local diabetes practice guidelines. It also incorporated the medication management service (MMS) model.

Module 3 encompassed a practice session on a patient interview to obtain medication management and compliance information. It also included a session on using the Simpler™ tool to facilitate provision of pharmaceutical care.

Module 4 comprised of the legal aspects pertaining to writing in patients' medical notes. It also included a practice session on recording of observations, interventions and writing a pharmacist care plan.

A more detailed Simpler™ training program outline consisting of modules 1 to 4 is at Appendix 4.3. Appendix 4.4 presents the hand-out version of modules one to four slide presentations. Figure 4.2 below summarises the flow of the training process.

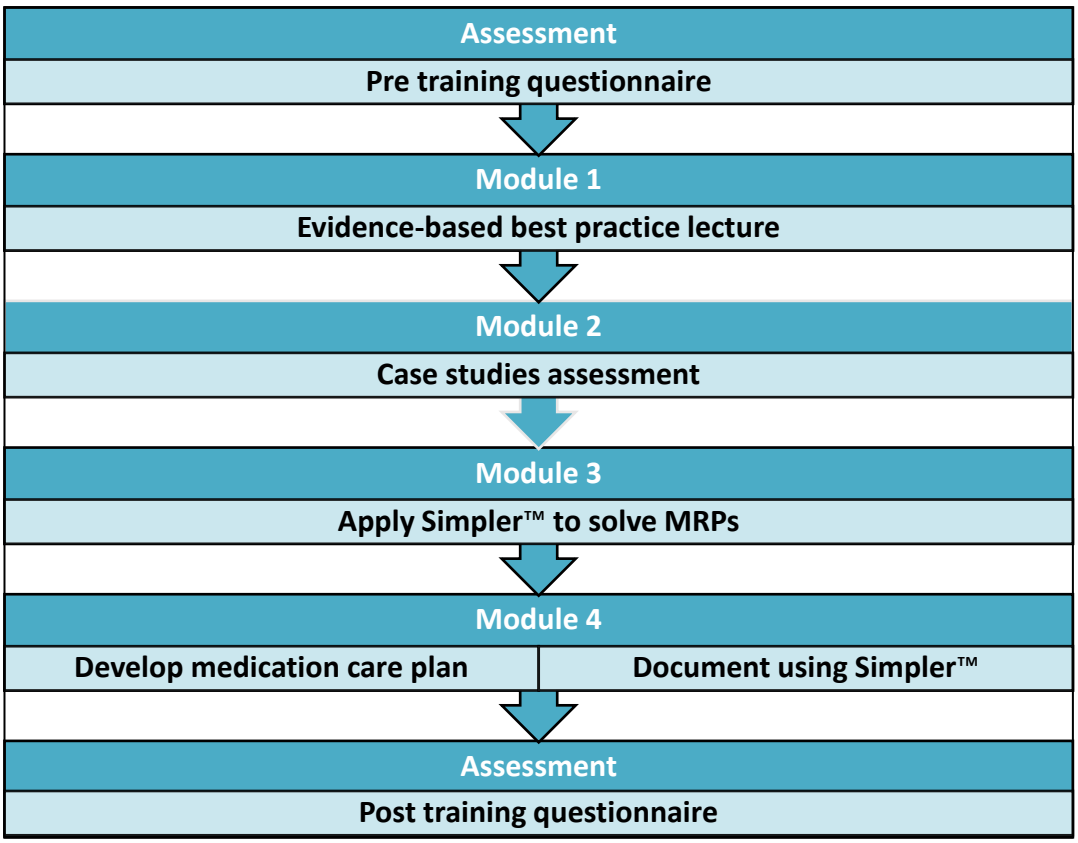


Figure 4.2: Flow chart summarises the flow of the Simpler™ tool training process

Although the contents of practice guidelines from Australia and Malaysia remained generally the same, they did differ in terms of cholesterol, BGL and BMI goals of treatment. Therefore, two versions of the training modules were designed. The Australian version comprised of diabetes management goals according to Australian general practice management of type 2 diabetes.(7) While the Malaysian modules incorporated diabetes management goals and targets according Malaysian guidelines for diabetes.(6) The Malaysian version of the modules were given a voice-over and pre-recorded. Subsequently they were uploaded into a cloud service, the Google drive. The link to the pre-recorded modules in Google drive were sent to the participant's email address. Participants from Malaysia could access the training modules by clicking on this link. A visual presentation of the training modules is shown in Figure 4.3.

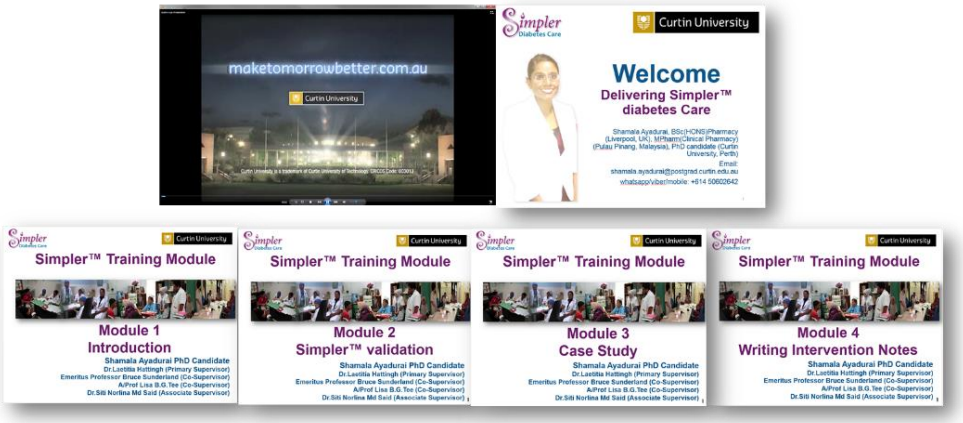


Figure 4.3: Overview of training modules uploaded into the cloud service.

4.3.3.2 Participant resources

Resources were provided to each pharmacist to facilitate the effective application of the Simpler™ tool in practice. These included:

- A hand-out version of the slide presentations (Appendix 4.4)
- A page with relevant websites mentioned in the training modules (Appendix 4.5)
- The Simpler™ tool hand-out (Appendix 4.6)
- Link to the video presentations of Modules 1-4 (only available to Malaysian participants)
- The researcher's (SA) telephone number. An Australian mobile number was available for Australian participants and Malaysian pharmacists used a mobile application called *WhatsApp*.

4.3.4 Recruitment of participants

The aim of qualitative analysis was to explore questions in detail until no new theories emerged known as the saturation point.(294) Literature on sample size determinants for qualitative study provided some guidance on selecting appropriate numbers of

participants.(295) For qualitative research on lived experience of a participant, a sample size between five and 25 is acceptable.(290, 296) Taking this factor into consideration and pharmacists' potential time constraints (297, 298), 13 pharmacists were recruited for Phase Two, namely seven from Australia and six from Malaysia.

The target participants were primary health care pharmacists who provided MMS for patients with diabetes and in full-time employment. As mentioned previously, in Malaysia this is known as Medication Therapy Adherence Clinic (MTAC Diabetes) and in Australia it is known as Diabetes MedsCheck. In addition, the participants chosen were not credentialed diabetes pharmacists.

Participants were recruited through personal contacts of the researchers as well as through snowball recruitment. Pharmacists in Australia worked at privately owned community pharmacies while pharmacists from Malaysia worked in government funded primary health care clinics. Six pharmacists from Johor, Malaysia and seven from Perth, Australia expressed interest. An introductory letter was sent to these pharmacists with details about the research (Appendix 4.7).

Participants who agreed were subsequently supplied with a participant information sheet (Appendix 4.8) and consent form (Appendix 4.9) (via email to participants who have given their email contact). Participants were given the opportunity to address any questions. One participant from Australia who had initially expressed interest to participate left the study, therefore the final number of participants were 12.

Once signed consent forms were received the training began. A link was given via email to participants who were doing it on-line. All participants were allocated a unique identification number. They were assigned the letter P. Participants from Australia were numbered 1 to 6 and letter A was assigned. Participants from Malaysia were also numbered 1 to 6 but instead letter M was assigned.

4.3.5 Training session evaluations

The face-to-face training sessions for the six Australian participants took two hours and were repeated to three groups of two pharmacists each to work around the participants' availabilities. Pharmacists were given 10 minutes to complete the pre-training questions as well as 10 minutes at the end of the training session to answer the post-training questions. Completed pre- and post-training questions were collected at the end of the sessions.

The six Malaysian participants had to complete the pre-training questions before being provided the link to the video presentations of Modules 1 to 4 which took approximately two hours to complete. They were given a two-week deadline to complete the modules. Upon completion, the pharmacists were requested to complete the post-training questions.

4.3.5.1 Pre- and post-training questionnaire

The intention of the pre- and post-training questionnaire was to assess the knowledge and skills of pharmacists before and after undergoing the training. The questionnaire was developed and validated by three university academics and four pharmacists with community and hospital backgrounds from Australia and Malaysia. The questionnaire contained two sections; section A and section B as follows:

Section A: Five closed ended questions directed at participants' training background and practices at the time of study.

Section B: This section aimed to test participants' knowledge on diabetes guidelines and skills in making medication management interventions in patients with diabetes. It included two open ended questions based on a patient case scenario. The questions from the second section were repeated following the training session

through the post-test. The pre- and post-training questionnaire is attached (Appendix 4.10).

A marking scheme was developed (Appendix 4.11). Each point answered correctly was awarded one mark. The marking scheme was validated by an independent pharmacist. Feedback on inconsistency and answer variations led to the amendment of the marking scheme and the revised version is at Appendix 4.12. Two markers marked both the pre- and post-training questionnaires, providing quality control. Final marks from each marker were analysed separately for significant improvement between pre- and post-training. The findings are presented in the results section.

4.3.6 Semi-structured interviews

Semi structured interviews were conducted to obtain detailed information on the participants' experience in using the Simpler™ tool. Face-to-face interviews were conducted with participants who were available to meet at an appropriate time and venue (i.e. private room in the community pharmacy). Telephone interviews were arranged for those who were not able to have face-to-face interviews mainly due to geographical reasons and work commitments. All interviews were conducted to ensure privacy and confidentiality. The main points covered in the interview were presented to the interviewees prior to the interview. The interviewer followed the interview guide, allowed room for probing questions but at the same time was able to follow interesting points raised during the conversation not covered in the interview guide but relevant to the aim of the study. At other times, the interviewer had to rephrase the questions in another language due to English being the second language for some interviewees. The interviewer ended the interview when all questions were exhausted and no new information was obtained. Interviews were recorded using an audio recorder to focus on the discussion. Audio recordings were

saved with the same corresponding identification code allocated earlier to participants. Recorded interviews were transcribed verbatim. Member of the research team checked all transcriptions for accuracy against the audio recordings as a quality check.

4.3.6.1 Interview guide

The interview guide was developed to obtain feedback on the effectiveness of the training modules and the Simpler™ tool. Questions focused on the perceived benefits, relevance and areas of improvement. Members of the research team reviewed the content and amendments including changing some of the questions from closed-ended to open-ended questions to obtain more information.

The aim of the interview questions was to serve as a guide during the interview session. The key overarching questions were questions such as; "Please comment on your experience in using the Simpler™ tool"; "How are the medication reviews with patients with diabetes different now compared to when you were not using the Simpler™ tool?" and "What recommendations would you make to enhance the feasibility of the tool?". Questions were divided into three sections (refer to Appendix 4.13 for interview guide). Below is an overview of the interview guide:

1. Section A: Eight close ended demographic questions on pharmacist practice experience, post-graduate qualifications, diabetes management training and practical experience.
2. Section B: Three close ended questions on their experience in conducting Diabetes MedsCheck or working as a MTAC diabetes pharmacist, existing tools or checklists used as an aid in making pharmaceutical interventions and reference to local diabetes practice guidelines.
3. Section C: Eight open ended questions with some sub-questions. Question one intended to probe participants on the relevance, ease of use and

practicality of the Simpler™ tool. Question two included question on the number of times pharmacists used Simpler™ to provide diabetes care. Questions three to seven talked about the positive aspect of Simpler™ and requested suggestions for improvement to the training modules and the tool. The final question number eight focussed on any additional comments from participants.

4.3.7 Data analysis

Data analysis was conducted separately for the pre- and post-training questionnaires and for the semi structured interview. The data were analysed using quantitative methods for close ended questions and qualitative methods for open ended questions. Descriptive data analysis was performed using SPSS 22.0.(233) To assess if there was a significant difference between pre and post-training scores, the Wilcoxon Signed Rank Test for non-parametric test was used. The Mann-Whitney U test was used to detect practice differences between Australian and Malaysian pharmacists. The non-parametric test was used as the sample size was too small and did not meet the sample size requirement for parametric testing.

For the qualitative analysis, the analytical process followed the framework method for thematic analysis.(287, 288) The task of transcribing the data was conducted by the candidate in order to become immersed and acquainted with the data as suggested by the qualitative framework method.(288) The open ended research questions were used as a guide in looking for emerging patterns. The transcripts were coded according to the interview questions which became the topics. Additional topics apart from the interview questions emerged during the analysis. Participants' raw data were highlighted in order to identify sentences or keywords which were assigned a descriptive label called 'codes'. The codes were subsequently sorted into categories. The transcribed data were read multiple times for the candidate to gain

familiarisation. Different viewpoints under the same category were grouped as subtopics. Nvivo 10 software (299) facilitated the categorizing and data organization. The candidate scrutinised the data again for new subtopics. Research project supervisors (HLH,VBS,LBGT) verified the analytical process before finalising the analysis.

4.4 Results

The findings from the pre- and post-training questionnaires and interviews with the 12 pharmacists from Malaysia and Australia are presented in the following sections. Section 4.4.1 represents the participants' demographic and practice experience data. The data was obtained from both section A of the pre-training questionnaire as well as section A of the interview guide. The thematic analysis results from sections B and C of the interview guide is represented in section 4.4.2.

4.4.1 Participant demographic and diabetes practice experience data

Participants' demographic data is presented in Table 4.2 with details on their age, country of practice, gender, working hours per week and practice information. As stated previously the inclusion criteria included not being a credentialed diabetes pharmacist and thus the participants did not previously undergo any credentialed formal training on diabetes management. Statistical representation of selected demographic information is shown in Table 4.3.

4.4.1.1 Demographic data

There was equal representation of participants from Australia (n=6) and Malaysia (n=6). The average age of participants were 30.3 years (range 25-48 years old) with the majority (7/12) under the 25 to 27 years' age range. The average working hours per week were 40.5 hours. Most participants were female (11/12).

Table 4.2: Australian and Malaysian participant demographics and practice information

ID	Age	Country	Gender	Average Working hours/week	Years of practice
P1M	30	Malaysia	Female	38.5	2
P2A	27	Australia	Female	38.0	4
P2M	25	Malaysia	Female	38.5	2
P3A	27	Australia	Female	41.5	2
P3M	26	Malaysia	Female	38.5	2
P4A	27	Australia	Female	45.0	3
P4M	37	Malaysia	Female	38.5	7
P5A	30	Australia	Male	42.0	6
P5M	35	Malaysia	Female	38.5	8
P6A	48	Australia	Female	45.0	27
P6M	26	Malaysia	Female	38.5	2
P7A	25	Australia	Female	35.0	3

Table 4.3: Statistical representation of participant demographic and practice information

Parameters	Mean (SD)	Median (IQR)	Minimum	Maximum
Age	30.3 (6.8)	27 (7.8)	25.0	48.0
Working hours/week	40.5 (2.9)	38.5(5.8)	38.0	45.0
Years practicing as pharmacist	5.7 (7.1)	2.6(5)	2.0	27.0

SD= standard deviation; IQR= interquartile range

4.4.1.2 Diabetes practice experience

Participants' pharmacy work experience ranged from two years to 27 years with an average of 5.7 years. The majority (66.7%; 8/12) had less than five years of pharmacy practice experience. However, in terms of experience conducting Diabetes MedsCheck services or MTAC Diabetes, the majority (75%; 9/12) of participants had less than three years' experience (see Figure 4.4)

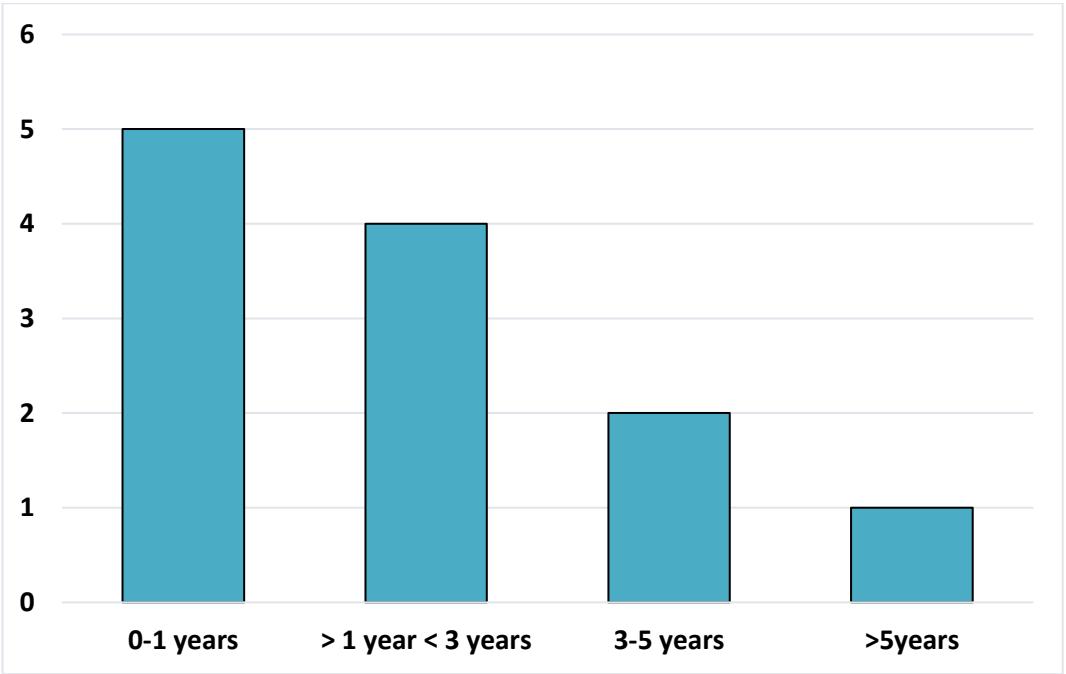


Figure 4.4: Length of years conducting diabetes MedsCheck or MTAC Diabetes

4.4.2 Training session evaluations

Training background included postgraduate degrees or qualifications. One participant was accredited with the Australian Association of Consultant Pharmacy to conduct medication reviews. The remaining participants did not have any postgraduate qualifications. Five participants from Malaysia and two from Australia previously attended a one-day training course on conducting diabetes medication management review.

4.4.2.1 Factors that motivated pharmacist to participate in research

Participants had to rank the reason for factors that impacted on their decision to participate in the study according to six categories using a Likert Scale: 1 to 5 (1= most motivating and 5= least motivating). The categories were as follows:

- Obtaining CPD points
- Financial reimbursements
- Interest in the subject
- It was recommended to me
- I want to improve patient outcomes
- Others

Figure 4.5 presents participants' responses. During analysis of the data the Likert scales were reversed to 1 being the least motivating and 5 being the most motivating to allow for easier data interpretation. In the *others* category, one participant mentioned "*want to learn more about this subject"* and another participant cited "*to improve my knowledge in MTAC Diabetes"* as reasons that motivated them to join the research.

The categories that most participants selected which fell in the upper quartile range of the Likert scale (namely 4 and 5) were *Interest in the subject* (83.3%; 10/12) and

Improve patient's outcomes (91.7%; 11/12). Of interest was that most participants (58.3%; 7/12) ranked *Financial reimbursements* as a low motivator (lower quartile range).

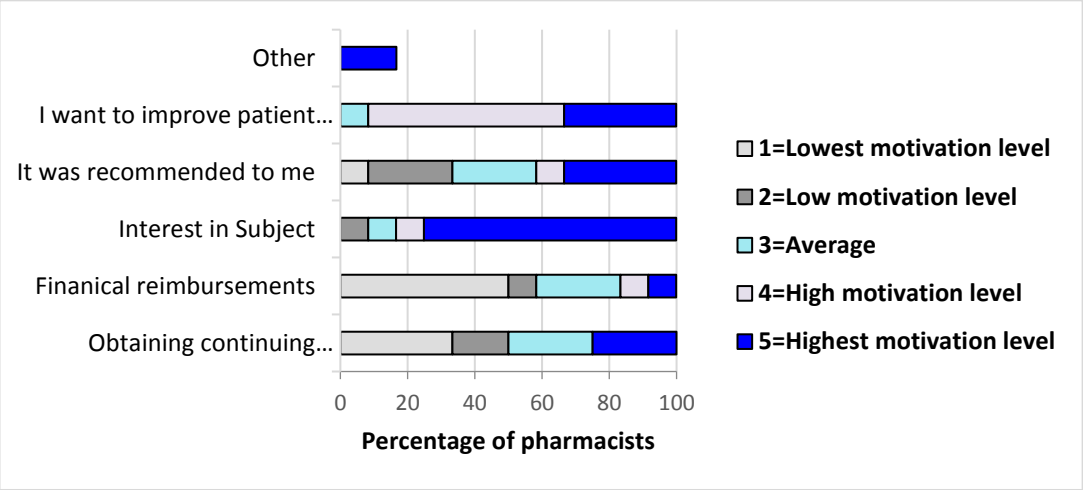


Figure 4.5: Breakdown of factors that motivated pharmacists to participate in the research

4.4.2.2 Pre- and post-training scores

Participants' knowledge was tested using the pre-training questions (before the training programme) and the same questions were repeated after the training (post-training). Two independent markers marked the answers. There was a significant improvement in post-training scores (*P*=0.002). Before attending the training session, the median test score for participants from 1st and 2nd markers were 6.0 (IqR 1.31). The full marks being 27 marks. After attending the training program, the scores improved to 13.25/27, IqR 2.56. The difference in pre- and post-test scores were as shown in Table 4.4.

Table 4.4: Pre- and post-training scores of participants (n=12)

	Median (IqR)		Z stat	[a]p value
	Pre-test	Post-test		
Test score (1st marker)	6.5 (1.4)	14.3 (4.5)	-3.063	*0.002
Test score (2nd marker)	5.3 (2.0)	11.3 (3.1)	-3.065	*0.002
1st and 2nd marker	6.0 (1.31)	13.25 (2.56)	-3.062	*0.002

IqR=interquartile range; Z-stat=number of standard deviations from the mean
[a] *p*-value from Wilcoxon signed ranks test; [b] statistically significant

4.4.3 Semi-structured interviews

The following sections report the findings obtained from sections B and C of the interview guide. The findings of participants' diabetes practice experience (section B of the interview guide) is presented first followed by a thematic analysis of section C data. The thematic analysis followed the COREQ requirements.(285) The analysis covered descriptive qualitative data followed by the thematic findings. Quotes from participants' data is included as supporting evidence for the key topics. As previously explained, participants' identity was replaced with codes to maintain anonymity.

All 12 pharmacists participated in the interview. Prior to being interviewed, participants were given one month to familiarize themselves with the Simpler™ tool. The average duration of the interview was 32 minutes. The length of the face-to-face interviews ranged between 19 to 32 minutes (average= 26 mins) and the telephone interviews ranged between 16 to 54 minutes (average= 36 mins). Face-to-face interviews were conducted with four pharmacists and telephone interviews with the remaining eight pharmacists.

4.4.3.1 Number of patients seen by participants

A comparison of baseline data between Australian and Malaysian participants revealed a difference between the average number of patients seen by participants per month, with 4.3 patients on average (SD=2.3) in Australia and 19.8 (SD=13.3) in Malaysia respectively. This difference was statistically different using the Mann-Whitney U test, P=0.015 (P<0.05 is significant). Figure 4.6 provides a graphical representation of this and other variables.

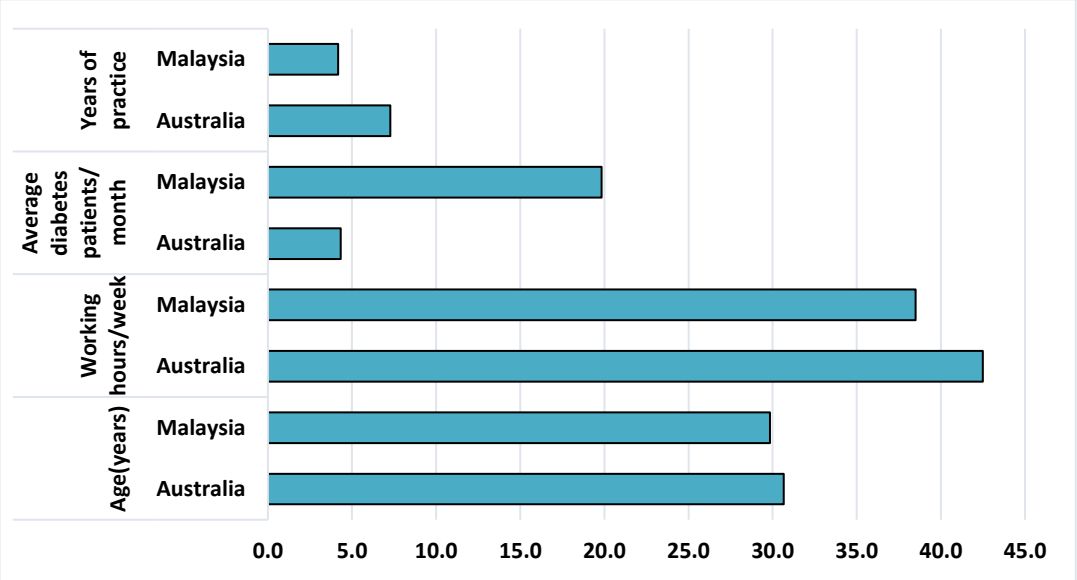


Figure 4.6: Pharmacy practice differences between Australian and Malaysian pharmacists

4.4.3.2 Diabetes practice guidelines as source of reference

All participants referred to a documentation guideline for MMS protocol on the management of patients with diabetes when asked about their reference sources. Most Malaysian pharmacists used the standardized MTAC diabetes form to report their interventions. Australian pharmacists on the other hand used a software program (GuildCare®) to document relevant information. Interestingly, most

pharmacists (66.7%; 8/12) had never or only sometimes referred to the Australian or Malaysian diabetes practice guidelines when providing diabetes MMS (Figure 4.7). The guidelines referred to was the Malaysian 'Clinical practice guidelines, management of type 2 diabetes, 2015 and the Royal Australian College of General Practitioners and Diabetes Australia, general practice management of type 2 diabetes, 2016-18.(6, 7)

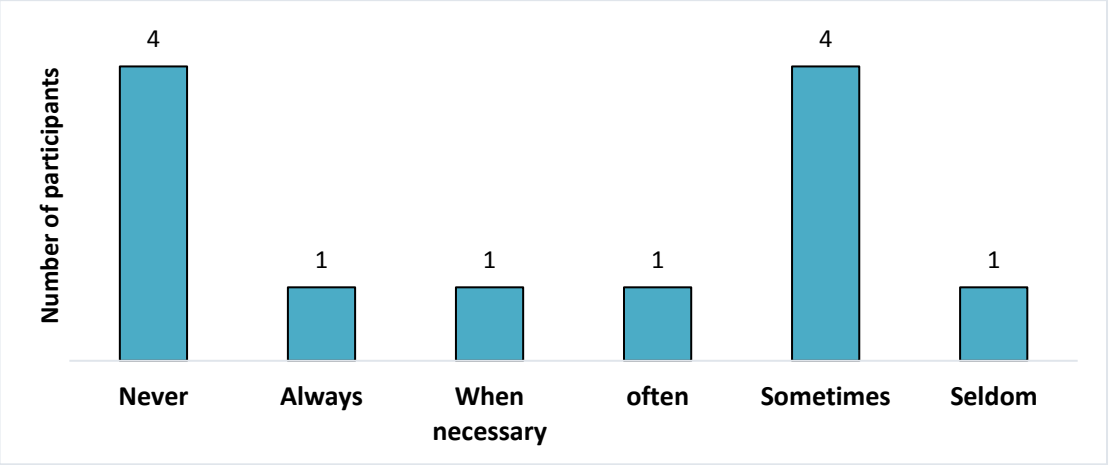


Figure 4.7: Participant referral frequency to Australian or Malaysian diabetes practice guideline

4.4.3.3 Perceived effectiveness of the Simpler™ tool

Participants' perception on the effectiveness of Simpler™ in utilising the seven diabetes factors to make evidence-based interventions was further explored (interview guide question 1 of Section C). All 12 interviewees found the Simpler™ tool to be useful when conducting medication reviews with patients. Three specific topics emerged around the perceived effectiveness of the tool namely:

1. The content was found to be relevant, structured, concise and easy to understand,
2. The tool was found to be a point of reference, and
3. The tool was a reminder of the factors associated with diabetes management.

4.4.3.4 Participants' view on Simpler™ tool's content

Participants used words such as 'organized', 'sequential', 'straight to the point', 'my accounting made relevant', 'compact', 'complete' and 'easiest tool' to describe the contents. Box 4.1 provides example quotes from participants.

Box 4.1: Key quotes from participants on the contents of the Simpler™ tool

Well I think that diabetes is so overwhelming, you just don't know where to start, how to begin so having a structured approach is very beneficial. (P6A)

The existing diabetes guide for pharmacists are not as complete as yours. (P4M)

I just want talk about education, the part about the medication storage. This is a very important thing because one always do not think about medication storage. (P2M)

We think this is straight to the point. The existing guide for pharmacists, can be irrelevant and quite time consuming for us to go through. (P5A)

Simpler tool is a compact tool and one of the easiest tool. In one word, you can summarize everything. (P1M)

Patients deviate, I come back I might have missed the blood pressure component but with this one, when they deviate, I need to go through all these checklist, all these points, so it's a good thing. (P3A)

4.4.3.5 The Simpler™ tool was found to be a point of reference

Participants from both Malaysia and Australia expressed their reliance on the Simpler™ tool:

Yes, because all the indicators in Simpler™ tool are proven from local guidelines and Australian guidelines so no one will dispute the contents. (P2M)

So far, I rely heavily on Simpler™ tool because it has all the targets and also it is based on Australian guidelines. (P2A)

The tool facilitated the recollection of the factors associated with diabetes management. One pharmacist described the tool as a 'simplification tool'. Whilst some pharmacists portrayed it as a 'supplementary tool' others defined it as a 'referral technique'.

4.4.3.6 Types of interventions made using the Simpler™ tool

The following findings were responses from Questions 2 and 3 under Section C of the interview guide. On average Australian participants applied the Simpler™ tool on three patients each (3±2) whereas the Malaysian participants applied it on 10 patients each (10±5.5) over the four-week period. Most of the participants (11/12) used the Simpler™ tool to facilitate their intervention process. Participants reported making interventions using one or more Simpler™ tool indicators as shown in the data extracted during the interview. Table 4.5 presents the types of interventions made, the corresponding intervention in the Simpler™ tool and the supporting participants' quotes. Participants showed more confidence in suggesting additional medicines and recommending dose adjustment and managed to detect the reasons patients did not achieve therapeutic outcomes.

Table 4.5: Types of interventions made by pharmacists using the Simpler™ tool

Corresponding letter of Simpler™ tool	Type of Interventions	Supporting quotes
S Statin/Cholesterol control	Initiate statin	*So basically with [the] first patient, he was not on [a] statin, with Simpler™ that's the first thing I actually spoke to him about, because he is at high risk* (P7A)
I (Insulin/glycaemic control)	Suggestion to initiate metformin	*My first patient was not on metformin even though [it] is not contraindicated.* (P6M)
I (Insulin/glycaemic control)	Initiate insulin	*Patients with HbA1c constantly above 7% (53mmol/mol), I gave suggestions to start insulin*. (P1M)
M (Medication management)	Patient's compliance	*Yes, it was simply compliance because he was not seeing that this medication is necessary for him and that includes his diabetes medication* (P3A)
M (Medication Management)	MRPs identified	*Because blood sugar is not controlled, [the] doctor increased [the] metformin dosage from 1gm to 2gm but the script is for just immediate-release metformin 1g, 2 tablets at night which is the wrong dose because immediate-release dosing should be 1 tablet twice daily* (P5A) *I managed to do a quick medication review and found that his lipid dose, fenofibrate actually, was too high for a patient with creatinine clearance of 45 and I suggested [to the] doctor to change it to 96mg daily rather than 145mg daily.* (P5A)
L (Lifestyle management) I (Insulin/Glycaemic control)	Diet, foot care, BMI Hypoglycaemia management	*... I did a lot was lifestyle, when we talked about lifestyle she had hypoglycaemia so we talked about hypoglycaemia. This other patient has her BMI as 29 so we talked about BMI. She is quite eager so we talked about plate model. (*P2A) *His diabetes levels weren't well controlled and when we went through Simpler™, I realised his diet wasn't very healthy. So I went through the diet and he also mentioned that he doesn't check his feet regularly as well because with diabetes*

Corresponding letter of Simpler™ tool	Type of Interventions	Supporting quotes
		you need to get your foot checked regularly so I advised him the importance of checking his foot regularly. (P4A)
R (CVD risk reduction strategies)	Suggestion to initiate aspirin based on Framingham risk score	*Based on that, the patient fit the criteria to start aspirin, therefore I advised the patient and recorded the intervention* (P1M)

CVD= cardiovascular disease; BMI= body mass index; HbA1c= glycated haemoglobin; MRP= medication related problem

4.4.3.7 Comparison to previous practice

Responses from Question 4 under Section C of the interview guide indicated participants' increased confidence levels and differences in the way they practised patient reviews compared with those performed previously. One participant commented:

> *In my practice, I learnt something new because previously I did not write any intervention, I mean I just counselled the patient based on their medication but now I am comfortable to make an intervention. (P1M)*

All participants agreed that the tool facilitated the writing of interventions in patients' medical records. One participant reported that doctors were impressed with her detailed patients' notes.

> *Because I'm using Simpler™, I wrote clearly inside the patients' book, the doctor complimented that it was good and well written. They salute the pharmacy, but before this I only used simple words and my notes were incomplete.* (P4M)

One participant felt that Simpler™ empowered pharmacists to extract relevant data from patients:

> *I guess the differences would be we don't just rely on existing computer tools, we can also check blood sugar level whereas before this we don't ask for laboratory results, we counsel patients based on their medications and dispense their medications. Now we try to contact the doctor and get the laboratory results so that we can conduct a detailed medication review. (P5A)*

Two participants agreed that Simpler™ allowed them to conduct more thorough reviews during consultations:

> *I go a bit thorough and ask more questions according to Simpler™ and find out a little more and counsel and educate patients a little bit more. So, usually when I'm doing my diabetes MedsCheck, I run through what's on the existing software program but then it's not enough so Simpler™ pushes [me] to do a bit more. (P7A)*
>
> *We are providing a bit more information to patients rather than just doing our normal MedsCheck. (P4A)*

4.4.3.8 Positive aspects of the Simpler™ training sessions

The following findings were responses from Question 5 under Section C of the interview guide. Pharmacists (10/12) opined that the training content was adequate and structured. The length of training was appropriate.

> *I think it's good actually, because you have provided us with the slide show and the guidelines. It is relevant*. (P5M)
>
> *Like all the study references you forwarded to us, all the evidence and all the readings that you emailed to us, they were relevant. We could do a letter to doctor and quote those studies or make a reference to those studies*. (P3A)

While some participants (41.7%; 5/12) found face-to-face training more interactive, 58.3% (7/12) preferred the online training:

> *I think it really depends on personal preference though, because if it's on-line, I would not do it, I generally I prefer to see face-to-face and listen to the person talk.* (P4A)

The Simpler™ training session increased their knowledge on evidence-based diabetes management and for some it served as a refresher:

> *Good. Because it's still can remind me, I mean like a revision. The Framingham risk score for example, I really forgot about that part*. (P6M)

The on-line training session was clear and relevant:

> *The video presentation was clear and your information is so relevant and you appropriately saying one thing clearly I think is good.* (P1M)

Training sessions increased participants' overall confidence in diabetes management. One participant expressed that she was more confident to record interventions on patient medical notes after the Simpler™ training session:

> *You know what's good, the example you gave us in the Simpler™ training of the little lecture that you sent to the doctor about the patients that is helpful. But I haven't sent anything to the doctor, but I still have the confidence to send the doctor something like that.* (P7A)

Facilitators for the training sessions were reported as Figure 4.8 shown below:

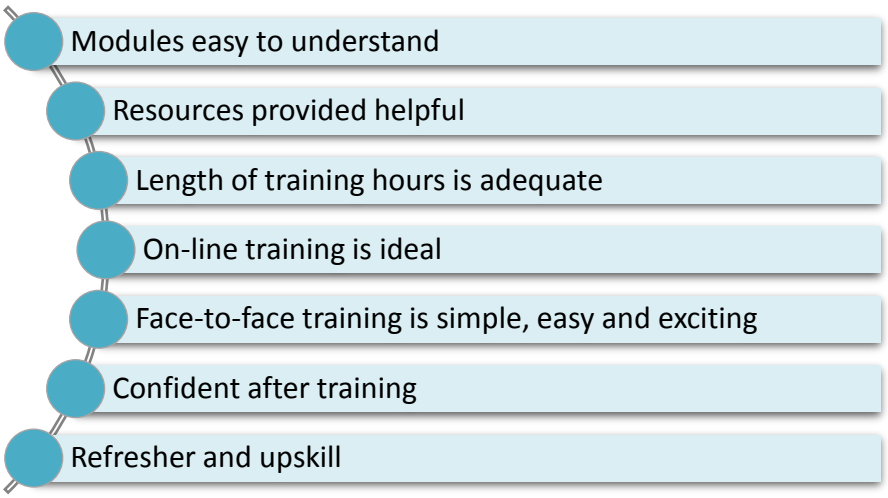


Figure 4.8: Training session facilitators

4.4.3.9 Suggestions for improvements

The following findings were responses from Question 7 under Section C of the interview guide. Participants were asked for recommendations to improve the training sessions and the tool's hand-out.

Improvements to training sessions

Two (of 12) participants believed the training content was too concise and recommended more focus on detection of medicine related problems and lifestyle issues. These suggestions and other recommendations for improvement with respect to future training sessions were summarised in Figure 4.9. These suggestions were incorporated into the training modules.

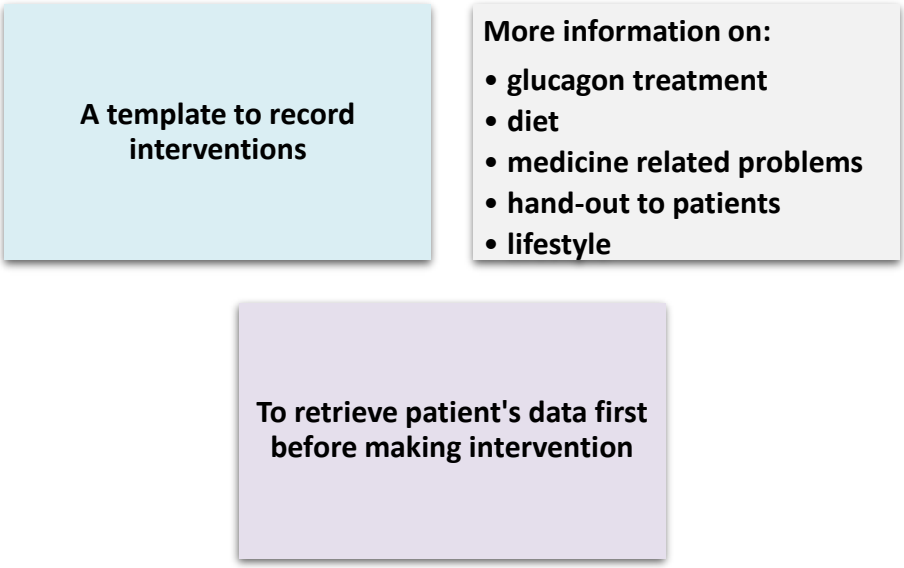


Figure 4.9: Recommendations to improve future training sessions

Simpler™ hand-out improvements

Three participants expressed a need to use visual prompts or larger fonts for headings in the Simpler™ tool. One participant could not recall the 8MMMAS (188) or the plate model for diet control (226) and therefore proposed their inclusion in the tool. As the tool contained both Malaysian and Australian clinical outcome targets, recommendations included to use either of the targets depending on the location the pharmacists were practising. However not all participants agreed with this as some preferred both targets considering different BMI recommendations for Asians compared to Caucasians. Suggestions for improvements are summarised as Figure 4.10 below:

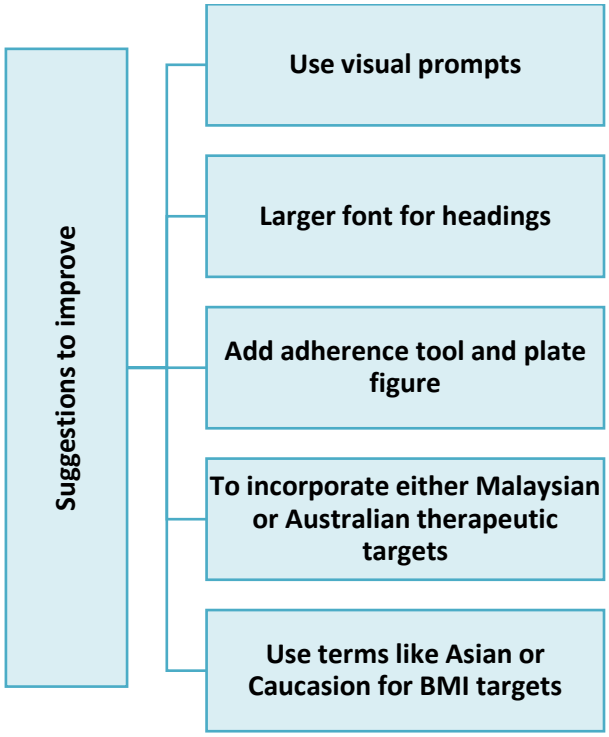


Figure 4.10: Participants' suggestions for improvement to the Simpler™ tool

4.4.3.10 Emerging qualitative analysis topics

There were several issues that emerged from the interviews when participants were asked to describe their experiences on using the Simpler™ tool. These issues were not part of the interview questions. These issues were grouped into topics; 1) implications of application of the Simpler™ in practice, 2) facilitators and 3) barriers experienced by the participants.

4.4.3.11 Implications of the Simpler™ tool in diabetes management

Although none of the issues below were specifically included in the interview questions, five subtopics emerged during the analysis presented in Figure 4.11. These subtopics were that the tool facilitated pharmacists' role; it was specific for diabetes management; it presents a competitive edge; it has wider usage than its original intention to facilitate the provision of MMS; and finally, to target glycaemic improvement.

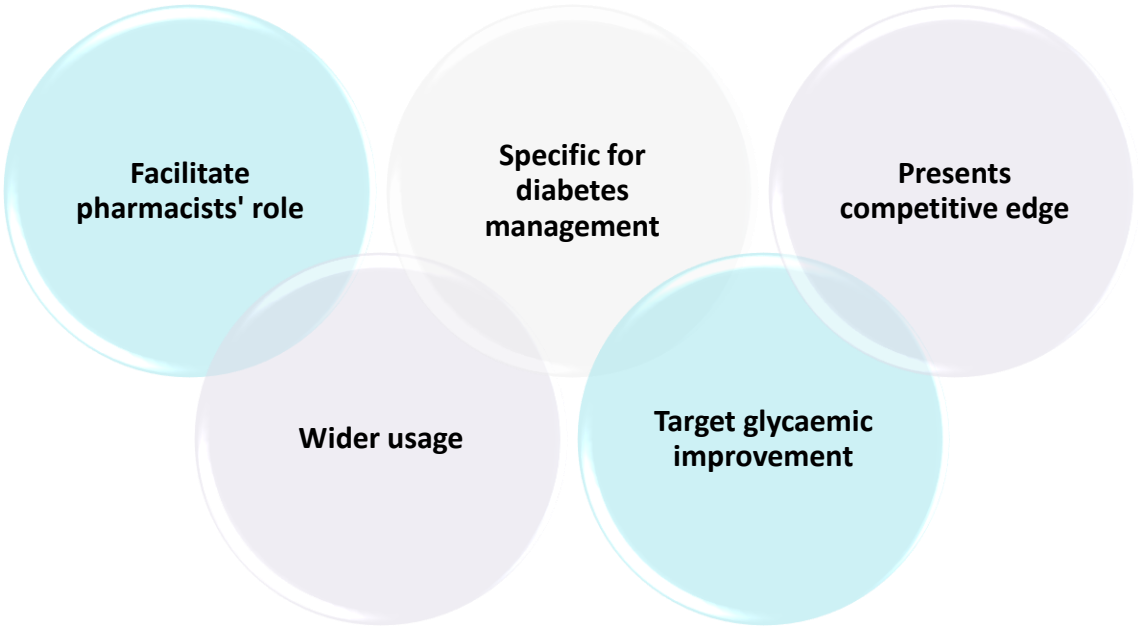


Figure 4.11: Five topics that emerged from the analysis

1. Facilitate pharmacists' role

The perception that Simpler™ facilitated pharmacists' role in diabetes management was raised by two participants. The participants felt positive that the tool facilitates their role as medication managers:

> *Really good thing and I think if a pharmacist can set themselves up to be a specialist in diabetes management through using the Simpler™ tool reporting back to the GP with 6 monthly progress. (P6A)*
>
> *I guess when it comes to [the] community setting, we are not exposed to detailed medication reviews but I think this is what we should be doing as a community pharmacist, service based, for us to compete against retail supermarket chains (P5A)*

2. Tool targets diabetes management

Simpler™ was viewed as a tool specific for diabetes management in comparison to the existing method such as Guildcare (Australia) software program used to document pharmacist's interventions. This is because the program was also used to document interventions for other chronic diseases and not specifically for diabetes.

> *That one you have to print from the GuildCare program [software to support provision of professional services] itself. Yes…You have to click, you just register your patients and you just print it out. It doesn't ask anything…all it asks is, does this patient have T2DM? And then classifies as diabetes MedsCheck so it doesn't have what your tool has, specifically for patients with diabetes. (P3A).*

3. Simpler™ presents competitive edge

When asked if participants would encourage other pharmacists to use Simpler™, all (n=11) except one (P6A) advocated for its use. Pharmacist P6A was not keen to recommend Simpler™ to other pharmacists because she believed from a business point of view, Simpler™ would give her pharmacy the advantage of delivering better diabetes care than other pharmacies:

> *Well no because I want a competitive edge. I don't want anybody else to know about it. (P6A)*

4. Potential application for wider usage

Some suggested to extend the use of Simpler™ for diabetes management during the routine dispensing processes, and some during pharmacist internship or pharmacist pre-registration:

> *We can also use it when we are doing dispensing. We can go through patient's profile whether they are taking statin medication. If they say no, you can ask them how their cholesterol is. And they can always ask their doctor for cholesterol test and we can do a clinical intervention. (P2A)*
>
> *In all setting of course. I will especially recommend Simpler™ to hospital pharmacist specifically intern pharmacists because it will help them so much because they are new and they do not how to write good comments in medical records. Since other health professionals read it, it's very important to write correctly. (P2M)*

The fresh graduates, some of them have been practicing in the community but not conducting diabetes MedsCheck. At least with Simpler™ and quick training they know what to do. Based on Simpler™ they will be more confident during consultation with the patient. (P5A)

5. Target glycaemic improvement

The fifth emerging topic was pharmacists' aim of diabetes management became more focused on clinical outcomes such as reduction in HbA1c.

Before this we only focussed on the education part, now the interesting part is the aim to reduce HbA1c. (P4M)

4.4.3.12 Emerging topics: perceived facilitators and barriers

In addition to the above, participants also perceived the following as Simpler™ tool facilitators, summarized in Figure 4.12. The Simpler™ tool provided structured and organized method for pharmacists to follow during the patient medication review process. The tool was found feasible in the practice setting as it reduced consultation time, facilitated the documentation process while providing relevant information to patients. Pharmacist were confident to use the tool as the contents were relevant and have previously been validated in Phase One of research.

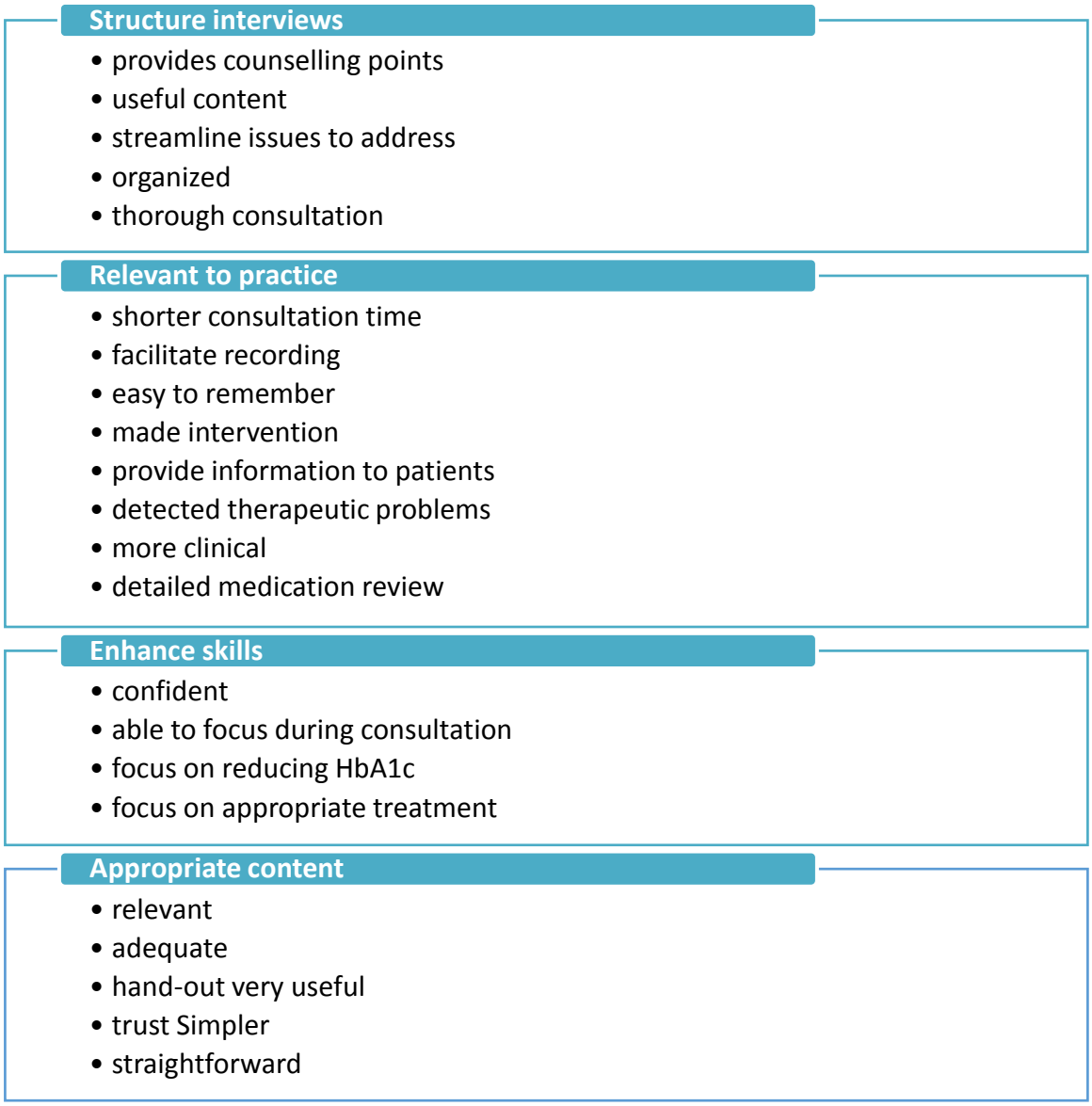


Figure 4.12: Facilitators of the Simpler™ tool

While Simpler™ was perceived as a facilitator to drive the delivery of evidence-based care by most of the participants, six participants (6/12) faced challenges that hindered them from using Simpler™ effectively. Three pharmacists reported that the tool was time consuming but perceived the tool's comprehensive medication review outweighed the increased duration it took to complete the review process. In addition, due to specific use, two pharmacists felt that training in diabetes management was required in order to use the tool effectively. Two pharmacists expressed the difficulty in obtaining laboratory data and thus were unable to conduct a detailed medication review. These barriers and supporting quotes are summarized in Table 4.6.

Table 4.6: Barriers and challenges in using Simpler

Barriers & Challenges	Supporting quotes
Time consuming	*Initially when we first applied it, since we are not familiar, it was more time consuming. The whole session took me about an hour for the first patient. (P5A)* *So it's quite lengthy because we need to, as you know, and control the time because there are a lot of patients so we have to be fast. (P6M)* *I need to go through all these checklists, all these points, so it's a good thing, it's longer but in a good way(P3A)*
Unable to make intervention unless a HMR pharmacist	*It's fine but the only thing from Simpler™ tool I found that it would be much more applicable for an HMR pharmacist as opposed to a regular pharmacist in a pharmacy unless that pharmacist has been specifically trained in or even a diabetes educator actually.* (P3A)
Need to be trained to use Simpler™	*…. but we need to be trained first to use Simpler™ otherwise that we don't have the basic knowledge to use it.* (P5A)
Difficult to access laboratory results (Australia)	*The only thing with diabetes MedsCheck and using the tool is that I can't actually have access to their blood HbA1C results and I even tried to get it from the surgery. (P2A)* *It was just at one point there was not enough laboratory test results in fact when I did medication review using Simpler™, I could only say" 'Yes that there is statin' but I do not know what the statin level was and what the cholesterol level was. (P3A)*

4.4.4 Modifications to the Simpler™ tool

The findings from Phase Two led to modifications to the Simpler™ training modules and the Simpler™ tool hand-out. Based on participants' recommendations, additional

PowerPoint slides on the identification of medicine related problems were included in Simpler™ training module 2. Information on glucagon administration was incorporated into Simpler™ module 3. Some participants wanted more information on lifestyle, diet and a hand-out for patients. In line with keeping the training modules to a two hour time frame, relevant websites on patient's education (300) and pharmaceutical care (61) were signposted into the presentation slides (module 2) to enable participants to read and download materials in their own time. These additional slides are presented as hand-out versions in Appendix 4.14.

A proposal from participants to incorporate more visual prompts and less text were acknowledged. As a result, the plate model (224) and questions from the 8-items MMMAS(188) were included in the hand-out. Larger fonts were used to highlight the primary word for each specific indicator. Since some of the clinical targets differed between the Australian and Malaysian guidelines, incorporating both countries' targets in the same Simpler™ hand-out posed confusion to some participants. Therefore, two separate hand-outs were constructed to account for the differences, as shown in Tables 4.7 and 4.8.

Table 4.7: Revised Simpler™ tool hand-out (Malaysian version)

Simpler™ Pharmacist Diabetes Management Tool (Malaysia)	
S=Statin	• **Statin** initiation in patients with CVD • Achieve targets: **LDL<2.6 mmol/L**, **TG<1.7 mmol/L**. • Statin initiation in patients **> 40 years** old without CVD
I=Insulin/Glycaemic control	• **Insulin** initiation if glycaemic control not achieved despite being on two or more oral hypoglycaemic agents • Target of **HbA1c ≤ 7% (53mmol/mol)** if no other complications • Management of **hypoglycaemia** • **Self-monitoring** of blood glucose (4.4-7.0 mmol/L fasting); (4.4-8.5 mmol/L-2h postprandial) • Aim a reduction of **HbA1c by 1%** if above target HbA1c • Initiate/continue **metformin** if not contraindicated
M=Medication	• Assess **medicine related problems** • Review medication adherence using 8-items modified **Morisky** medication adherence scale
P=Blood Pressure	• BP target: **≤135/75** • **ACEI/ARB** initiation in patients with/without microalbuminuria /proteinuria • **Reduce sodium** intake (<2400mg sodium/day; 6g/1 teaspoon/day) • One or more antihypertensive medicine to be taken at **bedtime**
L=Lifestyle	• **Exercise:** 30 mins walking (or equivalent) 5 or more days/week (total ≥150 min/week) • **Weight loss**: Caucasian (BMI< 25 kg/m2), Asian (BMI ≤ 23 kg/m2) • **Smoking cessation** • **Waist circumference**: Caucasian (<94 cm in men,<80 cm in women, Asian (≤90 cm in men,≤80cm in women) • **Alcohol** intake: ≤2 standard drinks (20 g) per day for men • Management of **stress** & diabetes related distress • **Erectile dysfunction**: recommend PDE-5 inhibitor as first line therapy for male patients • **Foot care** • Diet advice using **plate model** • Annual **eye** assessment • Address **sleep** hygiene
E=Education	• Knowledge & understanding of medicine • Medicine storage • Medication optimisation during fasting month for Muslims and other religious groups
R=Cardiovascular Risk	• **Aspirin** therapy as secondary prevention in those with diabetes with history of CVD • Use of **Framingham risk calculator** to calculate CVD risk and educate patients • Aspirin therapy (75mg-162mg/day) as primary prevention to decrease CVD risk (10 year risk>10%, Framingham) (patients **>65 years** old)

8-items Modified Morisky Medication Adherence Scale (page 2)

No.	Questions	Yes/No (Please circle)	
1.	Do you sometimes forget to take your pill?	Y=0	N=1
2.	People sometimes miss taking medications for reasons other than forgetting. Thinking over the past two weeks, were there any days when you did not take your medicine?	Y=0	N=1
3.	Have you ever cut back or stopped taking your medication without telling your doctor because you felt worse when you took it?	Y=0	N=1
4.	When you travel or leave home, do you sometimes forget to bring along your medications?	Y=0	N=1
5.	Did you take your medicine yesterday?	Y=1	N=0
6.	When you feel like your disease is under control, do you sometimes stop taking your medicine?	Y=0	N=1
7.	Taking medicine every day is a real inconvenience for some people. Do you ever get hassled about sticking to your treatment plan?	Y=0	N=1
8.	How often do you have difficulty remembering to take all your medication?	Never/Rarely	1
		Once in while	0.75
		Sometimes	0.5
		Usually	0.25
		All the time	0
Score	Low adherence=<6; Medium adherence=(6 to <8); High adherence=8	Total	___ /8

Plate Model

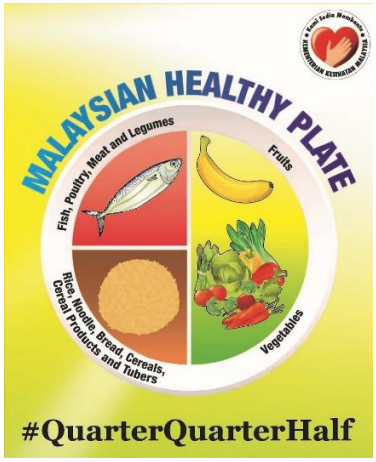


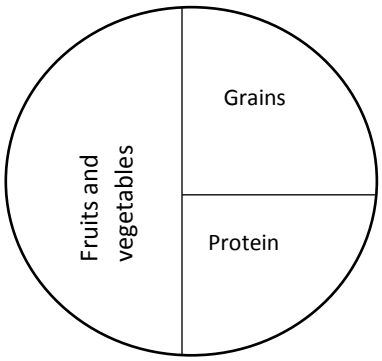
Table 4.8: Revised Simpler™ tool hand-out (Australian version)

Simpler™ Pharmacist Diabetes Management Tool (Australia)	
S=Statin	• **Statin** initiation in patients with CVD • Achieve targets: **LDL<2.0 mmol/L**, **TG<2.0mmol/L**. • Statin initiation in patients **> 40 years** old without CVD
I=Insulin/Glycaemic control	• **Insulin** initiation if glycaemic control not achieved despite being on two or more oral hypoglycaemic agents • Target of **HbA1c ≤ 7% (53mmol/mol)** if no other complications • Management of **hypoglycaemia** • **Self-monitoring** of blood glucose (6.0-8.0 mmol/L fasting); (8-10 mmol/L-2h postprandial) • Aim a reduction of **HbA1c by 1%** if above target HbA1c • Initiate/continue **metformin** if not contraindicated
M=Medication	• Assess **medicine related problems** • Review medication adherence using 8-items modified **Morisky** medication adherence scale
P=Blood Pressure	• BP target: **≤130/80** • **ACEI/ARB** initiation in patients with/without microalbuminuria /proteinuria • **Reduce sodium** intake. Malaysian CPG: (<2400mg sodium/day; 6g/1 teaspoon/day) • One or more antihypertensive medicine to be taken at **bedtime**
L=Lifestyle	• **Exercise:** 30 mins walking (or equivalent) 5 or more days/week (total ≥150 min/week) • **Weight loss**: Caucasian (BMI< 25 kg/m2), Asian (BMI ≤ 23 kg/m2) • **Smoking cessation** • **Waist circumference**: Caucasian (<94 cm in men,<80 cm in women, Asian (≤90 cm in men,≤80cm in women) • **Alcohol** intake: ≤2 standard drinks (20 g) per day for men • Management of **stress** & diabetes related distress • **Erectile dysfunction**: recommend PDE-5 inhibitor as first line therapy for male patients • **Foot care** • Diet advice using **plate model** • Annual **eye** assessment • Address **sleep** hygiene
E=Education	• Knowledge & understanding of medicine • Medicine storage • Medication optimisation during fasting month for Muslims and other religious groups
R=Cardiovascular Risk	• **Aspirin** therapy as secondary prevention in those with diabetes with history of CVD • Use of **Framingham risk calculator** to calculate CVD risk and educate patients • Aspirin therapy (75mg-162mg/day) as primary prevention to decrease CVD risk (10 year risk>10%, Framingham): 2016 ADA Standards of medical care in diabetes

8-items Modified Morisky Medication Adherence Scale (page 2)

No.	Questions	Yes/No (Please circle)	
1.	Do you sometimes forget to take your pill?	Y=0	N=1
2.	People sometimes miss taking medications for reasons other than forgetting. Thinking over the past two weeks, were there any days when you did not take your medicine?	Y=0	N=1
3.	Have you ever cut back or stopped taking your medication without telling your doctor because you felt worse when you took it?	Y=0	N=1
4.	When you travel or leave home, do you sometimes forget to bring along your medications?	Y=0	N=1
5.	Did you take your medicine yesterday?	Y=1	N=0
6.	When you feel like your disease is under control, do you sometimes stop taking your medicine?	Y=0	N=1
7.	Taking medicine every day is a real inconvenience for some people. Do you ever get hassled about sticking to your treatment plan?	Y=0	N=1
8.	How often do you have difficulty remembering to take all your medication?	Never/Rarely	1
		Once in while	0.75
		Sometimes	0.5
		Usually	0.25
		All the time	0
Score	Low adherence=<6; Medium adherence= (6 to <8); High adherence=8	Total	___ /8

Plate Model



4.5 Discussion

In the following section, the findings from this phase of the research will be discussed in relevance to Phase Two objectives in six sections: 1) Participants' demographic data and pharmacy practice experience 2) Perceived effectiveness of the Simpler™ tool 3) Positive aspects of the Simpler™ training sessions 4) Improvements made to the Simpler™ training modules and the tool based on participants' recommendations. 5) Overall implications of the tool and 6) Barriers and challenges limiting the tool's usage. An explanation of how the results from Phases One and Two were used to develop Phase Three are also presented.

4.5.1 Participant demographic and diabetes practice experience

In terms of average number of patients seen in the pharmacy during the period of research, Malaysian pharmacists had more patients than the Australian pharmacists. This could be due to a difference in the number of diabetes (Type 1 and Type 2 DM) population in each country. Malaysia's 15.2% of adults with diabetes (20) compared to Australia's 5.1%.(301) Furthermore, Malaysia's public health system provides more affordable healthcare compared to private institutions which motivates patients to seek treatment in government facilities.(302)

Most pharmacists reported unfamiliarity with practice guidelines as they relied on their existing knowledge and standardized documentation to assist diabetes care delivery. This could be due to lack of clinical support for community or primary care pharmacists compared to hospital pharmacists. For instance, the Australian DMAS program

conducted in 2007 which was part of Australian government plan to prepare pharmacist to deliver diabetes management service placed more emphasis on patient self-management and education rather than the clinical aspects.(132) In Malaysia, lack of support in terms of training programs other than for credentialed diabetes pharmacists may be a potential cause.(270) A short-term diabetes training programs specifically on clinical management according to practice guidelines such as Simpler™ may increase pharmacists' confidence and competency to deliver quality, evidence-based diabetes care.

4.5.2 Perceived effectiveness of the Simpler™ tool

The Simpler™ tool was perceived a beneficial intervention tool to be used by pharmacists. Potential benefits of guides to assist healthcare professionals to make interventions are known. Among the reported benefits are improved quality of interventions, clear recommendations offered to healthcare practitioners who are unsure of how to progress, provide evidence-based suggestions and consistent care.(303) Similar benefits were reported in studies using a defined approach to aid decision making such as the intervention tool for prescribing antibiotics (178, 182), asthma intervention tool for pharmacists (187), inappropriate medication use and prescribing indicators in the elderly Australian population (180) and a dietary intervention tool.(184) Participants' evaluation of the effectiveness of Simpler™ was similar to a hypothesis by Weed (177) who suggested two important features in order for the tool to be effective: (1)the tool should enable information retrieval and organization and (2) the tool should empower the user to use the information obtained and own judgement to make an intervention.

It is interesting to note that participants have successfully adopted and adapted the Simpler™ tool for making interventions in their respective countries. The Simpler™ tool did not pose issues such as difference in culture and healthcare systems as reported in one study conducted in multiple countries.(178) Although, the Australian guidelines contained BMI targets specifically for Caucasian patients and the Malaysian guidelines for Asian patients, some Australian participants opined the importance of having both BMI targets in Simpler™ owing to the increasing number of Asian patients visiting their pharmacy.

The present study raises the possibility that the Simpler™ tool can be used as a 'communication tool' between healthcare professionals and patients. This is because the effectiveness of Simpler™ as an intervention tool is dependent on the data obtained from patients' clinical outcomes, compliance issues, lifestyle habits and knowledge. To retrieve the data, pharmacists could utilise the tool to obtain responses from patients and also counsel patients. This is also evident from the types of intervention pharmacist made (section 4.4.3.6) using the Simpler™ tool. Pharmacists used the words; 'streamline issues to address', provide 'counselling points', 'provide information to patients', and 'detected therapeutic problems' to describe the Simpler™ tool.

4.5.3 Positive aspects of training sessions

While some pharmacists preferred direct face-to-face training, more preferred the on-line training. This finding corresponds to results of various studies which revealed pharmacists' preference for virtual training as it was ideal and relevant. This is because online training does not require travelling time to a specific location which may be time consuming. Furthermore, pharmacist daily work commitment will not be

interrupted.(281, 304-306) Similar to other studies (132, 278, 281), where pharmacists perceived increased confidence after MMS training, the Simpler™ training modules increased participant's confidence to deliver evidence-based diabetes care in their practice setting.

Participants' interviews revealed the need for additional information on MRPs. This was deemed unnecessary during the development of the training modules as the topic would have been covered in pharmacists' undergraduate degree programs in both countries.(307, 308) In addition, the design of the training modules called for succinct and concise information. However, despite these arguments, one study successfully incorporated relevant clinical elements in their web-based training program for pharmacists within a 60-minute time frame.(304) In contrast, another study required pharmacists to interpret pathophysiology and pharmacotherapy of T2DM as prerequisites prior to attending workshops as detailed discussion of these topics were not conducted during training.(132) To address the shortfall in Simpler™ training modules, additional slides were developed on pharmacotherapy workup. These slides summarised the thought processes required to make pharmaceutical care intervention according to Hepler and Strand.(61)

4.5.4 Overall implications of the Simpler™ tool

Participants' recommendations for more visual aids and less words on the Simpler™ tool was similar to a study on computer-based decision aids where users found the lengthy recommendations posed a problem.(309) Concise recommendations were also found to be more valuable in another study on decision aid tools.(310)

Simpler™ training managed to upskill the pharmacists as illustrated by the improvements in the post-training questions and number of interventions made during the one-month trial period. Most training programs which focused on pre- and post-training reported similar improved pharmacist performance immediately post training.(278, 281, 311) However, there is a lack of evidence of the longevity specifically in terms of reinforcement of the information in these training programs. The Simpler™ tool on the other hand consists of hand-out which remains with the pharmacists and therefore may encourage continued use.

The five topics that emerged from perceived effectiveness of the Simpler™ tool were associated with the Simpler™ tool's targeted use in diabetes management. Participants commented that the use of the Simpler™ tool could potentially be extended to pharmacists during routine dispensing activities and as a training tool for pre-registration or intern pharmacists. The tool motivated the pharmacists to facilitate improvements in glycaemic control. Lack of existing intervention tools, specifically for the management of patients, (14) may explain the reason why pharmacist found the tool helpful in their daily practice settings.

In addition, participants with no prior training in diabetes management and limited clinical experience could effectively make clinical interventions through application of the tool. These findings provide some support for the conceptual premise that pharmacists with limited clinical experience could effectively utilise the Simpler™ tool to facilitate diabetes medication reviews.

The Simpler™ tool was found to be feasible by community pharmacists in Australia and primary health care pharmacists in Malaysia as both countries had similar diabetes guidelines (6, 7) and similar diabetes MMS.(10, 157) This raises the possibility that the tool could be adapted to other countries with similar diabetes guidelines to Australia and Malaysia such as the UK, the USA and European countries and who offer diabetes MMS.

The Simpler™ tool was found to facilitate recordings of interventions. This was important as the intention of the tool is to promote quality, evidence-based interventions and communication between pharmacists and prescribers through patients' medical records (PMR). Participants found the training module on recording interventions in PMR helpful. The recording of interventions on patients' notes are usually done by a clinical pharmacists in the hospital setting but this is not traditionally practised by community or primary healthcare pharmacists.(61) Despite this, participants who completed the training expressed their willingness and were confident to record their clinical interventions.

4.5.5 Barriers and challenges using the Simpler™ tool

The Simpler™ tool was deemed easy to use as participants were assumed to have some knowledge of clinical practice guidelines and pharmacotherapy skills. However, participants highlighted the need to be trained prior to using the tool. This finding was similar to a study exploring general practitioners view on a web-based intervention tool which postulated similar need as they were unfamiliar with recent medical developments.(178)

One of the barriers faced by some pharmacists were access to PMRs. Two of the six Australian pharmacists found access to patient's medical data challenging. This could be due to differences in practice settings in Australia and Malaysia as pharmacists in Australian community settings were required to be proactive in acquiring laboratory results from doctors' practices. This issue could be the reason why one pharmacist commented on the need for a Home Medicines Review (HMR) accredited pharmacist to conduct interventions as patient data are more accessible to HMR pharmacists.(312)

Information from PMRs expedites pharmacists' assessment of pharmacotherapy issues and enable them to make quality interventions.(171) Pharmacists not able to access patients' laboratory results from PMRs were unable to make clinical interventions despite applying the Simpler™ tool. This finding further suggests that the Simpler™ tool is a clinical diabetes intervention tool and access to PMRs, including laboratory data, is essential to make meaningful recommendations.

4.5.6 Limitations and suggestions for future work

Most pharmacists considered Simpler™ a highly acceptable tool to be used in diabetes management. However, the risk of their views being biased towards a more positive response during the interview session is acknowledged as shown in some studies.(277) In addition, evaluation of the clinical outcomes in patients is needed to ascertain pharmacist application of knowledge and skill acquired through training. The small sample size from one state in Malaysia and Australia may not reflect the views of pharmacists as a whole. As there was no direct observation, therefore participant's practice experience could not be validated quantitatively. However, the content of the interviews revealed rich data which revealed topics and subtopics.

Majority of the participants in Phase Two comprised of the female gender. This was because participation in this research were voluntary and based on participants' availability. In addition, the unequal gender representation could also be due to the increasing number of young female pharmacists in both countries. The 2017 data from Pharmacy Board of Australia showed more female (62%) pharmacists than male (38%).(313) A 2015 report on women pursuing university degrees in Asia, found there were more female than male pharmacy undergraduates in Malaysia.(314) Nevertheless, this research aimed to compare pharmacists' views from both countries on the feasibility of the tool in practice. The intent of this research was not, however, to explore the views between the different genders. Therefore, equal representation of the genders was decided not a prerequisite for this research.

Although the Simpler™ tool provides guidance on diabetes targets in order to achieve therapeutic outcomes, it does not incorporate communication techniques such as motivational interviewing.(315) Increasingly, motivational interviewing has been suggested to increase patients' compliance to lifestyle issues in diabetes.(316) As the Simpler™ tool presents itself as a communication tool, it further reveals the need to include a section on motivational interviewing in the Simpler™ training modules. In addition, although the participants demonstrated improved knowledge and skills assessed as pre- and post-training results, pharmacists' effort in continuous education to update expanding new evidence in diabetes remains to be seen. Future studies on long-term impact of Simpler™ tool would provide evidence of its effectiveness.

4.6 Conclusion

This phase of the research resulted in the development of the Simpler™ training modules and both the training modules and the hand-out were refined based on proposals from participants in this research. This phase explored pharmacists' experience in application of the Simpler™ tool in the community (Australia) and primary healthcare setting (Malaysia). The Simpler™ training program and tool is a useful approach to upskill pharmacist and improve their confidence in delivering diabetes care. Pharmacists who have limited clinical experience compared to their counterparts in the hospital setting viewed the tool as relevant and beneficial in facilitating structured, evidence-based interventions in practice.

Chapter 5
Impact of the Simpler™ Multifactorial Diabetes Intervention on Type 2 Diabetes Patients in Johor, Malaysia: A Randomised Controlled Trial

5.1 Introduction

Pharmacists' contributions to improving glycaemic control and other clinical outcomes of patients with T2DM through provision of medication management services (MMS) are widely documented.(13, 14, 116) As a result, pharmacists are increasingly recognised for their role in T2DM management as important members of the healthcare team. However, the uptake of MMS provision in community practice remain low as was shown in a qualitative study.(317) One potential reason may be the lack of a specific standardised approaches for pharmacists to adopt, especially among pharmacists with limited clinical experience. Similar views were expressed in the findings from a recent review which highlighted the need for pharmacists to follow a structured approach in the management of T2DM patients.(13)

Most studies (RCTs, pre-and post-intervention, and retrospective) have reported interventions on one or more of the seven diabetes management factors such as lifestyle management, patient education, medication adherence, glycaemia, blood pressure, cholesterol and CVD risk management. However, studies lack in utilising all seven essential diabetes factors required to be addressed, mentioned previously in Chapter 2. This phase (Phase Three) of the research trialled the impact of the Simpler™ intervention tool on patients' clinical and QOL outcomes. The Simpler™ tool was designed to address all the seven factors required to be monitored in diabetes management. Phase Three of the research was conducted in Malaysia.

5.1.1 Malaysian healthcare system

Malaysia is in Southeast Asia and comprises of 13 states and three federal territories. Since it is in the equatorial region, Malaysia experiences tropical rainforest climate all year. Malaysia's population was estimated at 31.7 million people in 2016. The Malaysians are of diverse multicultural ethnic backgrounds namely the indigenous *Melayu* (68.6%), Chinese (23.4%) and Indian (7%) populations.(318) The national language of Malaysia is Bahasa Malaysia although English is widely spoken. Malaysia has experienced rapid urbanization and is the second most urbanized country in South East Asia after Singapore, with 70% of the population living in urban areas.(319)

The Malaysian healthcare system comprises of a dual tiered system which consists of government funded public services and privately funded services, referred to as private healthcare The public funded institutions consist of primary, secondary and tertiary care.(319) The primary health care clinics consist of *Klinik Kesihatan* (KK), *Klinik Desa*, *Klinik 1 Malaysia* and mobile health clinics. KK provides comprehensive medical care while *Klinik Desa* focuses on maternal and child health. *Klinik 1 Malaysia* are situated in highly populated urban and semi-urban areas while mobile health clinic services are provided in remote and rural areas. The private health care system focuses on provision of health services in urban locations through general practitioner clinics and private hospitals in addition to diagnostic laboratory and ambulance services.(319)

Whilst the primary care acts to treat and promote prevention of complications, patients requiring advanced care are referred to secondary care and those requiring specialised services are referred to tertiary care.(319) Malaysian citizens only pay a small fee for treatment in the public institutions in comparison to private healthcare.(320) The affordable care provided in the public sector meant more patients prefer public to

private care services. This has contributed to longer waiting times to receive treatment.(321, 322) Specifically to pharmacy, public institutions provide a variety of pharmacy services for ambulatory patients such as medication management services (MMS) for chronic disease such as diabetes, methadone replacement therapy, home medication reviews (HMR) and smoking cessation.(323)

In privately owned pharmacies, most patients visit community pharmacists for over the counter medications, general health items, health screening, smoking cessation and for medication information services.(324) In contrast to public pharmacists, community pharmacists in Malaysia offer limited professional services. Unlike Australia (273) or the UK (155), community pharmacists in Malaysia do not receive government funding for extended pharmacy services such as MMS or HMR. Despite this, participants in a recent qualitative study on community services in Malaysia did not recognize lack of funding as an issue in providing those services. Instead, lack of collaboration among healthcare professionals and regulatory constraints were cited as barriers.(325)

5.1.2 Determinants of glycaemia improvement

The overall prevalence of diabetes mellitus (DM) (known and undiagnosed) among adults of 18 years and above in Malaysia was 17.5% according to the 2015 National Health and Morbidity Survey.(21) Women had higher prevalence (18.3%) than men at 16.7% while urban areas had more patients with DM (17.7%, 95%CI: 16.7, 18.8) compared to rural locations at 16.7% (95% CI: 15.4, 18.1). Among the 13 states in Malaysia, Johor had the third highest diabetes prevalence at 19.8% (95%CI: 16.8,23.3).(21)

A literature search to June 2017 revealed a total of eight published pharmacists-led diabetes intervention studies conducted at primary healthcare centres and outpatient hospitals in Malaysia, listed in Table 5.1. However, diabetes intervention studies conducted in primary healthcare centres such as KKs were scarce. Most studies (6/8, 75%) were conducted in hospitals while only two (2/8, 25%) were conducted in KKs. In addition, there were no documented RCT studies performed at multiple KK sites.

While the impact of pharmacist led diabetes intervention studies is widely documented, specific improvement in glycated haemoglobin (HbA1c) has varied in Malaysian and international RCT studies.(13, 14) HbA1c level is selected as the relevant clinical marker in most diabetes studies as HbA1c 1% reduction is associated with a lower risk of complications as shown in the UKPDS study.(326) A review of previous diabetes intervention studies revealed several determinants were associated with HbA1c reductions.(13) Those are: 1) study setting (community or clinical); 2) baseline HbA1c levels; and 3) patients' age.

Table 5.1: Diabetes intervention studies conducted by pharmacists in Malaysia

	Authors, year	Design and setting	Arm size, mean age, mean baseline %HbA1c, %ethnicity, %gender	Number of patients' visits to pharmacists	Types of Intervention, Methods	Pharmacist experience	Results	Effect size
1.	Ayadurai, S et al, 2013(129)	Hospital, Johor, outpatient, Retrospective, cohort study	n=50, mean age:53.9; baseline HbA1c:11.72% (104.6mmol/mol); Ethnicity: *Melayu*:54%, Chinese:6%, Indian:40%; Gender: male:34%; female:68%	2-8 visits over 2 years	Medication adherence, drug related problem solutions, medication counselling, diabetes education and blood glucose monitoring	Credentialed diabetes pharmacist	HbA1c: Reduction from 11.72% (104.6mmol/mol) to 10.39% (90.1mmol/mol) =-1.33%; medication adherence and no. of hypoglycaemia events.	Cohen's d=0.54 Hedges'g= 0.54
2.	Butt M et al, 2016(158)	RCT, Outpatient teaching hospital, Kuala Lumpur	PC: n=33, mean age:57.4; baseline HbA1c: 9.66% (82.1mmol/mol), Ethnicity: *Melayu*:54.5%, Chinese:21.2%, Indian:24.2%; Gender: Male:39.45, Female:60.6% UC: n=33; mean age:57.1; baseline HbA1c:9.6% (81.4mmol/mol); Ethnicity: *Melayu*:60.6%, Chinese:24.2%, Indian:15.2%;	3 visits at 0, 3 and 6 months over 6 months	Patient Education by Pharmacist Programme (PEPP) on lifestyle, medication adherence and self-monitoring	Not reported	HbA1c PC:Reductioin from 9.66% (82.1mmol/mol) to 8.47% (69.1mmol/mol)= -1.19% UC: Reduction from 9.64% (81.9mmol/mol) to 9.26% (77.7mmol/mol) =-0.38%	Cohen's d = 0.49 Hedges' g = 0.49

	Authors, year	Design and setting	Arm size, mean age, mean baseline %HbA1c, %ethnicity, %gender	Number of patients' visits to pharmacists	Types of Intervention, Methods	Pharmacist experience	Results	Effect size
			Gender: male:42.4%, female:57.6%				BMI (29.34 to 28.92), 8-item MMMAS (5.83 to 6.77)	
3.	Chow EP et al, 2016(86)	RCT, KK, Pulau Pinang, Malaysia	PC: n=50; mean age:60.3; baseline HbA1c=8.92% (74mmol/mol); Ethnicity: *Melayu*:22%; Chinese:56%; Indian:20%, Gender: male:38%, female:62%; UC: n=69, mean age:60.3; baseline HbA1c:9.23% (77.4mmol/mol); Ethnicity: *Melayu*:49.28%; Chinese:33.33%; Indian:17.39%; Gender: male:36.23%, female:63.77%	2 visits over 2 months	Home based educational intervention, not specified	Not specified	PC: Reduction from HbA1c: 8.92% (74mmol/mol) to 8.19% (66mmol/mol)= -0.73% UC: No changes in HbA1c	Cohen's d = 0.57 Hedges' g= 0.56
4.	Chung WW et al, 2014(159)	RCT, Outpatient Teaching hospital, Kuala Lumpur	PC: n=120; mean age: 59.7; baseline HbA1c=9.6% (81.4mmol/mol); Ethnicity: *Melayu*:50.8%, Chinese:21.7%, Indian:26.7%, Gender: male:41.7%, female:58.3% UC: n=120; mean age:58.5; baseline HbA1c:9.5% (80.3mmol/mol);	12 visits over 12 months	Medication review, resolve drug related problem, patient education and medication adherence, monthly follow-up telephone calls, pill box and blood glucose	Experienced pharmacists but details not reported	Improvement in medication adherence; FBG; PC: Reduction from HbA1c: 9.6% (81.4mmol/mol) to 8.2% (66.1mmol/mol)= -1.4%, UC: Reduction from HbA1c: 9.5%	Cohen's d=0.70 Hedges' g = 0.70

	Authors, year	Design and setting	Arm size, mean age, mean baseline %HbA1c, %ethnicity, %gender	Number of patients' visits to pharmacists	Types of Intervention, Methods	Pharmacist experience	Results	Effect size
			Ethnicity: *Melayu*:38.8%, Chinese:19%, Indian:38.8%; Gender: male:46.3%, female:53.7%		meter to record self-monitoring of blood glucose		(80.3mmol/mol) to 9.3% (78.1mmol/mol)= -0.2%	
5.	Haron N et al, 2015(160)	Multicentre retrospective, 14 KK, Kuala Lumpur and Putrajaya	n=56; mean age: 54.8; baseline HbA1c: 10.7%; Ethnicity: *Melayu*:57.14%; Chinese:21.43%; Indian:21.43%; Gender: male:44.64%, female 55.36%	4 visits over 15 months	Dosage adjustment, changes of medications	Credentialed diabetes pharmacist	Reduction of HbA1c: 10.7% (93.4mmol/mol) to 9.7% (82.5mmol/mol)= -1%, significant improvement in medication understanding and adherence level	Cohen's d = 0.61 Hedges'g = 0.61
6.	Lim PC et al, 2016(161)	RCT, outpatient, Hospital Pulau Pinang	PC: n=39; mean age:57; baseline HbA1c:10.11% (87.0); Ethnicity: *Melayu*:28.2%; Chinese:46.2%, Indian:25.6%; Gender: male: 46.2%, female: 53.8%; UC: n=37; mean age:55.6; baseline HbA1c:9.71% (82.6mmol/mol); Ethnicity: *Melayu*:32.4%,	8 visits in 12 months	Medication reviews, adding and adjusting insulin doses within 4 units each time and laboratory tests ordered, education and lifestyle advice provided	Credentialed MTAC diabetes pharmacist	PC: Reduction of HbA1c: 10.11% (87mmol/mol) to 9.21% (77.2mmol/mol) =-0.9%, UC: HbA1c: 9.71% (82.6mmol/mol) to 9.63% (81.7mmol/mol) =-0.08%,	Cohen's d=1.50 Hedges' g = 1.50

	Authors, year	Design and setting	Arm size, mean age, mean baseline %HbA1c, %ethnicity, %gender	Number of patients' visits to pharmacists	Types of Intervention, Methods	Pharmacist experience	Results	Effect size
			Chinese:35.2%, Indian:32.4%; Gender: male:45.9%, female:54.1%				Improvement in FBG, TC and LDL	
7.	Lim PC et al, 2010(327)	Retrospective, outpatient, Hospital Pulau Pinang	n=43; mean age:47.9; baseline HbA1c:10.82% (94.8mol/mol); Ethnicity: *Melayu*:46.5%; Chinese:44.2%; Indian:9.3%; Gender: male:46.5%, female: 53.5%	8 visits in 12 months	Dosage adjustment, addition of OHA, insulin, statin and aspirin, medication adherence and education	Credentialed diabetes pharmacists	Reduction from HbA1c:10.82% (94.8mmol/mol) to9.09% (75.8mmol/mol) =-1.73%, FBG, LDL and improvement in medication adherence	Cohen's d = 6.24 Hedges' g = 6.24
8.	Navin KL et al, 2011(128)	RCT, outpatient, Hospital, Kuala Lumpur	PC: n= 42; mean age: not reported; baseline HbA1c: 10.6% (92.4mmol/mol); Ethnicity: not reported; Gender: not reported UC: n= 43; mean age: not reported, baseline HbA1c:10.7% (93.4mmol/mol); Ethnicity: not reported; Gender: not reported	9 visits in 12 months	Medication adherence, drug related problem solutions, medication counselling, diabetes education and blood glucose and weight monitoring	Credentialed diabetes pharmacists	PC: Reduction from HbA1c: 10.6% (92.4mmol/mol) to 8.9% (73.8mmol/mol) =-1.7%, UC: Reduction from HbA1c: 10.7% (93.4mmol/mol) to 10.1% (86.9mmol/mol)= -0.6%; improved medication	Calculation could not be performed as standard deviation was not reported

Authors, year	Design and setting	Arm size, mean age, mean baseline %HbA1c, %ethnicity, %gender	Number of patients' visits to pharmacists	Types of Intervention, Methods	Pharmacist experience	Results	Effect size
						adherence score (4.23 to 7.84)	

Melayu refers to ethnic Malay whose origin dates to Indian, Chinese, Cambodian and Indonesian heritage**(328)** and indigenous population in Malaysia; Indian refers to population from India, Sri Lanka, Pakistan and Bangladesh who migrated to Malaysia in the 3rd and 19th century(5); Chinese refers to population from China who migrated to Malaysia in the 3rd and 19th Century(5). FBG=fasting blood glucose; HbA1c= haemoglobin A1c; LDL= low density lipoprotein; MTAC= medication therapy adherence clinic; PC= pharmaceutical care; RCT= randomised controlled trial; TC=total cholesterol; UC=usual care;

The studies conducted in hospital settings showed larger mean improvements for HbA1c in comparison to the community or primary healthcare settings. Studies conducted in hospital settings showed mean differences of -0.9% to -1.73% after intervention while studies conducted in primary settings ranged from -0.73% to -1%. The effect size or the size of HbA1c changes based on sample size of the study between intervention and control arms ranged from 0.57-0.61 in primary settings and 0.49-1.5 in hospital outpatient settings. The increased HbA1c changes reported in hospital settings could be due to interventions by experienced clinical pharmacists whereas pharmacists in community settings may have less expertise in the clinical aspects of T2DM management. This view was supported by findings from a study which found pharmacists' educational background were facilitators of MMS provision and suggested enhanced practice experience and the need for clinical knowledge to build pharmacists' confidence.(264) Furthermore, the better outcomes among hospital outpatients may be due to enhanced self-care support provided by healthcare professionals (HCP). In comparison, primary care patients often lack the support due to constraints in the provision of care. The findings from a qualitative study conducted in Malaysia among T2DM and HCP in primary and secondary care supports this view.(329)

5.1.3 Diabetes management among Muslim patients

Malaysia is a secular country, as such while Muslims make up the majority of the population (61.3%), other religions such as Buddhism (19.8%), Christianity (9.2%) and Hinduism (6.3%) are also freely practised.(330) Of specific relevance is the Muslim population where individualised care is necessary among patients with diabetesdue to religious diet issues.(331)

During the Muslim month of Ramadan, Muslims worldwide, including those from Malaysia, practise fasting whereby they refrain from oral or intravenous substances from sunrise to sunset for a period of 30 days. Although Muslim patients are not required to fast according to their religion(6), some patients do participate in the practice of fasting. Thus, it becomes increasingly important for healthcare professionals to be educated in diabetes management, particularly the need for medication dose adjustments to avoid risks of hypoglycaemia, hyperglycaemia and dehydration.(332)

Malaysian diabetes practice guidelines outline several recommendations during fasting such as medication dose adjustment and timing, reduced physical activity, adequate fluid intake and breaking the fast when hypoglycaemia is experienced.(6) Several studies on fasting practice among Muslim patients documented significant improvements in HbA1c and fasting blood glucose after a three month education intervention which included medication dosage and timing adjustments.(332, 333) However diabetes intervention studies led by pharmacists in Malaysia have rarely reported intervention strategies adopted during the Ramadan fasting period.

5.1.4 The state of Johor, Malaysia

Johor is situated at the south of the peninsular of Malaysia with a population of 3.7 million. The major ethnic communities in Johor comprise of *Melayu* (2 million, 54.1%), Chinese (1.1 million, 29.7%) and Indians (0.23 million, 6.2%) and there are more men (1.9 million, 51.3%)) than women (1.7 million, 45.9%). Johor comprises of 10 districts namely; Batu Pahat, Johor Bahru, Kluang, Kota Tinggi, Kulai, Mersing, Muar, Pontian, Segamat and Tangkak. It consists of urban and semi urban areas.(318) Figure 5.1 shows the 10 districts of Johor state.

Figure 5.1: Location of the ten districts in the state of Johor

There are a total of 88 health clinics or KKs in Johor which provide primary healthcare services to its population.(334) Lack of diabetes intervention studies among KKs in Malaysia necessitated the need to conduct the Phase Three research in multiple KKs. A RCT method was selected to evaluate the effectiveness of pharmacist interventions using the Simpler™ tool. This research was the first multicentre RCT to use a specific method of diabetes intervention at KKs in the state of Johor and in Malaysia.

5.2 Objectives

The Phase Three research aimed to evaluate the impact of the tool's application in the management of T2DM patients through a RCT. The objectives of the Phase Three research were to:

1. Evaluate the changes in patients' clinical outcomes and cardiovascular risk score at the end of a six-month period between the intervention arm and the usual care arm.
2. Assess the impact of pharmacists' interventions using the seven diabetes factors namely:
    - Statin/cholesterol control
    - Insulin/glycaemic control
    - Medication management
    - Blood pressure control
    - Lifestyle management
    - Patient education
    - CVD risk reduction strategies
3. Determine the impact of pharmacists' interventions on patients' QOL at the end of the study period.

Phase Three tested the hypothesis that having a structured tool such as the Simpler™ tool would:

1. Result in reductions in HbA1c and blood glucose levels, blood pressure and lipid measurements in the SC arm after six months compared to the control group (SC vs UC).
2. Result in improved QOL scores between the arms at six months.

5.3 Methods

The Phase Three research was conducted between June 2016 and February 2017. The research method was informed by the findings from Phases One and Two. Johor state was chosen as the student researcher, SA, has previous work experience in a

tertiary hospital in Johor Bahru. In addition, associate supervisor, SNMS has a role in the management of clinical services provided in government hospitals and primary healthcare clinics in Johor.

This was a two-arm prospective, parallel arm, RCT, multi-centre research study. Participating sites were government funded primary healthcare clinics. Patients were randomised to either the intervention arm with pharmacists using the Simpler™ tool and providing Simpler™ care (SC), or the control arm with patients receiving usual care (UC). Patients in the SC arm were followed up for a duration of six months by pharmacists using the Simpler™ tool. Differences in clinical and QOL outcomes were quantitatively measured pre-and post-intervention and between arms. The research method followed the recommendations of the consolidated standards of reporting trials (CONSORT) 2010 guideline for randomised trials.(335)

The research procedure had a specific protocol and documentation process for participating pharmacists to follow which are explained in the following paragraphs. A summary of the overall research process including the sections where explained, is presented in Figure 5.2.

The Curtin University Human Research Ethics Committee (HREC) approved this research (HR214/2015) as well as the Malaysian Medical Research and Ethics Committee (NMRR-15-1831-28307) (refer to Appendices 5.1, 5.2 and 5.3). Additionally, a nonexclusive, royalty-free licence was obtained to use the World Health Organization QOL Questionnaire (WHOQOL-BREF) in three languages; English, Bahasa Malaysia and Mandarin languages (Appendix 5.4).

As the research period for Phase Three fell during the Ramadan fasting month (June), pharmacists were briefed on specific dose adjustment and timing in addition to patient education on diabetes management during that period. As explained in

Section 5.1.3, pharmacist training on pharmacotherapy and patient education was needed to prevent hypoglycaemia during the fasting period.

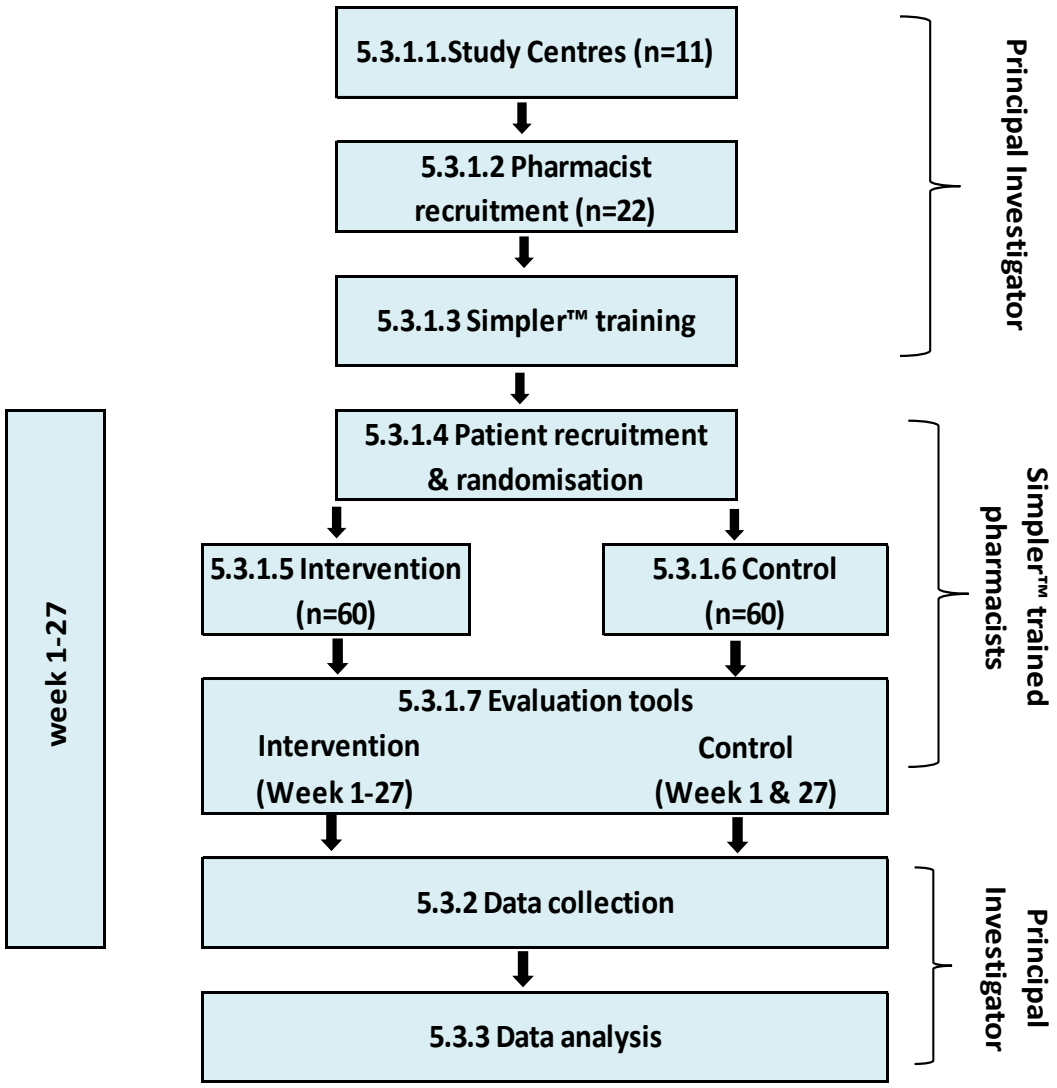


Figure 5.2: Flow diagram of the Phase Three research protocol

5.3.1 Recruitment process

5.3.1.1 Selection study centres

The study centres were government funded, outpatient primary health clinics (KK). The eligibility criteria included KKs which provided MMS as part of its pharmacy extended services and who employed two or more full time pharmacists who have not been credentialed as diabetes pharmacists. Recruitment of the KKs was conducted through personal contacts by the researcher (SA) and snowball recruitment. Out of the 88 KK's, the pharmacy managers of 11 KKs which fit the eligibility criteria, expressed their willingness to participate in the research.

5.3.1.2 Pharmacist recruitment

The eligibility criteria for pharmacists included having less than three years of clinical experience in diabetes management and having not undergone the credentialing process to become a credentialed diabetes pharmacist by the Pharmaceutical Services Division, Ministry of Health, Malaysia.

Pharmacists from the 11 KKs mentioned above were contacted by email and telephone calls. In addition, the benefits of this research were explained to each pharmacist to encourage their participation. An information sheet (Appendix 5.5) and consent form (Appendix 5.6), with copies of ethics approvals were sent as attachments. Pharmacists' participation was voluntary and two pharmacists were recruited from each KK to allow for pharmacist absences due to holidays, sickness or other reasons.

Subsequently, permission to conduct research at each KK was sought from the Deputy Director of Pharmaceutical Services Division of the State of Johor; and from

the Johor State Health Director. Letters to the Director of the Johor Health Department (a copy sent to the Deputy Director of Johor Pharmaceutical Services Division) are in Appendix 5.7. Additionally, an introductory letter was sent to the managers of each of the KKs (Appendix 5.8). A letter of approval to conduct research at the 11 KKs located in the seven districts by the Deputy Director of Johor Pharmaceutical Services Division was obtained before the start of research (Appendix 5.9).

5.3.1.3 The Simpler™ training

Training commenced once the pharmacists signed consent forms to participate in the research were received. Participating pharmacists completed two hours online Simpler™ training validated and trialled in Phase Two. The training was completed before the start of the trial. This was to ensure skills uniformity among the pharmacists as suggested in previous literature.(135) All participants were briefed on the protocol before the RCT commencement. The briefing took approximately four hours and was conducted face-to-face in a predetermined venue in Johor Bahru, Johor, Malaysia by SA. The agenda (Appendix 5.10) included an overview of the trial protocol, practice session on documentation process and role play on the patient recruitment procedure.

5.3.1.4 Patient recruitment and randomisation

The primary indicator was reduction of HbA1c ≥ 1% at the end of the study with respect to the control arm. A power analysis using the DSS research sample size calculator(336) indicated that at least 52 patients from each arm were needed. This number of patients were required to show a mean HbA1c difference of -1.33% between baseline and 6 months in the intervention arm compared to 0.4% for the control arm. The standard deviation was 1.9. These data were selected for the

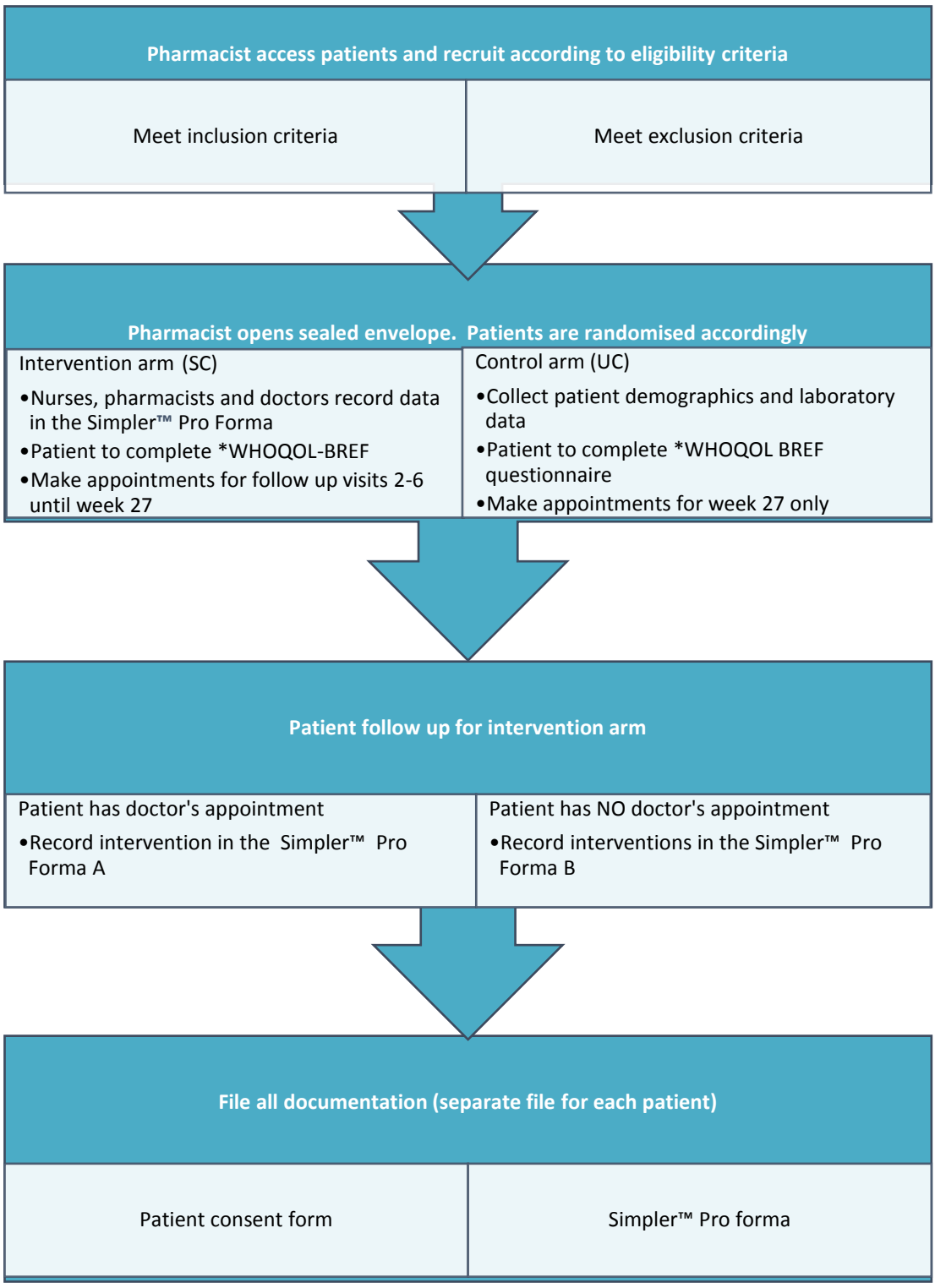
calculator based on findings from two previous studies conducted in the state of Johor and Selangor, Malaysia.(128, 129) Based on these numbers, a sample of 60 patients for each arm (intervention and control) was calculated, allowing for a drop-out rate of 15%.

The inclusion criteria for the patients were: T2DM diagnosis, aged > 21 years, on multiple medications/co-morbidities, HbA1c > 8% (63.9 mmol/mol) or fasting blood sugar > 7.0 mmol/L or two hours post prandial sugar level > 8.5 mmol/L.

The exclusion criteria were: if patients had been diagnosed with dementia or severe psychotic illness, on haemodialysis treatment, pregnant or lactating, intended to be pregnant within the next six months, diagnosed with cancer, or were involved in other research at the time of recruitment. Patients who were previously recruited into MMS such as the medication therapy adherence clinic (MTAC) diabetes prior to the start of the trial were excluded. This was to prevent possibility of bias as patients with previous exposure to MTAC diabetes may have increased knowledge of diabetes self-management in comparison to other patients.

Patients were recruited during their scheduled visit to the doctor. Recruitment processes were conducted either through proactively targeting patients who fulfilled the inclusion criteria or through referral by diabetes nurses. The patients were seen by the Simpler™ trained pharmacist prior to seeing the doctor. The Simpler™ trained pharmacist provided participants the information sheet and a brief explanation regarding the research. All patients were required to provide written consent and were subsequently admitted to the intervention or control arm according to the randomised schedule.

Patients were randomised to receive SC or UC using overall equal randomisation (1:1) at each of selected sites. The randomisation numbers were predetermined by the student researcher (SA) using an online random number generator based on a one block randomised block design.(337) The patients were blinded to the randomisation codes: intervention arm=1, control arm =2. Each KK were given a set of 24 sealed brown envelopes each containing a code and were labelled with continuous numbering of patient identification number. Whilst the patients were blinded the pharmacists were not and the pharmacists opened the envelopes in ascending order and depending on the randomisation code allocated patients to either the intervention or control arms. Figure 5.3 provides a summary of the steps involved.



*WHOQOL-BREF=abbreviated quality of life questionnaire developed through the World Health Organization

Figure 5.3: Flow diagram of the process involved in the intervention and control arms

5.3.1.5 Intervention (SC) arm

Patients in the intervention (SC) arm received usual care like patients in the control (UC) arm. In addition, they received a minimum of 20-30 minutes' face-to-face interview with the intervention pharmacist prior to seeing the doctor. During this interview the pharmacist utilised the Simpler™ tool to deliver pharmaceutical care.

Pharmacists utilised information gathered from patients and retrieved from medical records to make an assessment. Subsequently, by using the Simpler™ tool, they documented their interventions and individual goals for patients in the Simpler™ Pro Forma A and B (Appendix 5.11 and 5.12) and these were evaluated at each following visit. Simpler™ Pro Forma A was used on days when patients had appointment with doctor and nurse. The Simpler™ Pro Forma forms were then attached to patients' medical notes. The doctors were encouraged to record their interventions on the same forms. In most public health institutions in Malaysia, doctors would use black while nurses use blue ink. To differentiate each healthcare professionals' intervention, pharmacists used purple ink. Pharmacists then captured an image of each completed Simpler™ Pro Forma and sent it to the researcher, SA, through email once every month.

The Simpler™ Pro Forma B was used on days when patients had appointment with pharmacist only. During that time, pharmacists had autonomy to titrate insulin doses up to two units at each follow up visit for patients who do achieve the therapeutic target. In addition, pharmacists informed the doctors on any therapy change required and their recommendations. Subsequently, all interventions were documented using the Simpler Pro Forma B.

Patients were seen in a private consultation room located near doctors' consultation rooms when they had doctors' appointments and at a private counselling area at the

pharmacy when they did not have a doctor's appointment. An audit was performed on completed Simpler™ Pro Forma by SA to ensure the required information were recorded. In addition, current diabetes management information was sent to pharmacies periodically to keep them informed on recent developments.

In addition, patients completed the WHOQOL-BREF questionnaire once at the start (visit 1) and once at the end (visit 6) (Appendix 5.13, 5.14, 5.15). An image or scanned copy of the completed questionnaire for each visit was sent to the researcher. Pharmacists scheduled monthly appointments (five more times) for patients until the end of the trial (week 27). Additionally, pharmacists called patients the day before the appointment to remind them of their visit with the pharmacist.

The key tool used in the intervention arm was the previously developed and evaluated Simpler™ tool which consisted of the seven evidence-based factors from diabetes clinical practice guidelines. Each pharmacist received the Simpler™ tool resource pack which consisted of a number of resources as shown in Table 5.2.

Table 5.2: Simpler™ tool resource pack contents

No.	Item	Appendix
1.	Simpler Pro Forma A (when patient has a doctor's appointment)	Appendix 5.11
2.	Simpler Pro Forma B (when patient has no doctor's appointment)	Appendix 5.12
3.	WHOQOL-BREF questionnaire (Bahasa Malaysia, English and Mandarin)	Appendix 5.13, 5.14, 5.15
4.	Patient information sheet and consent forms in Bahasa Malaysia English languages	Appendix 5.16,5.17,5.18,5.19
5.	8-item MMMAS in English and Bahasa Malaysia languages.(1)	Appendix 5.20 and 5.21
6.	Naranjo probability scale for adverse drug reaction(338)	Appendix 5.22
7.	Researcher data collection form	Appendix 5.23
8.	Simpler™ tool hand-out	Appendix 5.24
9.	<u>For patients use</u> Appointment booklets for patients, SMBG record booklet and empty pocket files for each patient	Not applicable
10.	<u>Stationery for pharmacists' use</u> Stationery such as purple coloured pens and stapler. Folder containing hand-outs on Simpler™ training module; Simpler™ hand-out; oral hypoglycaemic and insulin treatment algorithm; efficacy and side effects profile of oral hypoglycaemic medicines; potential drug interactions, sealed brown envelopes containing information on participant ID and the arm they will be randomised	Not applicable
11.	<u>Monitoring device for pharmacists</u> Blood pressure monitor and tape measure to measure patient's waist circumference	Not applicable

8-item MMMAS=eight item modified Morisky medication adherence scale; SMBG=self-monitoring of blood glucose; WHOQOL-BREF=abbreviated quality of life questionnaire developed through the World Health Organization;

5.3.1.6 Control arm

Patients in the control arm received the usual care (UC). The routine medical care of patients with diabetes at primary health clinics in Malaysia consist of patient-doctor-nurse visits that ranges from between three to five visits per year. The role of the nurse is to take the blood glucose and blood pressure measurements. In addition, nurses record the height and weight of the patient and provide diabetes education to patients who have not achieved glycaemic control. It is also the nurse's

responsibility to schedule the patient's appointment with the doctor and organise laboratory tests as ordered by the doctor. In addition, patients received usual pharmacy care which includes monthly medication refills and patient counselling to promote safe and effective medicine use.

The number of scheduled doctors' appointments throughout the duration of this trial was the same for the both arms. As described above, they were seen once at the beginning of the trial (baseline) by research pharmacists to record baseline data. Subsequently, UC patients will continue their usual care with no other intervention. Pharmacist scheduled an appointment for patients to be seen once more at week 27 to record exit data. Similar to the SC arm, patients in the UC arm also completed the WHOQOL-BREF questionnaire once at the start (week 1) and once at the end (week 27). An image or scanned copy of patient demographics, laboratory data and completed WHOQOL BREF questionnaires were sent to the researcher.

5.3.1.7 Evaluation tools

Intervention pharmacists used the evaluation tools to record interactions with patients, assess medication management issues and measure blood pressure and glucose and waist circumference, both for when patients had doctors' appointments and during patients' visits to the pharmacy for prescription refills in-between doctors' appointments. The evaluation tools were therefore used in SC patients from weeks 1 to 27 but were only used for UC patients at the start (week 1) and the end (week 27) of the study.

Pharmacists performed blood pressure (BP) measurements using OMRON HEM/120 arm blood pressure monitors, blood glucose measurements using Abbott Freestyle Optiums and waist circumference measurements on patients during each visit. The BP monitor was procured by SA (part of the Scott Kimpton award for fieldwork

research) and was provided to pharmacists as part of their participation in the study. Pharmacists used the existing blood glucose monitors provided by their respective KKs. In addition to government funded and managed laboratories, HbA1c measurements were performed by a registered private laboratory, Pathlab (Pathology & Clinical Laboratory (M) Sdn.Bhd). WHOQOL-BREF questionnaires were self-administered. The primary and secondary outcome variables measured in this trial are shown in Table 5.3.

Table 5.3: Primary and secondary outcome variables measured at baseline and for the subsequent six months

Simpler™ factor evaluated	Variable	Evaluation Tools
Primary outcome variables		
Insulin/glycaemic	Glycaemic control	HbA1c measured at visit 1 and at visit 6 at hospital or private laboratory.
Secondary outcome variables		
Insulin/glycaemic	Glycaemic control	FBG measurement by pharmacist at each visit
BP	BP	Measurement by pharmacist at each visit. Measured twice. Third measurement taken only when the first two readings are different by more than 10mmHg and 6mmHg for systolic and diastolic BP.
Medication	Medication adherence	8-item MMMAS administered by pharmacists.
Statin/cholesterol	Blood lipids	measured at visit 1 and at visit 6 at hospital or private laboratory
Lifestyle	BMI	Calculated from height and weight measured by pharmacist during doctor's visit
Lifestyle	Waist circumference	Measured by pharmacist
Lifestyle	Physical activity	Self-reported by patient
Lifestyle	Health related QOL	WHOQOL-BREF questionnaire administered by pharmacist at week 1 and week 27
CVD risk	FRS	Using online calculator for risk score calculation using patients' BMI and lipid results at each visit.(89)
All factors	Pharmacists' interventions as per the Simpler™ tool	All interventions recorded in the Simpler™ Pro Forma A and B

BMI=body mass index; BP=blood pressure; FRS=Framingham risk score; HbA1c= glycated haemoglobin; MMMAS= modified Morisky medication adherence scale; SMBG=self-monitoring of blood glucose; QOL=quality of life; WHOQOL-BREF= abbreviated quality of life scale developed through World Health Organization;

5.3.2 Data collection

Sociodemographic information such as age, gender, ethnic origin, number of comorbidities, employment and education level were obtained through Simpler™ Pro Forma A and B forms for the SC arm and from medical notes and patient interviews for the UC arm. Information on patients' medication and laboratory results were obtained from patient medical records for both arms.

As mentioned previously, images sent by pharmacist were scrutinised by the researcher (SA) for missing information. Pharmacists were then contacted to obtain the required missing information. A data collection form (see Appendix 5.22) was used to record all required information.

5.3.3 Data analysis

Data analysis was performed on primary and secondary outcomes variables as outlined in Table 5.3. Information from the data collection forms mentioned in Section 5.3.2. were transferred into the IBM Statistical Package for Social Sciences (SPSS) software version 22.(233) An excerpt of the data from SPSS is shown in Appendix 5.25. The data were then analysed using the same statistical program. Outcomes from the intervention and control arms were compared at baseline using independent t-tests for parametric data and Mann-Whitney U-test for non-parametric data. Pearson chi-square test was used for categorical parameters. Paired t-test was used to detect significant differences at baseline and at 6 months. Occasionally one-way analysis of variance (Anova) was used to determine significant differences between three or more categories. An alpha level of ≤ 0.05 was used for all statistical tests to denote significance level.

5.4 Results

Prior to the start of the trial, 11 KKs expressed their willingness to participate. One of the pharmacists from one of the KKs who commenced training was a credentialed diabetes pharmacist which did not conform to the eligibility criteria for pharmacists. Three KKs withdrew due to staff shortages and increasing workload. Therefore, only pharmacists from the remaining seven KK's signed the consent form.

All participating pharmacists were trained on diabetes management and medication-related interventions using the Simpler™ tool. The online training session ran from mid-April to end May 2016. On completion, pharmacists were invited to a four-hour face to face RCT briefing session held in Johor Bahru, Malaysia. Depending on pharmacist availability, pharmacists were given an option to attend the briefing session on separate dates. Seven pharmacists attended the briefing on 4th June 2016 while five attended the briefing on 11th June 2016. One pharmacist could not attend on both dates and was therefore briefed at his normal place of work on 23rd June 2016 and the 14th pharmacist was trained at a later date (7th February 2017). The RCT commenced in mid-June 2016 and was completed by early March 2017.

5.4.1 Demographic characteristics of pharmacists

There was a total of 14 pharmacists who were initially recruited. One pharmacist dropped out during the research because she was relocated to another pharmacy, therefore the new pharmacist who replaced her in that clinic was conveniently recruited and trained. Hence, 14 pharmacists were recruited and trained in total. Pharmacists recruited worked in seven KKs situated in six out of the total 10 different districts in the state of Johor. The names of the KKs were: Bukit Besar and Bandar

Tenggara in the Kota Tinggi district; Tenggaroh 2 in the Mersing district; Bukit Pasir in the Muar district; Paya Mas in the Tangkak district; Segamat in the Segamat district; and Tebrau in the Johor Bahru district. A map of Johor state in Figure 5.4 marks the location of each participating site (KK), showing that the sites were spread throughout the state and hence represented a wide geographical area.

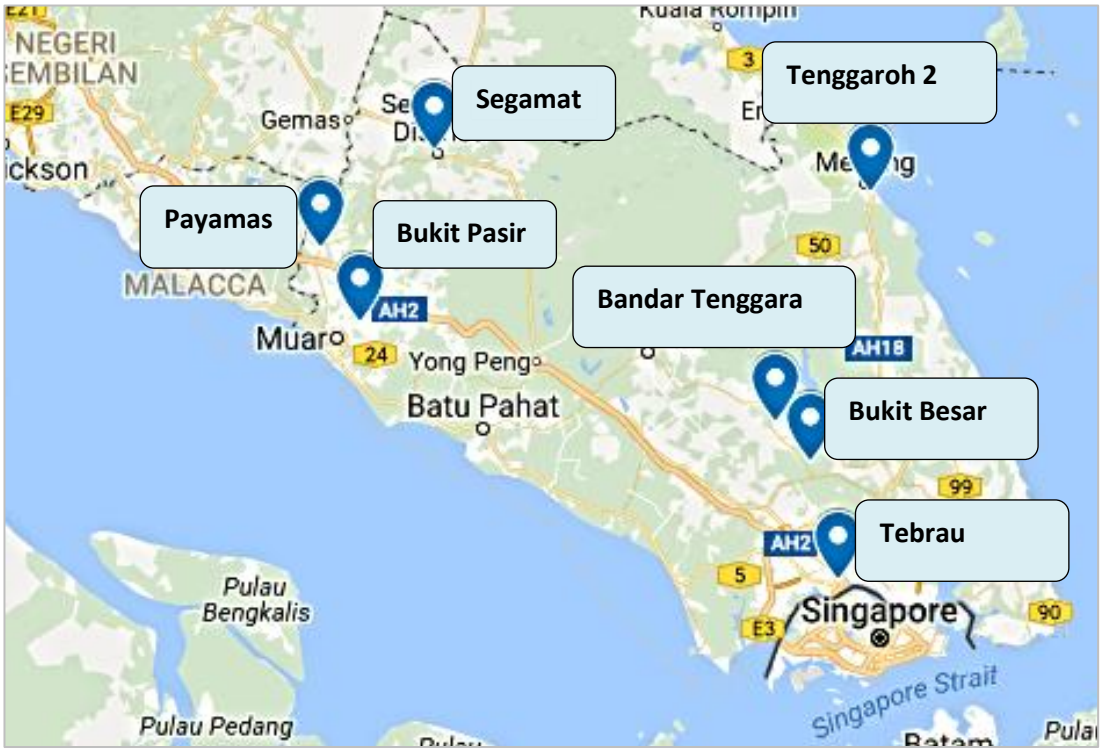


Figure 5.4: Location of participating sites in the state of Johor, Malaysia using Google maps.(339)

The majority of the participating pharmacists were female (12/14; 85.7%). All pharmacists worked full time and on average 37.5 hours per week. Half of the pharmacists (7/14; 50%) recruited were practicing pharmacists for a period of less than 3 years. None of the pharmacists had been credentialed or received any formal diabetes training. Most pharmacists (10/14; 71.4%) had been conducting diabetes management services for less than one year. Collectively all pharmacists had less

than three years' experience in the management of T2DM patients. Table 5.4 presents pharmacists' practice experience.

Table 5.4: Participating pharmacists practice experience (years)

Years qualified	**Number of pharmacists n (%)**
0-1	2 (14.3)
>1 and <3	5 (35.7)
3-5	3 (21.4)
>5	4 (28.6)
Total	14 (100)
Years of conducting diabetes MMS	**Number of pharmacists n (%)**
0-1	10 (71.4)
>1 and <3	4 (28.6)
Total	14 (100)

Pharmacists were asked to rank the main motivating factors that induced their participation in this research. The two main reasons that were ranked in the upper quartile range of the Likert scale (4 and 5) were "improve patients' outcome" (13/14; 92.9%) and "interested in subject" (9/14; 64.3%) as shown in Figure 5.5. The other factors which got the highest rankings (4 and 5) are also presented.

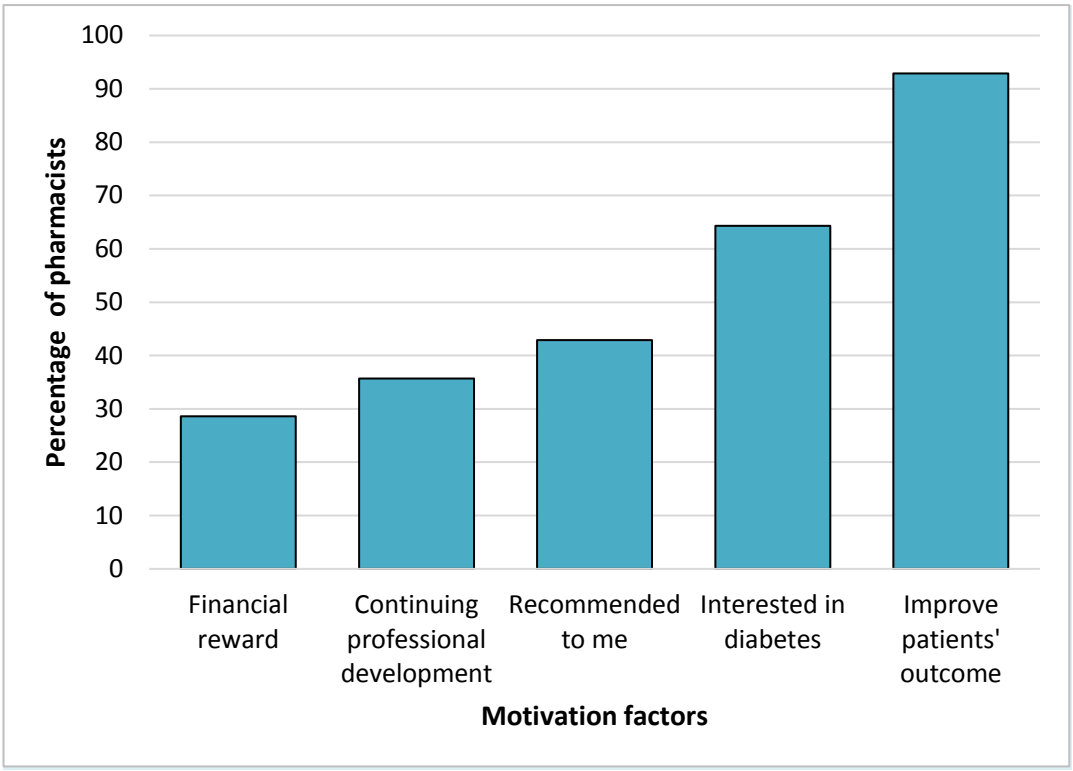


Figure 5.5: Factors that motivated pharmacists to participate in Phase Three research

5.4.2 Results from pre-and post-training questionnaire

Overall there was significant improvement in the post-test results compared to the pre-test (p=0.001). The median pre-test score for the 1st and 2nd markers was 5.75 (IqR 3.6) out of 27. The median post-test score for the 1st marker and 2nd marker was 14.29 out of 27 marks. The statistical results are presented in Table 5.5.

Table 5 5: Pharmacists pre- and post-training scores of participants (n=14)

	Median (IqR)		Z stat	[a]*p* value
	Pre-test	Post-test		
Test score (1st marker)	5.5 (3.8)	14 (5.3)	-3.303	[b]0.001
Test score (2nd marker)	6.0 (4.3)	13.5 (4.8)	-3.193	[b]0.001
(1st and 2nd marker)	5.75 (3.6)	13.25 (4.1)	-3.299	[b]0.001

[a]statistical test using Wilcoxon signed rank test for non-parametric data; [b]statistically significant

5.4.3 Demographic characteristics of patients

A total of 154 T2DM patients (77 SC: 77 UC) attending the seven KKs were recruited into the study. Table 5.6 shows the number of patients recruited from each KK and the numbers excluded from the final analysis.

There were 89.6% (69/77) of patients in the UC arm who completed the study. Reasons for non-completion included patients absent on follow up visits despite repeated reminders and telephone calls, patients did not have outcome measures or passed away.

In the SC arm, 79.2% (61/77) patients completed the study. The average number of visits to the pharmacists was 5 (SD=1.43). The number of visits ranged from two to six visits for each patient. Each visit lasted between 20 and 30 minutes. However only the 55 patients out of the total 61 patients who attended a minimum of three visits (55/77; 71.4%) were included in data analysis. The reasons why patients completed less than the agreed six visits were, not able to meet at predetermined dates agreed with pharmacists. In other instances, pharmacists were not able see patients due to heavy dispensing workloads caused by lack of staffing.

Table 5.6: Number of patients recruited and number of dropouts from each KK

KK	No. patients recruited (%)		No. patients dropped out (%)		No. patients' data used in analysis for final visit (%)	
	SC	UC	SC	UC	SC	UC
Bukit Besar	12 (15.6)	12 (15.6)	0	0	12 (21.8)	12 (17.4)
Bandar Tenggara	12 (15.6)	12 (15.6)	5 (22.7)	1 (12.5)	7 (12.7)	11 (15.9)
Bukit Pasir	12 (15.6)	12 (15.6)	0	0	12 (21.8)	12 (17.4)
Paya Mas	12 (15.6)	12 (15.6)	6 (27.3)	5 (62.5)	6 (10.9)	7 (10.1)
Segamat	12 (15.6)	12 (15.6)	1 (4.5)	0	11 (20.0)	12 (17.4)
Tebrau	5 (6.5)	5 (6.5)	2 (9.1)	2 (25.0)	3 (5.5)	3 (4.3)
Tenggaroh 2	12 (15.6)	12 (15.6)	8 (36.4)	0	4 (7.3)	12 (17.4)
Total	77 (100)	77 (100)	22 (100)	8 (100)	55 (100)	69 (100)

For the purpose of this research, the HbA1c values are expressed in the International Federal Clinical Chemistry Working Group (IFCC-WG) unit as mmol/mol and are used interchangeably with National Glycohaemoglobin Standarization Program (NGSP) unit as %.(340)

Figure 5.6 presents the CONSORT(341) diagram illustrating the flow chart of the research participants from enrolment to final analysis.

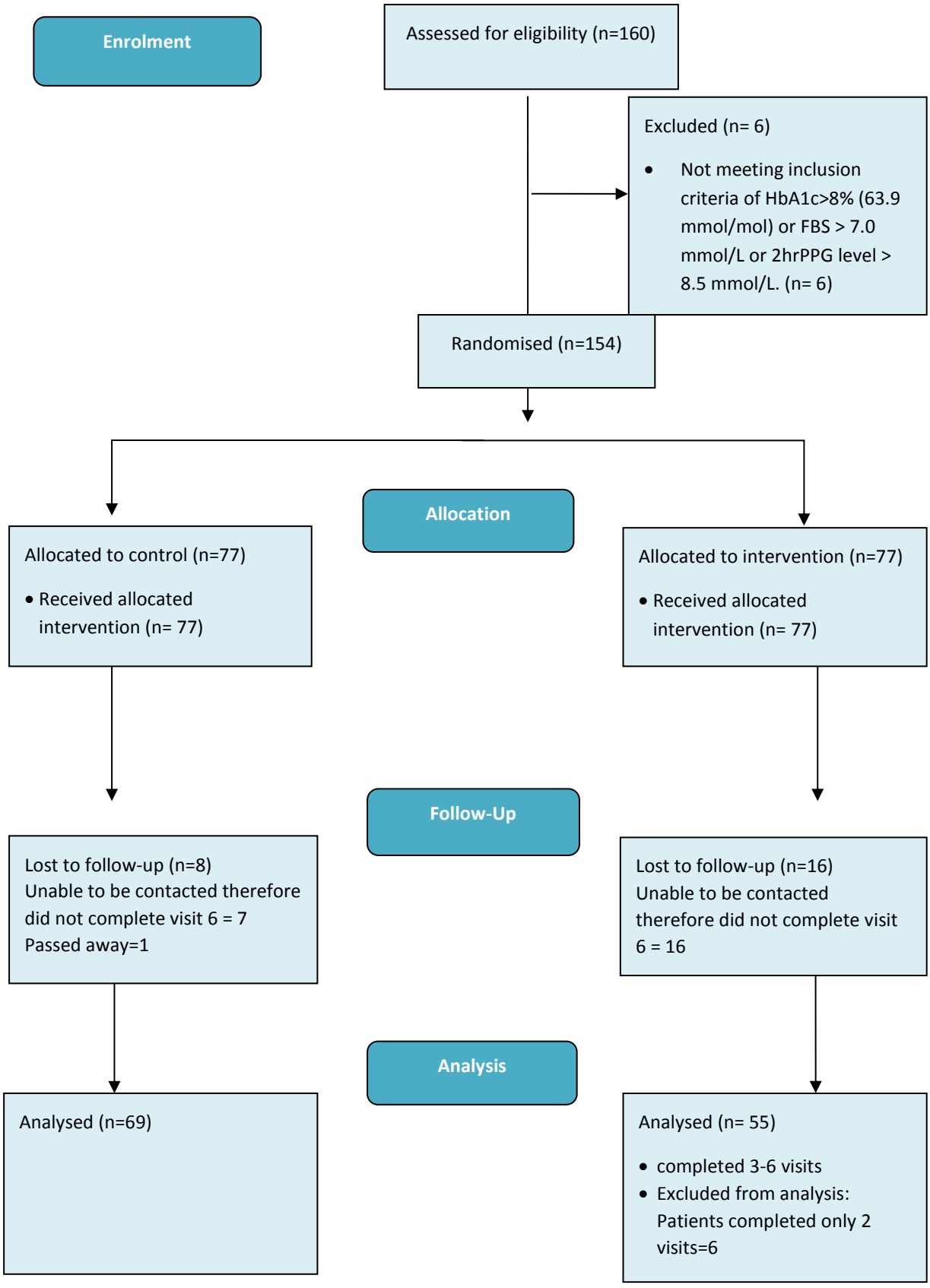


Figure 5.6: CONSORT diagram of patients' recruitment and completion.

There were six patients in the SC arm who completed only two visits to the pharmacy. Appendix 5.26 presents the demographic data of the six patients who completed only two visits. As stated, the analysis of results in this chapter included data for SC patients who completed the study and who attended a minimum of three visits. A required minimum of three visits to pharmacists was agreed by the research team as this allowed patient education on various aspects of diabetes medication and self-management throughout the trial period. Table 5.7 presents the breakdown of number of patients and their completed number of visits to pharmacists.

Table 5.7: Breakdown of SC patients who completed the three to six visits with the pharmacist

No. visits with pharmacists	No. SC patients (%)
3	7 (12.7)
4	7 (12.7)
5	7 (12.7)
6	34 (61.8)
Total	55 (100)

The baseline characteristics of patients in the SC and UC arms are shown in Table 5.8. A comparison of SC and UC patients with respect to demographic, family history, types and number of comorbidities and current employment showed no significant differences. The mean age from both arms were 56.5 years and there were more female patients recruited in comparison to male patients. Ethnic *Melayu* patients outnumbered other races in both arms and hypertension was the most identified comorbidity. There were slightly more patients in the SC arm who were working (52.7%) compared to the UC arm but this difference was not significant. There was a significant difference between patients' overall highest education level between the

SC and UC arms. Nevertheless, the percentage of patients who were educated and those who were not did not differ among SC and UC arms (p=1.000).

Table 5.8: Baseline characteristics of the study population

Characteristics	SC (n=55)	UC (n=69)	*p*-value
Mean age (years)	55 (SD=8.9)	58 (SD=10)	0.068
Existing family history of diabetes	29 (53.7%)	21 (38.2%)	0.106
Gender			0.854
Female	32 (58.2%)	39 (56.5%)	
Male	23 (41.8%)	30 (43.5%)	
Ethnic origin			0.837
[a]*Melayu*	43 (78.2%)	53(76.8%)	
Chinese	8 (14.5%)	11 (15.9%)	
Indian	4 (7.3%)	5 (7.2%)	
Comorbidities			
Hypertension	49(76.6%)	61 (69.3%)	0.905
CVD	1 (1.6%)	1 (1.1%)	
Nephropathy	5 (7.8%)	12 (13.6%)	0.182
Retinopathy	3 (4.7%)	3 (3.4%)	
Neuropathy	3 (4.7%)	1 (1.1%)	
≥2 comorbidities	12 (21.8%)	21 (30.4%)	0.393
Highest education level			[b]0.028
Primary	10 (18.2%)	29 (42.0%)	
Secondary	34 (61.8%)	34 (49.3%)	
Diploma	6 (10.9%)	3 (4.3%)	
University	3 (5.5%)	1 (1.4%)	
Not educated	2 (3.6%)	2 (2.9%)	
Current employment			0.080
Caring for family	18 (32.7%)	34 (49.3%)	
Working	28 (50.9%))	30 (43.5%)	
Unemployed	2(3.6%)	0 (0%)	
Retired	7 (12.7%)	5 (7.2%)	
Clinical parameter	SC mean (SD)	UC mean (SD)	p-value
HbA1c (%)/(mmol/mol)	10.68/93 (2.22)	10.32/89 (1.50)	0.337
Systolic BP (mmHg)	136.97(16.78)	137.82 (18.33)	0.791
Diastolic BP (mmHg)	80.95(12.00)	79.87 (10.47)	0.592
LDL (mmol/L)	3.09(1.13)	3.35 (1.16)	0.317
HDL (mmol/L)	1.28(0.34)	1.19 (0.24)	0.158
TG (mmol/L)	1.93(1.23)	1.97 (0.92)	0.870
Creatinine (mmol/L)	78.46(24.20)	80.74 (25.11)	0.657
BMI (kg/m^2)	28.82 (5.43)	29.32 (5.26)	0.606
Waist circumference (cm)	96.51(11.31)	95.78 (10.71)	0.717

[a] *Melayu* refers to ethnic Malay and indigenous population in Malaysia

[b]Chi-square and Fisher's exact tests was used to determine significance, denoted as $p<0.05$, between intervention (SC) and usual care (UC) arms.

BP=blood pressure; BMI=body mass index; CVD=cardiovascular disease; HbA1c= haemoglobin A1c; LDL=low density lipoprotein; HDL=high density lipoprotein; SD=standard deviation; TG=triglyceride

5.4.4 Medication use at baseline and changes at six months

The average number and types of medication used by patients in both arms are presented in Table 5.9. Patients' medication lists included mostly antidiabetic, antihypertensive and lipid lowering medicines and a daily antiplatelet medication. The changes at 6 months from baseline were not statistically different between the two arms except for a daily antiplatelet as primary prevention to decrease CVD risk (p=0.02). Other medications used related to patients' other comorbidities as shown in Table 5.10. The other medications at the final visit were mostly vitamin B complex (SC=24% vs UC=20%).

At 6 months, 72.7% of SC patients were prescribed metformin compared to 61.8% of patients at baseline. There was a slight increase in the number of patients on metformin at 6 months for both SC (10.7%) and UC arms (6%). However, these differences between arms were not statistically significant between baseline (p=0.408) and at 6 months (p=0.337). Similarly, there was no significant difference in the number of prescribed insulin between arms at 6 months, (p=0.414). The SC arm had a non-significant increase (5.4%) in the number of patients on prescribed insulin at 6 months compared to baseline, while the UC arm initiated two patients on insulin, a non-significant increase of 2.9% at 6 months from baseline. Of interest, the SC arm had a higher proportion of patients (74.5%) on insulin as required by the Malaysian diabetes guidelines when compared to UC arm (72.5%).

Pharmacist interventions on ACEI/ARB initiation contributed to a slight increase (11%) in prescribed ACEI/ARB for the SC arm at the end of the study at 6 months, however, this increase was not statistically significant (baseline vs 6 months). Equally, UC patients had a non-significant increase (12.5%) of prescribed ACEI/ARB at 6 months.

Table 5.9: Medication use and changes over six months in SC and UC arms

	SC (n=55) n (%)		UC (n=69) n (%)		SC vs UC [a]*p*-value	
	Baseline	6 months	Baseline	6 months	Baseline	6 months
Use of Insulin					0.51	0.41
Short	5 (9.1)	6 (10.9)	11 (15.9)	13 (18.8)		
Intermediate	18 (32.7)	20 (36.4)	21 (30.4)	23 (33.3)		
Long	1 (1.8)	2 (3.6)	2 (2.9)	0		
Premixed	19 (34.5)	19 (34.5)	25 (37.7)	28 (40.6)		
OHA						
Metformin	34 (61.8)	40 (72.7)	40 (58.0)	44 (63.8)	0.41	0.33
Sulphonylurea	15 (27.3)	15 (27.3)	18 (26.1)	17 (24.6)		
Metformin+sulphonylurea	11 (20.0)	9 (16.4)	12 (17.4)	9 (13.0)		
Acarbose	1 (1.8)	3 (5.5)	3 (4.3)	4 (5.8)		
DPP-4 Inhibitor	0	0	1 (1.4)	1 (1.4)		
SGLT-2 Inhibitor	0	1 (1.8)	0	0		
Antihypertensive						
ACEI	35 (63.6)	38 (69.1)	37 (53.6)	41 (59.4)	0.40	0.29
ARB	1 (1.8)	2 (3.6)	3 (4.3)	4 (5.8)		
CCB	30 (54.5)	31 (56.4)	40 (58.0)	44 (63.8)		
Beta blocker	8 (14.5)	9 (16.4)	14 (20.3)	16 (23.2)		
Alpha blocker	3 (5.5)	3 (5.5)	3 (4.3)	4 (5.8)		
Diuretic	15 (27.3)	13 (23.6)	15 (21.7)	14 (20.3)		
Coversyl Plus (Perindopril+indapamide)	0	0	1 (1.4)	0		
Lipid lowering						
Simvastatin	44 (80.0)	47 (85.5)	52 (75.4)	52 (75.4)	0.43	0.12
Others	3 (5.5)	3 (5.5)	4 (5.8)	4 (5.8)		

	SC (n=55) n (%)		UC (n=69) n (%)		SC vs UC [a]*p*-value	
	Baseline	6 months	Baseline	6 months	Baseline	6 months
Daily antiplatelet						
Aspirin	16 (29.1)	22 (40.0)	15 (21.7)	16 (23.2)	0.25	[b]0.02
Ticlopidine	1 (1.8)	2 (3.6)	0	0		

[a]*p*-value from Pearson chi-square test; [b] statistically significant

ACEI=angiotensin converting enzyme inhibitor; ARB=angiotensin renin blocker; CCB=calcium channel blocker; DPP-4 inhibitor=dipeptidyl -4 inhibitor; OHA=oral hypoglycaemic agent; SC=Simpler ™ care intervention; SLGT2=sodium glucose cotransporter-2; UC=usual care

Table 5.10: Other medication used by patients in both SC and UC arms

	SC (n=55) n (%)		UC (n=69) n (%)	
	Baseline	6 months	Baseline	6 months
Inhalers for asthma	2 (3.6)	2 (3.6)	2 (2.9)	2 (2.9)
Allopurinol	0	0	0	1 (1.4)
Calcium carbonate	1 (1.8)	0	0	0
Empagliflozin	0	2 (3.6)	0	0
Glyceryl trinitrate	1 (1.8)	2 (3.6)	2 (2.9)	3 (4.3)
Isosorbide mononitrate	1 (1.8)	2 (3.6)	3 (4.3)	4 (5.8)
L-thyroxine	0	0	1 (1.4)	0
Omeprazole	1 (1.8)	0	1 (1.4)	1 (1.4)
Potassium chloride	0	0	3 (4.3)	3 (4.3)
Ranitidine	4 (7.3)	4 (7.3)	1(1.4)	1 (1.4)
Vitamin B complex	10 (18.2)	13 (23.6)	11 (15.9)	13 (18.8)
Traditional medications	4 (7.3)	1 (1.8)	-	-

SC=Simpler™ care intervention; UC= usual care; n=sample size

5.4.5 Doctor's visits and hospital admissions at 6 months

There was a total of five hospital admissions during the six months' study period. Two hospital admissions in the SC arm and three hospital admissions in the UC arm. Although the UC arm had one more hospital admission than the SC arm, this difference was not statistically significant (p=0.868).

Similarly, there was no significant difference between the average number of patients' visits to doctors between the SC (2.73; SD=0.971) and UC arm (2.75; SD=1.322; p=0.902). The frequency of visits to the doctor in the SC and UC arm is presented graphically in Figure 5.7.

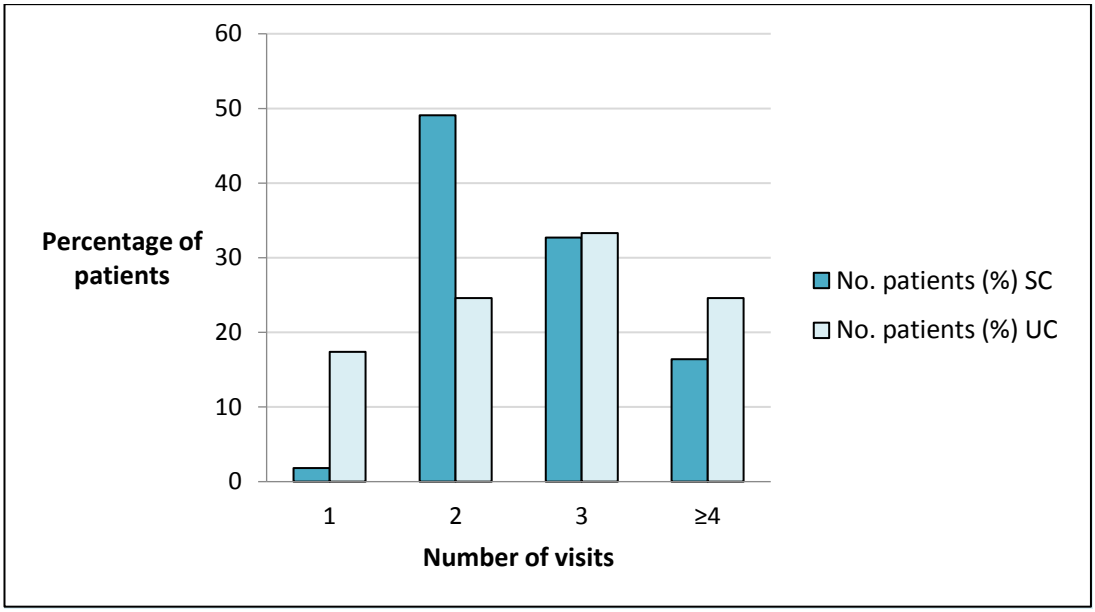


Figure 5.7: Comparison of patients' visits to the doctor for SC and UC arms

5.4.6 Pharmacists' interventions

The number of patients in the SC arm whom interventions were recorded over the 6 month follow up is shown in Table 5.11. SC pharmacists managed to address all the

indicators in most patients (>60%) in the SC arm. The number of patients who achieved treatment targets according to the guidelines(6) is discussed separately in section: 5.4.7.1.

Table 5.11: Simpler™ interventions conducted on SC patients over the 6 months follow up

Indicators	No.patients (%) (n= 55)		
	Yes (%)	No (%)	Not relevant (%)
S=Statin			
Statin initiation in patients with CVD	13 (23.6)	0	42 (76.4)
Achieve targets: LDL<2.6 mmol/L, TG<1.7 mmol/L		See Table 5.13	
Statin initiation in patients > 40 years old without CVD	38 (69.1)	0	17 (30.9)
I=Insulin/Glycaemic control			
Insulin initiation if glycaemic control not achieved despite being on two or more oral hypoglycaemic agents	41 (74.6)	14 (25.5)	0
Target of HbA1c ≤ 7% (53mmol/mol) if no other complications		See Table 5.13	
Management of hypoglycaemia	48 (87.3)	7 (12.7)	0
Self-monitoring of blood glucose	51 (92.7)	4 (7.3)	0
Aim a difference for HbA1c of -1% if above target HbA1c		See Table 5.13	
Initiate/continue metformin if not contraindicated	50 (90.9)	4 (7.3)	1 (1.8)
M=Medication			
Assess medicine related problems	55 (100)	0	0
Review medication adherence using 8-items MMMAS	55 (100)	0	0
P= Blood pressure			

Indicators	No.patients (%) (n= 55)		
	Yes (%)	No (%)	Not relevant (%)
Achieve BP target ≤135/75		See Table 5.13	
ACE-I/ARB initiation in patients with/without microalbuminuria /proteinuria	45 (81.8)	6 (10.9)	4 (7.3)
Reduce sodium intake (<2400mg sodium/day; 6g/1 teaspoon/day)	51 (92.7)	4 (7.3)	0
Take one or more antihypertensive at bedtime	37 (67.3)	13 (23.6)	5 (9.1)
L=Lifestyle			
Exercise: 30 mins walking (or equivalent) 5 or more days/week (total ≥ 150 min/week)		See Table 5.13	
Weight loss: BMI ≤ 23kg/m^2		See Table 5.13	
Advise on smoking cessation	5 (9.1)	0	50 (90.9)
Waist circumference: ≤ 90cm in men, ≤ 80cm in women		See Table 5.13	
Alcohol intake: ≤2 standard drinks (20 g) per day for men	54 (98.2)	1 (1.8)	0
Management of stress and diabetes related distress	35 (63.6)	20 (36.4)	0
Erectile dysfunction: recommend PDE-5 inhibitor as first line therapy for male patients			55(100)
Foot care	47 (85.5)	8 (14.5)	0
Diet advice using plate model	51 (92.7)	4 (7.3)	0
Annual eye assessment	39 (70.9)	16 (29.1)	0
Address sleep hygiene	40 (72.7)	15 (27.3)	0

Indicators	No.patients (%) (n= 55)		
	Yes (%)	No (%)	Not relevant (%)
E=Education			
Knowledge and understanding of medicine	55 (100)	0	0
Medicine storage	52 (94.6)	3(5.5)	0
Medication optimisation during fasting month for Muslims and other religious arms	1 (1.8)	0	54 (98.2)
R= CVD risk			
Aspirin therapy as secondary prevention in those with diabetes with history of CVD	37 (67.3)	6 (10.9)	12 (21.8)
Use of Framingham risk calculator to calculate CVD risk and educate patients	39 (70.9)	16 (29.1)	0
Aspirin therapy (75mg-162mg/day) as primary prevention to decrease CVD risk (10-year risk>10%, Framingham) (patients >65 years old)	37 (67.3)	5 (9.1)	13(23.6)

ACEI=angiotensin converting enzyme inhibitor; ARB=angiotensin renin blocker; BMI= body mass index; CVD= cardiovascular disease HbA1c= haemoglobin A1c; BMI=body mass index; BP=blood pressure; TG=triglyceride; LDL=low density lipoprotein; MMMAS= modified Morisky medication adherence scale; HDL=high density lipoprotein

5.4.7 Clinical outcomes of patients in both arms

Table 5.12 presents the results of the statistical test analyses of patients between the SC and UC arms and at baseline and at 6 months' intervention. Results show significant improvement in HbA1c (p=<0.001) and systolic BP (p=0.028) at 6 months between arms. The effect size for HbA1c differences in this research is 0.702 for Cohen's d and 0.722 for Hedges'g.

The SC arm showed significant differences in HbA1c and systolic BP at 6 months compared to the UC arm. In this study, a separate analysis was done for each variable in Table 5.12. These variables were not dependent on each other therefore Bonferroni adjustments were not applicable. This is in accordance to suggestions by Perneger.(342)

The number of patients who achieved treatment targets at 6 months according to the Malaysian diabetes guidelines is shown in Table 5.13. More patients in the SC arm achieved the treatment targets compared to the UC arm for all clinical parameters listed except for diastolic BP. However, only the number of patients who achieved the treatment targets for HbA1c, LDL and systolic BP were significantly different between the two arms.

Table 5.12: Clinical parameters of participants at baseline and on 6 months follow up in SC and UC arms

Variables	SC vs UC	*n*	Baseline Mean (SD)	6 months Mean (SD)	Mean difference (95% CI)	Baseline vs 6- months [a]*p*-value	SC vs UC (6 months) [b]*p*-value
HbA1c (%)/mmol/mol	SC	49	10.68/93 (2.22)	9.08/76 (2.26)	-1.59 (-2.2 to -0.9)	[c] <0.001	[c] <0.001
	UC	63	10.32/89 (1.50)	10.07/86 (1.80)	-0.25 (-0.62 to 0.11)	0.171	
BMI (kg/m$^{2)}$	SC	55	28.82 (5.43)	28.72 (5.33)	-0.1 (-0.6 to 0.4)	0.710	0.481
	UC	68	29.32 (5.26)	29.52 (5.22)	0.20 (-0.4 to 0.8)	0.529	
Waist circumference (cm)	SC	54	96.51(11.31)	95.02(8.84)	-1.49(-3.6 to 0.6)	0.164	0.249
	UC	65	95.78 (10.71)	95.71 (11.17)	-0.06 (-1.44 to 1.31)	0.928	
Systolic BP (mmHg)	SC	55	136.97(16.78)	130.68(14.35)	-6.28(-10.5 to -2.0)	[c] 0.005	[c] 0.028
	UC	69	137.82 (18.33)	138.07(13.35)	0.26 (-3.74 to 0.43)	0.897	
Diastolic BP (mmHg)	SC	55	80.95(12.00)	78.49(9.65)	-2.46(-5.8 to -0.8)	0.141	0.705
	UC	69	79.87 (10.47)	78.21 (9.15)	-1.66 (-4.37 to 1.05)	0.225	
Total Cholesterol (mmol/ml)	SC	44	5.19(1.25)	5.02 (1.19)	-0.17(-0.6 to 0.3)	0.419	0.943
	UC	53	5.36 (1.30)	5.21(1.43)	-0.15 (-0.5 to 0.2)	0.373	
TG (mmol/ml)	SC	44	1.93(1.23)	1.67(0.94)	-0.26(-0.6 to 0.1)	0.138	0.202
	UC	54	1.97 (0.92)	1.99 (1.15)	0.03 (-0.26 to 0.31)	0.856	
LDL (mmol/ml)	SC	38	3.09(1.13)	2.61(1.09)	-0.49(-0.9 to -0.1)	[c] 0.017	0.553
	UC	49	3.35 (1.16)	3.01 (1.25)	-0.33(-0.68 to 0.012)	0.058	
HDL (mmol/ml)	SC	37	1.28(0.34)	1.40(0.39)	0.12 (1.2 to 2.3)	[c] 0.010	0.598
	UC	50	1.19 (0.24)	1.28 (0.30)	0.09 (0.012 to 0.17)	[c] 0.024	

[a]*p* values from paired t-test. Changes over 6 months are mean difference (95% CI); [b]*p* values from independent t-test; [c]statistically significant
SC=Simpler™ care; UC= Usual care; SD=standard deviation; CI= confidence interval; HbA1c= haemoglobin A1c; BMI=body mass index; BP=blood pressure; TG=triglyceride; LDL=low density lipoprotein; HDL=high density lipoprotein

Table 5.13: Comparison of participants in SC and UC arms who met treatment target at 6 months according to the 2015 Malaysian clinical practice guidelines on of T2DM.(6)

Variables	Arm	n	Total patients (%)	[a]*p*-value SC vs UC
HbA1c ≤ 6.5%/48mmol/mol	SC	49	7(14.3)	[c] 0.020
	UC	65	1(1.5)	
BMI ≤ 23 kg/m2	SC	55	7 (12.7)	0.484
	UC	68	6 (8.8)	
Waist circumference ≤90 cm in men	SC	23	7 (30.4)	0.667
	UC	30	7 (23.3)	
Waist circumference ≤80cm in women	SC	32	3 (9.4)	0.657
	UC	39	2 (5.1)	
Systolic BP target: ≤135 mmHg	SC	55	44 (80.0)	[c] 0.001
	UC	69	29 (42.0)	
Diastolic BP target: ≤75 mmHg	SC	55	15 (27.3)	0.577
	UC	69	22 (31.9)	
TG ≤ 1.7 mmol/L	SC	45	32 (71.1)	0.080
	UC	59	32 (54.2)	
LDL ≤ 2.6 mmol/L	SC	43	26 (60.5)	[c]0.046
	UC	57	23 (40.4)	
HDL > 1.0 (male)	SC	17	13 (76.5)	1.000
	UC	22	17 (77.3)	
HDL > 1.2 (female)	SC	20	15 (75.0)	0.226
	UC	28	15 (53.6)	
[b]CVD risk (10 year risk < 10%) using lipid values	SC	42	17(40.5)	-
[b]CVD risk (10 year risk < 10%) using BMI values	SC	55	5 (9.1)	-

[a] *p*-value from Pearson chi-square test; [b] data could only be obtained for SC patients; [c]statistically significant; BMI=body mass index; BP=blood pressure; CI=confidence interval; CVD=cardiovascular disease; HbA1c= Haemoglobin A1c; HDL=high density lipoprotein; LDL=Low density lipoprotein; SC=Simpler™ care; SD=standard deviation; TG=triglyceride; UC=usual care;

5.4.7.1 Lipid values at baseline and at 6 months

Findings in this section refers to Table 5.12. Both arms had improvements in TC, TG, LDL and HDL at 6 months compared to baseline. However, these improvements were not significantly different between arms. Of interest, there was significant reductions (p=0.017) in the LDL level for the SC arm (baseline vs. 6 months) but this was not the case for the UC arm.

There was a 5% increase in the number of statins prescribed at 6 months compared to baseline for patients in the SC arm due to intervention recommendations by SC pharmacists. However, this increase was not statistically significant. In contrast, the UC patients had no change in the number of statins prescribed to them at 6 months.

5.4.7.2 Glycaemia control at baseline and outcomes at 6 months

The primary outcome measure, HbA1c were similar at baseline for both arms, showing that the patients from the two arms were comparable at baseline. However, there were significant decreases in HbA1c levels between the arms at 6 months intervention (p<0.001). The patients in the SC arm who received care from pharmacists using the Simpler™ tool showed average mean reductions in HbA1c of 1.59%, (p=0.001) at 6 months, whilst the UC arm differences was 0.25% (p=0.171) at 6 months compared to baseline levels. Figure 5.8 presents standard error for mean HbA1c differences in both arms. Additionally, the standard error bars of each arm did not overlap, meaning the Simpler™ intervention made a difference in the HbA1c outcomes among patients in this research.

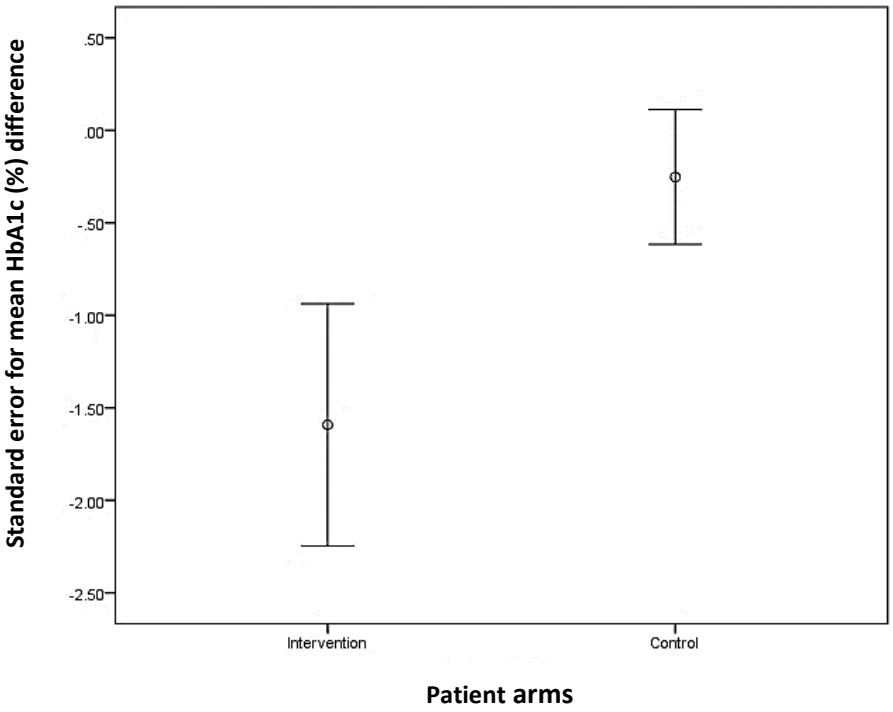


Figure 5.8: Standard error of mean HbA1c difference levels between baseline and 6 months for both arms

Of interest, the percentage of patients who obtained target HbA1c levels less than 7% (53mmol/mol) as set by the American Diabetes Association guidelines(16) were greater 11/49 (22.4%) in the SC than the UC arm 4/65 (6.2%) at 6 months. These differences were statistically significant (p=0.011). Similarly, in accordance with the Malaysian diabetes guidelines (6), more participants 7/49 (14.3%) from the SC arm achieved the target HbA1c of ≤6.5% (47.5mmol/mol) compared to the UC arm 1/65 (1.5%). Additionally, these differences were statistically significant (p=0.020) between the arms (Table 5.13).

A majority of SC patients (57.1%) achieved a mean HbA1c reduction of 1% compared to 28.6% of UC patients. This difference was found to be statistically significant (p=0.002). Subgroup analysis found that patients of *Melayu* ethnicity, female

patients and patients with mean baseline levels of more than 9% in the SC arm had significantly improved HbA1c results compared to patients in UC arm as presented in Table 5.14.

Table 5.14: Comparison of patients who achieved a mean reduction of 1% HbA1c between arms

Variable	No. patients (%)	[a] *p*-value
Overall		
SC (n=49)	28 (57.1%)	[b] 0.002
UC (n=63)	18 (28.6%)	
Patients of *Melayu* ethnicity		
SC (n=40)	23 (57.5%)	[b] 0.003
UC (n=49)	13 (26.5%)	
Patients of non *Melayu* ethnicity		
SC (n=9)	5 (55.6%)	0.349
UC (n=14)	5 (35.7%)	
Female patients		
SC (n=27)	16 (59.3%)	[b] 0.006
UC (n=36)	9 (25.0%)	
Male patients		
SC (n=22)	12 (54.5%)	0.136
UC (n=27)	9 (33.3%)	
Patients with mean baseline HbA1c≤9.0%/75 mmol/mol		
SC (n=10)	5 (50%)	0.204
UC (n=14)	3 (21.4%)	
Patients with mean baseline HbA1c>9.0%/75 mmol/mol		
SC (n=39)	23 (59.0%)	[b]0.008
UC (n=49)	15 (30.6%)	

[a] *p*-value from Pearson chi-square test; [b] statistically significant; SC= Simpler™ care; UC= usual care; HbA1c= glycated haemoglobin

Comparison of FBG readings (baseline vs 6 months) showed significant improvement for the SC arm, a reduction of 3.76 mmol/L ($p<0.001$) as shown in Table 5.15. In comparison, FBG readings reduced by 0.63 mmol/L ($p=0.524$) in the UC arm. These reductions were significantly different between arms ($p<0.002$). However, the FBG results at six months were not significantly different between the arms. Figure 5.9 shows a graphical presentation of the changes in FBG values throughout the six months. The different sizes of the box plots at each visit suggests different FBG values

during each patients' visit. The shorter box plot at visit six compared to other visits suggests that overall, SC patients had similar FBG values at this visit.

Table 5.15: Changes in blood glucose parameters at baseline and at 6 months follow up in both arms

	Arm	n	Baseline Median (IQR)	6 months Median (IQR)	Z stat	Baseline vs 6 months *p*-value	SC vs UC [a]*p*-value (6 months)	SC vs UC [a]*p*-value [c](changes)
FBG	SC	30	10.4 (4.0)	7.95 (3.45)	-3.764	*[b]0.001	0.154	*0.002
	UC	29	9.2 (2.0)	9.1 (3.70)	-0.638	[b]0.524		
RBG	SC	9	12.45(0)	7.15 (0)	-1.960	0.050	0.831	0.756
	UC	9	11.6 (3.15)	9.1 (4.6)	-1.475	0.140		
PPG	SC	2	12.1 (0)	11.0 (0)	-1.342	0.180	-	
	UC	0	-	-	-	-		

[a]*p*-value from Mann-Whitney U test for independent samples; [b]Wilcoxon signed ranks test; *statistically significant; [c]changes refer to difference of 6 months values from baseline values; FBG=fasting blood glucose; PPG=post prandial glucose; RBG=random blood glucose

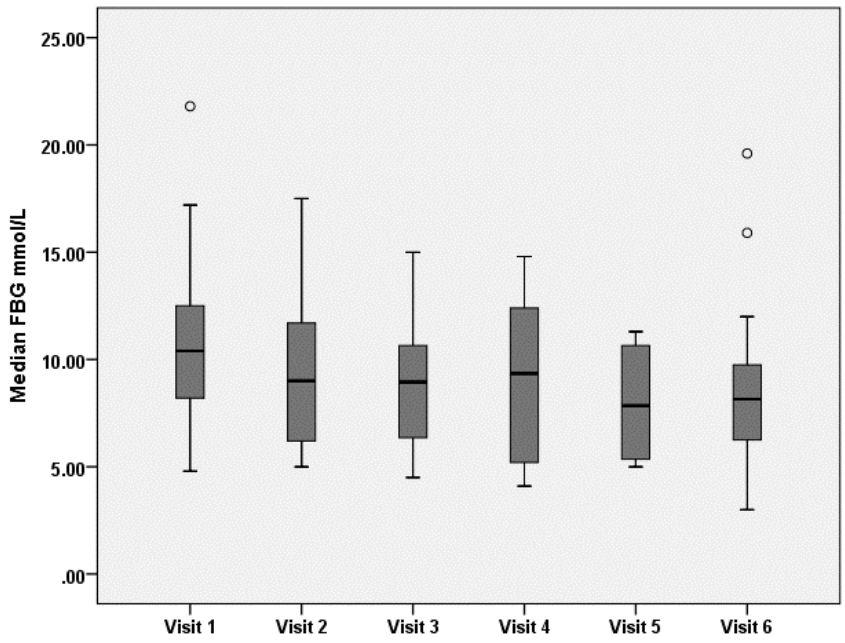


Figure 5.9: Median fasting blood glucose (FBG) in the SC arm during each visit to the pharmacy

5.4.7.3 Medication management

1) Patients' medication adherence

Patients in the SC arm self-reported medication adherence using the 8-item MMMAS score which revealed significant improvement, $p<0.001$ at 6 months (7.57, SD=1.12) compared to baseline (5.86, SD=1.93). The number of patients who showed high adherence (8-item MMMAS score =8) was 13 (23.6%, n=55) at baseline and increased to 44 (80%, n=55) at 6 months. Figure 5.10 presents the mean adherence scores for each visit in the SC arm. Table 5.16 reflects SC patients' self-reported responses for each of the 8-item MMMAS questions. Scores from all questions except one (question no.5) showed significant differences pre-and post-intervention.

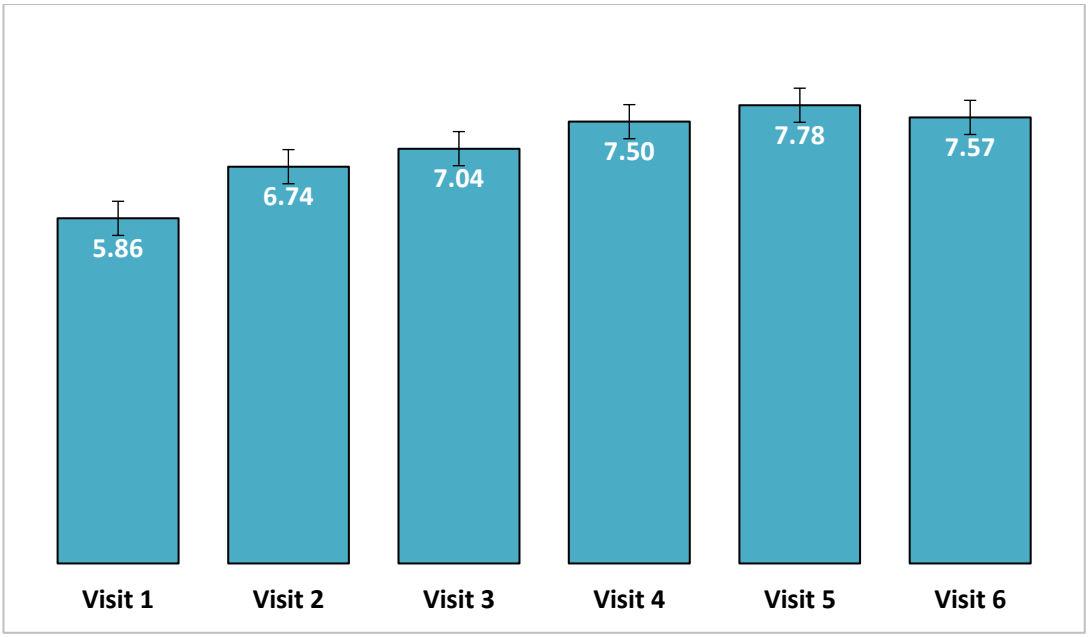


Figure 5.10: Changes in adherence scores in the SC arm according to 8-item MMMAS tool

Table 5.16: 8-item MMMAS responses at baseline and at 6 months in SC arm (n=55)

No.	Questions	Baseline		6 months' intervention		Baseline vs 6 months
		Yes N (%)	No N (%)	Yes N (%)	No N (%)	[a]*p*-value
1.	Do you sometimes forget to take your pill?	33(60.0)	22(40.0)	5(9.1)	50(90.9)	[b] <0.001
2.	People sometimes miss taking medications for reasons other than forgetting. Thinking over the past two weeks, were there any days when you did not take your medicine?	17(30.9)	38(69.1)	5(9.1)	50(90.9)	[b] 0.004
3.	Have you ever cut back or stopped taking your medication without telling your doctor because you felt worse when you took it?	9(16.4)	46(83.6)	2(3.6)	53(96.4)	[b] 0.027
4.	When you travel, or leave home, do you sometimes forget to bring along your medications?	17(30.9)	38(69.1)	5(9.1)	50(90.9)	[b] 0.004
5.	Did you take your medicine yesterday?	49(89.1)	6(10.9)	53(93.4)	2(3.6)	0.145
6.	When you feel like your disease is under control, do you sometimes stop taking your medicine?	8(14.5)	47(85.5)	1(1.8)	54(98.2)	[b] 0.016
7.	Taking medicine every day is a real inconvenience for some people. Do you ever get hassled about sticking to your treatment plan?	11(20.0)	44(80.0)	2(3.6)	53(96.4)	[b] 0.008
8.	How often do you have difficulty remembering to take all your medication?					
	Never/Rarely	24(43.6)		48(87.3)		[b] <0.001
	Once in while	11(20.0)		1(1.8)		
	Sometimes	13(23.6)		3(5.5)		
	Usually	6(10.9)		3(5.5)		
	All the time	1(1.8)		0		

[a] *p*-value from independent t- test; [b] Statistically significant

Of interest, the questions that had the most improvement at 6 months compared to baseline were question 1: pertaining to remembering to take medication, question 2: reasons for forgetting to take medications other than the reasons stated in question 1, and question 4: on taking medications when travelling.

2) Medication-related problems

The MRPs identified for each SC patient during visits were recorded in the Simpler™ pro forma forms. The most common MRPs was patients' non-adherence problems which accounted for 135 of the 301 recordings (44.9%) of the total MRPs followed by sub therapeutic dose (65/135, 21.6%) and needs additional therapy (52/135, 17.3%). Table 5.17 presents the types of MRP identified and the causes of non-adherence. The most frequent causes of non-adherence to medications was patients forgetting to take their medicine (124, 68.1%) followed by patients preferring not to take their medicine (42, 23.1%).

There were four recordings of adverse drug reactions, which were related to side effects. Those were: 1) metformin (patient unable to tolerate the nausea and vomiting), 2) vitamin B complex (caused drowsiness and vomiting), 3) perindopril (caused dizziness), and 4) fluoxetine (caused insomnia). In all instances, pharmacists communicated suggestions for alternative medications to doctors. In addition, SC patients reported hypoglycaemia-like symptoms. There was a total of 23 episodes among seven (12.7%) patients during the 6 months' period. Pharmacists educated patients on prevention and management of hypoglycaemia. Regrettably, pharmacists were unable to assess the adverse drug reactions experienced by UC patients.

Table 5.17: Number of medicine related problems identified by pharmacists for SC arm over 6 months

Medicine related problems	Frequency (%)
Unnecessary drug therapy	10 (3.3)
Needs additional drug therapy	52 (17.3)
Ineffective drug	29 (9.6)
Sub therapeutic dose	65 (21.6)
Adverse drug reaction	4 (1.3)
Dosage too high	6 (2.0)
Non-adherence	135 (44.9)
Total	**301 (100)**
Causes of non-adherence	**Frequency (%)**
Does not understand instructions	14 (7.7)
Patient prefers not to take	42 (23.1)
Patient forgets to take	124(68.1)
Cannot swallow or administer drugs	2 (1.1)
Total	**182 (100)**

Out of the 301 MRPs recorded, pharmacists documented 111 (36.9%) interventions made in collaboration with patients and doctors to resolve the MRPs as listed in Table 5.18. The interventions for non-adherence, focused on patient education and counselling to improve medication adherence, is presented in Section 5.4.7.6.

Table 5.18: Number of pharmacist collaborations with SC patients and doctors

Collaboration with patient	Frequency (%)
Reinitiated drug therapy in patients	21 (35.0)
Pill reminder chart or device for patients	39 (65.0)
Total	**60 (100)**
Collaboration with doctor	**Frequency (%)**
Changed drug product	6 (11.8)
Discontinued drug therapy	5 (9.8)
Changed dosage	17 (33.3)
Not resolvable	0
Added additional medicine	23 (45.1)
Total	**51(100)**

The most common interventions provided by pharmacists to improve adherence among SC patients were recommendations to buy a pill reminder device or providing medication timing chart (39,65.0%) followed by reinitiating drug therapy based on patient collaborations (21,35.0%). The most common suggestion accepted by doctors and consequent therapy change was adding a medicine (23, 45.1%) out of total doctor collaborations followed by a dosage change (17, 33.3%). Pharmacists' recommendations to add medications included initiation of metformin, ACE-I/ARB, statin and aspirin. However, there was a non-significant difference between the number of patient prescribed medications at 6 months compared to baseline between the two arms. Details of these differences are discussed in the following sections. Pharmacists' actions to resolve causes of non-adherence problems through education and pharmacotherapy may have contributed to the increased number of patients achieving high adherence score (8-item MMMAS=8) at 6 months compared to baseline, approximately a three-fold increase.

5.4.7.4 Blood pressure (BP) control

There was a significant reduction in the systolic BP at 6 months compared to baseline in the SC arm (p=0.005). In contrast, the UC arm showed an increase in systolic BP at 6 months compared to baseline. The difference in systolic BP at 6 months for the SC arm was found to be significantly different from the UC arm. Although the diastolic BP showed reduction in both SC and UC arms, the difference was not statistically different between the arms (Table 5.12).

Figure 5.11 presents systolic BP and FBG values for the SC arm at each visit. Of interest, there was a sharp decrease at visit 2, however the value increased at visits 3 and 4 before it decreased in visit 5 and remained at a similar value at visit 6. The increase in systolic BP during visit 4 before decreasing at visit 5 was similar to FBG values, which showed a similar trend.

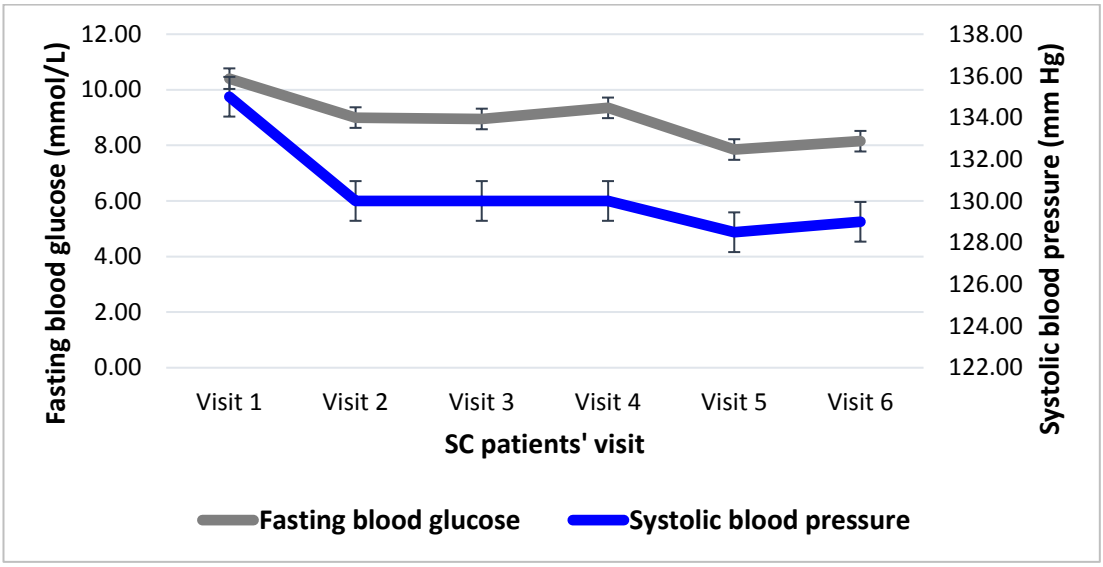


Figure 5. 11: Comparison between mean FBG and mean systolic BP between each visit

Further analysis found weak, positive association between FBG changes (visit 1 and visit 6) and systolic BP changes (visit 1 and visit 6) for SC patients using the Spearman's

rank correlation. This association was statistically significant (r_s=0.330, *p*=0.011). Of interest, there was a similar weak but significant association between changes for mean HbA1c and mean systolic BP changes pre-and post-intervention. (r_s = 0.255, p=0.007).

5.4.7.5 Lifestyle management

SC patients showed more reductions in BMI and waist circumference values compared to UC patients, however, these improvements were not significantly different between both arms at 6 months' study. Of interest, time spent exercising increased at 6 months (57.38 minutes; SD=77.34) compared to baseline (35.83 minutes; SD=56.51) among the SC arm and this increase was statistically significant. (P=0.041).

Additionally, the number of SC patients who smoked at visit 1 (6/55; 10.9%) was reduced to five patients by the end of visit 6 as one patient stopped smoking.

5.4.7.6 Education

All patients in the SC arm were given education on diabetes self-management during each visit. The types of education given followed recommendations in the Simpler™ tool and are summarized in Table 5.19.

Table 5.19: Types of education provided to patients in the SC arm

	Types of education	Frequency (%) (n=55)
1.	Management of hypoglycaemia	48 (87.3)
2	Self-monitoring of blood glucose	51 (92.7)
3	Reduce sodium intake	51 (92.7)
4	Management of stress and diabetes related distress	35 (63.6)
5	Foot care	47 (85.5)
6	Diet advice using plate model	51 (92.7)
7	Sleep hygiene	40 (72.7)
8	Knowledge and understanding of medicines	55 (100.0)
9	Medicine storage	52 (94.6)
10	Simple exercises	55 (100.0)
11	Use of Framingham risk calculator to educate patients	39 (70.9)
12	Medication optimisation during fasting month for Muslims and other religious arms	7 (12.7)

5.4.7.7 Cardiovascular risk reduction strategies

The cardiovascular risk scores for patients in the SC arm were calculated using two calculators. One using the Framingham risk score (FRS) utilising patients' lipid values and the other using their BMI results. Patients in the SC arm had a statistically non-significant reduction of CVD risk (1.05%) at 6 months compared to baseline: 21.96 (SD=14.27) vs 20.91 (SD=15.51)) using the FRS lipid calculator. There was a similar non-significant reduction (2.91%) when using the FRS BMI calculator: 29.03 (SD=15.71) at baseline vs 26.12 (SD=14.68) at 6 months. Regrettably the FRS calculation for the UC arm were not performed as some information required were unable to be retrieved.

Interestingly, the SC arm had an increased number of total daily antiplatelet medication prescribed for primary prevention to reduce CVD risk at the end of the study in comparison to the UC arm and this difference was found to be significant, p=0.016.

5.4.8 Comparison of QOL outcomes between the Simpler™ care and usual care

The overall WHOQOL BREF score improved significantly (p=0.007) in both arms at 6 months. Note that a higher WHOQOL BREF score denotes higher QOL.(148) The overall scores comprise of questions on self-evaluation of QOL and self-assessment of health. The SC arm had significant improvements at all four domains at 6 months compared to baseline: physical health (p=0.002), psychological (p=0.042), social relationships (p=0.031) and environment (p=<0.001).

The two following domains were significantly improved in the SC arm with respect to the UC arm at 6 months: physical health [14.68 (SD=2.31) vs 13.70 (SD=2.30); p=0.021]; and environment [15.37(SD=2.16)] vs [14.53 (SD=2.05); p=0.030]. Physical health incorporates activities of daily living, mobility and work capacity while environment includes financial resources, home environment, health and social care and opportunities for acquiring new information and skills. The remaining two domains psychological (bodily image and appearance, self-esteem, spirituality, negative and positive feelings, thinking, learning, memory and concentration) and social relationship (personal relationships, social support, sexual activity) showed no significant improvement between the arms. Table 5.20 compares the summary statistics for the WHOQOL BREF scores converted to scores between 4-20 which is comparable with the WHOQOL100.(11) Table 5.21 on the other hand shows the scores that were converted to a 0-100 scale according to the WHOQOL-BREF manual.

Table 5.20: Changes in WHOQOL-BREF domain scores between both arms from baseline to 6 months follow-up [scores transformed from 4-20 according to WHOQOL-BREF manual.(11)]

Domain	Mean at Baseline (SD)	6 months mean (SD)	Mean difference (95% CI)	Baseline Vs 6 months	SC vs UC (Baseline)	SC vs UC (6 months)
				[a]*p*-value	[b]*p*- value	[b]*p*-value
Overall						
SC (n=55)	13.64(2.08)	15.38(2.31)	1.75 (0.97 to 2.52)	*<0.001	0.730	*0.007
UC (n=67)	13.79(2.85)	14.09(2.73)	0.30 (-0.34 to 0.94)	0.353		
Physical health						
SC (n=55)	13.8061 (2.04)	14.68(2.31)	0.87 (0.33 to 1.42)	*0.002	0.741	*0.021
UC (n=68)	13.9398 (2.37)	13.70 (2.30)	0.24(-0.68 to 0.20)	0.276		
Psychological						
SC (n=54)	14.4568 (1.62)	15.03(2.34)	0.62 (0.02 to 1.21)	*0.042	0.354	0.147
UC (n=68)	14.1275 (2.28)	14.44 (2.14)	0.31 (-0.14 to 0.76)	0.177		
Social relationships						
SC (n=53)	14.6038 (2.03)	15.12(2.84)	0.74 (0.07 to 1.42)	*0.031	0.500	0.169
UC (n=65)	14.2974 (2.74)	14.44(2.60)	0.30 (-0.28 to 0.88)	0.310		
Environment						
SC (n=55)	14.2961(1.51)	15.37(2.16)	1.07 (0.51 to 1.63)	<0.001	0.770	*0.030
UC (n=68)	14.3897(2.03)	14.53(2.05)	0.14 (-0.25 to 0.53)	0.477		

[a]*p* values from paired t-test; [b]*p* values from independent t-test; *statistically significant

CI= confidence interval; n= sample size; SC= Simpler™ care; SD=standard deviation; UC= usual care

Table 5.21: Changes in WHOQOL-BREF domain scores between both arms from baseline to 6 months follow-up [scores transformed from 0-100 according to WHOQOL-BREF manual.(11)]

Domain	Mean at Baseline (SD)	6 months mean (SD)	Mean difference (95% CI)	Baseline Vs 6 months	SC vs UC (Baseline)	SC vs UC (6 months)
				[a]*p*-value	[b]*p*- value	[b]*p*-value
Self-evaluation of QOL						
SC (n=55)	65.91(15.49)	74.09(17.32)	8.18 (2.21 to 14.15)	*0.008	0.648	*0.020
UC (n=67)	64.55(16.94)	65.81(21.56)	1.12 (-4.74 to 6.98)	0.704		
Self-assessment of health						
SC (n=55)	54.55(19.89)	68.18(16.98)	13.64 (8.30 to 18.97)	<0.001	0.379	*0.018
UC (n=68)	58.09(24.60)	60.66(17.45)	2.57 (-1.63 to 6.77)	0.226		
Physical health						
SC (n=55)	61.29(12.78)	66.74(14.44)	5.45 (2.04 to 8.87)	*0.002	0.741	* 0.021
UC (n=68)	62.12(14.81)	60.61(14.38)	-1.51 (-4.27 to 1.24)	0.276		
Psychological						
SC (n=54)	65.35(10.14)	69.21(14.63)	3.86 (0.14 to 7.57)	*0.042	0.354	0.147
UC (n=68)	63.30(14.28)	65.25(13.38)	1.95 (-0.90 to 4.80)	0.177		
Social relationships						
SC (n=52)	66.27(12.79)	70.91(16.20)	4.65 (0.43 to 8.86)	*0.031	0.500	0.169
UC (n=65)	64.36(17.15)	66.22(15.68)	1.86 (-1.77 to 5.49)	0.310		
Environment						
SC (n=55)	64.35(9.42)	71.04(13.48)	6.69 (3.19 to 10.18)	*<0.001	0.770	* 0.030
UC (n=68)	64.94(12.70)	65.82(12.82)	0.88 (-1.57 to 3.33)	0.477		

[a]*p* values from paired t-test; [b]*p* values from independent t-test; *statistically significant

5.4.8.1 Impact of patients' characteristics on overall QOL score

The findings presented here refer to results presented in Table 5.22. Older patients, aged more than the average age (56.6 years) in this study constituted 47.2% in the SC arm and 71.6% in the UC arm. Interestingly older patients in both arms reported better overall QOL than the younger patients. Similarly, SC patients reported better QOL scores (15.46, SD=2.23) than patients in the UC arm (14.33, SD=2.38). This difference was statistically significant (p=0.038).

The majority of patients in the SC (69%) and UC (70%) arms were using insulin. SC patients who were using insulin reported lower QOL scores than SC patients without insulin. Conversely, the QOL scores among patients in the UC arm were the same for patients with or without insulin. In contrast, patients who were on OHA only, reported better QOL in both arms compared to patients who were not prescribed OHA. The QOL score difference was statistically significant (p=0.018) between arms.

Doctors' visits consisted of usual patient monitoring which is conducted on average four times yearly but less frequently if patients' disease is well controlled and more frequently if it is not. There was no significant difference in QOL scores between the two arms for patients who had more than two doctors' visits throughout the six months' duration.

Patients in the SC arm who had hypertension reported better QOL scores (15.42; SD=2.35) than SC patients who did not have hypertension (15.00; SD= 2.10). In addition, they scored significantly (p=0.009) better than the UC patients who had hypertension (14.13, SD=2.68). The majority of patients in the SC (89.1%) and UC (89.6%) arms had hypertension.

As expected, patients without nephropathy self-evaluated better QOL scores than patients with nephropathy and the difference between SC (15.52, SD=2.23) and UC arms (14.11, SD=2.73) was significantly different (p=0.005)

Table 5.22: Impact of patients' characteristics on overall WHOQOL-BREF score

Patients' characteristics	Overall score after 6 months (with characteristics and without characteristics)				SC vs UC *p*-value	
	Existing Mean (SD)	Non-existing Mean (SD)	Existing Mean (SD)	Non-existing Mean (SD)	Existing	Non-existing
Sociodemographic						
[+]Age (≥56.6 year)	15.46(2.23)	15.31(2.41)	14.33(2.38)	13.60(3.41)	*[b]0.038	[b]0.080
Family history of diabetes	15.31(2.29)	15.44(2.42)	15.33(2.22)	13.82(2.84)	[b]0.836	*[b]0.030
Severity						
Use of insulin	15.11(2.26)	16.00(2.35)	14.13(2.74)	14.10(2.72)	[a]0.076	*[b]0.031
Use of OHA only	15.60(2.24)	14.40(2.46)	14.32(2.92)	13.56(2.01)	*[a]0.018	[b]0.555
Resource utilization						
Doctor visit ≥2times	15.37(2.33)	16.00(0)	14.43(2.80)	12.67(1.78)	[a]0.058	[b]0.154
Comorbidity						
Hypertension	15.42(2.35)	15.00(2.10)	14.13(2.68)	14.00(3.21)	*[a]0.009	[b]0.414
Nephropathy	14.00(2.83)	15.52(2.23)	14.17(2.76)	14.11(2.73)	[b]1.00	*[a]0.005
Number of medical conditions ≥2	15.00(2.63)	15.49(2.22)	14.60(2.91)	13.92(2.64)	[b]0.774	*[a]0.003

OHA= oral hypoglycaemia agent; [a] p-value from independent t-test; [b] *p*-value form Mann Whitney-U test; *Statistically significant;[+]average age of cohort

Understandably, patients in the SC arm who had two or more medical conditions reported lower overall QOL scores than patients who did not. Surprisingly, patients in the UC arm who had two or more medical conditions reported better QOL scores. However, this difference between SC and UC arms was not significant. Accordingly, patients who had less than two medical conditions in the SC arm recorded significantly better scores (15.49, SD=2.22) than UC patients (13.92, SD=2.64), p=0.003.

5.4.9 Analysis of patient case studies

Pharmacists' application of the Simpler™ intervention tool improved patients' clinical and QOL outcomes. The following three patient case studies have been selected as they showed the most improved HbA1c levels at six months compared to baseline. Details of pharmacists' interventions and comparisons of clinical parameters for each visit are presented in Boxes 5.1 to 5.3 and in Figures 5.12 to 5.14.

1. Patient ID 417

Box 5.1: Case study for patient ID 417

Patient ID 417 was a 37-year-old man of Melayu ethnicity with a family history of diabetes. His highest education level was secondary education and he worked as security guard at a local school. He was diagnosed with T2DM in 2013. He complained of chest pain during his first visit and was prescribed glyceryl trinitrate tablets (GTN) and consequently sent for further medical examinations. His medications before the intervention were statin, CCB, aspirin intermediate acting insulin, metformin and sulphonylurea and neurobion. At visit six, GTN was added to his list of medications.

Achieved HbA1c reduction of 8.8% (96.2mmol/mol) [from 16.8% (160.1mmol/mol) to 8.0% (63.9mmol/mol)], LDL reduced from 2.80 mmol/l to 1.90 mmol/l and his waist circumference reduced from 105cm to 90cm. His self-reported physical exercise improved from none to 60 minutes per week and consequently his BMI decreased from 33kg/m2 to 31kg/m2.

The pharmacist identified MRPs such as sub-therapeutic dosage and non-medication adherence as reasons for therapeutic failure.

The reasons for non-adherence were 'patient prefers not to take medication' and 'patient forgets to take'.

The patient developed fear towards insulin administration and was dependent on his carer (mother) to administer it. Therefore he was unfamiliar with the insulin administration technique. The pharmacist educated him on the correct technique of administration and the beneficial effects of insulin.

Education was provided on weight loss; simple exercises; foot care; stress and sleep hygiene; medicine storage; hypoglycaemia management; salt intake; medication and smoking cessation.

The pharmacist provided him with a pill reminder chart and collaborated with the doctor to titrate insulin and add aspirin as primary prevention to reduce CVD risk.

The patient scored social relationships the lowest (50.0) and physical domain (75.0) the highest at pre-intervention, while at post-intervention he scored environment domain the lowest (71.9) and physical domain the highest (85.7). The largest improvement in his QOL assessment was social relationships (50 to 75).

There was a marked improvement in FBG and systolic BP when the patient's medication adherence score increased, as shown in Figure 5.13. This was expected as medication adherence is associated with achieving therapeutic goals. This is further discussed in section 5.5.1.3.

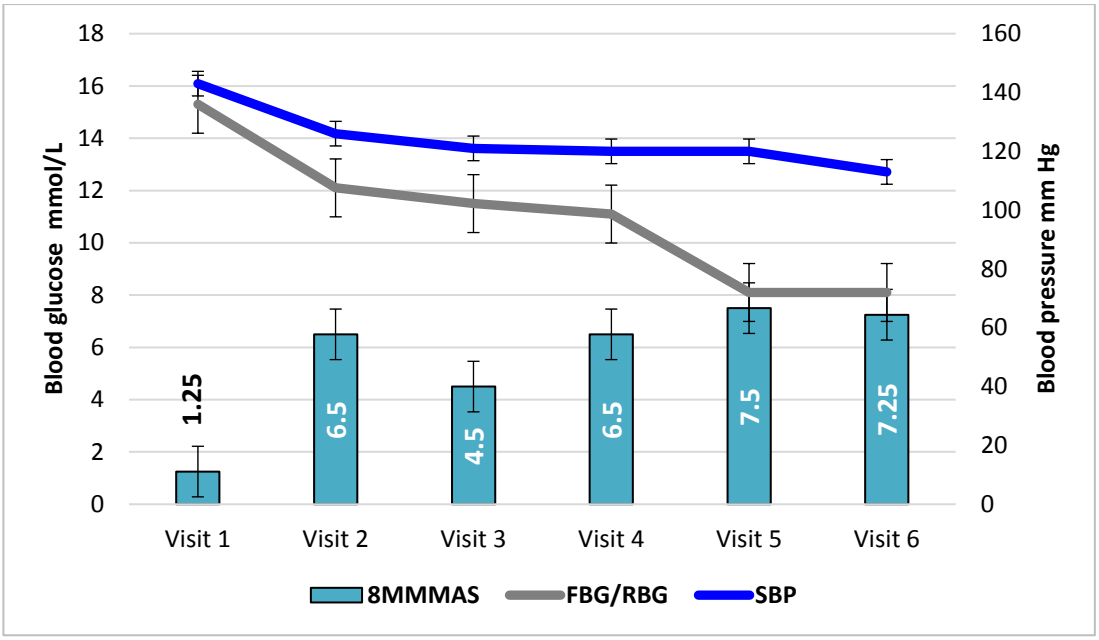


Figure 5.12: Comparison of 8-item MMMAS scores, blood glucose levels and systolic BP at each visit for patient ID 417

2. Patient ID 416

Box 5.2: Case study for patient ID 416

Patient ID 416 was a 56-year-old lady of Chinese descent with a family history of diabetes. Her highest level of education was at primary level. She was married and was taking care of her family and grandchild. She was first diagnosed with diabetes and hypertension when she was 42 years old. She also suffered from anxiety disorder. Similar to patient ID 417 above, her increased medication adherence through the pharmacists' input led to reduction in blood glucose and systolic BP levels. Her HbA1c showed a reduction of 6.8% [from 13.20% (120.8mmol/mol) to 6.40% (46.4mmol/mol)]. Her LDL reduced from 3.40 mmol/L to 2.30 mmol/L, however her waist circumference and BMI did not show any changes. Her self-reported physical exercise (walking, household chores) improved from none to 30 minutes per week. Her medications before the intervention were statin, CCB, aspirin, intermediate acting insulin, metformin and sulphonylurea and calcium carbonate. At visit six, calcium carbonate was stopped, however all other medications remained the same.

The major cause of her medication non-adherence was 'forget to take and 'prefers not to take' her medications including insulin particularly when travelling or staying over at relative's house.

The patient reported difficulty in sleeping from visits 1 to 3. The pharmacist's collaboration with the doctor resulted in discontinuation of her fluoxetine. Consequently, there were no complaints of sleep by visit 4.

The pharmacist titrated insulin doses for optimum blood glucose levels.

Pharmacist education included sleep hygiene, hypoglycaemia management, medication knowledge and storage, insulin injection technique and guidance on self-monitoring of blood glucose.

She scored physical health (60.7) the lowest and social relationship the highest (66.7) pre-intervention. At post-intervention, she scored physical health (64.3) the

lowest and psychological domain the highest (70.8). Psychological domain (62.5 to 70.8) scores showed most improvement in her QOL assessment pre-and post-intervention.

A comparison of systolic BP, blood glucose and medication adherence score is shown in Figure 5.14

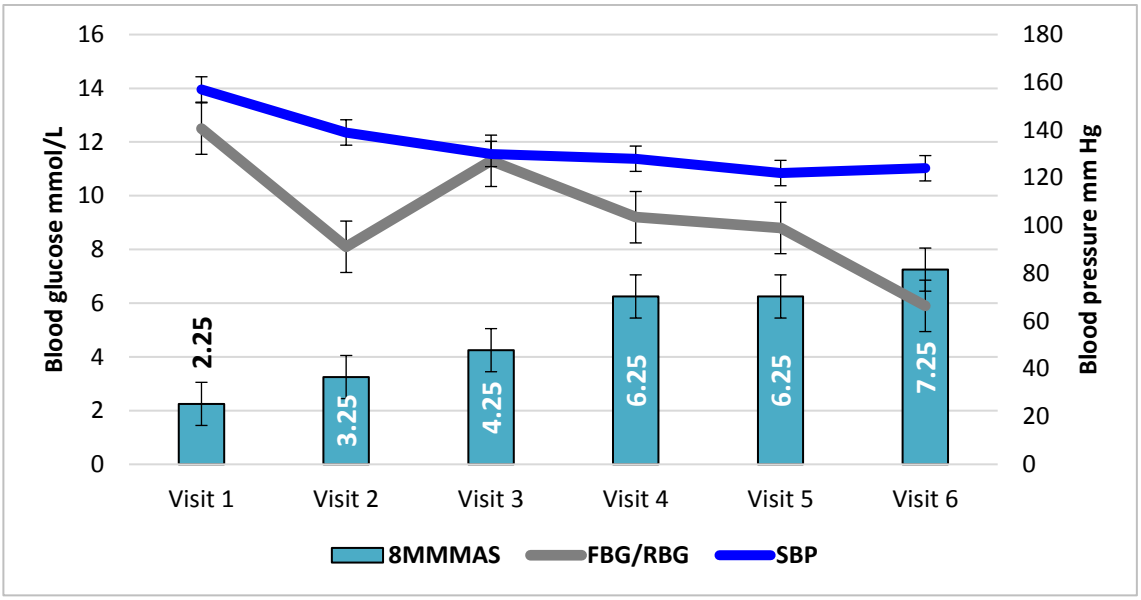


Figure 5.13: Comparison of 8-item MMMAS scores, blood glucose levels and systolic BP at each visit for patient ID 416

3. Patient ID 508

Box 5.3: Case study for patient ID 508

Patient ID 508 was a 68-year-old man of Melayu ethnicity who also had hypertension. He lived with his wife on a small landholder (palm oil plantation) that he owned. His highest level of education was at primary level. His HbA1c results reduced by 6.2% (67.7mmol/mol) [from 15.10% (141.5mmol/mol) to 8.90% (73.8mmol/mol)]. His lipid value, waist circumference and BMI did not change. However, his physical activity improved from 60 to 105 minutes per week. His medications before the intervention were statin, CCB, ACEI, beta blocker, frusemide, metformin and gliclazide. At visit six, premix insulin was added and gliclazide was stopped.

Ineffective medication and patient non-adherence to medication were identified as reasons for not achieving therapeutic targets.

The pharmacist also identified the need for insulin as patient's did not achieve glycaemia targets with his current OHA (metformin and sulphonlyurea)

Pharmacist also recommended aspirin to be added due to increasing FRS (lipid = 31.80, BMI =51.40) at visit 1. Furthermore, he was more than 65 years old as required by the 2015 Malaysian diabetes guideline. However, the pharmacist suggestion was not accepted as the doctor was concerned of increased bleeding caused by aspirin in his age group.

There was a need to simplify his medication regime to a fixed-dose combination to increase medication adherence and the pharmacist suggested telmisartan + amlodipine. The doctor decided on perindopril + indapamide.

The reasons for non-adherence were 'patient prefers not to take' and 'patient forgets to take'. The patient misunderstood dosage instructions: he took one tablet of perindopril + indapamide twice daily instead of two tablets once daily as instructed. This was rectified at visit 5.

The pharmacist collaborated with the doctor to initiate insulin at visit 3 which the patient refused at visits 1 and 2.

Patient education was provided on insulin, salt intake, medication adherence, diet, foot care, sleep hygiene, simple exercise, hypoglycaemia management, medication knowledge and storage and dose administration time. He scored psychological domain the lowest (62.5) and scored high marks on both social relationships and environment domains (75.0) equally. At post intervention, he scored psychological domain the lowest (50.0) and environment domain the highest (75.0). The physical health domain showed the largest improvement pre-and post-intervention (64.3 to 70.8).

In contrast to the previous two patients mentioned above, patient ID 508 did not achieve therapy outcomes even though he achieved the highest score for medication adherence from visits 1 to 5 as shown in Figure 5.15. This was because the doses prescribed for his antihypertensive and OHA medications were not the optimum doses to achieve required outcomes. However, his glycaemic and BP improved at the final visit after pharmacist educated him on the correct dosage instructions at visit 5.

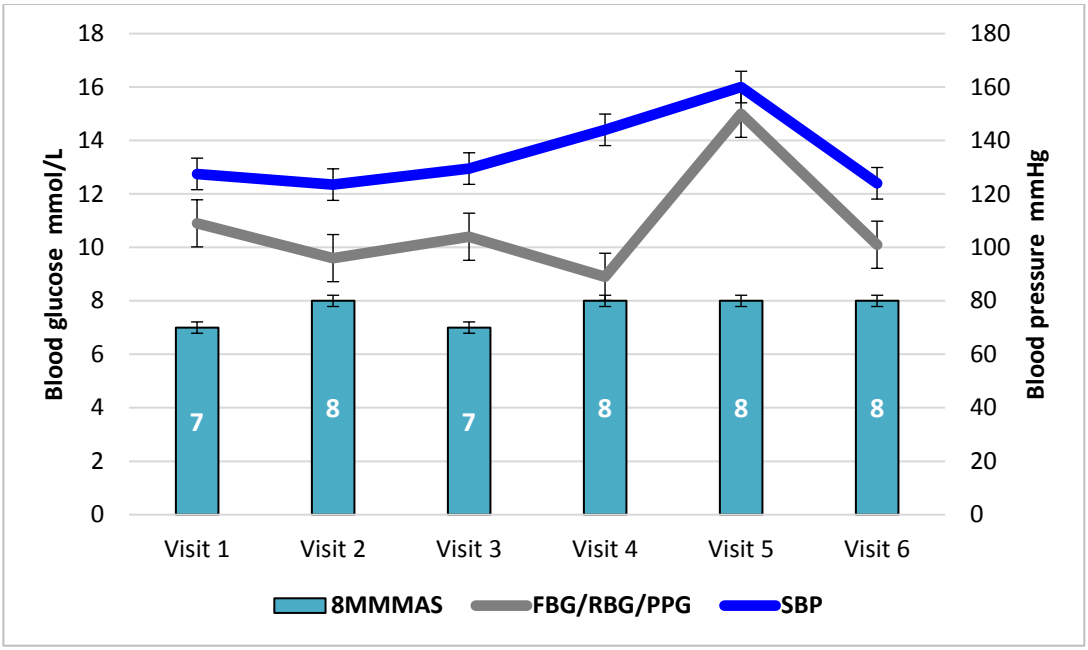


Figure 5.14: Comparison of 8-item MMMAS scores, blood glucose levels and systolic BP at each visit for patient ID 508

5.5 Discussion

The Simpler™ intervention tool was successfully implemented in seven primary health care clinics in six districts in the state of Johor, Malaysia. A RCT was chosen as the methodology to assess the impact of the use of the tool as it reduces selection and confounding biases. Thus it provided the most reliable evidence in terms of measuring effectiveness of healthcare interventions.(3)

5.5.1 Patients' clinical outcomes based on the Simpler™ tool indicators

In Phase Three research the pharmacists in the intervention arm used the Simpler ™ tool in the management of patients with T2DM. At baseline, patient in both arms were similar in clinical and QOL assessments. However, at 6 months, the clinical outcomes of the intervention patients showed positive results through a significant decrease in the HbA1c levels and systolic BP compared to control arm. In addition, the Simpler™ intervention also improved other clinical outcomes such as FBG, LDL and HDL levels at 6 months compared to baseline. The intervention also led to increases in prescribed statins and a significant increase in daily antiplatelet use as well as significant improvements in QOL assessments between arms.

The magnitude of HbA1c improvements pre-and post-intervention measured by Cohen's d and Hedges'g between both arms were comparable to most RCTs performed among hospital outpatients in Malaysia.(158, 159) Patients in the intervention arm also self-reported significantly better QOL outcomes than the control patients in the physical and environment domain of the WHOQOL-BREF questionnaire. Specifically, older patients, without a family history of diabetes, on OHA, with hypertension, without nephropathy and having two or less medical comorbidities self-evaluated better QOL scores.

In this phase, there were 27/61 (44.3%) SC patients who missed their appointments and thus did not complete the required six visits to the pharmacy as per protocol. However, the research team agreed to include patients who attended a follow up meeting with the pharmacist at least three times during the six months research period for data analysis. This is consistent with previous studies which found that patients showed a significance difference in their clinical outcomes at three months of follow up. (123, 158)

5.5.1.1 Cholesterol control

The intervention arm showed significant improvements in LDL and HDL at six months compared to baseline (baseline LDL: 3.09 mmol/L; baseline HDL: 1.28 mmol/L). The improvement in LDL is consistent with previous RCT diabetes intervention and retrospective studies conducted by pharmacists in hospital settings in Malaysia (161, 327) and Hong Kong (130). Their baseline values ranged from 2.11 to 3.22 mmol/L. A RCT conducted in one community pharmacy in Brazil also had similar improvements in LDL and HDL levels as this research from baseline value: LDL (3.18mmol/L) and HDL (baseline value: 1.38mmol/L).(136) Similar to this research, the higher baseline levels in the aforementioned studies enabled higher potential for decreases in cholesterol levels.

Although the improvements in LDL values were not significant between arms, the proportion of patients in the intervention arm who achieved the LDL target set by the Malaysian diabetes guidelines was significantly more than the patients in the control arm. Additionally, more patients in the intervention arm achieved the HDL target level compared to the control arm. Both improvements in LDL and HDL can be associated with the increase in prescribed statins which is able to induce an increase in HDL and decrease in LDL .(343) In addition, the increase in exercise and diet changes recommended by pharmacists could have contributed to the improvements.

5.5.1.2 Glycaemia control

The overall decrease of HbA1c levels for the intervention arm patients in this research was consistent with the findings from RCT studies conducted in community and hospital settings in Malaysia (128, 158, 159) and in other parts of the world.(13, 14)

The results from the UKPDS trial (326) were used to estimate the effectiveness of the Simpler™ intervention tool on blood glucose control. The UKPDS trial found a 1% change in HbA1c before and after intervention was associated with a 14% reduction risk for myocardial infarction, 37% for microvascular complications and 21% for deaths related to diabetes. The method of using HbA1c levels to measure the effectiveness of an intervention has been used by previous studies.(13, 14, 135) In this research, pharmacists utilising the Simpler™ tool reduced the patients' mean HbA1C by more than 1%.

The proportion of patients who achieved a 1% reduction pre-and post the study in HbA1c was significantly more in the intervention arm compared to the control arm. The number of patients with baseline HbA1c > 9% (74.9 mmol/mol) that achieved a mean reduction of 1% in the intervention arm was significantly more compared to patients with baseline values of <9% (74.9 mmol/mol). This results are similar to findings from a systematic review on diabetes interventions conducted internationally that showed a greater reduction in HbA1c with higher baseline levels [more than 9% (74.9 mmol/mol)].(13) Nevertheless, the intervention pharmacists managed to improve HbA1c values in these patients who represented the majority (71.0%) of patients in our baseline population.

Even though, this research was not statistically powered initially to account for differences among different ethnicities and gender, significantly more patients in the intervention arm from *Melayu* ethnicity and female gender achieved a mean reduction of 1% for HbA1c. The FBG readings between both arms did not significantly differ at six months. This could be because only small numbers of patients from both arms were being measured for FBG. There were other contributing factors that could affect the results such as medications taken, posture, current illness, stress and time FBG was taken, for instance in the morning or afternoon as suggested by a review study.(344) However, the magnitude of change at six months from baseline for the intervention arm

were significantly different when compared with changes in the control arm. This further suggests the impact of Simpler™ interventions on glycaemic improvement.

The variation in FBG levels among intervention patients during each visit was found to be associated with systolic BP values. This is consistent with findings from a recent cross sectional study on 2092 elderly Chinese patients conducted in China that reported increased FBG was associated with high systolic BP values.(345) In addition, previous epidemiological research has documented increased hypertension among patients.(346) Of interest, most patients (110, 88.7%) from both the intervention and control arms had hypertension.

Pharmacists were not able to confirm whether the hypoglycaemia like symptoms encountered by patients (12.2%) in this study were true hypoglycaemia. However, the proportion of patients in this study who reported similar hypoglycaemia symptoms were less than a before-after diabetes intervention study conducted for six months, during which 58.1% of patients reported hypoglycaemia like symptoms.(133)

5.5.1.3 Medication management

Reasons for increased medication adherence were probably due to increased patient education on knowledge and understanding of medication as well as self-management skills, discussed in Section 5.5.1.6. This finding is consistent with two recent studies conducted in Malaysia and with another study conducted in Hong Kong.(86, 130, 347) In this study, the main causes of self-reported non-adherence was 'patient forgets to take' (68.1%). Most patients were on a minimum of four different medications namely metformin, ACEI, CCB and simvastatin. Twelve (21.8%) patients had more than two

comorbidities which further increased their medication regimen complexity and the importance of being adherent. Indeed, a recent review identified medication regimen complexity being related to medication non-adherence.(348)

In this study 'sub therapeutic dose' and 'needs additional drug therapy' was the most frequent MRPs encountered and consequently was solved by pharmacists' recommendations to prescriber and titrating the doses in the case of insulin. Pharmacists collaborated with doctors to initiate medications such as ACEI, insulin, metformin and statins. This is similar to a retrospective study that involved multiple KKs conducted in Malaysia where half of pharmacists' interventions involved dosage adjustment and the remainder were changes to OHA, cholesterol and antihypertensive medications.(160) In addition, pharmacists' efforts in identifying other MRPs such as adverse drug reactions, ineffective drugs and high medication doses and solving these issues could have increased adherence levels. A large RCT study conducted in the USA supports this view.(62)

Previous studies conducted in hospital settings in Malaysia as well as other countries have also shown that pharmacists' recommendations resulted in positive outcomes and were favourably accepted by doctors.(64, 120, 125) Nevertheless, in this study setting, the fact that pharmacists and doctors were in close proximity enabled effective communication. However in settings where community pharmacies are not located in the same premise as the GP clinic/practice, there is often a time difference between identification of medication problems and subsequent correspondence with GPs which can impact on outcomes.(64)

Additionally, the pharmacists had autonomy to titrate insulin doses up to two units at each time as part of an agreed collaboration with the doctors. This avoided a time lag

between pharmacists' recommendations and communication with the prescriber during follow-up visits when patients did not have a doctor's appointment. Published meta-regression analysis found independent insulin titration by pharmacists resulted in improvement in HbA1c if patients' mean baseline was more than 9% (74.9mmol/mol).(13) In this research, Phase Three participants' average HbA1c for both control and intervention arms were 10.65% (92.9mmol/mol) and similar to the study, the intervention arm reported greater reduction of mean HbA1c compared to the usual care patients.

5.5.1.4 Blood pressure control

In this study, systolic but not diastolic BP significantly reduced in the intervention arm at six months compared to baseline and between arms. This is similar to a recent RCT study conducted in a hospital setting in Malaysia (161). However, other studies conducted in KK settings or other hospitals in Malaysia have not achieved significant improvements in either systolic or diastolic BP.(64, 86, 158-160) This BP improvement is also consistent with RCTs conducted among multiple primary health care centres in Brazil, Canada the UK, (136, 349, 350) but not achieved in other similar settings in Pakistan and Australia.(122, 140)

The significant decrease in systolic BP is associated with a 50% reduction in stroke or myocardial infarctions and was equally as important as glycaemia control in the UKPDS trial.(26) There are numerous published studies on the association of high salt intake and hypertension.(351) Pharmacists in the intervention arm actively educated patients on the importance of reduction of salt intake as recommended by the 2015 Malaysian diabetes guidelines.(6) Furthermore, this is consistent with the findings from the TONE trial (trial of non-pharmacological intervention in the elderly) among 875 men in the USA.

The trial found reduced salt intake in the elderly (60-80 years of age) led to a decrease in BP and reduction in the need for antihypertensive medications.(352) This could explain a higher proportion of patients in the intervention arm achieving systolic BP targets compared to the control arm.

The average BMI for both intervention and control arms at baseline were 29kg/m^2. This is classified as obese (BMI≥23kg/m^2) in Malaysia. A study conducted among 399 patients in China found that patients' BMI and waist circumference were associated with their BP. This study found obese patients tend to have increased salt intake and consequently had higher BP compared to patients with low salt intake.(353)

With regards to diastolic BP targets, slightly more patients in the control arm than the intervention arm achieved the target BP. This could be contributed to patients' age factor. Systolic BP has been shown to rise between the ages 30 and 84 and over, the diastolic BP tends to decrease from the age of 60 to 84 onwards according to a recent study conducted in the UK.(354) The average age of patients in the intervention arm was 55 years while the average age for the control arm was 58 years which was closer to the age range mentioned above for diastolic BP decrease. However findings from the MRFIT trial showed greater CVD risk with each increment of systolic BP increase and individuals with increased systolic and not diastolic BP were at greater risk of stroke(355) and mortality(356).

The reduction of BP in visit 2 and gradual increase to visit 4 before achieving a constant level in visit 5 and visit 6 could be explained by patients' follow up visits with pharmacists which coincided with doctors' appointments. Therefore, systolic BP increase in these visits could be the 'white coat effect,' documented in previous studies.(357)

5.5.1.5 Lifestyle management

The non-significant reductions in BMI and waist circumference among intervention patients compared to the control arm at six months is consistent with several published RCTs conducted in Malaysia, the UK, the USA, Hong Kong, Iran, Jordan, Australia and Brazil.(64, 123-125, 127, 130, 134, 136)

Although pharmacists actively educated SC patients on diet and exercise the intervention did not match the intensive approach adopted in the Look AHEAD study which was conducted in the USA from 2001 to 2012.(358) The 5145 participants in the Look AHEAD study were provided meal replacements with liquid shakes and meal bars and were instructed to achieve exercise target ≥ 175min/week by month six of the study. They participated in counselling as well as individualised interventions twice monthly. Consequently, there were significant improvement in weight loss and physical exercise in the intervention patients compared to the control. Conversely, a systematic review on the impact of improved diet and increased exercise found significant reductions in BMI and waist circumference if education and motivation were given at the early phase of newly diagnosed patients with diabetes.(359)

These studies highlight the need for a comprehensive approach and ideally pharmacists' diet advice needs to be coupled with frequent monitoring and possibly nutritional supplements although this may not be feasible in daily practice due to time and funding constraints. Alternatively, paid nutritional services which deliver nutritionally balanced meals and slimming centres which focus on weight loss technology may facilitate patients achieve their BMI and waist circumference targets. However, the costs of using these services may pose a barrier to some patients. Nevertheless, this research showed non-significantly reduced BMI and waist circumference averages in the SC arm of 0.35%

and 1.54%. In contrast, the control patients had non-significantly increased BMI of 0.68% but reduced waist circumference by 0.06%. Previous studies have reported that uptake of physical exercise may be difficult among older and obese patients which constitutes majority of Phase Three research population.(360) Another reason may be that exercise in hot and humid conditions can exert physiological strain as shown in a previous study.(361) Therefore, exercise may be more difficult to implement in a tropical climates where patients have little air conditioning and no access to air conditioned gymnasiums. However, a study on follow-up of unsupervised gymnasium-based home exercise, following a 12 weeks supervised exercise training improved exercise tolerance among T2DM patients.(362) This findings might help patients implement an active lifestyle.

5.5.1.6 Patient education

The intervention patients were given education on diabetes self-management and on medication knowledge during their multiple visits to the pharmacist. This may have improved their adherence to medication and application of the lifestyle indicators. The findings from this RCT is comparable to other RCTs conducted in Malaysia that incorporated patient education in their methodology.(86, 160, 161)

In this study, education given by pharmacists was culturally and religiously sensitive for patients from different ethnicity and customs. Each of the pharmacists could speak two to four different languages which further enhanced the patient pharmacist relationship. This is consistent with similar studies worldwide regarding culturally sensitive educational programs.(96, 252)

A low number of patients were given education on medication consumption during fasting (indicator for education factor in the Simpler™ tool) for religious (Muslim) groups. This was because only one patient practiced fasting during the research period. The fasting month for Muslim patients ran from 6th June to 5th July 2017. Phase Three

recruitment started during the second week of June and the majority of patients were recruited by pharmacists during the second week of July. This explains the reason why only one patient was recorded to receive education on this indicator.

Pharmacists' education on the beneficial effects of insulin in glycaemia control contributed to overall improvement in HbA1c levels. This is mainly because some patients in this study 'preferred not to take' insulin as they had negative associations with insulin. This is consistent with two Malaysian qualitative studies which found lack of knowledge related to diabetes and constraints in patients' ability to control diabetes the biggest barrier in achieving therapeutic targets.(71, 363) .

5.5.1.7 Cardiovascular risk reduction strategies

Despite reductions in BP and LDL levels, both of which are factors incorporated in the FRS calculation, the overall FRS reductions were not significant at six months from baseline. This could be due to the age factor as the risk of having CVD increases with age. In this research the average age for the SC arm was 55 years. Despite this, the CVD risk factor reduction of 1.05% using lipid results was consistent with two RCTs conducted in Australia and Hong Kong which achieved 1% and 1.64% respectively.(130, 364) Similar to this RCT, the intervention patients in both studies mentioned had increased antiplatelet medications prescribed at the end of study compared to the control patients.

5.5.2 Quality of life outcomes

Baseline QOL scores were statistically similar among both arms, suggesting that the baseline characteristics were homogenous. However, at six months, all single domains

improved significantly in the intervention arm compared to baseline values. This was not the case for the control arm. The improvement in the single domains reflects patients' management of their daily tasks and could possibly be attributed to compliance to pharmacists' lifestyle advice as also suggested in a similar RCT.(137) The two domains that showed significantly improved scores at six months comparing the intervention arm with the control arm were physical health and environment. Our study is also compatible with QOL results from a specific educational intervention conducted among patients in a diabetes clinic in Iran. Similar to our results, there were significant improvements in self-evaluation of QOL, self-assessment of health and the physical health domain comparing the intervention arm with the control arm.(365)

Our research findings are also consistent with pharmacist led diabetes intervention studies conducted in hospitals in Nigeria and in India.(137, 366) The results from this study are also consistent with a study conducted among outpatients in a medical centre in Malaysia.(158) Although a different QOL instrument was used (EQ-5D-3L), the significant improvement in mobility corresponds to the physical health domain in WHOQOL-BREF used in our study. However, the medical centre study also showed significant improvement in anxiety levels among the intervention arm versus control arm which our study did not demonstrate (psychological domain).

The psychological domain in this research did not show significant improvement between arms. One reason could be attributed to the non-significant reduction in weight loss (BMI) for both arms which is associated with body image. This view is consistent with a systematic review conducted on 36 studies which found improved body image was associated with weight loss.(367) Body image is a facet relating to the psychological domain of the WHOQOL-BREF questionnaire. In addition, previous studies have found that weight loss led to improved mood and self-confidence.(368, 369)

Likewise, there were no significant improvement between groups for the social relationships domain. However, this domain was ranked the highest at baseline and at 6 months compared to the other three domains for both arms in this research. Similar high scores were found in a 2015 cross sectional study conducted among T2DM patients from primary healthcare clinics in Malaysia (370) and in a 2016 study in Iran.(371) Correspondingly, the high social relationship domain scores could be attributed to the existing strong social support through individual, community and healthcare in Malaysia as reported in a Malaysian study conducted among 175 patients in a primary care centre.(372) Social support was considered important as it decreases diabetes distress and subsequently lead to improved outcome as documented in a systematic review on 30 studies.(373) Nevertheless, in contrast to the UC patients, the SC patients had significant improvement pre-and post-intervention for this domain.

5.5.2.1 Impact of patients' characteristics on QOL outcomes

In a systematic review study on QOL assessment among patients with diabetes found that younger patients may benefit more from pharmacists intervention.(13). In contrast, this research helped older patients improve their glycaemic control and reported improved QOL scores.

The use of insulin in our study was associated with negative impact on QOL compared with the use of an OHA. This was consistent with a recent audit of patients with diabetes from major ethnic arms in Malaysia and in Taiwan.(19, 146) The audit found that insulin usage necessitated patients to adhere to additional requirements such as daily self-monitoring of blood glucose and diet restrictions. The additional restrictions could have caused the patients to rate their QOL scores lower. Similar to the Taiwan national health management system(19), the Malaysian public health care system(319) subsidises

patients for consultations with healthcare professionals and for medications, however needle costs for insulin administration and blood glucose monitoring costs are not covered. Possible collaboration with insurance schemes and medical companies would be ideal to support these additional costs.

The majority of patients in both arms diagnosed with hypertension and on antihypertensive medications reported better QOL than patients who did not have hypertension. This finding is consistent with a study conducted in Brazil where improvements in physical health scores and medication adherence were reported after educational interventions among this patient group.(374)

The lower QOL score among patients with multiple comorbidities in the intervention arm is similar to several studies conducted in Malaysia and elsewhere (137, 370, 375) highlighting that patients with illnesses in addition to diabetes have a significant health burden.

5.5.3 Strengths of Phase Three study

The Phase Three study had a number of strengths which were different from previous documented intervention studies. All Simpler™ trained pharmacists were from the community setting, previously not formally trained in diabetes management and had less than three years' experience of providing diabetes management services. Yet, the overall HbA1c improvement was comparable to that of RCTs employing pharmacists who have more than three years of clinical experience and who are trained to provide services in the hospital setting.(122, 124, 130)

This study demonstrated that pharmacists with limited clinical experience but with adequate support through the Simpler™ intervention tool effectively improved clinical and QOL outcomes of patients in primary healthcare clinics in Malaysia. This suggests that the Simpler™ tool can be utilised by a greater pool of pharmacists. Overall, the findings from this study may be generalizable to pharmacists working in any community setting providing diabetes management services; have access to patients' medical records; in countries with similar diabetes guidelines; and applies similar inclusion and exclusion criteria as this research. This study however was done in an environment of close contact with prescribers.

Since the Simpler™ tool was a multifactorial structured intervention, it was difficult to isolate a single contributing factor. Therefore, it was highly probable that the combination of improved glycaemic, cholesterol and blood pressure levels, increased medication adherence and the slight increase in physical activity may have contributed to patients' improvement as was postulated in a previous RCT study conducted in Australia.(140) Furthermore, several studies have found that multifactorial interventions resulted in greater improvements in clinical outcomes compared to a single intervention.(94, 95)

5.5.4 Limitations

This RCT also had limitations. First, the RCT was conducted in seven clinics encompassing six districts in the state of Johor and some variation could have occurred with pharmacists' relationships with doctors.

Second, there were problems obtaining baseline clinical values such as HbA1c, lipid and creatinine results from both arms. Hence the values obtained ranged from the previous month to previous four months. However, every effort was made to obtain the most recent results before the trial commenced and on completion for both arms.

Third, as both intervention and control patients were recruited from the same primary care health centre, contamination in the control arm was likely. While patients were unaware to receiving the intervention or the usual care, pharmacists, nurses and doctors knew which patients were in the intervention or usual care arms. This could have influenced the type of care the patients in each arm received. This is because it was possible that the same doctors were involved in treating intervention as well as control patients and could have applied pharmacists' recommendations for intervention patients to control arm patients. Nevertheless, the effect of any contamination did not impact the improvements seen in the intervention arm.

Fourthly, the Hawthorne effect (awareness of research participation) in this RCT may only be partially neutralised.(376) This is because although both arms were given appointments by the pharmacists and were aware of their participation in this research, some of the effect may still exist in the intervention arm as they had more visits to the pharmacist than the patients in the control arm. Therefore, increased contact time with

pharmacists may have influenced patients' compliance towards their treatment as shown in several diabetes intervention studies.(377, 378) Nevertheless, patients in the control arm also made frequent visits to dispensing pharmacists who equally provided counselling and advice on medications and lifestyle modifications although not as intensive and extended as the intervention pharmacists.

In this research, pharmacists were required to follow up the patient every month for six months. However, it showed to be a difficult process as over half of the patients recruited missed appointments or visited the pharmacy when pharmacists were busy with dispensing tasks. Therefore only 34 (44.2%) out of 77 patients recruited managed to complete all six visits. Pharmacists' efforts to remind patients of their appointments placed extra burden on their increasing workload. Thus, future research should focus on optimum face to face or telephone interventions intervals between patient and pharmacists to improve diabetes end points while still allowing room for self-care management.

Certain information for both intervention arms and the control arm were missing for some patients during the research period. Accordingly, pharmacists were contacted to retrieve a majority of the missing data. Other times, pharmacists had to contact patients to retrieve information such as education and occupational background. Regardless, some data such as HbA1c results and lipid results from both arms could not be obtained. Some patients had taken their meals prior to the finger pricking tests. Subsequently their finger pricking test result was therefore categorised as random blood glucose (RBG) which reduced the number of patient with FBG results. As the average age of patients in the SC arm of Phase Three research was 55 years, there is a need to evaluate the compliance level in younger age group patients. Finally, some recommendations by pharmacists such as addition of antihypertensive therapy were only implemented close

to the end of the study period, hence the beneficial effects may not have shown until after the trial period ended.

5.6 Conclusions

The aim of the present phase was to determine the impact of utilising all seven diabetes indicators in improving patients' clinical as well as QOL outcomes. This study has shown the benefits of pharmacists utilising a structured and consistent diabetes tool, the Simpler™ tool, to make individualised, evidence-based interventions in the clinical management of T2DM. Most notably were the improvements in glycaemia, blood pressure and medication adherence results in addition to QOL outcomes. This study contributes to the body of evidence that suggests the need for multifactorial interventions which includes all seven diabetes factors to reduce diabetes related complications. The results indicate that pharmacists in community or hospital settings with or without prior formal diabetes training can be trained to use an appropriate tool, such as the Simpler™ tool, to deliver quality diabetes care.

Chapter 6

General Discussion and Conclusions

6.1 General discussion

The prevalence of diabetes is increasing worldwide, and particularly in Malaysia.(21) Of significance is the number of diabetes related complications which are also on an increasing trend.(23) Diabetes management is complex and requires multifactorial care to reduce the risk of complications. The multifactorial intervention, the Simpler™ tool consisted of seven essential factors as outlined in diabetes guidelines.(6, 7, 16, 17) These are cholesterol, glucose, blood pressure control, medication, lifestyle and CVD risk management, as well as provision of education. The need for a multifactorial intervention was exemplified in several landmark trial studies, namely the UKPDS, ADVANCE and ACCORD studies (26, 27, 30) which successfully reduced the rates of premature morbidity and mortality associated with T2DM. To the best of our knowledge, the role of a structured multifactorial diabetes intervention tool which incorporates all seven evidence-based diabetes management factors has not been evaluated.

Many studies have documented the beneficial outcomes due to pharmacists' provision of care in collaboration with other healthcare professionals.(13, 14) Yet, other studies have identified pharmacists' insufficient knowledge and skills as barriers to provide medication management services.(135, 264) Thus, some diabetes intervention studies conducted by pharmacists (379) have not achieved a 1% reduction or greater for HbA1c which is the required percentage to reduce CVD and mortality risk recommended in the UKPDS trial.(326) There are two postulations for these varied patient outcomes. Firstly, it is not clear if all the guideline required diabetes factors mentioned above were necessarily addressed in these studies. Secondly, there were variations in pharmacists' skills and experience during the medication review process. To be able to provide quality diabetes care, knowledge and skills on pharmaceutical issues such as MRPs, dosage adjustments and modification of medications are important. As most of these studies

were conducted by pharmacists with extensive clinical experience, it remained unknown if similar outcomes could be achieved in community practice settings by pharmacists with limited clinical experience. Accreditation programs for pharmacists wishing to specialise in diabetes care such as to become a credentialed diabetes pharmacist exist in Malaysia and Australia. However, a relatively small number of pharmacists undergo this training and pharmacists are not required to be credentialed to provide diabetes management services. Both postulations were supported by findings from systematic reviews.(13, 380)

The overall aim of this research was to: 1) develop and validate a structured pharmacist type 2 diabetes (T2DM) intervention tool, referred to as the Simpler™ tool; 2) explore the impact of targeted training addressing pharmacists' knowledge and ability to deliver evidence-based diabetes care and; 3) determine the effectiveness of a multifactorial evidence-based diabetes intervention tool among T2DM patients. To achieve the overall aim, it was essential systematically to develop and evaluate the intervention tool through Phases One and Two. Since this research was exploratory in conception, the outcomes of each phase informed the development of the next phase. It was deemed important to collectively apply all factors and indicators required in diabetes management guidelines and obtain consensus on the content, format and design of the tool. An acronym was obtained through rearranging the first or second alphabet letter from the words in the seven diabetes management factors. The seven factors and indicators were then developed into the acronym Simpler™ whereby each letter of the word represented each of the seven diabetes factors. The notion to use an acronym that represents each required intervention was based on tools such as the SOAP note (an acronym for subjective, objective, assessment, and plan) which followed a similar technique.(187, 189, 190, 237) SOAP is used widely by healthcare professionals to document patients' assessment and care plans.

The Simpler™ tool, allows users to retrieve and organize information and use their judgement based on that information to make an intervention if necessary, as recommended by Weed.(177) The Simpler™ tool is grouped according to each outcome such as glycaemia, cholesterol, BP and medication adherence. Once the acronym, Simpler™ was developed, the indicators corresponding to the factors were listed. The decision on the list of indicators to be included and the order it should appear was achieved through Phase One during which 12 diabetes experts from Australia and Malaysia reached consensus using the Delphi method. The Delphi method explored disagreements and attained consensus among the panellists(200, 213) and has been used in similar studies on tool validation in healthcare.(179, 202-209, 212) This methodology was selected as it enabled respondents to consider their answers and to subsequently amend their initial decisions.

Phase Two aimed to explored pharmacists' perceptions of the tool's relevance and usefulness to deliver quality diabetes care in daily practice settings. To achieve this, a training program incorporating the application of the Simpler™ tool was developed. Phase Two methodology followed the format of previous studies which had explored pharmacists' views during application of new skills and knowledge on completion of training programs.(381, 382) Participants recruited were pharmacists from community settings without any formal diabetes training. Upon using the tool in practice for a month, pharmacists' interviews revealed the Simpler™ tool to be beneficial and functional when conducting diabetes MMS. Overall participants from both countries agreed that the Simpler™ tool was structured, comprehensive, evidence-based and user friendly. The most obvious finding was the need for participants to be pre-trained for effective use of the tool and the need to supplement the tool with clinical knowledge to facilitate assessment of MRPs. In addition, access to PMR was indicated as crucial. Phase Two showed that the application of the tool was useful specifically for diabetes management and prompted pharmacists to provide structured and consistent

interventions. The suggestions for improvements from this phase led to refinement of the Simpler™ training modules and the Simpler™ tool hand-out. The barriers and challenges of pharmacists utilising the tool were acknowledged and informed the methodology of the next phase.

Once the essential steps in the development and refinement in Phases One and Two were accomplished, the overall aim of the research was then evaluated moving forward to Phase Three. Phase Three evaluated the effectiveness of the tool on pharmacists' evidence-based recommendations including patients' clinical and health related QOL through a randomised controlled trial (RCT). Patients were randomised to receiving care from pharmacists using the Simpler™ tool and to receiving the usual customary care and were followed up for 6-months. RCT was chosen as the study method as it reduces selection and confounding biases. In addition, previous studies have recommended this method to measure the effectiveness of healthcare interventions.(3)

The process involved in Phases One, Two and Three and their findings are summarised in Figure 6.1.

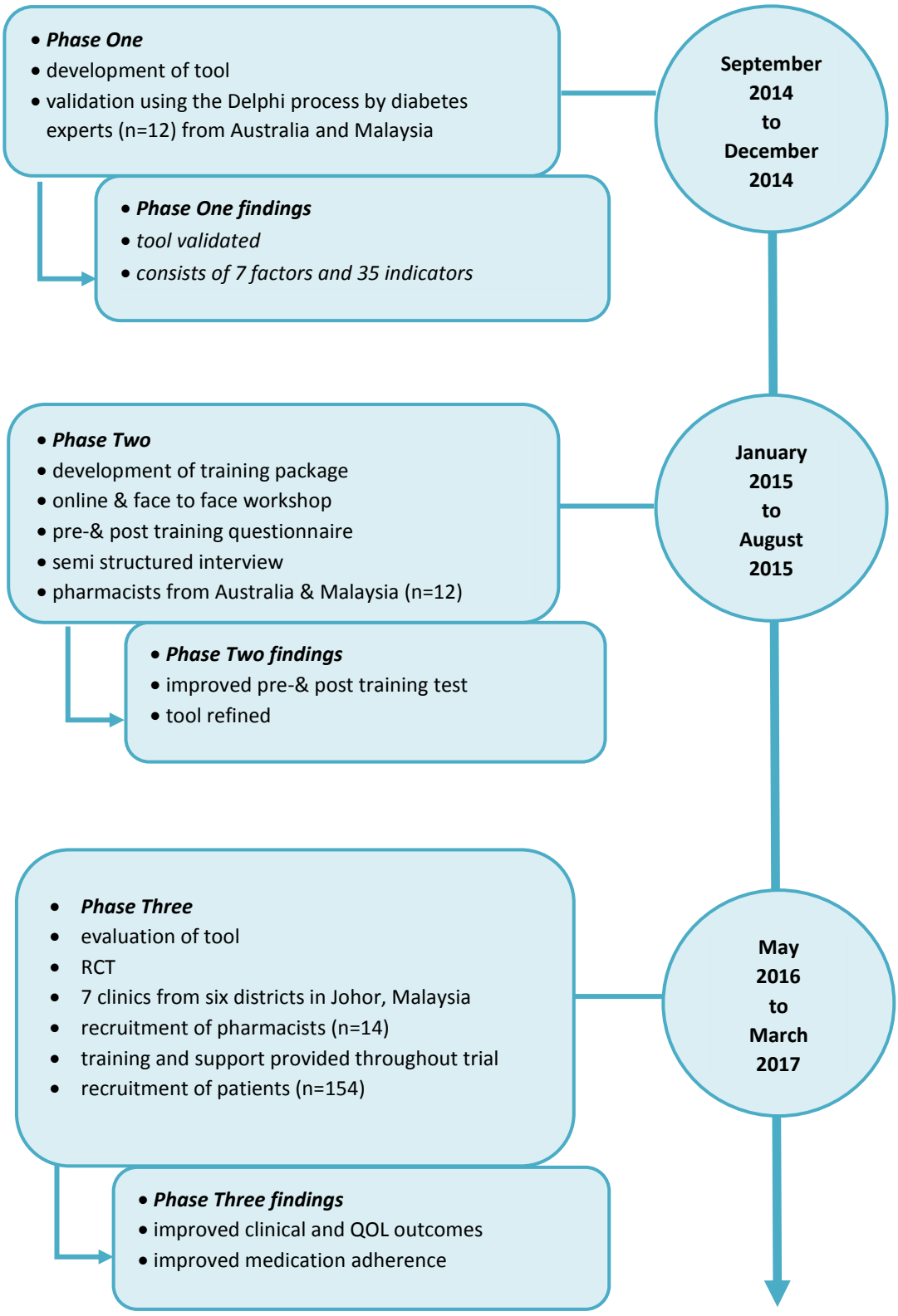


Figure 6. 1: Flow chart shows the summary of research process and finding

The primary aim of the trial was to achieve ≥ 1% HbA1c reduction. The reason being, this level of reduction has been shown to improve patient outcomes with respect to secondary risk factors.(326) The secondary outcomes of Phase Three of this research was that patients in the intervention arm showed statistically significant improvement in FBG, systolic BP, LDL and HDL levels at six months compared to baseline. Overall, HbA1c, systolic BP and QOL showed significant improvements at six months with respect to the control arm. Importantly, reductions of >1% HbA1c levels occurred in the intervention arm. This is a direct result of pharmacists' interventions using the multifactorial approach. The findings support the beneficial effects of the Simpler™ tool in improving medication adherence, increase evidence-based recommendations, clinical as well as health related QOL outcomes among T2DM patients.

Overall the Simpler™ training program improved pharmacists' skills, knowledge and confidence post training in both Phases Two and Three. This correlates with findings from review studies that concluded the need to upskill pharmacists to deliver quality diabetes care.(264, 383, 384) Due to the concise format of the Simpler™ tool, prior training is required for its effective use. Pharmacists used the Simpler™ tool to identify MRPs in each patient and worked towards resolving the problems. Several studies have shown that addressing medication adherence problems can improve glycaemia outcomes.(385) However, a systematic review found that while 22 intervention studies improved medication adherence, only nine improved both medication adherence and glycaemic control.(380) This indicates the need for a multifactorial intervention so that the other diabetes factors involved are addressed. In the Phase Three RCT, the impact of multifactorial interventions incorporating the seven factors in addition to pharmacists' expertise on medicine use enhanced the quality of diabetes care pharmacists provided.

Phase Three pharmacists documented 301 MRPs. Of these, 299 (96.3%) interventions to resolve the problems (including addressing causes of non-adherence) were recorded by

both pharmacists and doctors using the Simpler™ template forms. A majority of pharmacist interventions included evidence-based recommendations to prescribers on appropriate choice of medications and dosage modifications to achieve optimum therapy outcomes. Undoubtedly, the validation process in Phase One by diabetes experts from Australia and Malaysia may have increased pharmacists' confidence to use the tool. Pharmacists' interventions using the Simpler™ tool may have enhanced the communication process and doctors' trust in the pharmacists' recommendations. Consequently, this could have improved doctor and pharmacist cooperation as highlighted in a review study on pharmacists' extended role.(386)

The Simpler™ tool incorporated a template for documentation of information (Simpler™ Pro Forma A) for pharmacists, doctors and nurses to document their interventions on the same form. Although healthcare professionals (HCPs) are required to document and communicate patients' current health status so that the information is available to the rest of the healthcare team, documentation by HCPs and communication among team members were found to be inadequate in a systematic review study.(387) The Simpler™ tool on the other hand guided pharmacists to not only make evidence-based interventions but also to document the interventions. Additionally, the Simpler™ forms could be sent to doctors by email if further discussion is required and hence enhance communication between HCP. The Simpler™ tool facilitated the process of HCPs working towards achieving shared goals. In the practice settings used for the intervention, doctors were available in the same clinic therefore facilitating better communication. Although the level of communication may have varied from one clinic to another, the close housing of pharmacists and doctors may have been an advantage. This would also be feasible in other general practice settings.

Pharmacists in both Phases Two and Three found the Simpler™ tool feasible and of benefit in diabetes management. The Simpler tool was designed to be concise and structured, considering pharmacists' time constraints. Additionally, the Simpler™ tool

was intended to facilitate the process of pharmacist-patient consultation and not to add additional tasks to their existing MMS process. In addition, the inclusion criteria for patients recruited into the Phase Three research were aged more than 21 years old, on multiple medications and HbA1c of more than 8% (63.9 mmol/mol) or fasting blood sugar > 7.0 mmol/L or two hours post prandial sugar level > 8.5 mmol/L. As such, the results of the Phase Three RCT could be generalised to patients with similar criteria.

The Simpler™ tool provided specific indicators to address and therapeutic targets to achieve, whilst also offering individualised, patient centred care. Pharmacists followed guidelines for less stringent glycaemic targets for patients with severe hypoglycaemia and advanced complications.(388) In addition, the Simpler tool prompted pharmacists to address patients' self-care management. For instance, the education factor in the tool facilitated each patient to receive education on self-care specifically on areas they need improvement.(251) The tool is culturally sensitive especially in making dosage adjustments and when providing counselling advice.

6.2 Conclusions

Pharmacist without specialist diabetes training successfully applied the Simpler™ tool to improve the primary and secondary outcomes in T2DM. Furthermore, the tool's application in the community and primary health care settings was found to be relevant and feasible in both Australia and Malaysia. The Simpler™ tool was systematically developed and evaluated to prompt pharmacists to provide structured interventions in the management of T2DM. Pharmacists as part of collaborative team can use the Simpler™ tool to provide recommendations to doctors. It is evident that the beneficial outcomes achieved in this study have been facilitated by a structured and multi-faceted

intervention, rather than focusing on a single factor such as patient compliance. With the increasing prevalence of T2DM worldwide new models for its management need to be developed and this study has demonstrated that pharmacists using a structured intervention tool can achieve positive patient outcomes in several domains important to overall disease management. This approach could be broadened to MMS practices for T2DM management.

6.3 Future directions

This research identified gaps in the delivery of quality diabetes care. Most diabetes studies identified, incorporated one or a combination of intervention strategies but not all seven factors. Systematic review studies that focused on specific intervention strategies showed improved outcomes although the intervention strategies were inconclusive or unclear. This research therefore took a multifactorial approach whereby all seven factors were considered important to achieve the desired outcome.

Considering the learning from this study, the following recommendations are made for future research.

1. Australia and Malaysia have similar diabetes guidelines and provide diabetes MMS, which broadens the scope to apply the tool. Using the same premise, countries with similar diabetes guidelines which include the UK, Europe and the USA may find the tool beneficial when providing diabetes MMS. Therefore, other multi centre studies are necessary to evaluate the effectiveness of the tool in other countries.
2. Although this research evaluated the application of evidence-based interventions, clinical and QOL outcomes as well as pharmacists' view on the tool,

it did not assess the economic impact, as was proposed by a review study on pharmacist intervention tools.(389) Future studies should ideally also evaluate the cost effectiveness of Simpler™ interventions especially in reducing the risk of hospitalizations or onset of diabetes related complications like nephropathy or CVD.

3. In this research, Phase Three period was only for six months. Previous long term studies have shown that patient improvement waned after six months.(158) Therefore future studies should look into strategies to sustain patient improvements after the RCT study has ended or involve long term studies. In addition, the frequency of pharmacist interventions should be considered.
4. Pharmacists' expanding role and delivery of new services are currently moving towards the need for collaborative drug therapy management (CDTM) as opposed to current medication management services (MMS).(118) In CDTM, pharmacists independently change, add and modify doses of medications as part of an agreed protocol with the prescriber and other members of the healthcare team. The Simpler™ tool contains a list of guideline-based indicators which CDTM pharmacists working in collaboration with general practitioners could utilise to make medication changes. In addition, the Simpler™ tool could be used to assist pharmacist deliver structured intervention during remote monitoring such as telemedicine or tele pharmacy.(390)
5. The pharmacists in Phase Two identified that access to patients' medical record was necessary for efficient use of the Simpler™ tool. In other pharmacy services, such as home medication review, pharmacists' access to PMRs may enable pharmacists to utilise the Simpler™ tool more efficiently.
6. The tool has not been evaluated among privately owned community pharmacy settings in Malaysia. Future studies can explore its effectiveness in this setting.

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Appendices

Appendix 3. 1: Phase One ethics approval

Curtin University

Memorandum

Faculty of Health Sciences

School of Pharmacy

TELEPHONE 9266 7418
FACSIMILE 9266 3793
EMAIL Ausana.Naidoo@curtin.edu.au

To	Shamala Ayadurai
From	Ausana Naidoo, Form C Coordinator
Subject	Protocol Approval **PH-18-14**
Date	10 September 2014
Copy	Laetitia Hattingh

Thank you for your "Form C Application for Approval of Research with Low Risk (Ethical Requirements)" for the project titled *"Development and Evaluation of a Pharmacist Diabetes Management Tool: a Mixed Methods Study"* On behalf of the Human Research Ethics Committee, I am authorised to inform you that the project is **approved**.

Approval of this project is for a period of 4 years **10/09/2014** to **10/09/2018**.

Your approval has the following conditions:

(i) **Annual Progress Reports** on the project must be submitted to the Ethics Office.

(ii) It is your responsibility, as the researcher, to **meet the conditions** outlined and to retain the necessary records demonstrating that these have been completed.

(iii) It is the investigator's responsibility to complete **Risk Assessments** as appropriate to the research activities, prior to commencement of this research. The Curtin University Risk Assessment form is available here.

The approval number for your project is **PH-18-14**. Please quote this number in any future correspondence. If at any time during the approval term changes/amendments occur, or if a serious or unexpected adverse event occurs, please advise me immediately.

Sincerely,

Ausana Naidoo
Research & Development Support Coordinator
School of Pharmacy

Please Note: The following standard statement must be included in the information sheet to participants:
This study has been approved under Curtin University's process for lower-risk Studies (Approval Number PH-18-14). This process complies with the National Statement on Ethical Conduct in Human Research (Chapter 5.1.7 and Chapters 5.1.18-5.1.21). For further information on this study contact the researchers named above or the Curtin University Human Research Ethics Committee. c/o- Office of Research and Development, Curtin University, GPO Box U1987, Perth 6845 or by telephoning 9266 9223 or by emailing hrec@curtin.edu.au.

Appendix 3. 2: Phase One participant information sheet

Curtin University
GPO Box U1987
Perth Western Australia 6845

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INFORMATION SHEET

Development and Evaluation of a Pharmacist Diabetes Management Tool: a Mixed Methods Study

Purpose of the study? As part of my PhD I need to evaluate a diabetes tool called the SIMPLER tool. This tool will be used to facilitate pharmacists in making structured, consistent and quality interventions.

What will the study involve? The study will involve completing a series of surveys to evaluate the use of the SIMPLER tool. This is expected to take a maximum of 30 minutes for each survey. The first survey will involve ranking each category of indicators for diabetes management as they should appear in the accompanying hand-out. In addition, participants will be required to rank indicators not previously included in diabetes guidelines and whether they should be included in the SIMPLER tool. Group consensus will be achieved when 60% or more respondents give the same response to a question.

Why have you been asked to take part? You have been asked because of your expertise and vast experience in diabetes.

Do you have to take part? The answer is no! Participation is voluntary. You have the option of withdrawing before the study commences or discontinuing after data collection has started without penalty.

Will your participation in the study be kept confidential? Yes. The identity of each participant will not be revealed to other participants. Any information about your identity will not appear in the thesis or publications. Any extracts from your comments will be entirely anonymous.

What will happen to the information which you give? The data will be kept confidential for the duration of the study and up to 5 years post completion of the study. On completion of the thesis, they will be retained for a further six months and then destroyed.

What will happen to the results? The results will be presented in the thesis and publications. They will be seen by my supervisor, a second marker and the external examiner. The thesis may be read by future students in the course.

What are the possible disadvantages of taking part? I don't envisage any negative consequences for you in taking part.

Who has reviewed this study? Approval must be given by the Faculty of Health and Science, Curtin University, Bentley, Western Australia before the survey takes place. Curtin University conducts research in accordance with the *National Statement on Ethical Conduct in Human Research.*

Any further queries? If you need any further information, you can contact me: Shamala Ayadurai, shamala.ayadurai@postgrad.curtin.edu.au

This study has been approved under Curtin University's process for lower-risk studies (Approval Number PH-18-14). This process complies with the National Statement on Ethical Conduct in Human Research (Chapter 5.1.7 and Chapters 5.1.18-5.1.21). For further information on this study contact the researchers named above or the Curtin University Human Research Ethics Committee. C/- Office of Research and Development, Curtin University, GPO Box U1987, Perth 6845 or by telephoning 9266 9223 or by emailing hrec@curtin.edu.au.

Appendix 3. 3: Introductory letter to Phase One participants

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The Delphi Survey– Round 1

Title of Research: Development and evaluation of a pharmacy diabetes management tool: a mixed methods study

By way of introduction I am Shamala Ayadurai, a pharmacist from Malaysia with experience in diabetes care. I am undertaking this research study as part of my Doctor of Philosophy.

Thank you for agreeing to participate in this Delphi survey on a diabetes tool for pharmacists. This survey is based on current diabetes guidelines and evidence based best practice. Responses from participants will be used to validate the diabetes tool, entitled the SIMPLER tool. This tool will be used by pharmacists to facilitate the provision of structured and consistent interventions in providing pharmaceutical care to patients and making treatment suggestions to prescribers. Pharmacists will be integrating this tool as part of existing diabetes management programmes such as Medication Therapy Adherence Clinic (MTAC Diabetes) in Malaysia and the Diabetes Medscheck service in Australia.

Survey Round 1 is the first of three rounds of the survey. Please answer all questions. You will have an opportunity to revise your answers with subsequent rounds of the survey. An information sheet explaining the references to each question is attached (Appendix 2).

You will be requested to rate each indicator in order of importance as it will appear in the hand-out (Appendix 3a/3b). There will be a section on whether you agree or disagree with interventions recommended from randomised clinical trials. Where appropriate, a space is also provided for you to comment and provide reasons for your responses or additional suggestions.

Participants will be given two weeks to give their responses for each round. Once responses have been received from all participants, findings will be incorporated and the second questionnaire will be formulated. We assure you that your participation in the survey and your individual responses will be strictly confidential to the research team and will not be disclosed to any outside party, including other participants.

Yours sincerely,

Shamala Ayadurai
PHD Candidate
School of Pharmacy, Curtin University
Perth, Western Australia
Tel: 04 50602642
Email: shamala.ayadurai@postgrad.curtin.edu.au

Dr.Laetitia Hattingh
PhD Supervisor and Senior Lecturer
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This study has been approved under Curtin University's process for lower-risk Studies (Approval Number: PH-18-14). This process complies with the National Statement on Ethical Conduct in Human Research (Chapter 5.1.7 and Chapters 5.1.18-5.1.21). For further information on this study contact the researchers named above or the Curtin University Human Research Ethics Committee. c/- Office of Research and Development, Curtin University, GPO Box U1987, Perth 6845 or by telephoning 9266 9223 or by emailing hrec@curtin.edu.au

Appendix 3. 4: Round 1 questionnaire

1. Below is a list of diabetes indicators recommended by diabetes guidelines from Malaysia, Australia, America, and the United Kingdom. The questionnaire is divided into two parts. In Part I you are asked to rate each of the indicators in order of importance as it should appear in the accompanying hand-out (appendix). Note that 1 is ranked as most important and will appear as the first subheading, 2 as the second subheading, and 3 as the third subheading and so on. Only one number can be circled per subheading. In formulating your responses, you are not expected to assess the feasibility or cost of monitoring the indicators. The table below shows an example of this:

Code:	**Indicator Name And Description**	**Appearance Of Indicator In Hand-out In Order Of Importance.** **Please Choose One Number For Each Indicator. The Same Number Cannot Be Picked More Than Once For Each Of The Indicator.**	**Order of appearance in hand-out**
1.	3.3 Statin initiation in patients with CVD	□1 ☒2 □ 3	This will be the second bullet point to appear in the hand-out (appendix3).
2.	3.4 Statin initiation in patients over age 40 years without CVD	☒1 □2 □ 3	This will be the first bullet point.
3.	3.5 Achieve targets: LDL, Malaysia (LDL<2.6mmol/L, TG<1.7mmol/L) Australia (LDL<2.5mmol/L), TG (<1.5mmol/L).	□1 □2 ☒ 3	This will be the third bullet point.

2. In Part 2 of the questionnaire, you are asked to rate the indicator in terms of its value in making diabetes interventions, where 1 indicates it is least important or redundant and 5 indicates it is most important.
3. Once consensus is achieved, these indicators will appear in the hand-out. This hand-out will be used to aid pharmacists to make their interventions.
4. A space is provided for you to briefly explain the reason for your rating if you wish to. This additional information is optional and could help us understand the reasons some indicators receive a more important ranking than others. The space could also be used

for additional suggestions or interventions that should be included according to indications mentioned.

5. As the *Simpler™* tool is quite unique, we would like to stress that all materials discussed here will remain the intellectual property of the researchers and protected by copyright laws. All such rights are reserved. Materials may not be reproduced, distributed or otherwise exploited in any manner without prior written permission.

Part 1

Code	Indicator Name And Description	Appearance of indicator in hand-out in order of importance. Please choose one number for each indicator. The same number cannot be picked more than once for each of the indicator.	Additional Comments
Statin Initiation: 3 indicators			
	3.6 Statin initiation in patients with CVD	☐1 ☐2 ☐3	Click here to enter text.
	3.7 Statin initiation in patients over age 40 years without CVD	☐1 ☐2 ☐3	Click here to enter text.
	3.8 Achieve targets: LDL, Malaysia (LDL<2.6mmol/L, TG<1.7mmol/L) Australia (LDL<2.5mmol/L), TG (<1.5mmol/L).	☐1 ☐2 ☐3	Click here to enter text.
Insulin Initiation: 6 indicators			
	3.9 Insulin initiation if glycaemic control not achieved despite being on two or more oral hypoglycaemic agents	☐1 ☐2 ☐3 ☐4 ☐5 ☐6	Click here to enter text.
	3.10 Management of hypoglycaemia	☐1 ☐2 ☐3 ☐4 ☐5 ☐6	Click here to enter text.
	3.11 Self-monitoring of blood glucose Malaysia & Australia CPG (4.0-6.0mmol/L fasting); NHMRC (6-8mmol/L (fasting), (6-10mmol/L, 2h postprandial). Malaysia CPG (6-8mmol/L-2h postprandial)	☐1 ☐2 ☐3 ☐4 ☐5 ☐6	Click here to enter text.
	3.12 Target of HbA1c ≤ 7% (53mmol/mol) if no other complications	☐1 ☐2 ☐3 ☐4 ☐5 ☐6	Click here to enter text.
	3.13 Aim a reduction of HbA1c by 1%	☐1 ☐2 ☐3 ☐4 ☐5 ☐6	Click here to enter text.
	Initiate metformin if not contraindicated	☐1 ☐2 ☐3 ☐4 ☐5 ☐6	Click here to enter text.

Medication: 2 indicators			
	3.14 Review medication adherence using 8-items modified Morisky medication adherence scale	☐1 ☐2	Click here to enter text.
	3.15 Assess medicine related problems(pharmacotherapy): contraindicated medicine, inappropriate dosing, adverse reaction, duplication of therapy, medicine and food interaction, unnecessary medicine use	☐1 ☐2	Click here to enter text.
Blood Pressure (BP) Control: 5 indicators			
	3.16 BP target: ≤130/80	☐1 ☐2 ☐3 ☐4 ☐5	Click here to enter text.
	4.2 Reduce sodium intake	☐1 ☐2 ☐3 ☐4 ☐5	Click here to enter text.
	4.3 ACEI/ARB initiation in patients without microalbuminuria/proteinuria	☐1 ☐2 ☐3 ☐4 ☐5	Click here to enter text.
	4.4 ACEI/ARB initiation in patients with microalbuminuria/proteinuria	☐1 ☐2 ☐3 ☐4 ☐5	Click here to enter text.
Lifestyle Intervention: 8 indicators			
	5.1 Moderate alcohol intake: ≤2 standard drinks (20g) per day for men and women with max 4 standard drinks on any occasion	☐1 ☐2 ☐3 ☐4 ☐5 ☐6 ☐7 ☐8	Click here to enter text.
	5.2 Exercise: 30 mins walking (or equivalent) 5 or more days/week (total ≥150 min/week)	☐1 ☐2 ☐3 ☐4 ☐5 ☐6 ☐7 ☐8	Click here to enter text.
	5.3 Smoking cessation	☐1 ☐2 ☐3 ☐4 ☐5 ☐6 ☐7 ☐8	Click here to enter text.
	5.4 Advice on foot care	☐1 ☐2 ☐3 ☐4 ☐5 ☐6 ☐7 ☐8	Click here to enter text.
	5.5 Weight loss: Australia (BMI<25kg/m^2) Malaysia (BMI <23kg/$m^{2)}$	☒1 ☐2 ☐3 ☐4 ☐5 ☐6 ☐7 ☐8	Click here to enter text.

	Waist circumference Australia (<94cm in men,<80cm in women, waist circumference), Malaysia (≤90cm in men,≤80cm in women)	☐1 ☐2 ☐3 ☐4 ☐5 ☐6 ☐7 ☐8	Click here to enter text.
	5.7Erectile dysfunction: recommend PDE-5 inhibitor as first line therapy for male patients	☐1 ☐2 ☐3 ☐4 ☐5 ☐6 ☐7 ☐8	Click here to enter text.
	5.8Management of stress & diabetes related distress	☐1 ☐2 ☐3 ☐4 ☐5 ☐6 ☐7 ☐8	Click here to enter text.
Education: 3 indicators			
	6.1 Knowledge and understanding of medicine	☐1 ☐2 ☐3	Click here to enter text.
	6.2 Medicine storage	☐1 ☐2 ☐3	Click here to enter text.
	6.3 Medication optimisation during fasting month for muslims	☐1 ☐2 ☐3	Click here to enter text.
CVD Risk factors: 3 indicators			
	7.1 Aspirin therapy (75mg-162mg/day) as primary prevention to decrease CVD risk (10 year risk>10%, Framingham)	☐1 ☐2 ☐3	Click here to enter text.
	7.2 Aspirin therapy as secondary prevention in those with diabetes with history of CVD	☐1 ☐2 ☐3	Click here to enter text.
	7.3 Use of Framingham risk calculatorto calculate CVD risk and educate patient	☐1 ☐2 ☐3	Click here to enter text.

Part 2

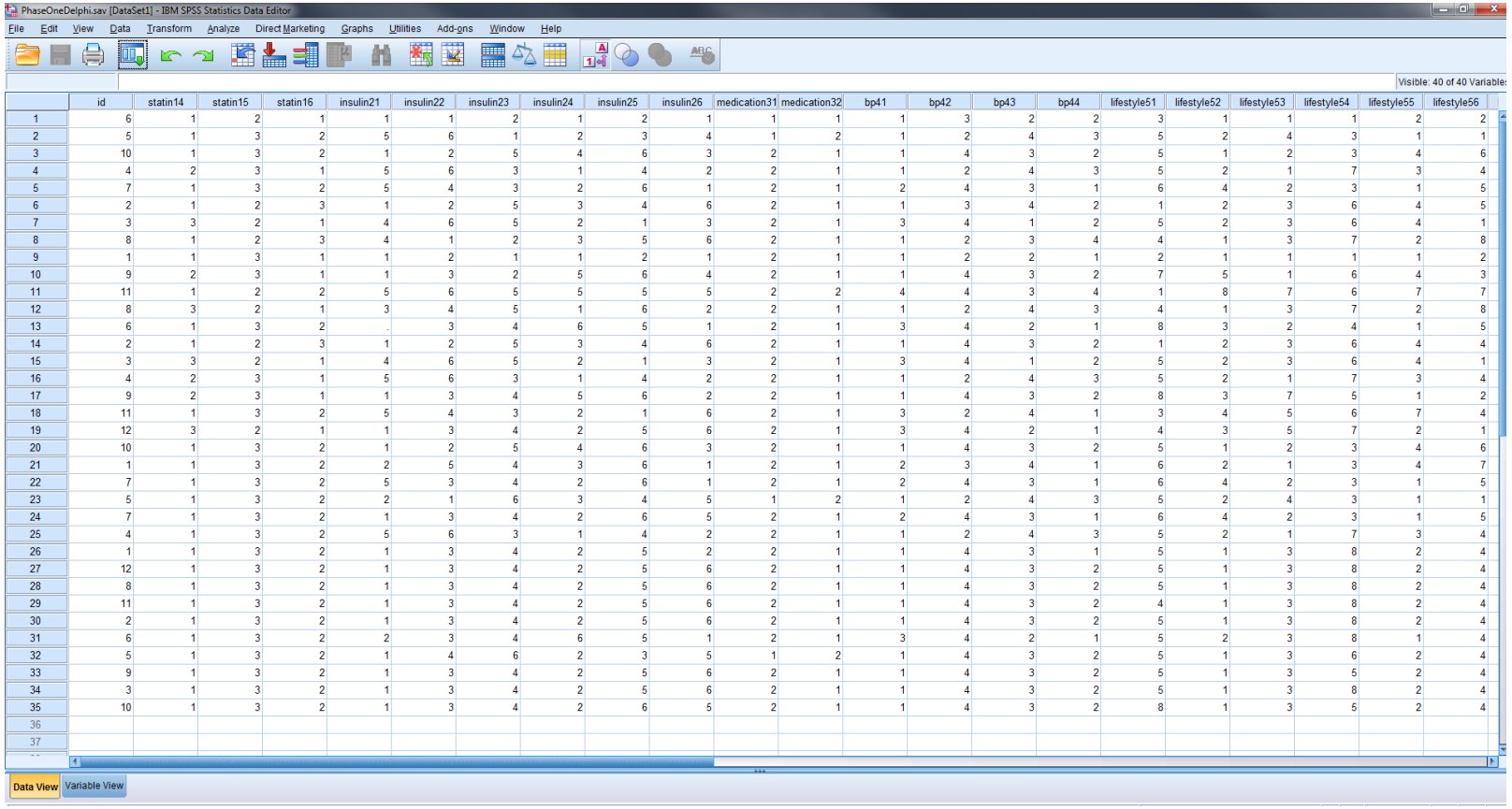
Code:	Indicator Name And Description	Rating (1=least preferred ⟶ 5=most preferred) Please choose your preference.	
8.	Hand-out Design Preference		
	8.1 Appendix 3a (bookmark design)	☐1 ☐2 ☐3 ☐4 ☐5	Click here to enter text.
	8.2 Appendix 3b (wheel design)	☐1 ☐2 ☐3 ☐4 ☐5	Click here to enter text.
9.	Additional Indicators to be included in hand-out	Rating (1=least preferred ⟶ 5=most preferred) Please choose your preference.	
	9.1 Administer once daily antihypertensive at bedtime	☐1 ☐2 ☐3 ☐4 ☐5	Click here to enter text.
	9.2 Diet advice using plate model	☐1 ☐2 ☐3 ☐4 ☐5	Click here to enter text.
	9.3 Annual eye assessment	☐1 ☐2 ☐3 ☐4 ☐5	Click here to enter text.
	9.4 Address sleep hygiene	☐1 ☐2 ☐3 ☐4 ☐5	Click here to enter text.
	9.5 1g-3g cinnamon intake per day	☐1 ☐2 ☐3 ☐4 ☐5	Click here to enter text.
	9.6 Vitamin B12 supplement in patients on long term metfomin	☐1 ☐2 ☐3 ☐4 ☐5	Click here to enter text.
	9.7 Encourage daily Intake of tree nuts (almonds, brazil nuts, cashews, hazelnuts, macadamia, pecans, pine nuts, pistachios and walnuts)	☐1 ☐2 ☐3 ☐4 ☐5	Click here to enter text.

Appendix 3. 5: Excerpt from Round 2 Questionnaire

Code	Indicator Name And Description Part 1	Your Score	Median Score	Round 2 Score Please choose one number for each indicator. The same number cannot be picked more than once for each of the indicator.
1.	Statin Initiation: 3 indicators			
	1.1 Statin initiation in patients with CVD	2	1	☐1 ☐2 ☐3
	1.2 Statin initiation in patients over age 40 years without CVD	3	3	☐1 ☐2 ☐3
	1.3 Achieve targets: LDL, Malaysia (LDL<2.6mmol/L, TG<1.7mmol/L) Australia (LDL<2.5mmol/L), TG (<1.5mmol/L).	1	2	☐1 ☐2 ☐3

Code:	Indicator Name And Description Part 2	Your Score	Median Score	Round 2 Score (1=least preferred ⟶ 5=most preferred) Please choose your preference.
8.	Hand-out Design Preference			
	8.1 Appendix 3a (bookmark design)	3	4	☐1 ☐2 ☐3 ☐4 ☐5
	8.2 Appendix 3b (wheel design)	5	3	☐1 ☐2 ☐3 ☐4 ☐5

Appendix 3. 6: Excerpt of SPSS data set for Phase One data



	id	statin14	statin15	statin16	insulin21	insulin22	insulin23	insulin24	insulin25	insulin26	medication31	medication32	bp41	bp42	bp43	bp44	lifestyle51	lifestyle52	lifestyle53	lifestyle54	lifestyle55	lifestyle56
1	6	1	2	1	1	1	2	1	2	1	1	1	1	3	2	2	3	1	1	1	2	2
2	5	1	3	2	5	6	1	2	3	4	1	2	1	2	4	3	5	2	4	3	1	1
3	10	1	3	2	1	2	5	4	6	3	2	1	1	4	3	2	5	1	2	3	4	6
4	4	2	3	1	5	6	3	1	4	2	2	1	1	2	4	3	5	2	1	7	3	4
5	7	1	3	2	5	4	3	2	6	1	2	1	2	4	3	1	6	4	2	3	1	5
6	2	1	2	3	1	2	5	3	4	6	2	1	1	3	4	2	1	2	3	6	4	5
7	3	3	2	1	4	6	5	2	1	3	2	1	3	4	1	2	5	2	3	6	4	1
8	8	1	2	3	4	1	2	3	5	6	2	1	1	2	3	4	4	1	3	7	2	8
9	1	1	3	1	1	2	1	1	2	1	2	1	1	2	2	1	2	1	1	1	1	2
10	9	2	3	1	1	3	2	5	6	4	2	1	1	4	3	2	7	5	1	6	4	3
11	11	1	2	2	5	6	5	5	5	5	2	2	4	4	3	4	1	8	7	6	7	7
12	8	3	2	1	3	4	5	1	6	2	2	1	1	2	4	3	4	1	3	7	2	8
13	6	1	3	2	.	3	4	6	5	1	2	1	3	4	2	1	8	3	2	4	1	5
14	2	1	2	3	1	2	5	3	4	6	2	1	1	4	3	2	1	2	3	6	4	4
15	3	3	2	1	4	6	5	2	1	3	2	1	3	4	1	2	5	2	3	6	4	1
16	4	2	3	1	5	6	3	1	4	2	2	1	1	2	4	3	5	2	1	7	3	4
17	9	2	3	1	1	3	4	5	6	2	2	1	1	4	3	2	8	3	7	5	1	2
18	11	1	3	2	5	4	3	2	1	6	2	1	3	2	4	1	3	4	5	6	7	4
19	12	3	2	1	1	3	4	2	5	6	2	1	3	4	2	1	4	3	5	7	2	1
20	10	1	3	2	1	2	5	4	6	3	2	1	1	4	3	2	5	1	2	3	4	6
21	1	1	3	2	2	5	4	3	6	1	2	1	2	3	4	1	6	2	1	3	4	7
22	7	1	3	2	5	3	4	2	6	1	2	1	2	4	3	1	6	4	2	3	1	5
23	5	1	3	2	2	1	6	3	4	5	1	2	1	2	4	3	5	2	4	3	1	1
24	7	1	3	2	1	3	4	2	6	5	2	1	2	4	3	1	6	4	2	3	1	5
25	4	1	3	2	5	6	3	1	4	2	2	1	1	2	4	3	5	2	1	7	3	4
26	1	1	3	2	1	3	4	2	5	2	2	1	1	4	3	1	5	1	3	8	2	4
27	12	1	3	2	1	3	4	2	5	6	2	1	1	4	3	2	5	1	3	8	2	4
28	8	1	3	2	1	3	4	2	5	6	2	1	1	4	3	2	5	1	3	8	2	4
29	11	1	3	2	1	3	4	2	5	6	2	1	1	4	3	2	4	1	3	8	2	4
30	2	1	3	2	1	3	4	2	5	6	2	1	1	4	3	2	5	1	3	8	2	4
31	6	1	3	2	2	3	4	6	5	1	2	1	3	4	2	1	5	2	3	8	1	4
32	5	1	3	2	1	4	6	2	3	5	1	2	1	4	3	2	5	1	3	6	2	4
33	9	1	3	2	1	3	4	2	5	6	2	1	1	4	3	2	5	1	3	5	2	4
34	3	1	3	2	1	3	4	2	5	6	2	1	1	4	3	2	5	1	3	8	2	4
35	10	1	3	2	1	3	4	2	6	5	2	1	1	4	3	2	8	1	3	5	2	4
36																						
37																						

Appendix 3. 7: Excerpt from Round 3 questionnaire

Code	Indicator Name And Description Part 1	Your Score	Median Score	Round 2 Score Please choose one number for each indicator. The same number cannot be picked more than once for each of the indicator.
1.	Statin Initiation: 3 indicators			
	3.17 Statin initiation in patients with CVD	1	1	☐1 ☐2 ☐3
	3.18 Statin initiation in patients over age 40 years without CVD	consensus achieved		3
	3.19 Achieve targets: LDL, Malaysia (LDL<2.6mmol/L, TG<1.7mmol/L) Australia (LDL<2.5mmol/L), TG (<1.5mmol/L).	3	2	☐1 ☐2 ☐3

9.	Additional Indicators to be included in hand-out Part 2	Your Score	Median Score	Round 2 Score (1=least preferred ⟶ 5=most preferred) Please choose your preference.
	9.5 1g-3g cinnamon intake per day	2	1	☐1 ☐2 ☐3 ☐4 ☐5
	9.6 Vitamin B12 supplement in patients on long term metfomin	1	2	☐1 ☐2 ☐3 ☐4 ☐5

Appendix 4. 1: Phase Two ethics approval (Australia)

MEMORANDUM

Curtin University

To:	Laetitia Hattingh
	School of Pharmacy
CC:	Shamala Ayadurai
From	Professor Peter O'Leary, Chair HREC
Subject	Ethics approval
	Approval number: RDHS-06-14
Date	18-Dec-14

Office of Research and Development
Human Research Ethics Office

TELEPHONE 9266 2784
FACSIMILE 9266 3793
EMAIL hrec@curtin.edu.au

Thank you for your application submitted to the Human Research Ethics Office for the project: 5845

Development and Evaluation of a Pharmacist Diabetes Management Tool: a Mixed Methods Study

Your application has been approved through the low risk ethics approvals process at Curtin University.

Please note the following conditions of approval:

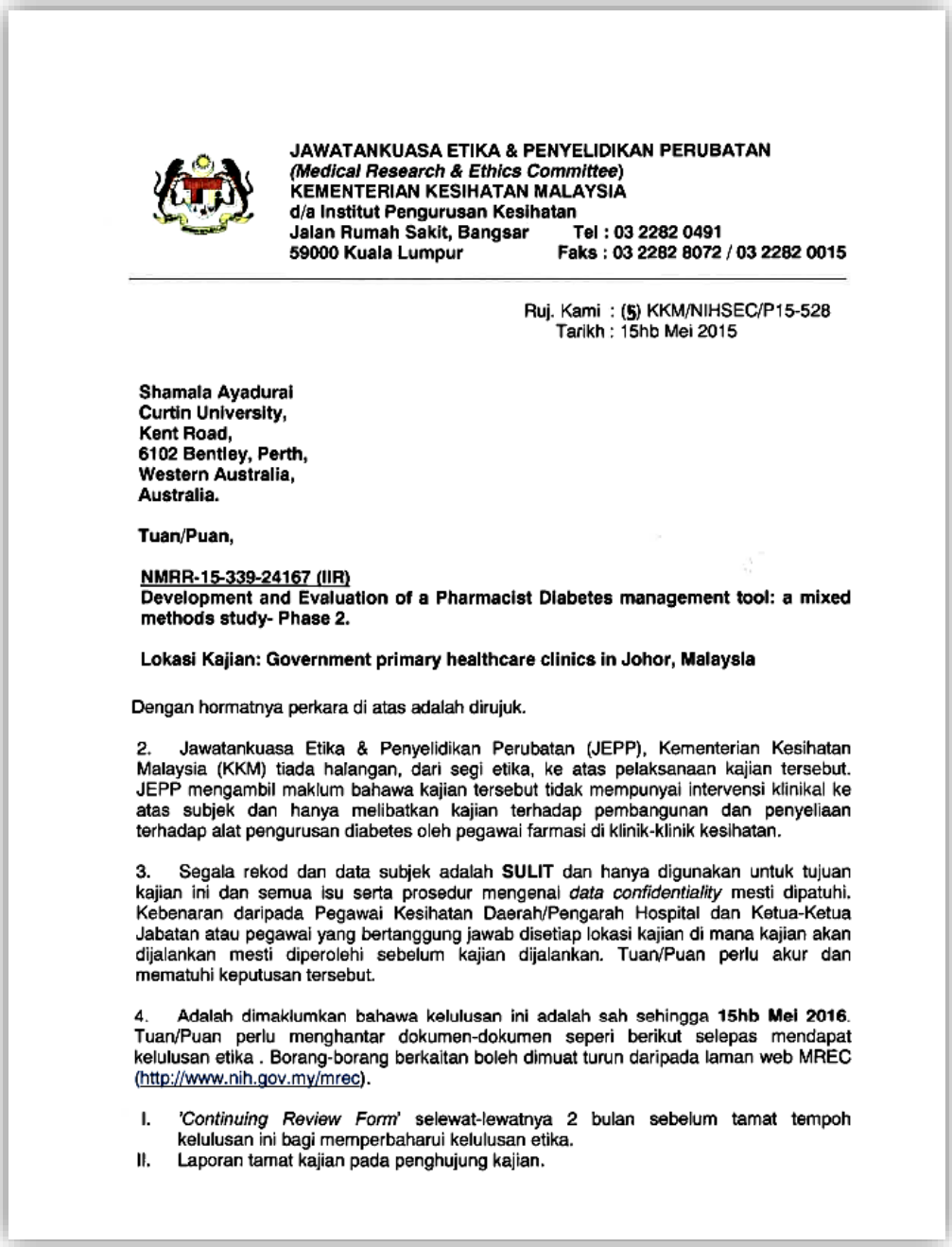
1. Approval is granted for a period of four years from **18-Dec-14** to **18-Dec-18**
2. Research must be conducted as stated in the approved protocol.
3. Any amendments to the approved protocol must be approved by the Ethics Office.
4. An annual progress report must be submitted to the Ethics Office annually, on the anniversary of approval.
5. All adverse events must be reported to the Ethics Office.
6. A completion report must be submitted to the Ethics Office on completion of the project.
7. Data must be stored in accordance with WAUSDA and Curtin University policy.
8. The Ethics Office may conduct a randomly identified audit of a proportion of research projects approved by the HREC.

Should you have any queries about the consideration of your project please contact the Ethics Support Officer for your faculty, or the Ethics Office at hrec@curtin.edu.au or on 9266 2784. All human research ethics forms and guidelines are available on the ethics website.

Yours sincerely,

Professor Peter O'Leary
Chair, Human Research Ethics Committee

Appendix 4. 2: Phase Two ethics approval (Malaysia)



JAWATANKUASA ETIKA & PENYELIDIKAN PERUBATAN
(Medical Research & Ethics Committee)
KEMENTERIAN KESIHATAN MALAYSIA
d/a Institut Pengurusan Kesihatan
Jalan Rumah Sakit, Bangsar **Tel : 03 2282 0491**
59000 Kuala Lumpur **Faks : 03 2282 8072 / 03 2282 0015**

Ruj. Kami : (5) KKM/NIHSEC/P15-528
Tarikh : 15hb Mei 2015

Shamala Ayadurai
Curtin University,
Kent Road,
6102 Bentley, Perth,
Western Australia,
Australia.

Tuan/Puan,

NMRR-15-339-24167 (IIR)
Development and Evaluation of a Pharmacist Diabetes management tool: a mixed methods study- Phase 2.

Lokasi Kajian: Government primary healthcare clinics in Johor, Malaysia

Dengan hormatnya perkara di atas adalah dirujuk.

2. Jawatankuasa Etika & Penyelidikan Perubatan (JEPP), Kementerian Kesihatan Malaysia (KKM) tiada halangan, dari segi etika, ke atas pelaksanaan kajian tersebut. JEPP mengambil maklum bahawa kajian tersebut tidak mempunyai intervensi klinikal ke atas subjek dan hanya melibatkan kajian terhadap pembangunan dan penyeliaan terhadap alat pengurusan diabetes oleh pegawai farmasi di klinik-klinik kesihatan.

3. Segala rekod dan data subjek adalah **SULIT** dan hanya digunakan untuk tujuan kajian ini dan semua isu serta prosedur mengenai *data confidentiality* mesti dipatuhi. Kebenaran daripada Pegawai Kesihatan Daerah/Pengarah Hospital dan Ketua-Ketua Jabatan atau pegawai yang bertanggung jawab disetiap lokasi kajian di mana kajian akan dijalankan mesti diperolehi sebelum kajian dijalankan. Tuan/Puan perlu akur dan mematuhi keputusan tersebut.

4. Adalah dimaklumkan bahawa kelulusan ini adalah sah sehingga **15hb Mei 2016**. Tuan/Puan perlu menghantar dokumen-dokumen seperi berikut selepas mendapat kelulusan etika . Borang-borang berkaitan boleh dimuat turun daripada laman web MREC (http://www.nih.gov.my/mrec).

I. '*Continuing Review Form*' selewat-lewatnya 2 bulan sebelum tamat tempoh kelulusan ini bagi memperbaharui kelulusan etika.
II. Laporan tamat kajian pada penghujung kajian.

III. Laporan mengenai "*All adverse events, both serious and unexpected*"/*Protocol Deviation* atau *Violation* kepada Jawatankuasa Etika & Penyelidikan Perubatan, KKM jika berkenaan.
IV. Memaklumkan jika terdapat pindaan keatas sebarang dokumen kajian.

5. Sila ambil maklum bahawa sebarang urusan surat-menyurat berkaitan dengan penyelidikan ini haruslah dinyatakan nombor rujukan surat ini untuk melicinkan urusan yang berkaitan.

Sekian terima kasih.

BERKHIDMAT UNTUK NEGARA

Saya yang menurut perintah,

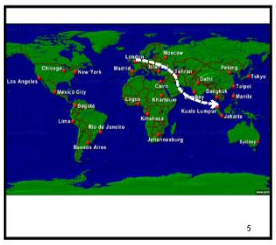
(DATO' DR CHANG KIAN MENG)
Pengerusi
Jawatankuasa Etika & Penyelidikan Perubatan
Kementerian Kesihatan Malaysia

Appendix 4. 3: The Simpler™ training modules outline

<table>
<tr><td colspan="3">MODULE 1- INTRODUCTION (15 MINS)</td></tr>
<tr><td colspan="3">Learning Objectives
Describe the pharmacist's role in management of Type 2 Diabetes Mellitus
Explain the research objectives and significance
Outline the research plan and present results of the Phase 1 study</td></tr>
<tr><td>Content
Introduction on research objectives
Background information on prevalence of diabetes in Australia & Malaysia
Phase 1 Delphi results</td><td>Process
Presentation 15 minutes</td><td>Resources
Slides</td></tr>
<tr><td colspan="3">MODULE 2- SIMPLER™ VALIDATION (30 MINS)</td></tr>
<tr><td colspan="3">Learning Objectives
Outline and describe the seven indicators incorporated into Simpler™
Explain the benefits of Simpler™ using evidence-based information</td></tr>
<tr><td>Content
Simpler™ diabetes indicators
Additional indicators: findings from Phase 1
Recent updates on diabetes management</td><td>Process
Presentation 30 minutes</td><td>Resources
Slides</td></tr>
<tr><td colspan="3">MODULE 3 – CASE SCENARIO (45 MINS)</td></tr>
<tr><td colspan="3">Learning Objectives
Outline the information gathering process
Practise effective intervention using the Simpler™ tool</td></tr>
<tr><td>Content
Extracting information from patient and case notes
Systematic intervention using the Simpler™ tool</td><td>Process
Presentation 15 minutes</td><td>Resources
Case study</td></tr>
<tr><td>Case study (1 scenario)</td><td>1. Participants to practise intervention using Simpler™
2. Feedback 30 minutes</td><td>Diabetes Guidelines
Simpler™ tool</td></tr>
<tr><td colspan="3">MODULE 4 – WRITING INTERVENTION NOTES (30 MINS)</td></tr>
<tr><td colspan="3">Learning Objectives
Writing case notes using the Simpler™ tool</td></tr>
<tr><td>Content
Legal aspects
Describing observations and interventions
Use of correct spelling and grammar.
Writing case note using the Simpler™ tool</td><td>Process
Presentation 15 minutes</td><td>Resources
Slides</td></tr>
<tr><td>Case study (1 scenario)</td><td>1. Documenting patient case notes</td><td>Diabetes Guidelines and Simpler™ tool</td></tr>
</table>

	2.Feedback 15 minutes	

Appendix 4. 4: The Simpler™ hand-out version of the slide presentations



1

Training Module Outline

Module 1
- Pharmacist's role in diabetes management
- Background of research

Module 2
- Outline of seven diabetes indicators
- Benefits of SIMPLER

Module 3
- Outline the information gathering process
- Practise effective intervention using SIMPLER

Module 4
- Write case notes/ GuildCare using SIMPLER

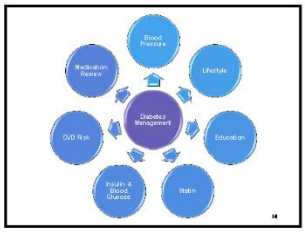
Overview (1)

- **Prevalence of diabetes:**
  - Malaysia 15.2% in 2011[1]
  - Australia 4.1% in 2008[2]
- **Complications:**
  - Australia 58% CVD, 60% microvascular (2007-08)[2]
  - Malaysia 28.9% CVD, 75% microvascular (2008)[3]

Overview (2)

Country	Total health expenditure for diabetes in 2010	Mean diabetes related expenditure per person in 2010
Malaysia[4]	USD 1,005,095,000	USD 325
	RM 3,224,646,000	RM 1043
Australia[4]	USD 7,701,169,000	USD 3780
	AUD 8,212,526,000	AUD 4030

Clinical Practice Guidelines(CPG)



Guidelines Adherence

- **Evidence of following CPG**[5-8]
  - ↓ kidney failure
  - ↓ amputation
- **Guideline adherence-** significant positive association with hypertension control[9]

Medication Therapy Adherence

- **Pharmacists collaborate with other healthcare professionals**[10-12,13-15,16]
  - ↕ Therapy outcome
  - ↓ GP visits & hospitalisation
- Diabetes MedsCheck Australia
- Medication therapy adherence clinic (MTAC Diabetes) Malaysia

Key Landmark Studies (1)

1993: DCCT
(Diabetes Control and Complications Trial)

1998: UKPDS
(United Kingdom Prospective Diabetes Study)

2008: ADVANCE
(Action in Diabetes and Vascular Disease, Preterax and Diamicron MR controlled evaluation)

2008:VADT
(Veteran Affairs Diabetes Trial)

2008: ACCORD
(Action to control cardiovascular risk in diabetes trial)

Key Landmark Studies (2)

- **Glycaemic, Blood Pressure, Cholesterol control**
- **Targets individualised to each patient**
- **Reduction by1% HbA_{1c}**
  - 21% diabetes death
  - 37% microvascular complications
  - 43% amputation/peripheral vascular death
  - 14% myocardial infarction

Diabetes Intervention Studies

Reduction of HbA_{1c} is 0.6%-1.9%

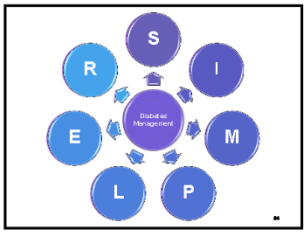
- Outcomes may be positive due to regular contact with healthcare professional[21,22]

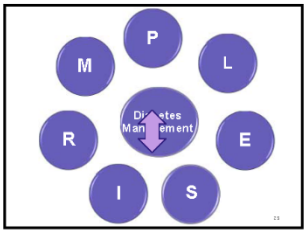
RCTs – did not incorporate 7 factors

- only focus on education[23-26]
- education, medicine management, pharmaceutical care and lifestyle counselling, HbA_{1c} and cholesterol levels[10]
- self management[27, 28-30]

Pharmacist Intervention Studies

- **Pharmacists have a minimum of 3 years practice**[10-13,23-26,31-33,35-37]
- **Is Intervention sustainable?**
  - If Pharmacist has limited experience in clinical practice





- **S** Statin initiation, Cholesterol targets
- **I** Insulin initiation, hypoglycaemia management
  - Oral antidiabetes, SMBG, sick day, HbA1c target
- **M** Medication adherence
  - Medication related problems
- **P** Blood Pressure target
  - ACEI/ARB initiation
- **L** Lifestyle - exercise, diet, foot, alcohol, smoking, eye assessment, stress, sleep, cinnamon intake
- **E** Education on medicine,diabetes knowledge
  - fasting for Muslims & other religious groups
- **R** Aspirin initiation for CVD 10 year Risk >10% - Framingham

Aims

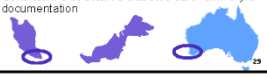
- **Develop, evaluate & assess the application of SIMPLER**
- **Support Pharmacists:**
  - structured and consistent diabetes care
  - primary and secondary health care settings
- **Integrate into MTAC Diabetes**

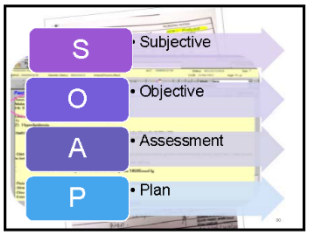
Objectives

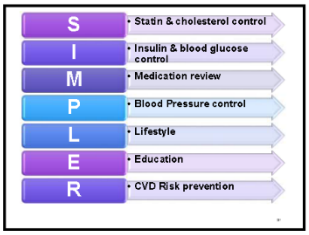
1. Design, validate and refine SIMPLER tool
2. Measure pharmacists' application of diabetes guidelines
3. Measure clinical outcomes & QOL
4. Measure cost effectiveness of HbA_{1c} reduction: intervention vs usual care

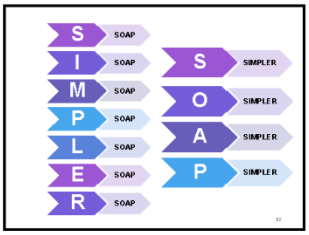
Significance

- Train pharmacists with limited clinical experience – evidence based, straightforward diabetes care
- Increase application of diabetes guideline
- Design, validate, pilot of tool: 2 countries
- Consistent & structured diabetes care- delivery & documentation

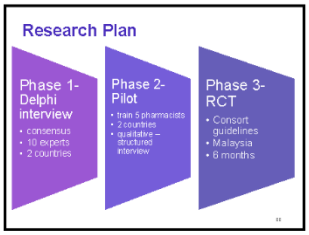








Research Plan



Phase 1 Participants

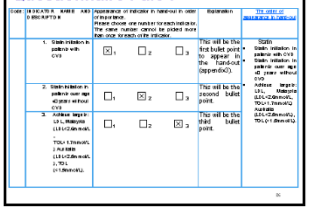
- 12 participants
- 7: Malaysia, 5: Australia

Profession	Malaysia	Australia
Pharmacist	3	2
GP	3	1
Endocrinologists	1	1
Diabetes Nurse	0	1
Total	7	5

Delphi Interview Questionnaire

- 7 key factors – SIMPLER
- Based on recent diabetes guidelines from both Malaysia and Australia
- Consensus achieved in 3 rounds

Questionnaire Part 1



Appearance in Hand-Out

S
I
M
P
L
E
R

- HbA1c% in patients <65 years without CVD
- HbA1c% in patients with CVD
- Achieve LDL% target

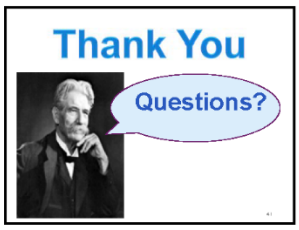
Questionnaire Part 11

Code	INDICATOR NAME AND DESCRIPTION	Your Score	Median Score	Round 2 Score (1=least preferred ⟶ 5=most preferred) Please choose your preference.
8.	Hand-out Design Preference			
	8.1 Appendix 2a (bookmark design)	5	4	1 2 3 4 5
	8.2 Appendix 2b (wheel design)	3	3	1 2 3 4 5
9.	Additional indicators to be included in hand-out			Round 2 Score (1=least preferred ⟶ 5=most preferred) Please choose your preference.
	9.1 Administer once daily antihypertensive at bedtime	3	3	1 2 3 4 5
	9.2 Diet advice using plate model	4	4	1 2 3 4 5
	9.3 Annual eye assessment	5	4	1 2 3 4 5
	9.4 Address sleep hygiene	5	4	1 2 3 4 5

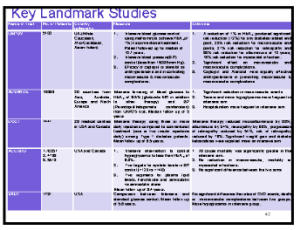
Phase 1: Determining Consensus

- consensus achieved in Round 3
- Part 1: **> 60%** of participants pick the same number
- Part 11: score of **4 or 5** chosen by **>60%** of participants

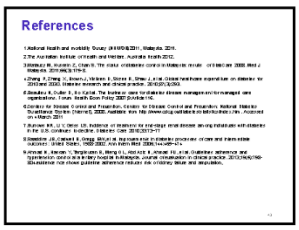
Only these numbers and indicators chosen by majority will be included in **SIMPLER**



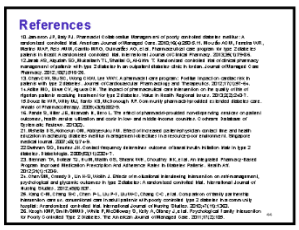
Key Landmark Studies



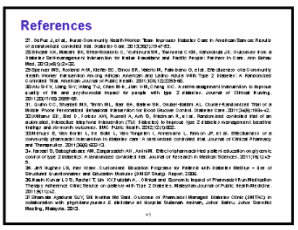
References



References



References



Curtin University

SIMPLER Training Module

Module 2
SIMPLER validation

Sham ala Ayadurai PhD Candidate
Dr.Laetitia Hattingh (Primary Supervisor)
A/Prof Lisa B.G.Tee (Co-Supervisor)
Dr.Siti Norlina Md Said (Associate Supervisor)

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Statin – Results of Delphi

Statin

- •Statin initiation in patients with CVD
- •Achieve targets: LDL, Malaysia (LDL<2.6 mmol/L, TG<1.7 mmol/L) Australia (LDL<2.0 mmol/L), TG(<2.0 mmol/L)
- •Statin initiation in patients >40 years without CVD

Blood Glucose(1) – Results of Delphi

Insulin/ Blood Glucose

- Insulin initiation if glycaemic control not achieved despite being on two or more oral hypoglycaemic agents
- Target of HbA1c ≤ 7% if no other complications
- Management of hypoglycaemia

Blood Glucose(1) – Results of Delphi

Monotherapy		Combination therapy	
Sulponylurea	0.9 to 2.5	SU+metformin	1.7
Biguanides (metformin)	1.1 to 3	SU+rosiglitazone	1.4
Thiazolidinediones	1.5 to 1.6	SU+pioglitazone	1.2
Alpha glucosidase inhibitors	0.6 to 1.3	SU+acarbose	1.3
DPP IV inhibitor	0.8	Repaglinide+metformin	1.4
Insulin	No limit	Pioglitzone+metformin	0.7
Non insulin injectables		Rosiglitazone+metformin	0.8
Pramlintide	0.43 to 0.56	DDPIV i+metformin	0.7
Exenatide	0.8 to 0.9	DDPIVI+pioglitazone	0.7

Clinical Pharmacy Working Committee Endocrine – Diabetes, Pharmaceutical Services Division, MOH, Malaysia

Blood Glucose(2) – Results of Delphi

Insulin/ Blood Glucose

- Self-monitoring of blood glucose Malaysia & Australia CPG (4.0-6.0 mmol/L fasting), Australia (8-10 mmol/L, 2h postprandial), Malaysia CPG (6-8 mmol/L-2h postprandial)
- Aim a reduction of HbA1c by 1%
- Initiate metformin if not contraindicated

Medication – Results of Delphi

Medication

- Assess medicine related problems(pharmacotherapy)
- Review medication adherence using 8 item Modified Morisky Medication Adherence Scale

Drug Related Problem Assessment

1. Correlation between drug therapy and medical problem
2. Appropriate therapy
3. Drug regimen
4. Therapeutic duplication/polypharmacy
5. Side effect/ Adverse drug reaction
6. Interactions, drug-drug, drug disease, drug food, drug herbal
7. Drug allergy or intolerance
8. Risk and Quality of Life Impact
9. Social or recreational drug use (drug abuse)
10. Financial impact
11. Patient knowledge or therapy
12. Adherence/ compliance
13. Self monitoring

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Morisky Medication Adherence Scale

No.	Questions	Yes/No
1.	Do you sometimes forget to take your pills?	Y=0, N= 1
2.	People sometimes miss taking medications for reasons other than forgetting. Thinking over the past 2?2, were there any day when you did not take your medicine?	Y=0, N=1
3.	Have you ever cut back or stopped taking your medications without telling your doctor because you felt worse when you took it?	Y=0, N=1
4.	When you travel or leave home, do you sometimes forget to bring along your medications?	Y=0, N=0
5.	Did you take your medicine yesterday?	Y=1, N=0
6.	When you feel like your disease is under control, do you sometimes stop taking your medicine?	Y=0, N=1
7.	Taking medicines everyday is a real inconvenience for some people. Do you ever get hassled about sticking to your treatment plan?	Y=0, N=1
8.	How often do you have difficulty remembering to take all your medication?	
	(a) Never/rarely	1
	(b) Once in a while	0.75
	(c) Sometimes	0.5
	(d) Usually	0.25
	(e) All the time	0

Morisky, D. E., et al. (2008). "Predictive Validity of a Medication Adherence Measure in an Outpatient Setting." Journal of Clinical Hypertension (NY) 10(5): 348-354.

Blood Pressure – Results of Delphi

Blood Pressure

- BP target: ≤130/80
- ACEI/ARB initiation in patients with microalbuminuria / proteinuria
- ACEI/ARB initiation in patients without microalbuminuria /proteinuria
- Reduce sodium intake

Blood Pressure – Update from AACE/ACE guidelines

- **Previous: <130/80**
- **Current BP targets <140/80 to 90**

Lifestyle(1) – Results of Delphi

Lifestyle

- Exercise: 30 mins walking (or equivalent) 5 or more days/week (total ≥150 min/week)
- Weight loss: Australia (BMI<25 kg/m^2) Malaysia (BMI <23 kg/m^2)
- Smoking cessation

Lifestyle(2) – Results of Delphi

Lifestyle

- Waist circumference Australia (<94 cm in men,<80 cm in women, waist circumference), Malaysia (≤90 cm in men,≤80 cm in women)
- Moderate alcohol intake: ≤2 standard drinks (20 g) per day for men and women

Lifestyle(3) – Results of Delphi

Lifestyle

- Management of stress& diabetes related distress
- Erectile dysfunction: recommend PDE-5 inhibitor as first line therapy for male patients
- Foot care

Education– Results of Delphi

Education

- Knowledge and understanding of medicine
- Medicine storage
- Medication during fasting month for Muslims & other religious groups

Name	Normal Daily Dose	Dose adjustment during fasting
Metformin 500mg	2 tablets to be taken twice daily after food	2 tablets on breaking fast (sunset) & 2 tablets after morning meal (dawn)
Metformin 500mg XR	4 tablet to be taken once daily with evening meal	4 tablets to be taken on breaking fast (sunset)
Gliclazide 30mg MR	3 tablets to be taken with morning meal	3 tablets on breaking fast (sunset)
Gliclazide 80mg or Glibenclamide 5mg	2 tablets to be taken with morning meal & 2 tablets to be taken with dinner	a) Morning meal (dawn): take half of normal dose b) Breaking fast (sunset) take full dose eg: 1 tablet before morning meal (dawn) & 2 tablets on breaking fast (sunset)
Rosiglitazone 4mg / 8mg Sitagliptin 100mg or Saxagliptin 5mg	1 tablet to be taken daily	To be taken at morning meal (dawn)
Glibenclamide + Metformin	2 tablets to be taken twice daily after food	a) Morning meal (dawn) take half of normal dose b) Breaking fast (sunset) take full dose eg: 1 tablet before morning meal (dawn) & 2 tablets on breaking fast (sunset)
Vildagliptin + Metformin (Galvumet)or Sitagliptin + Metformin (Janumet)or Vildagliptin 50mg	1 tablet to be taken twice daily after food	No difference. Take during morning meal (dawn) and during breaking fast (sunset)

Name	Normal Daily Dose	Dose adjustment during fasting
Insulin premixed (Humulin 30/70 or Mixtard)	40 iu half an hour before breakfast & 28 iu half an hour before dinner	a) Reverse breakfast and dinner doses b) Morning meal (dawn): reduce dose by 20-50 % of nightime dose c) Breaking fast (sunset): same morning dose eg: 14-22 iu half an hour before morning meal (dawn) & 40 iu half an hour before breaking fast (sunset)
Insulin premixed analogue (Novomix or Humalog Mix 25/75)	32 iu during breakfast & 30 iu during dinner	a) Reverse breakfast and dinner doses b) Morning meal (dawn): reduce dose by 20-50 % of nightime dose c) Breaking fast (sunset): same morning dose eg: 10-16 iu during morning meal (dawn) & 32 iu on breaking fast (sunset)
Insulin short-acting (Actrapid or Humulin R)	24 iu 3 times daily half an hour before meals	a) Skip lunchtime dose b) Morning meal (dawn): reduce dose by 25 % of usual dose c) Breaking fast (sunset) take usual dose eg: 18 iu half and hour before morning meal (dawn) & 24 iu half an hour before breaking fast (sunset)
Insulin rapid-acting (Novorapid or Humalog)	16 iu 3 times daily during meals	Skip lunchtime dose b) Morning meal (dawn): reduce dose by 25 % of usual dose c) Breaking fast (sunset) take usual dose eg: 12 iu during morning meal (dawn) & 16 iu on breaking fast (sunset)
Insulin intermediate & long-acting (Insulatard/ Humulin N/ Glargine/Detemir)	34 iu before bedtime	34 iu before bedtime

Cardiovascular Risk(1) – Results of Delphi

Cardiovascular Risk

- Aspirin therapy as secondary prevention in those with diabetes with history of CVD
- Use of Framingham risk calculator to calculate CVD risk and educate patient

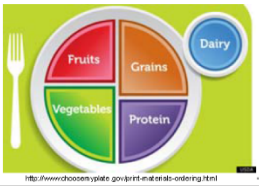
Cardiovascular Risk(2) – Results of Delphi

Cardiovascular Risk	• Aspirin therapy (75mg-162mg/day) as primary prevention to decrease CVD risk (10 year risk>10%, Framingham)

Additional Indicators – Results of Delphi

Additional Indicators	• Diet advice using plate method • Annual eye assessment • Address sleep hygiene

Plate method



http://www.choosemyplate.gov/print-materials-ordering.html

Sleep Hygiene

Centre for clinical intervention, Department of health, Western Australia

http://www.cci.health.wa.gov.au/resources/infopax_doc.cfm?MInI_ID=50

Indicators: Consensus not achieved

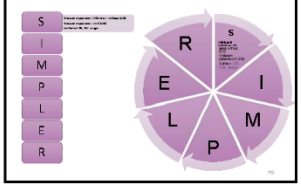
- Administer once daily antihypertensive at bedtime
- 1g-3g cinnamon supplement (capsules) intake per day
- Vitamin B12 supplement in patients on long term metformin
- Encourage daily intake of tree nuts (almonds, brazil nuts, cashews, hazelnuts, macadamia, pecans, pine nuts, pistachios and walnuts)

Dietary Supplements for diabetes management

Medscape Pharmacists

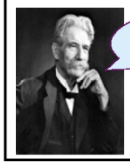
http://www.medscape.com/features/slideshow/dietary-supplements-for-diabetes?src=nm-slfhs

SIMPLER Design – Results of Delphi

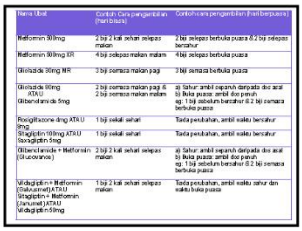


- **S** Statin initiation, Cholesterol targets
- **I** Insulin, HbA1c, hypoglycaemia, SMBG, Blood glucose target, metformin
- **M** Medication related problems
- medication adherence score
- **P** Blood Pressure target
- ACEI/ARB initiation
- **L** Lifestyle - exercise, weight loss, smoking cessation, waist size, alcohol, stress, foot care, diet, eye, sleep, erectile dysfunction (male)
- **E** Education on medicine,diabetes knowledge
- fasting for muslims & other religious groups
- **R** Aspirin for diabetes patients with CVD, Aspirin for CVD 10 year Risk >10% - Framingham, Framingham risk calculator to educate patient

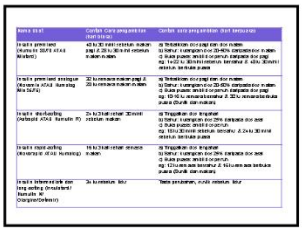
Thank You



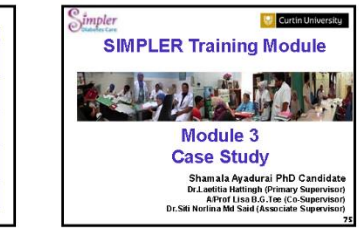
Questions?

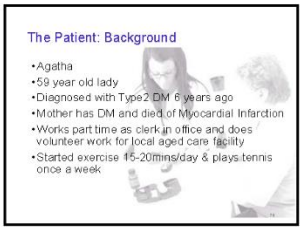


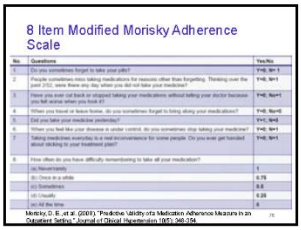
Nama Ubat	Cadangan Cara penggunaan (Pemberian)	Cadangan cara penggunaan dan tempoh (Pemberian)
Metformin 500mg	2 biji 2 kali sehari selepas makan	2 biji selepas berbuka puasa & 2 biji selepas bersahur
Metformin 500mg ER	4 biji selepas makan malam	4 biji selepas berbuka puasa
Gliklazide 30mg MR	2 biji semasa makan pagi	2 biji semasa berbuka puasa
Gliklazide 60mg ATAU Glibenclamide 5mg	2 biji semasa makan pagi & 2 biji semasa makan malam	a) Sahur: ambil separuh daripada dos asal b) Buka puasa: ambil dos penuh eg: 1 biji sebelum bersahur & 2 biji semasa berbuka puasa
Rosiglitazone 4mg ATAU 8mg	1 biji sekali sehari	Tanda perubahan, ambil waktu bersahur
Sitagliptin 100mg ATAU Saxagliptin 5mg	1 biji sekali sehari	Tanda perubahan, ambil waktu bersahur
Glibenclamide + Metformin (Glucovance)	2 biji 2 kali sehari selepas makan	a) Sahur: ambil separuh daripada dos asal b) Buka puasa: ambil dos penuh eg: 1 biji sebelum bersahur & 2 biji semasa berbuka puasa
Vildagliptin + Metformin (Galvumet) ATAU Sitagliptin + Metformin (Janumet) ATAU Vildagliptin 50mg	1 biji 2 kali sehari selepas makan	Tanda perubahan, ambil waktu sahur dan waktu buka puasa

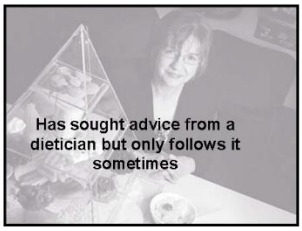


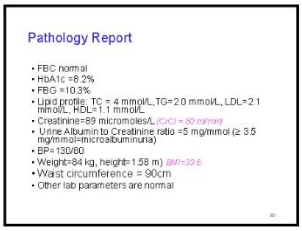
Nama Ubat	Cadangan Cara penggunaan (Pemberian)	Cadangan cara penggunaan dan tempoh (Pemberian)
Insulin premixed (Actrapid & NOVO MIX 30/70 ATAU Mixtard)	40 hingga 50 unit sebelum sarapan pagi & 20 hingga 30 unit sebelum makan malam	a) Tetapkan dos pagi dan dos malam b) Sahur: tambahkan dos 20-40% daripada dos malam c) Buka puasa: ambil dos penuh daripada dos pagi eg: 1st/2 hingga 30 unit sebelum bersahur & 40 hingga 50 unit sebelum berbuka puasa
Insulin premixed analogue (Humalog MIX50 ATAU Apidra SOLOSTAR)	20 hingga makan pagi & 20 hingga makan malam	a) Tetapkan dos pagi dan dos malam b) Sahur: tambahkan dos 20-40% daripada dos malam c) Buka puasa: ambil dos penuh daripada dos pagi eg: 10-15 u semasa bersahur & 30 u semasa berbuka puasa (Sumber dari makanan)
Insulin short-acting (Actrapid ATAU Humulin R)	2x hingga 3x sehari sebelum makan	a) Tingkatkan dos tingkatkan b) Sahur: tambahkan dos 20% daripada dos asal c) Buka puasa: ambil dos penuh eg: 10hingga 30 unit sebelum bersahur & 2x hingga 3x unit sebelum berbuka puasa
Insulin short-acting (Actrapid & NOVO Humalog)	10 hingga 20 unit sebelum sarapan & makan	a) Tingkatkan dos tingkatkan b) Sahur: tambahkan dos 20% daripada dos asal c) Buka puasa: ambil dos penuh eg: 10 hingga 20 unit sebelum bersahur & 1 hingga 2 unit sebelum berbuka puasa (Sumber dari makanan)
Insulin intermediate dan long acting (Insulatard/ Humulin N/ Glargine/Detemir)	2x hingga 3x sehari	Tanda perubahan, ambil waktu sahur dan waktu buka puasa

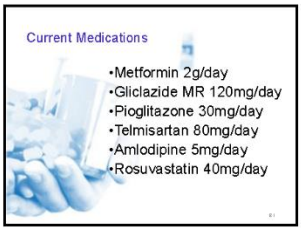












Cholesterol Management

1. What is the target for LDL, TG in Australian/Malaysian diabetes guideline?
   LDL: Malaysia (LDL<2.6 mmol/L, TG<1.7 mmol/L) Australia (LDL<2.0 mmol/L), TG(<2.0 mmol/L)
2. Do you routinely monitor cholesterol targets?
   6-12 weekly
3. What treatment intervention would you make if LDL and TG levels are not on target?
   Statin (simvastatin 20mg).
4. When do you suggest initiating Statin?
   Statin initiation in patients >40 years with or without CVD (Malaysia and USA)

Statin Updates

- 90,000 – diabetes risk 9% higher in those taking statins
- Labels - 1 fasting serum & HbA_{1c}
- FDA, USA – diabetes risk small – statin effective in reducing CVD events
- Statin inhibition of insulin secretion & down regulation of a glucose transporter in adipocytes
- Small risks; higher with rosuvastatin & atorvastatin

Relative LDL-lowering Efficacy of Statin and Statin-based Therapies

% LDL-C	Atorva	Fluva	Pitava	Lova	Prava	Rosuva	Vytorin	Simva
30%	—	40 mg	1 mg	20 mg	20 mg	—	—	10 mg
38%	10 mg	80 mg	2 mg	40 or 80 mg	40 mg	—	—	20 mg
41%	20 mg	—	4 mg	80 mg	80 mg	5 mg	10/10 mg	40 mg
47%	40 mg	—		—	—	10 mg	10/20 mg	80 mg
55%	80 mg	—		—	—	20 mg	10/40 mg	—
63%		—		—	—	40 mg	10/80 mg	—

Cholesterol Lowering Efficacy Of Statin And Fibrate

	LDL ↓	HDL ↑	TGL ↓
Lovastatin	✓	No evidence	✓
Simvastatin	✓	✓	✓
Atorvastatin	✓	✓	✓
Pravastatin	✓	No evidence	✓
Rosuvastatin	✓	✓	✓
Fibrate	-	✓	✓

FDA Drug Safety Communication

Contraindicated with **simvastatin**:
- Itraconazole
- Ketoconazole
- Posaconazole (New)
- Erythromycin
- Clarithromycin
- Telithromycin
- HIV protease inhibitors
- Nefazodone
- Gemfibrozil
- Cyclosporine
- Danazol

Do not exceed 10 mg simvastatin daily with:
- Verapamil
- Diltiazem

Do not exceed 20 mg simvastatin daily with:
- Amiodarone
- Amlodipine (New)
- Ranolazine (New)

Avoid large quantities of grapefruit juice (>1 quart daily=4-6 cups)

http://www.fda.gov/Drugs/DrugSafety/ucm293101.htm

FDA Drug Safety Communication

Contraindicated with **lovastatin**:
- Itraconazole
- Ketoconazole
- Posaconazole
- Erythromycin
- Clarithromycin
- Telithromycin
- HIV protease inhibitors
- Boceprevir
- Telaprevir
- Nefazodone

Avoid with lovastatin:
- Cyclosporine
- Gemfibrozil

Do not exceed 20 mg lovastatin daily with:
- Danazol
- Diltiazem
- Verapamil

Do not exceed 40 mg lovastatin daily with:
- Amiodarone

Avoid large quantities of grapefruit juice (>1 quart daily=4-6 cups)

http://www.fda.gov/Drugs/DrugSafety/ucm293101.htm

Blood Glucose Management

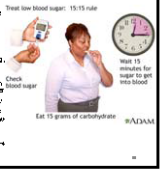
1. What is the target for fasting and 2hrs post prandial blood glucose according to Australian diabetes guideline?
   (4.0-6.0 mmol/L fasting); Australia (5-10 mmol/L, 2h postprandial).
2. When do you suggest initiating insulin?
   Insulin initiation if glycaemic control not achieved despite being on two or more oral hypoglycaemic agents
3. Which type of insulin would you start?
   Basal or premixed insulin
4. How do you increase the dose and what are the intervals?
   2-4 units every 3-7 days

Blood Glucose Management

1. What is the target $HbA1_c$?
   Aim a reduction of HbA1c by 1%, 53 mmol/mol (range 49–58), 57% (range 6.5–7.5)
2. What is the prescribing indication for Metformin?
   Initiate metformin if not contraindicated
3. What problems due to OHA and insulin do you encounter?
   Hypoglycaemia. Also causes of hypoglycaemia in this patient. It could be due to diet or timing of doses.
4. How do you manage it?
   Rule of 15 & manage causes of hypoglycaemia

Rule of 15

- Provide 15 grams of quick-acting carbohydrate that is easy to consume (e.g. half can of regular – non diet – soft drink, half glass fruit juice, 3 teaspoons of sugar or honey, 6-7 tablets of glucose tablets).
- Wait 15 minutes and repeat blood glucose check. If the result is not rising, suggest treating another quick-acting carbohydrate from the above list.
- If the patient's next meal is more than 15 minutes away, provide some longer acting carbohydrate (e.g. a sandwich, 1 glass of milk or soy milk, 1 piece of fruit, 2 tablespoons of dried apricots, figs or other dried fruit, 1 tub of natural low fat yoghurt, 6 small dry biscuits and cheese).
- Test glucose again during the next 2–4 hours.



Medication Assessment

1. How do you monitor medication adherence?
   8MMMAS: Score 3.5/8.0
2. How do you identify medicine related problems?
   SIMPLER

Medication Assessment

3. How do you solve the problem?
   - *i. Reduce glicazide dose to 90 mg/daily*
     or
     stop pioglitazone, reduce gliclazide dose and start basal insulin 10 units
   - *ii. Add simvastatin 20 mg/daily*
   - *iii. To solve compliance suggest combination:*
     - *Sitagliptin 50mg & metformin (controlled release) 1000mg*
     - *Perindopril 5mg & Amlodipine 10mg*
       or
     - *Telmisartan 40mg & Amlodipine 10mg*

Blood Pressure Control

1. What is the BP target according to guideline?
   BP target: ≤130/80 mmHg
2. Which antihypertensive is strongly recommended for diabetes in the absence of contraindications?
   ACEI or ARB
2. What is the best practice in administration time of antihypertensive according to American Diabetes Association, consensus statement (ADA)?
   Bedtime

Lifestyle

1. When you make an intervention on diet, do you refer to any tools or guidelines?
2. What does the guideline recommend on exercise?
   30 mins walking (or equivalent) 5 or more days/week (total ≥150 min/week)
3. What is the target for BMI and waist circumference according to the guidelines?
   (BMI<25 kg/m²) (<94 cm in men,<80 cm in women)
4. What other lifestyle interventions should be made in a diabetes patient?
   (smoking cessation, alcohol intake, stress, foot care, erectile dysfunction (male)

Cardiovascular (CVD) Risk Factor

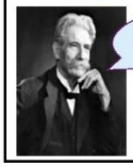
1. When would you recommend aspirin as prevention strategy?
   Aspirin therapy (75mg-162mg/day) as primary prevention to decrease CVD risk (10 year risk>10%, Framingham)
   Agatha has 15.9% risk of CVD in Next 10 years-Framingham

Framingham risk calculator

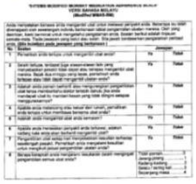
Aspirin therapy (75mg-162mg/day) as primary prevention: (10 year risk>10%, Framingham)

https://www.cvdriskchecksecure.com/FraminghamRiskScore

Thank You



Morisky Medication Adherence Scale



SIMPLER Training Module

Module 4
Writing Intervention Notes

Shamala Ayadurai PhD Candidate
Dr.Laetitia Hattingh (Primary Supervisor)
A/Prof Lisa B.G.Tee (Co Supervisor)
Dr.Siti Norlina Md Said (Associate Supervisor)

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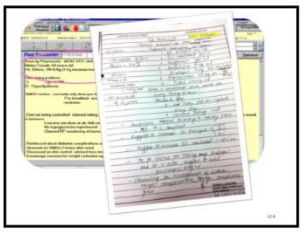


S • Subjective

O • Objective

A • Assessment

P • Plan

Subjective

- patient's report of how he or she has been doing since last visit and includes current visit
- include patient's complaints, feelings, concerns, plans or goals
- record key words or brief phrase if using patient's quotes

Objective

- that can be seen, heard, smelled, counted or measured
- includes BP, blood glucose, pulse, temperature, results of lab tests, physical exam

Assessment

- synthesize and analyze data from subjective and objective portions of the notes

Plan

- types of interventions used
- treatment suggestions
- date of next appointment
- include anticipated gains from the interventions

Guidelines for SOAP(1)

- brief and concise
- keep quotes to a minimum
  use an active voice, eg
  'A report will be sent to your doctor.' (passive)
  'We will send a report to your doctor.' (active)
- use precise and descriptive terms
- record immediately after each session

Guidelines for SOAP(2)

- start each new entry with date and time of session
- write legibly and neatly
- use proper spelling, grammar, punctuation
- use only black ink if notes are handwritten
- sign-off using signature plus your title, contact number

Guidelines for SOAP(3)

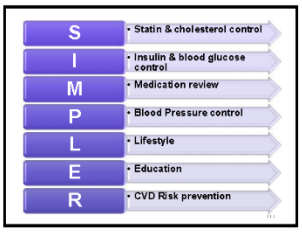
- avoid terms like seems, appears
- avoid names of family members or others named by patient
- avoid opinionated statements
- do not erase, obliterate, use correction fluid, or in any way attempt to obscure mistakes instead
- do not leave blank spaces between entries
- do not try to squeeze additional commentary between lines or in margins

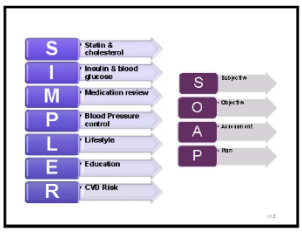
Medico-Legal (1)

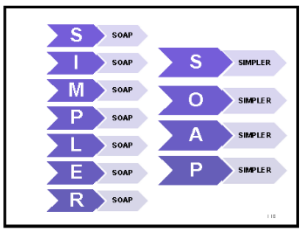
- Write "*Patient's daughter is today. She said, 'leave the room. We're busy,*' rather than "*Patient's daughter is rude today.*"
- use sentences. Rather than "*progressive hypotension*", write "*Blood pressure dropped from 110/60 at 0500 to 100/50 at 515 to 80/40 at 0545.*"

Medico-Legal(2)

- Document any recommendations you make. eg education, counselling given
- Limit your entries to descriptions of observations and services provided, rather than making conclusions about causes
- Keep all medical records in a safe and secure place
- Medical records are confidential
- Do not tell/allow anyone to touch or look at medical record unless they are taking care of that patient





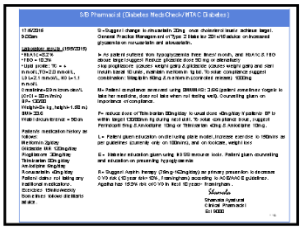


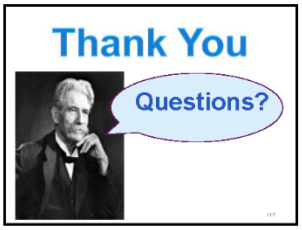
Reference

- Cameron S, Learning to write case notes using the SOAP format. Journal of counseling & development. 2002;80:286-92
- Nurses:What is the most important documentation advice? Carolyn Buppert, NP, JD August21,2012
- Medical Record documentation and Legal Aspects Appropriate to Nursing Assistants http://study.materials.healthmanagementventures.com/pdf/Medical RecordDocumentation

Practice Session

Write intervention in case note for case study in Module 3





Appendix 4. 5: The Simpler™ training list of websites

SIMPLER Training List of Websites

No	Resources	Website
1.	Management of Type 2 Diabetes Mellitus	http://www.moh.gov.my/attachments/3878.pdf
2.	Practical Guide to Insulin therapy in Type 2 DM	http://www.mems.my/file_dir/3308086634dc0e0f9e1c72.pdf
3.	General Practice Management of Type 2 Diabetes 2014/15	http://www.racgp.org.au/your-practice/guidelines/diabetes/
4.	Standards of Medical Care 2015, American Diabetes Association	http://professional.diabetes.org/admin/UserFiles/0%20-%20Sean/Documents/January%20Supplement%20Combined_Final.pdf
5.	AACE/ACE Comprehensive diabetes management algorithm 2015	https://www.aace.com/publications/algorithm
6.	Plate method	http://www.choosemyplate.gov/print-materials-ordering.html
7.	Sleep hygiene	http://www.cci.health.wa.gov.au/resources/infopax_doc.cfm?Mini_ID=50
8.	Dietary Supplements for diabetes management	http://www.medscape.com/features/slideshow/dietary-supplements-for-diabetes?src=emailthis *Note: Please register in order to access. Medscape registration is free.*
9.	Creatinine Clearance Calculator (cockroft-Gault Formula)	http://www.palms.com.au/clinical/egfr.shtml
10.	PSA Guidelines Medscheck and Diabetes MedsCheck	http://5cpa.com.au/programs/medication-management-initiatives/medscheck-diabetes-medscheck/
11.	Australian Absolute CVD risk calculator	http://www.cvdcheck.org.au
12.	Framingham Risk Calculator	https://www.cvdriskchecksecure.com/FraminghamRiskScore.aspx
13.	FDA Drug Safety Communication on Simvastatin	http://www.fda.gov/Drugs/DrugSafety/ucm256581.htm
14.	FDA Drug Safety Communication on lovastatin	http://www.fda.gov/Drugs/DrugSafety/ucm293101.htm
15.	NDSS Information sheets on diabetes	http://www.ndss.com.au/en/About-Diabetes/Information-Sheets/About-Diabetes/
16.	NDSS information for patient booklet	http://www.ndss.com.au/Global/NDSS%20Information%20Pack/317552%20Diabetes_Web.pdf

Appendix 4. 6: The Simpler™ tool hand-out for Phase Two participants

SIMPLER Pharmacist Diabetes Management Tool

S=Statin	• Statin initiation in patients with CVD • Achieve targets: LDL, Malaysia (LDL<2.6 mmol/L, TG<1.7 mmol/L) Australia (LDL<2.0 mmol/L), TG (<2.0 mmol/L) • Statin initiation in patients over age 40 years without CVD
I=Insulin/Glycaemic control	• Insulin initiation if glycaemic control not achieved despite being on two or more oral hypoglycaemic agents • Target of HbA1c ≤ 7% if no other complications • Management of hypoglycaemia • Self-monitoring of blood glucose Malaysia & Australia CPG (4.0-6.0 mmol/L fasting); Australia (8-10 mmol/L, 2h postprandial). Malaysia CPG (6-8 mmol/L-2h postprandial) • Aim a reduction of HbA1c by 1% • Initiate metformin if not contraindicated
M=Medication	• Assess medicine related problems • Review medication adherence using 8 item Modified Morisky Medication Adherence Score
P=Blood Pressure	• BP target: ≤130/80 • ACEI/ARB initiation in patients with microalbuminuria /proteinuria • ACEI/ARB initiation in patients without microalbuminuria /proteinuria • Reduce sodium intake
L=Lifestyle	• Exercise: 30 mins walking (or equivalent) 5 or more days/week (total ≥150 min/week) • Weight loss: Australia (BMI< 25 kg/m2), Malaysia (BMI ≤ 23 kg/m2) • Smoking cessation • Waist circumference Australia (<94 cm in men,<80 cm in women, waist circumference), Malaysia (≤90 cm in men,≤80cm in women) • Moderate alcohol intake: ≤2 standard drinks (20 g) per day for men • Management of stress & diabetes related distress • Erectile dysfunction: recommend PDE-5 inhibitor as first line therapy for male patients • Foot care • Diet advice using plate model • Annual eye assessment • Address sleep hygiene
E=Education	• Knowledge and understanding of medicine • Medicine storage • Medication optimisation during fasting month for Muslims and other religious groups
R=Cardiovascular Risk	• Aspirin therapy as secondary prevention in those with diabetes with history of CVD • Use of Framingham risk calculator to calculate CVD risk and educate patients • Aspirin therapy (75mg-162mg/day) as primary prevention to decrease CVD risk (10 year risk>10%, Framingham)

ShamalaAyadurai Phase2SIMPLER 02/06/2015

Appendix 4. 7: Introductory letter to Phase Two participants

Curtin University

School of Pharmacy

GPO Box U1987
Perth Western Australia 6845

Telephone +61 8 9266 7369
Facsimile +61 8 9266 2769
Email pharmacy@curtin.edu.au
Web curtin.edu.au

26 March 2015

Dear Pharmacist,

Diabetes is a complex disease and there are many factors involved in treating and preventing diabetes related complications. Many of these factors are based on findings from landmark randomised controlled trials and have been incorporated into diabetes guidelines. Yet, evidence suggests that diabetes patients do not always receive diabetes care according to the guidelines. We are conducting research that involves the development and evaluating of a patient-centred diabetes tool, called the Simpler™ tool, to be used by pharmacists to facilitate making structured interventions.

Our research will involve a two-hour training session on the Simpler™ tool. Trained pharmacists will then be given a month to use the Simpler™ tool in their own practices setting. This will be followed by an exploratory interview to obtain feedback about the use and feasibility of the Simpler™ tool. This interview will take approximately 30 minutes and will be conducted by Shamala Ayadurai who is undertaking this research to meet the requirements of the Doctor of Philosophy. Your participation is completely voluntary. If you choose to participate you will receive remuneration of AUD$100 (AUD$50 for Malaysian participants) as a token of our appreciation for your time and effort.

If you have any questions about our research, we are more than happy to provide you with the necessary information.

Thanking in advance for your time and consideration.

Yours sincerely,

Shamala Ayadurai
PHD Candidate
School of Pharmacy, Curtin University
Perth, Western Australia
Tel: 04 50602642
Email:shamala.ayadurai@postgrad.curtin.edu.au

Dr. Laetitia Hattingh
PhD Supervisor and Senior Lecturer
School of Pharmacy, Curtin University
Perth, Western Australia
Tel: +61 892667376
Email: L.Hattingh@curtin.edu.au

*This study has been approved by the Curtin University Human Research Ethics Committee (Approval Number **RDHS-06-14**). The Committee is comprised of members of the public, academics, lawyers, doctors and pastoral carers. If needed, verification of approval can be obtained either by writing to the Curtin University Human Research Ethics Committee, c/- Office of Research and Development, Curtin University, GPO Box U1987, Perth, 6845 or by telephoning 9266 2784 or by emailing hrec@curtin.edu.au*

Appendix 4. 8: Phase Two participant information sheet

School of Pharmacy

GPO Box U1987
Perth Western Australia 6845
Telephone +61 8 9266 7369
Facsimile +61 8 9266 2769
Emailshamala.ayadurai@
postgrad.curtin.edu.au
Webcurtin.edu.au

INFORMATION SHEET

Development and Evaluation of a Pharmacist Diabetes Management Tool: a Mixed Methods Study

Purpose of the study? My name is Shamala and I am a PhD student at the School of Pharmacy, Curtin University. As part of my PhD I need to evaluate a diabetes tool called the Simpler™ tool. This tool will be used by pharmacists to facilitate making structured interventions.

What will the study involve? The study will involve the use of the SIMPLER training modules to train five community pharmacists in Western Australia and five primary health care pharmacists in Malaysia as part of a pilot study. The training session will takeapproximately two hours. The training modules will be evaluated through pre- and post-training questionnaires. The questions will test the pharmacists on knowledge and practice behaviour on evidence-based diabetes care. Trained pharmacists will then have one month to use the tool, followed by a qualitative interview which will take approximately 30 minutes to explore the usefulness of the tool.

Why have you been asked to take part? You have been asked because of your expertise and experience in diabetes management.

Do you have to take part? The answer is no! Participation is voluntary. You have the option of withdrawing before the study commences or discontinuing after data collection has started without penalty.

Will your participation in the study be kept confidential? Yes. The identity of each participant will not be revealed to other participants. Any information about your identity will not appear in the thesis or publications. Any extracts from your comments will be entirely anonymous.

What will happen to the information which you give? The data will be kept confidential for the duration of the study and up to 5 years post completion of the study. On completion of the thesis, they will be retained for a further six months and then destroyed.

What will happen to the results? The results will be presented in the thesis and publications. They will be seen by my supervisor, a second marker and the external examiner. The thesis may be read by future students in the course.

What are the possible disadvantages of taking part? I don't envisage any negative consequences for you in taking part.

Who has reviewed this study? Approval must be given by the Faculty of Health and Science, Curtin University, Bentley, Western Australia before the survey takes place. Curtin University conducts research in accordance with the *National Statement on Ethical Conduct in Human Research.* Approval must also be given by Medical Research and Ethics Committee, MREC, Ministry of Health, Malaysia.

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Any further queries? If you need any further information, please contact my Principal Supervisor Dr Laetitia Hattingh at l.hattingh@curtin.edu.au

*This study has been approved by the Curtin University Human Research Ethics Committee (**Approval Number**: **RDHS-06-14**). The Committee is comprised of members of the public, academics, lawyers, doctors and pastoral carers. If needed, verification of approval can be obtained either by writing to the Curtin University Human Research Ethics Committee, c/- Office of Research and Development, Curtin University, GPO Box U1987, Perth, 6845 or by telephoning 9266 2784 or by emailing hrec@curtin.edu.au*

Appendix 4. 9: Phase Two consent form

School of Pharmacy

GPO Box U1987
Perth Western Australia 6845
Telephone +61 8 9266 7369
Facsimile +61 8 9266 2769
Emailshamala.ayadurai@postgrad.curtin.edu.au
Webcurtin.edu.au

Development and Evaluation of a Pharmacist Diabetes Management Tool: a Mixed Methods Study

Consent Form

I, ……. agree to participate in the above study. I have been provided with a copy of the Participant Information Sheet explaining the study, which I have read and understood. I have been given the opportunity to ask questions about the study and any questions asked have been answered to my satisfaction. I understand that I may withdraw from the study at any time without prejudice. I am aware that all research data collected will only be used for the purpose of this study and will be kept confidential and that my participation will not be disclosed without my consent. Any information which might potentially identify me will not be used in published material.

Signed:	……..	Date:	……
Signature of person obtaining consent:	……	Date:	……..
Name of person obtaining consent:	Shamala Ayadurai		

Receipt of Gift Card

I declare that I have received AUD$100/AUD$50 gift card as a token of appreciation for my time to participate in the study.

Signed:	……..	Date:	……
Signature of person giving out gift card:	……	Date:	……..
Name of person giving out gift card:	…….		

Contact Information

For further information contact Shamala Ayadurai(Mobile: 0450602642 or email shamala.ayadurai@postgrad.curtin.edu.au)

*This study has been approved by the Curtin University Human Research Ethics Committee (Approval Number **RDHS-06-14**). The Committee is comprised of members of the public, academics, lawyers, doctors and pastoral carers. If needed, verification of approval can be obtained either by writing to the Curtin University Human Research Ethics Committee, c/- Office of Research and Development, Curtin University, GPO Box U1987, Perth, 6845 or by telephoning 9266 2784 or by emailing hrec@curtin.edu.au*

Appendix 4. 10: Pre-and post training questionnaire

Instructions

1. This Pre and Post training questionnaires contains two sections: (1) **Section A** and (2) **Section B**

2. **Section A** focuses on participants' training background and current practice.

3. **Section B** covers knowledge and use of current diabetes guidelines in managing patients with diabetes. It consists of open ended questions based on a case scenario.

4. Participants will answer Sections A and B before the training session and Section B again after the training session.

ID:

Simpler™ tool
Pre-training Questionnaire

SECTION A

The first section gathers some basic information about your training background and current practice.

1. Have you had any specific diabetes management education or training after your initial pharmacy degree training?

☐	NO (go to Q3)
☐	YES

2. If you answered YES to the above question, please provide details of education and training/qualification, when it was undertaken and how many hours it involved.

Name of training/Institution where the training was conducted	When completed	Duration (eg.hours,months,years)

3. How long have you been a registered pharmacist?

☐	0-1 years
☐	More than 1 year but less than 3 years
☐	3-5 years
☐	>5 years

4. How long have you practising as MTAC Diabetes/ Diabetes MedsCheck/Endocrine Ward Pharmacist?

☐	0-1 years
☐	More than 1 year but less than 3 years
☐	3-5 years
☐	>5 years

5. What motivated you to participate in this research? (Rank from 1 to 5; where 1 = most motivating and 5 = least motivating).

☐	Obtaining CPD points
☐	Financial reimbursement
☐	Interest in the subject
☐	It was recommended to me
☐	I want to improve patient outcomes
☐	Others. Please specify_____

Simpler™ tool
Pre-training Questionnaire

ID:

SECTION B

This section covers your knowledge and skills about working with people with diabetes.

As this is not a test PLEASE do not check resources to answer the questions.

Please answer the questions based on the case scenario below.

Lily is a 54-year-old teacher, with a six year history of type 2 Diabetes Mellitus (DM). Her medical record details are as below:

Laboratory test results

Average Fasting Blood Glucose:	9 mmol/l
Average 2 hr post prandial blood glucose:	14 mmol/l
Recent HbA1c:	10% (85.8mmol/mol)
BP:	144/95 mmHg
TG:	3.1 mmol/L(<1.69 mmol/L)
LDL:	3.1 mmol/L (<4 mmol/L)
HDL:	0.94 mmol/L (0.9-1.9 mmol/L)

Kidney and Liver Function Tests are normal

Medications

Gliclazide 160 mg bd
Amlodipine 10 mg od
Simvastatin 20 mg nocte
Metformin 1 g tds

1. **What additional information about Lily do you need to know in order to manage her diabetes more effectively?**

Answers

---

2. **What interventions would you recommend for this patient and give your reasons?**

Answers

Simpler™ tool
Post-training Questionnaire

ID:

SECTION B

This section covers your knowledge and skills about working with people with diabetes.

As this is not a test PLEASE do not check resources to answer the questions.

Please answer the questions based on the case scenario below.

Lily is a 54 year old teacher, with a six year history of type 2 Diabetes Mellitus (DM). Her medical record details are as below:

Laboratory test results

Average Fasting Blood Glucose:	9 mmol/l
Average 2 hr post prandial blood glucose:	14 mmol/l
Recent HbA1c:	10% (85.8mmol/mol)
BP:	144/95 mmHg
TG:	3.1 mmol/L(<1.69 mmol/L)
LDL:	3.1 mmol/L (<4 mmol/L)
HDL:	0.94 mmol/L (0.9-1.9 mmol/L)

Kidney and Liver Function Tests are normal

Medications

Gliclazide 160 mg bd
Amlodipine 10 mg od
Simvastatin 20 mg nocte
Metformin 1 g tds

1. **What additional information about Lily do you need to know in order to manage her diabetes more effectively?**

Answers

---

2. **What interventions would you recommend for this patient?**

Answers

Appendix 4. 11: Marking scheme for pre-and post training questionnaire (trial version)

Simpler™ tool
Training Questionnaire

ID:

SECTION B

This section covers your knowledge and skills working with people with diabetes.

As this is not a test PLEASE do not check resources to answer the questions.
Considering the case scenario below please answer the questions.

Lily is a 54 year old teacher, with a six year history of type 2 Diabetes Mellitus (DM). Her record summary sheet is as below:

Patient Details

Average Fasting Blood Glucose:	9 mmol/l
Average 2 hr post prandial blood glucose:	14 mmol/l
Recent HbA1c:	10% (85.8mmol/mol)
BP:	144/95 mmHg
TG:	3.1 mmol/L(<1.69mmol/L)
LDL:	3.1 mmol/L (<4mmol/L)
HDL:	0.94 mmol/L(0.9-1.9mmol/L)

Kidney and Liver function tests are normal

Medications:

1. Gliclazide 160mg bd
2. Amlodipine 10mg od
3. Simvastatin 20mg nocte
4. Metformin 1g tds

3. What additional information about Lily do you need to manage her diabetes more effectively?

Answers

a) Allergies: Lily claims NKDA
b) Family history: Mother has Type 2 DM and died from myocardial infarction aged 74
c) Weight: 67
d) Height:1.52m
e) Alcohol: 22 units per week
f) Smoking: 10 cigarettes per day
g) Rarely exercise
h) Traditional medications: Chinese herbal pills for energy
i) Medication adherence: 8-items MMMAS = 5.5, L has missed several doses while out with friends, has difficulty remembering to take medications sometimes, finds troublesome to stick to treatment plan.

j) Suffered from hypoglycaemia twice last month mainly in the middle of the night
k) Finds blood glucose monitoring strips expensive, so rarely monitors blood glucose
l) Knowledge, time, dose, Frequency of medication administration
m) Total cholesterol: 4 mmol/L

What interventions would you recommend for this patient?

Answers

a) Address compliance issues
b) Start insulin, insulatard 10unit on or start DPP 4 inhibitor(sitagliptin 100mg od) minimal weight gain and hypoglycaemia
c) Dose of metformin 1g bd or combination sitagliptin & metformin
d) Stop gliclazide if suspect causing hypoglycaemia
e) Simvastatin 40mg od
f) Start ACE Inhibitor, perindopril 4mg od
g) Education to prevent hypoglycaemia
h) Education on SBMG, foot care
i) Exercise, smoking, alcohol
j) Address traditional medication
k) Aspirin needed based on Framingham CVD risk score (16% Australian absolute CVD risk calculator, Framingham risk score 15.9%)
l) Insulin technique and management

Appendix 4. 12: Marking scheme for pre and post training questionnaire (revised)

Simpler™ tool
Marking Scheme for Training Questionnaire

Lily is a 54-year-old teacher, with a six-year history of type 2 Diabetes Mellitus (DM). Her record summary sheet is as below:

Patient Details

Average Fasting Blood Glucose:	9 mmol/l
Average 2 hr post prandial blood glucose:	14 mmol/l
Recent HbA1c:	10% (85.8mmol/mol)
BP:	144/95 mmHg
TG:	3.1 mmol/L (<1.69mmol/L)
LDL:	3.1 mmol/L (<4mmol/L)
HDL:	0.94 mmol/L (0.9-1.9mmol/L)

Kidney and Liver function tests are normal

Medications:

1. Gliclazide 160mg bd
2. Amlodipine 10mg od
3. Simvastatin 20mg nocte
4. Metformin 1g tds

1. What additional information about Lily do you need to manage her diabetes more effectively?

No.	Answers	Marks
1.	Allergies, Previous adverse drug reaction	1
2.	Any hypoglycaemia? SMBG results Monitoring knowledge eg measures correct time of day	2
3.	Address compliance issues using 8MMMAS Address issues with traditional medication if any (possible interaction with modern medication) If current medications are causing side effects?	2
4.	Sodium intake	1
5.	Alcohol, Smoking, Exercise, Weight & Height, Waist Circumference Diet, stress, sleep hygiene eye assessment foot care	3
6.	Knowledge, time, dose, frequency of medication administration,	1
	Medication storage	1
7.	CVD risk using Framingham Risk Calculator Total Cholesterol Family history	2
	Total	13

2. What interventions would you recommend for this patient?

	Answers	Marks
S	Add ezetimibe 10mg od to lower LDL and TG. (Reduce LDL by 47% according to data by FDA drug safety communication). Change Simvastatin 20mg to Atorvastatin 20mg (reduce LDL by 41%).	1
I	Start insulin, insulatard 10units ON or start DPP4inhibitor (sitagliptin 100mg od causes minimal weight gain and hypoglycaemia) Dose of metformin should be 1g bd /To improve compliance can suggest combination of sitagliptin & metformin Reduce dose of gliclazide to 80mg bd Counsel patient on insulin technique and management Counsel patient on monitoring blood glucose (SMBG)	3
M	Address compliance issues Address compliance issues using 8MMMAS Address issues with traditional medication if any (possible interaction with modern medication) If current medications are causing side effects suggest suitable alternative	2
P	Start ACE inhibitor or ARB, eg perindopril 4mg od, as BP>130/80	1
	Sodium intake	1
L	Address the following: BMI Waist Circumference Alcohol, Smoking, Exercise, Diet, stress, sleep hygiene eye assessment foot care	3
E	Education to prevent hypoglycaemia and management of hypoglycaemia (rule of 15) Knowledge, time, dose, frequency of medication administration Storage of medication	2
R	Aspirin 75mg od needed based on Framingham CVD risk score according to American Diabetes Guidelines 2015	1
	Total	14

Interview Guide: Development and Evaluation of a Pharmacist Diabetes Management Tool: a Mixed Methods Study

Thank you for taking the time to talk to me today.

To start off, I will give a brief summary. The key question is will a diabetes tool increase the number of patients receiving guideline-adherent therapy. I understand you have been using this tool for about a month in patients during Diabetes MedsCheck/MTACDM. In particular, I will be asking questions about the practicability and ease of use of this tool.

I have a series of questions to help guide the interview. There are no wrong answers to these questions, feel free to share your point of view and experience. Everything you say will remain confidential and your name will not appear in any reports or publications. I would like to record this, so we can focus on our discussion. Do you agree with me recording the interview?

Section A: Details and experience of Pharmacist

1. What is your age?
2. Were you trained to practise Diabetes MedsCheck/ MTAC diabetes?
3. If yes, how did you undertake this training?
4. Do you have any post-graduate qualifications? If yes, what qualifications?
5. On average, how many hours do you work per week in the community setting?
6. How many years have you been practising as a pharmacist in the community?
7. In which year did you first obtain your registration to practise as a pharmacist?
8. How would you consider your current role in the pharmacy?
9. Prompt: Dispensary pharmacist, patient care-focused, managerial role, MTAC pharmacist, clinical pharmacist….

Section B: Experience in providing Diabetes MedsCheck service before being trained on Simpler™ tool

1. On average, how many patients do you provide Diabetes MedsCheck service to in a day/week/month?

2. How do you normally review patients?
   Prompt: use MTAC diabetes/Diabetes MedsCheck checklist, own checklist, tools from the web, etc
3. How often do you refer to the Australian Diabetes Guidelines/Malaysia CPG on diabetes?

Section C: Experience in using Simpler™ tool

1. Please comment on your experience in using the Simpler™ tool.
   Prompts:
   a. Relevance when reviewing patient?
   b. Ease of Use? Content simple to understand?
   c. Relevance to local practice and guidelines?
   d. Managing consultation time with patients?
   e. Intervention format?
   f. Ease of remembering?
   g. Guide pharmacists to make interventions?
   h. Record intervention notes in a consistent, structured manner?
   i. Clarity of tool?
   j. Providing evidence-based information to GP, patients?
2. How many patients did you use SIMPLER on?
3. Talk about the interventions you made using SIMPLER?
4. Are the medication reviews with patients with diabetes different now compared to when you were not using the Simpler™ tool? If yes in what way?
5. How was the SIMPLER training session?
6. Would you recommend Simpler™ tool to other community pharmacists?
7. Are they any recommendations you like to make to enhance the usability of the tool?
8. Thank you again for your time. Before we finish, do you have any comments you'd like to make, about the research topic or training or about the interview?

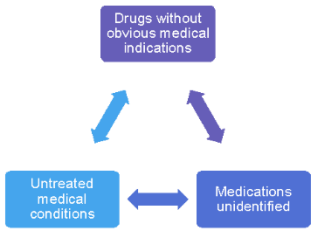
Appendix 4. 14: Hand-out version of additional slide presentations (revised)

Drug Related Problem Assessment

1. Correlation between drug therapy and medical problem
2. Appropriate therapy
3. Drug regimen
4. Therapeutic duplication/polypharmacy
5. Side effect/ Adverse drug reaction
6. Drug allergy or intolerance
7. Interactions, drug-drug, drug disease, drug food, drug herbal
8. Risk and Quality of Life Impact
9. Social or recreational drug use (drug abuse)
10. Financial impact
11. Patient knowledge of therapy
12. Adherence/ compliance
13. Self monitoring

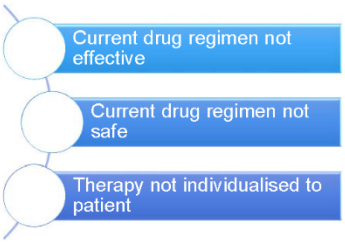
9

1. Correlation between drug therapy and medical problem



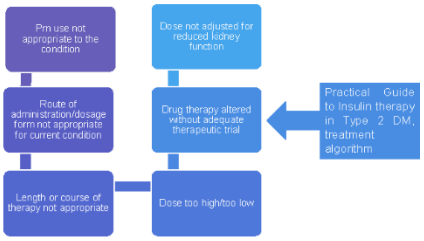
10

2. Appropriate therapy



11

3. Drug regimen



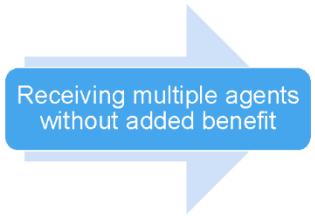
12

Treatment recommendations: Patients on follow-up

Glycaemic Control / Current Treatment	A1c 6.5-< 7.5% or FPG 6-<8 mmol/L	A1c 7.5-<8.5% or FPG 8-<10 mmol/L	A1c 8.5-10.0% or FPG 10-13 mmol/L	A1c >10.0% or FPG >13 mmol/L
Lifestyle Treatment	Add Metformin (or if metformin cannot be tolerated add either SU / Glinides / AGI / TZD / DPP-4i / GLP-1 RA / SGLT2i	Add Metformin and another agent (Dual therapy)	Add Metformin and another 2 agents not used for the dual therapy (Triple therapy)	Dual or Triple therapy + insulin (basal or premixed)
Monotherapy (Metformin preferred)	Add another agent (Dual therapy)	Add 2 agents not used for the dual therapy (Triple therapy)	Dual or Triple therapy + insulin (basal or premixed)	Optimise insulin (basal plus/multiple premixed) ± OAD
Dual Therapy	Add another agent not used for the dual therapy (Triple therapy)	Dual or Triple therapy + insulin (basal or premixed)	Optimise insulin (basal plus/multiple premixed) ± OAD	Intensify insulin (basal bolus/multiple premixed) ± OAD
Triple Therapy	Dual or Triple therapy + insulin (basal or premixed)	Optimise insulin (basal plus/multiple premixed) ± OAD	Intensify insulin (basal bolus/multiple premixed) ± OAD	Intensify insulin (basal bolus/multiple premixed) ± OAD

13

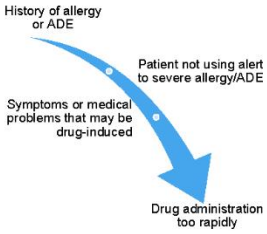
4. Therapeutic duplication



14

1

5. Side effect / adverse drug reaction
6. Drug allergy or intolerance



Efficacy of OHA

	MET	SU	GLN	AGI	TZD	DPP4-i	SGLT2-i	GLP-1 RA	Insulin
A1c reduction, %	1.0-1.5	1.5	1.0-1.2	0.5-0.8	0.5-1.4	0.5-0.8	0.7	0.5-1.0	>1.5
FPG vs PPG	FPG	FPG	Both	PPG	FPG	Both	Both	Both	Both
Hypoglycaemia	↔	↑↑	↑	↔	↔	↔	↔	↔	↑↑
Weight change	↓	↑↑	↑	↔	↑↑	↔	↓↓	↓↓	↑↑
GI symptoms	↑↑	↔	↔	↑↑	↔	↑	↔	↑↑	↔
Congestive heart failure	↔	↔	↔	↔	↑	↔?	↔	↔	↔
Cardiovascular disease	↓	↔?	↔	↔	↔	↔	↔	↔	↔
Bone loss	↔	↔	↔	↔	↑	↔	↔	↔	↔
CKD	Avoid GFR<30	Hypo-glycaemia	Hypo-glycaemia	↔	Fluid retention	Dose adjustment	Avoid GFR<60	Avoid GFR<30	Hypo-glycaemia
References									

MET = metformin; SU = sulphonylureas; GLN = glinides; GLP-1 RA = glucagon-like peptide-1 receptor agonists; DPP4-i = dipeptidyl peptidase-4 inhibitors; SGLT2-i = sodium-glucose co-transporter 2 inhibitors; AGI = α-glucosidase inhibitor; TZD = thiazolidinediones

The efficacy data for the above anti-diabetic agents were established with baseline A1c level below 10%. Efficacy of all OADs is dependent on the baseline A1c levels. The higher the A1c level, the more efficacious is the agent.

Beneficial
Possible benefit
Neutral
Minimal risk
Increased risk

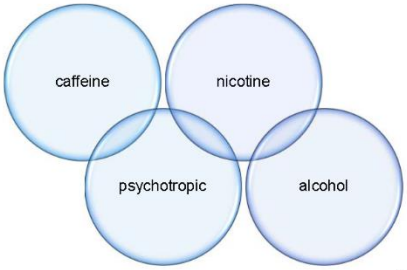
7. Interactions, drug-drug, drug disease, drug food, drug herbal

- RACGP General practice management of type 2 DM
- Appendix K: Potential drug interactions

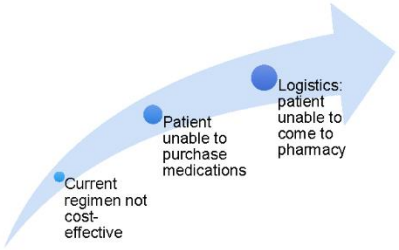
8. Risk and quality of life impact

- Measure using Quality Of Life assessment
- Eg. WHOQOL BREF questionnaire

9. Social/recreational drug use



10. Financial impact



11. Patient knowledge of therapy

- Patient does not understand the purpose of drug therapy
- Does not understand the directions
- Does not understand potential side effects
- Current regimen not consistent with patient's beliefs

12. Adherence/compliance

13. Self monitoring

- Side effects
- BP
- SMBG
- Hypoglycaemia
- Food Diary
- Exercise Diary

Diet & Lifestyle: Resources

Nutriweb:
http://www.nutriweb.org.my/

NDSS:
https://www.ndss.com.au/

Glucagon Administration

- If patient cannot swallow 15g of carbohydrate
- Administer 1 vial of glucagon IM
- Measure glucose after 15 mins
  - Should be >4 mmol/L
  - Test again after 1 hour

Appendix 5. 1: Phase Three ethics approval (Australia)

MEMORANDUM

Curtin University

To:	Dr.Laetitia Hattingh School of Pharmacy
CC:	Shamala Ayadurai
From	Professor Peter O'Leary, Chair HREC
Subject	Ethics approval Approval number: HR214/2015
Date	16-Nov-15

Office of Research and Development
Human Research Ethics Office

TELEPHONE 9266 2784
FACSIMILE 9266 3793
EMAIL hrec@curtin.edu.au

Thank you for your application submitted to the Human Research Ethics Office for the project: 6480

Development and Evaluation of a Pharmacist Diabetes Management Tool: a Mixed Methods Study - Phase 3

Your application was reviewed by Human Research Ethics Committee at Curtin University at their meeting on the 3/11/2015

Thankyou for providing the additional information requested by the Human Research Ethics Committee. The information you provided was satisfactory and your proposal is now approved.

Please note the following conditions of approval:

1. Approval is granted for a period of four years from **17-Nov-15** to **17-Nov-19**
2. Research must be conducted as stated in the approved protocol.
3. Any amendments to the approved protocol must be approved by the Ethics Office.
4. An annual progress report must be submitted to the Ethics Office annually, on the anniversary of approval.
5. All adverse events must be reported to the Ethics Office.
6. A completion report must be submitted to the Ethics Office on completion of the project.
7. Data must be stored in accordance with WAUSDA and Curtin University policy.
8. The Ethics Office may conduct a randomly identified audit of a proportion of research projects approved by the HREC.

Should you have any queries about the consideration of your project please contact the Ethics Support Officer for your faculty, or the Ethics Office at hrec@curtin.edu.au or on 9266 2784. All human research ethics forms and guidelines are available on the ethics website.

Yours sincerely,

Professor Peter O'Leary
Chair, Human Research Ethics Committee

Appendix 5. 2: Phase Three ethics approval (Malaysia)

JAWATANKUASA ETIKA & PENYELIDIKAN PERUBATAN
(Medical Research & Ethics Committee)
KEMENTERIAN KESIHATAN MALAYSIA
d/a Institut Pengurusan Kesihatan
Jalan Rumah Sakit, Bangsar
59000 KUALA LUMPUR

Tel.: 03-2287 4032/2282 0491/2282 9085
03-2282 9082/2282 1402/2282 1449
Faks: 03-2282 0015

Ref : (9)KKM/NIHSEC/ P15-1522
Date : 5 January 2016

Protocol Title:
NMRR-15-1831-28307
Development and Evaluation of a Pharmacist Diabetes Management Tool: a Mixed Methods Study - Phase 3

PRINCIPLE INVESTIGATOR
Shamala Ayadurai
CURTIN UNIVERSITY

Hendrika Laetitia Hattingh
CURTIN UNIVERSITY

Documents received and reviewed with reference to the above study:

1. Study Protocol Version 3.0 Dated 30-12-2015
2. Patient Information Sheet (English) & Informed Consent Form (English) Version 3 dated 30-12-2015
3. Follow up review report version 1 dated 29-12-2015
4. Curriculum vitae of :

a. **Hendrika Laetitia Hattingh**
b. **Shamala Ayadurai**
c. **Siti Norlina Md Said**

Please note that the approval is valid until **4 January 2017**. The following items are to be submitted to the Medical Research and Ethics Committee (MREC) as appropriate. The required forms can be obtained from the MREC website (**http://www.nih.gov.my/mrec**).

I. The **Continuing Review Form** is to be submitted to MREC at least 2 months before the expiry of the approval.
II. The **Study Final Report** is to be submitted to MREC upon study completion.

III. Ethical approval is required in the case of **amendments/ changes** to the **study documents/ study sites/ study team**.

IV. **Applicable for Clinical interventional Studies only:** Report occurrences of **all Serious Adverse Events (SAEs), Suspected Unexpected Serious Adverse Reaction (SUSARs)** and **Protocol Deviation/Violation** at all MREC approved sites to MREC. SAEs are to be reported within 15 calendars days from awareness of event by investigator. Initial report of SUSARs are to be reported as soon as possible but not later than 7 calendar days from awareness of event by investigator, followed by a complete report within 8 additional calendar days.

2. The number of subjects/ patients/ respondents targeted to enroll in this study in Malaysia is 120.

3. Please take note that the reference number for this letter must be stated in all correspondence related to this study to facilitate the process.

Comments (if any):

Project Sites: **JABATAN KESIHATAN NEGERI JOHOR**

Decision by Medical Research & Ethics Committee:
(√) Approved
( ) Disapproved

Date of Approval: 5 January 2016

(DATO' DR. CHANG KIAN MENG)
Pengerusi
Jawatankuasa Etika & Penyelidikan Perubatan
Kementerian Kesihatan Malaysia

Appendix 5. 3:Phase Three ethics renewal (Malaysia)

JAWATANKUASA ETIKA & PENYELIDIKAN PERUBATAN
(Medical Research & Ethics Committee)
KEMENTERIAN KESIHATAN MALAYSIA
d/a Institut Pengurusan Kesihatan
Jalan Rumah Sakit, Bangsar
59000 Kuala Lumpur

Tel.: 03-2287 4032/2282 0491/2282 9085
03-2282 9082/2282 1402/2282 1449
Faks: 03-2282 0015

Ruj.Kami:(7)KKM/NIHSEC/ P15-1522
Tarikh : 30-December-2016

Dr Hendrika Laetitia Hattingh
CURTIN UNIVERSITY

Dato'/ Tuan/ Puan,

Annual Ethical Renewal for 2016

NMRR-15-1831-28307 (IIR)
Protocol No :
Development and Evaluation of a Pharmacist Diabetes Management Tool: a Mixed Methods Study - Phase 3

With reference to the 'Continuing Review Form' submitted 28-December-2016, we are pleased to inform that the conduct of the above study has been granted approval (via Expedited Review by Chairperson) for a year by the Medical Research & Ethics Comittee, Ministry of Health Malaysia. Please note that the approval is valid until 29-December-2017. To renew the approval, a completed 'Continuing Review Form' has to be submitted to MREC **within 1 month** before the expiry of the approval.

The MREC, Ministry of Health Malaysia operates in accordance to the International Harmonization Good Clinical Practice Guidelines.

Thank you.

"BERKHIDMAT UNTUK NEGARA"

Yours sincerely,

.....
(DATO' DR CHANG KIAN MENG)
Chairman
Medical Research & Ethics Committee
Ministry of Health Malaysia

Appendix 5. 4: User agreement for WHOQOL-BREF

User Agreement for "WHOQOL-100" and/or WHOQOL-BREF and related materials

This agreement is between the World Health Organization ("WHO") and Dr.H Laetitia Hattingh. WHO hereby grants the User a nonexclusive, royalty-free license to use the World Health Organization Quality of Life Questionnaire and/or related materials (hereafter referred to as "WHOQOL-100" or "WHOQOL-BREF") in User's study outlined below. The term of this User Agreement shall be for a period of 1 year, commencing on (date) 1st March 2016.

The approved study for this User Agreement is:

Study Title	Development and Evaluation of Pharmacist Diabetes Management Tool: A mixed methods study
Principal Investigator	Dr.Laetitia Hattingh
Sample characteristics	Type 2 Diabetes patients who have glycated hemoglobin (HbA1c) above 8%, having multiple medications and other health conditions.
Sample size	120 Type 2 diabetes patients
Treatment Intervention	This research aims to evaluate the application of a tool that has been developed earlier in this PhD research. A randomised controlled trial(RCT) will be conducted to evaluate whether there is significant difference between patients receiving care from pharmacists using the tool and patients receiving usual care.
Total number of assessments	Twice for each patient
Assessment time points	Once in the beginning and once at the end of six months
"WHOQOL-100" or WHOQOL-BREF version – *Please specify language version(s) you would like to receive.*	WHOQOL-BREF version in English, Bahasa Malaysia and Chinese (Mandarin) languages
Other measures	In addition to QOL outcome, pharmacists will be required to record the demographics, pharmaceutical care interventions and clinical outcomes of patients in both groups.

This User Agreement is based upon the following conditions:

1. User shall not modify, abridge, condense, translate, adapt, recast or transform the WHOQOL-100 or BREF in any manner or form, including but not limited to any minor or significant change in wording or organization, or administration procedures, of the WHOQOL-100 or BREF. If User thinks that changes are necessary for its work, or if translation is necessary, User must obtain written approval from WHO in advance of making such changes.

2. User shall not reproduce WHOQOL-100 or BREF, except for the limited purpose of generating sufficient copies for its own uses and shall in no event distribute copies of the WHOQOL-100 or BREF to third parties by sale, rental, lease, lending, or any other means. In addition, User agrees that it will not use the WHOQOL-100 or BREF for any purpose other than conducting studies as specified above, unless agreed in writing by WHO. In any event, the WHOQOL-100 or BREF should not be used for research or clinical purposes without prior written authorization from WHO.

3. User agrees to provide WHO with an annual update regarding activities related to the WHOQOL-100 or BREF.

4. User agrees to provide WHO with a complete copy of User's raw data and data code books, including the WHOQOL-100 or BREF and any other instruments used in the study. This data set must be forwarded to WHO upon the conclusion of User's work. While User remains the owner of the data collected in User's studies, these data may be used in WHO analyses for further examining the psychometric properties of the WHOQOL-100 or BREF. WHO asserts the right to present and publish these results, with due credit to the User as the primary investigator, as part of the overall WHOQOL-100 or BREF development strategy.

5. WHO shall be responsible for preparing and publishing the overall WHOQOL-100 or BREF results under WHO copyright, including:

a. the overall strategy, administrative set-up and design of the study including the instruments employed;

b. common methods used by two or more Users;

c. the data reported from two or more Users ;

d. the comparisons made between the data reported from the Users;

e. the overall findings and conclusions.

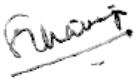
6. User shall be responsible for publications concerning information developed exclusively by User and methods employed only by User. Publications describing results obtained by User will be published in User's name and shall include an acknowledgement of WHO. User agrees to send to WHO a copy of each such paper prior to its submission for publication.

7. WHO may terminate this User Agreement at any time, in any event. Should WHO terminate this User Agreement, User shall immediately cease all use of the WHOQOL100 or BREF and destroy or return all copies of the WHOQOL-100 or BREF. In the event of such termination, all other collateral materials shall be destroyed and no copy thereof shall be retained by User. Notwithstanding the return or destruction of the WHOQOL-100 or BREF and its collateral materials, User will continue to be bound by the terms of this User Agreement.

8. It is understood that this User Agreement does not create any employer/employee relationship. User and its affiliates are not entitled to describe themselves as staff members of WHO. User shall be solely responsible for the manner in which work on the project is carried out and accordingly shall assume full liability for any damage arising therefrom. No liability shall attach to WHO, its advisers, agents or employees.

Please confirm your agreement with the foregoing by signing and returning one copy of this letter to WHO, whereupon this letter agreement shall become a binding agreement between User and WHO.

WHO:



Dr. Somnath Chatterji
Health Statistics and Health Information Systems (HSI)
World Health Organization
Avenue Appia
Geneva 27
CH 1211 Switzerland

Date:

USER:

By: _____
Title: Senior Lecturer
Institution: School of Pharmacy, Curtin University
Address: Kent Street, Bentley, Perth
6102, Western Australia
Australia
Date: 10 November 2015

Appendix 5. 5: Phase Three pharmacist information sheet (pharmacist)

Curtin University

School of Pharmacy

GPO Box U1987
Perth Western Australia 6845
Telephone +61 8 9266 7369
Facsimile +61 8 9266 2769
Emailshamala.ayadurai@postgrad.curtin.edu.au
Webcurtin.edu.au

INFORMATION SHEET FOR PHARMACISTS

Development and Evaluation of a Pharmacist Diabetes Management Tool: a Mixed Methods Study

1. **What is this study about?** This research aims to develop and evaluate a decision-support tool to support pharmacists in delivering diabetes care at primary health care settings in Malaysia. We will investigate the effectiveness of the tool to improve control of blood glucose, blood pressure and cholesterol levels as well as quality of life. We will also determine the potential cost effectiveness of the tool compared to usual care.

2. **Who is doing this research?** Dr. Laetitia Hattingh, Prof.Bruce Sunderland and Associate Prof.Dr.Lisa Tee from Curtin University in Western Australia and chief pharmacist of Sultanah Aminah Hospital, Johor Bahru, Dr.Siti Norlina Md Said in Malaysia are supervising this project. The results of this study will be used by Shamala Ayadurai as part of her PhD project.

3. **Why am I being invited to participate and what do I have to do?** You have been invited to participate because you are involved in diabetes management. Your involvement in this research will start with a 2 hour training session on the use of this tool. Each primary health clinic (*Klinik Kesihatan*) will be asked to recruit 20 patients who will be followed up for six months. These 20 patients will be randomised to two arms: 10 patients for the intervention and 10 patients for the control arm. Pharmacists will administer the health related quality of life questionnaire to the 20 patients (intervention and control arm) twice, once in the beginning and again at the end of six months. A scanned copy of the completed questionnaire will be sent via email to the researcher, Shamala Ayadurai. The patients in the intervention arm will be followed up every month for six months while the patients in the control arm will only be seen twice by the intervention pharmacist namely once in the beginning and once at the end of the six months. Pharmacists will be asked to use the diabetes tool to suggest interventions to doctors. Pharmacists will take an image of their intervention notes and patients' laboratory data and send it via email to Shamala every month for recording in a data collection form. As for patients in the control arm, image of patients' demographic data and laboratory data will be sent to Shamala at the beginning and once more at the completion of the study at 6 months. As a token of your time and effort, you will receive a remuneration of AUD100/RM300.

4. **What are the possible disadvantages of taking part?** You may spend more time to consult with patients when using the tool in the beginning of the research project.

5. **Who has access to my information and what will happen to it after the project ends?** The identity of each participant will not be revealed to other participants. Any information we collect will be treated as confidential and used only in this project. The data we collect in this study will be kept under secure conditions at Curtin University for 25 years after the research has ended and then it will be destroyed. The results of this research may be

presented at conferences or published in professional journals, but you will not be identified in any results that are published and you will remain anonymous.

6. **Do I have to participate and how can I withdraw?** Taking part in a research project is voluntary. It is your choice to take part or not. You do not have to agree if you do not want to. If you decide to take part and then change your mind, that is okay, you can withdraw from the project. You do not have to give us a reason; just tell us that you want to stop. Please let us know you want to stop so we can make sure you are aware of any thing that needs to be done. If you chose not to take part or start and then stop the study, it will not affect your relationship with the university, staff or colleagues. If you chose to leave the study we will use any information collected unless you tell us not to.

7. **Any further queries?** If you would like to know more at any stage, please do not hesitate to contact Shamala at shamala.ayadurai@postgrad.curtin.edu.au or Dr.Laetitia Hattingh L.Hattingh@curtin.edu.au or The Secretary, Medical Research & Ethics Committee, Ministry of Health Malaysia, at telephone number 03- 22874032.

Curtin University Human Research Ethics Committee (HREC) has approved this study (HR214/2015). The Malaysian Medical Research and Ethics Committee has also approved the study (NMRR-15-1831-28307). Should you wish to discuss the study with someone not directly involved, in particular, any matters concerning the conduct of the study or your rights as a participant, or you wish to make a confidential complaint, you may contact the Ethics Officer on (08) 9266 9223 or the Manager, Research Integrity on (08) 9266 7093 or email hrec@curtin.edu.au.

Appendix 5. 6: Phase Three pharmacist consent form

Curtin University

School of Pharmacy

GPO Box U1987
Perth Western Australia 6845
Telephone +61 8 9266 7369
Facsimile +61 8 9266 2769
Emailshamala.ayadurai@postgrad.curtin.edu.au
Webcurtin.edu.au

Development and Evaluation of a Pharmacist Diabetes Management Tool: a Mixed Methods Study

Consent Form

I, ……. agree to participate in the above study. I have been provided with a copy of the Participant Information Sheet explaining the study, which I have read and understood. I have been given the opportunity to ask questions about the study and any questions asked have been answered to my satisfaction. I understand that I may withdraw from the study at any time without prejudice. I am aware that all research data collected will only be used for the purpose of this study and will be kept confidential and that my participation will not be disclosed without my consent. Any information which might potentially identify me will not be used in published material.

Signed:	……..	Date:	……
Signature of person obtaining consent:	……	Date:	……..
Name of person obtaining consent:	Shamala Ayadurai		

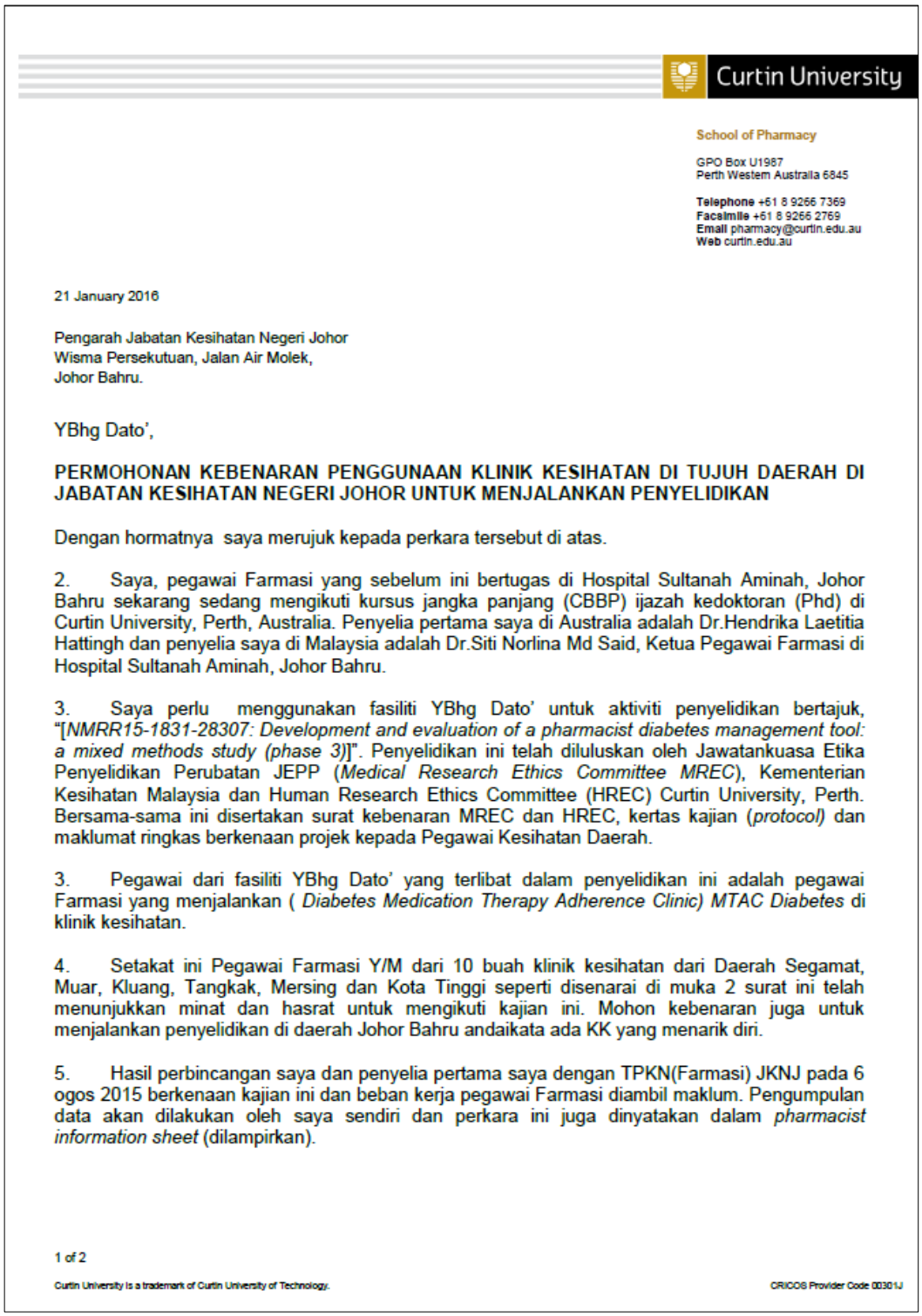
Receipt of Gift Card

I declare that I have received AUD$100/AUD$50 gift card as a token of appreciation for my time to participate in the study.

Signed:	……..	Date:	……
Signature of person giving out gift card:	……	Date:	……..
Name of person giving out gift card:	…….		

Curtin University Human Research Ethics Committee (HREC) has approved this study (HR214/2015). The Malaysian Medical Research and Ethics Committee has also approved the study (NMRR-15-1831-28307). Should you wish to discuss the study with someone not directly involved, in particular, any matters concerning the conduct of the study or your rights as a participant, or you wish to make a confidential complaint, you may contact the Ethics Officer on (08) 9266 9223 or the Manager, Research Integrity on (08) 9266 7093 or email hrec@curtin.edu.au.

Appendix 5. 7: Application for conducting research to director of Johor State Health Department



Curtin University

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Telephone +61 8 9266 7369
Facsimile +61 8 9266 2769
Email pharmacy@curtin.edu.au
Web curtin.edu.au

21 January 2016

Pengarah Jabatan Kesihatan Negeri Johor
Wisma Persekutuan, Jalan Air Molek,
Johor Bahru.

YBhg Dato',

PERMOHONAN KEBENARAN PENGGUNAAN KLINIK KESIHATAN DI TUJUH DAERAH DI JABATAN KESIHATAN NEGERI JOHOR UNTUK MENJALANKAN PENYELIDIKAN

Dengan hormatnya saya merujuk kepada perkara tersebut di atas.

2. Saya, pegawai Farmasi yang sebelum ini bertugas di Hospital Sultanah Aminah, Johor Bahru sekarang sedang mengikuti kursus jangka panjang (CBBP) ijazah kedoktoran (Phd) di Curtin University, Perth, Australia. Penyelia pertama saya di Australia adalah Dr.Hendrika Laetitia Hattingh dan penyelia saya di Malaysia adalah Dr.Siti Norlina Md Said, Ketua Pegawai Farmasi di Hospital Sultanah Aminah, Johor Bahru.

3. Saya perlu menggunakan fasiliti YBhg Dato' untuk aktiviti penyelidikan bertajuk, "[*NMRR15-1831-28307: Development and evaluation of a pharmacist diabetes management tool: a mixed methods study (phase 3)*]". Penyelidikan ini telah diluluskan oleh Jawatankuasa Etika Penyelidikan Perubatan JEPP (*Medical Research Ethics Committee MREC*), Kementerian Kesihatan Malaysia dan Human Research Ethics Committee (HREC) Curtin University, Perth. Bersama-sama ini disertakan surat kebenaran MREC dan HREC, kertas kajian (*protocol)* dan maklumat ringkas berkenaan projek kepada Pegawai Kesihatan Daerah.

3. Pegawai dari fasiliti YBhg Dato' yang terlibat dalam penyelidikan ini adalah pegawai Farmasi yang menjalankan (*Diabetes Medication Therapy Adherence Clinic) MTAC Diabetes* di klinik kesihatan.

4. Setakat ini Pegawai Farmasi Y/M dari 10 buah klinik kesihatan dari Daerah Segamat, Muar, Kluang, Tangkak, Mersing dan Kota Tinggi seperti disenarai di muka 2 surat ini telah menunjukkan minat dan hasrat untuk mengikuti kajian ini. Mohon kebenaran juga untuk menjalankan penyelidikan di daerah Johor Bahru andaikata ada KK yang menarik diri.

5. Hasil perbincangan saya dan penyelia pertama saya dengan TPKN(Farmasi) JKNJ pada 6 ogos 2015 berkenaan kajian ini dan beban kerja pegawai Farmasi diambil maklum. Pengumpulan data akan dilakukan oleh saya sendiri dan perkara ini juga dinyatakan dalam *pharmacist information sheet* (dilampirkan).

Kami berharap mendapat kebenaran YBhg Dato'. Jika ada sebarang pertanyaan sila hubungi saya di emel seperti di bawah.

Sekian, terima kasih.

Saya yang menurut perintah,

.....

(Shamala Ayadurai)
Ketua Penyelidik;
Calon PhD (PhD Candidate)
Curtin University
Perth, Australia
Emel: shamala.ayadurai@postgrad.curtin.edu.au
Tel: 012 2702642 (aktif sehingga 5 Februari 2016)

s.k.
Dr.Siti Norlina Md.Said,
Penyelidik bersama (Co-Invesigator)
Ketua Pegawai Farmasi Hospital Sultanah Aminah;
Curtin University Associate, Perth, Australia.

Senarai Klinik Kesihatan yang telah menunjukkan minat untuk menyertai projek ini.

Bil.	Klinik Kesihatan	Daerah
1)	Segamat	Segamat
2)	Bandar Putra (IOI)	Segamat
3)	Paya Mas	Tangkak
4)	Jalan Mengkibol	Kluang
5)	Maharani	Muar
6)	Bukit Pasir	Muar
7)	KK Tenggaroh 2	Mersing
8)	KK Bandar Tenggara	Kota Tinggi
9)	KK Bukit Besar	Kota Tinggi
10)	KK Bandar Mas	Kota Tinggi
11)	Belum direkrut	Johor Bahru

Appendix 5. 8: Letter to the manager of each clinic (KK)

Curtin University

School of Pharmacy
GPO Box U1987
Perth Western Australia 6845
Telephone +61 8 9266 7369
Facsimile +61 8 9266 2769
Email pharmacy@curtin.edu.au
Web curtin.edu.au

Pegawai Kesihatan Daerah,
Pejabat Kesihatan Daerah

14th January 2016

Dear Doctor,

Ref: Permission to conduct diabetes research

Diabetes is a complex disease and there are many factors involved in treating and preventing diabetes-related complications. We are conducting a randomised controlled trial that aims to evaluate a patient-centred diabetes tool which will enable pharmacists to make structured, consistent and quality interventions. This research will involve MTAC Diabetes pharmacists and we hope you would allow these pharmacists to participate. Pharmacists will not be expected to do anything beyond their usual practice as we understand their workload.

Our research will involve a training session on using this tool and on diabetes management which will take two hours. Pharmacist will then be asked to recruit 12 patients each who will be followed up for six months. These 12 patients will be randomised to two groups, namely six patients for intervention and six patients for the control group. The patients in the intervention group will receive care from pharmacists trained to use the tool. The control group will receive the usual care from pharmacists who are not trained to use the tool.

Pharmacist will administer the health related quality of life questionnaire to the 12 patients (intervention and control group) twice, once in the beginning and again at the end of six months. A scanned copy of the completed questionnaire will be sent via email to the researcher, Shamala Ayadurai. Shamala is undertaking this research to meet the requirements of a Doctor of Philosophy.

Patients in the intervention group will be managed by pharmacists who will be using the diabetes tool to make interventions and suggestions to doctors. Pharmacist will be required to take an image of their intervention notes and patients' laboratory data and send it via email to Shamala every month. Shamala will then be recording the information in a data collection form. Pharmacist will be required to do the same for the control group but only have to send the image of their intervention notes and patients' laboratory data twice: once in the beginning and once at the end of six months.

If you have any questions about our research we are more than happy to provide you with the necessary information.

Thanking in advance for your time and consideration.

Yours sincerely,

Shamala Ayadurai
PHD Candidate
School of Pharmacy, Curtin University, Perth, Western Australia

Dr.Siti Norlina Md Said
PhD Supervisor and Curtin University Associate
Hospital Sultanah Aminah, Johor Bahru, Johor, Malaysia

Appendix 5. 9: Letter of approval to conduct research at the seven districts in Johor

JABATAN KESIHATAN NEGERI JOHOR
BAHAGIAN PERKHIDMATAN FARMASI
D/A HOSPITAL PERMAI LAMA
JALAN PERSIARAN PERMAI
81200 JOHOR BAHRU
JOHOR DARUL TA'ZIM

TELEFON : 07-235 5120
FAKS : 07-235 5130
Email : farmasijb@moh.gov.my

Ruj. Kami: Bil (8)JKNJ(FAR) 05/053 Jld.2
Tarikh: 2 November 2016

Shamala Ayadurai
Curtin University

Hendrika Laetitia Hattingh
Curtin University

Puan,

KEBENARAN MENJALANKAN KAJIAN PENYELIDIKAN DI KLINIK KESIHATAN DI TUJUH DAERAH DI JABATAN KESIHATAN NEGERI JOHOR (NMRR-15-1831-28307)

Adalah saya dengan segala hormatnya merujuk kepada perkara tersebut di atas.

2. Sukacita dimaklumkan bahawa Bahagian Perkhidmatan Farmasi, Jabatan Kesihatan Negeri Johor memberi kebenaran kepada pihak puan untuk menjalankan kajian penyelidikan di klinik kesihatan di tujuh daerah di Jabatan Kesihatan Negeri Johor yang mana ia melibatkan pegawai farmasi yang menjalankan MTAC Diabetes di fasiliti berkenaan.

3. Pihak puan diminta untuk mematuhi arahan dan garis panduan oleh NIH bertajuk "NIH Guidelines for Conducting Research in Ministry of Health Institutions and facilities". Pihak puan juga diminta untuk menghantar satu laporan penuh hasil kajian ke bahagian ini pada penghujung kajian untuk makluman pihak kami. Jika terdapat sebarang pertanyaan, sila hubungi Pn. Suraya Hani Binti Sharon (Tel: 07-235 5120 atau emel farmasijb@moh.gov.my).

Sekian, terima kasih.

"BERKHIDMAT UNTUK NEGARA

Saya yang menurut perintah,

.....
(ROSIDAH BT MD DIN)
Timbalan Pengarah Kesihatan Negeri (Farmasi) Johor

s.k. 1. Pegawai Kesihatan Kanan
Pejabat Kesihatan Daerah Johor Bahru / Muar / Kluang / Segamat / Kota Tinggi / Tangkak / Mersing

2. Pegawai Farmasi Kesihatan
Pejabat Kesihatan Daerah Johor Bahru / Muar / Kluang / Segamat / Kota Tinggi / Tangkak / Mersing

Appendix 5. 10: Agenda for Phase Three RCT briefing

Simpler Diabetes Care

Agenda for Phase 3 Simpler© Trial Meeting

Date: 4 & 11 June 2016

Registration	12.00-12.30pm
Overview of protocol followed by role play	12.30-1.00pm
Lunch (KSL)	1.00-2.00pm
Practice session: Simpler© Pro Forma A Documentation	2.00-2.15pm
Practice session: Simpler© Pro Forma B Documentation	2.15-2.30pm
Practice session: WHO QOL-BREF questionnaire	2.30-3.00pm
Practice session: Morisky & Naranjo	3.00-3.15pm
Other relevant issues	3.15-3.45pm
End of Briefing session	3.45pm

Appendix 5. 11: The Simpler™ Pro forma A

Time:_____ Date:_____	**Simpler™ Pro Forma A (to be used during doctor's appointment)**	
	Patient ID:_____Visit No:_____ **Patient RN:_____**	**Blue Ink: Nurse** **Purple Ink: Pharmacist** **Black Ink: Doctor**

Gender	Age	Ethnic	Drug allergies	FHx of diabetes	Current social Hx	Other diseases

Medicines list: Current, regular, 'prn' (taken when necessary) medicines including prescription, non-prescription and complementary medicines

Name	Dose	Frequency

Statin/Cholesterol control

Subjective & Objective observations: TC=_____mmol/L. TG=_____mmol/L. LDL=_____mmol/L. HDL=_____mmol/L

Creatinine=_____micromoles/L CrCL=_____ml/min

Interventions:

Plan:

Insulin/Glycaemic control

Subjective & Objective observations: HbA1c_____%. FBG=_____mmol/L. RBG=_____mmol/L. 2HoursPPG=_____mmol/l No. hypoglycaemia like symptoms since previous visit on_____:_____times
Hospital Admission on_____.

Interventions:

Plan:

Medication
Subjective & objective observations: Patient compliance assessed using 8-item MMMAS. Score =_____/8. See attached. Patient claims taking/not taking any traditional medications. Interventions: Plan:
Blood pressure
Subjective & objective observations: BP=_____mmHg. Interventions: Plan:
Lifestyle

Weight:	_____kg	Height:	___m	BMI:	_____ kgm^2	Waist Circumference:	_____ cm

Exercises:	___ /mins_____/day ___week	Smoking:	_____cigarettes ___day____week____month	Alcohol:	_____ standard drinks/ day.

Subjective & objective observations:
Patient does/does not follow plate model.

Interventions:

Plan:

Education

Subjective & objective observation: Patient compliance assessed using 8-item MMMAS. Score =_____/8. See attached.

Interventions:

Plan:

CVD Risk

Subjective & objective observation: Patient has____% risk of CVD in Next 10 years- Framingham.

Interventions:

Plan:

Signature:		Signature:		Signature:	
Name of Nurse:		Name of Pharmacist:		Name of Doctor:	
Ext:		Ext:		Ext:	

Appendix 5. 12: The Simpler™ Pro forma B

Time:_____ ___ Date:_____ ___	**Simpler © Pro Forma B (Follow up form when patient has no doctor's appointment)** **Patient ID:_____Visit No:_____** **Patient RN:_____**

Medicines list(if different from previous visit): Current, regular, 'prn' (taken when necessary) medicines including prescription, non-prescription and complementary medicines

Name	Dose	Frequency

Statin	Subjective observation: Intervention: Monitor:
Insulin	Subjective & objective observation: include SMBG readings & no hypoglycaemic like symptoms BG Range: Breakfast:_____mmol/L; 2hr post breakfast:_____mmol/L; Lunch:_____mmol/L; 2hr post lunch:_____ mmol/L; Dinner:_____mmol/L; 2hr post dinner:_____mmol/L; Bedtime:_____mmol/L; Intervention: Monitor:

Medicat ion	Subjective & objective observation: Patient compliance assessed using 8-item MMMAS. Score =__ /8. State the questions patient showed low adherence. Patient claims taking/not taking any traditional medications. Intervention: Monitor:

B**P**	Subjective & objective observation: BP=_____mmHg Intervention: Monitor:
Lifestyle	Subjective observation: Patient does/does not follow plate model Waist circumference = _____cm Smoking:___cigarettes___day__week__month. Alcohol=_____standard drinks/day. Exercises:___ /mins_____/day ___week Intervention: Monitor:
Educati on	Subjective observation: Comment Patient knowledge of name, dose, frequency, indication and timing of medicine Intervention: Monitor:

CVD **R**isk	Subjective & objective observation: Hospital admission on:_____ Intervention: Monitor:	
Signature and name of Pharmacist:		

Appendix 5. 13: WHOQOL-BREF questionnaire (Bahasa Malaysia)

No Siri kajian:

WHOQOL-BREF

		Sangat tidak baik	Tidak baik	Sederhana	Baik	Sangat baik
1(G1)	Bagaimanakah anda menilai kualiti kehidupan anda?	1	2	3	4	5

		Sangat tidak berpuas hati	Tidak berpuas hati	Sederhana	Berpuas hati	Sangat Berpuas hati
2(G4)	Setakat manakah anda berpuas hati dengan kesihatan anda?	1	2	3	4	5

Soalan-soalan berikutnya bertanyakan tentang berapa banyakkah anda telah mengalami sesuatu perkara **dalam dua minggu yang lepas.**

		Tiada langsung	Sedikit sahaja	Sederhana	Sangat banyak	Teramat banyak
3(F1.4)	Setakat manakah anda berasa kesakitan (fizikal) menghalang anda dari melakukan apa yang anda perlu lakukan?	1	2	3	4	5
4(F11.3)	Berapa banyakkah rawatan perubatan yang anda perlu untuk berfungsi dalam kehidupan harian anda?	1	2	3	4	5
5(F4.1)	Berapa banyakkah anda menikmati keseronokan dalam hidup anda?	1	2	3	4	5
6(F24.2)	Setakat manakah anda rasa hidup anda bermakna?	1	2	3	4	5

		Tiada langsung	Sedikit sahaja	Sederhana	Sangat	Teramat
7(F5.3)	Berapa baikkah anda dapat memberi tumpuan?	1	2	3	4	5
8(F16.1)	Berapa selamatkah anda rasa dalam kehidupan seharian anda?	1	2	3	4	5
9(F22.1)	Berapa sihatkah persekitaran fizikal anda?	1	2	3	4	5

Soalan-soalan berikutnya bertanyakan **bagaimana sempurnanya** anda mengalami atau berupaya melakukan sesuatu perkara dalam **dua minggu yang lepas.**

		Tiada langsung	Sedikit sahaja	Sederhana	Kebanyak-kannya	Sepenuhnya
10(F2.1)	Adakah anda mempunyai cukup tenaga untuk kehidupan harian anda?	1	2	3	4	5
11(F7.1)	Adakah anda dapat menerima rupa dan bentuk tubuh anda?	1	2	3	4	5
12(F18.1)	Adakah anda mempunyai wang yang cukup untuk memenuhi keperluan anda?	1	2	3	4	5
13(F20.1)	Setakat manakah kemudahan bagi anda untuk mendapatkan maklumat yang diperlukan dalam kehidupan harian?	1	2	3	4	5
14(F21.1)	Setakat manakah anda mendapat peluang untuk aktiviti riadah?	1	2	3	4	5

		Sangat Tidak baik	Tidak baik	Sederhana	Baik	Sangat baik
15(F9.1)	Sebaik manakah keupayaan anda bergerak dari satu tempat ke satu tempat yang lain?	1	2	3	4	5

Soalan-soalan berikut bertanyakan tentang perasaan anda terhadap beberapa aspek tertentu dalam kehidupan anda **sepanjang dua minggu yang lepas**.

		Sangat tidak berpuas hati	Tidak Berpuas hati	Sederhana	Berpuas hati	Sangat Berpuas hati
16(F3.3)	Adakah anda berpuas hati dengan tidur anda?	1	2	3	4	5
17(F10.3)	Adakah anda berpuas hati dengan keupayaan anda melaksanakan aktiviti kehidupan harian anda?	1	2	3	4	5
18(F12.4)	Adakah anda berpuas hati dengan keupayaan anda bekerja?	1	2	3	4	5
19(F6.3)	Adakah anda berpuas hati dengan diri anda?	1	2	3	4	5
20(F13.3)	Adakah anda berpuas hati dengan perhubungan peribadi anda?	1	2	3	4	5
21(F15.3)	Adakah anda berpuas hati dengan kehidupan seks anda?	1	2	3	4	5
22(F14.4)	Adakah anda berpuas hati dengan sokongan yang anda dapati dari kawan-kawan anda?	1	2	3	4	5
23(F17.3)	Adakah anda berpuas hati dengan keadaan tempat tinggal anda?	1	2	3	4	5
24(F19.3)	Adakah anda berpuas hati dengan kemudahan mendapatkan perkhidmatan kesihatan ?	1	2	3	4	5
25(F23.3)	Adakah anda berpuas hati dengan pengangkutan anda?	1	2	3	4	5

Soalan berikut merujuk kepada kekerapan anda merasa atau mengalami sesuatu emosi **sepanjang dua minggu yang lepas.**

		Tidak pernah	Jarang-jarang	Kerap	Sangat kerap	Sentiasa
26(F8.1)	Berapa kerapkah anda mempunyai perasaan-perasaan negatif, seperti susah hati, kecewa, kegelisahan atau kemurungan?	1	2	3	4	5

Adakah anda mempunyai sebarang maklumbalas tentang soal-jawab ini?

TERIMA KASIH ATAS PERTOLONGAN ANDA
HUSM: Dr. Hasanah

Appendix 5. 14: WHOQOL-BREF questionnaire (English)

Please read each question, assess your feelings, and circle the number on the scale for each question that gives the best answer for you.

		Very poor	Poor	Neither poor nor good	Good	Very good
1(G1)	How would you rate your quality of life?	1	2	3	4	5

		Very dissatisfied	Dissatisfied	Neither satisfied nor dissatisfied	Satisfied	Very satisfied
2 (G4)	How satisfied are you with your health?	1	2	3	4	5

The following questions ask about **how much** you have experienced certain things in the last two weeks.

		Not at all	A little	A moderate amount	Very much	An extreme amount
3 (F1.4)	To what extent do you feel that physical pain prevents you from doing what you need to do?	1	2	3	4	5
4(F11.3)	How much do you need any medical treatment to function in your daily life?	1	2	3	4	5
5(F4.1)	How much do you enjoy life?	1	2	3	4	5
6(F24.2)	To what extent do you feel your life to be meaningful?	1	2	3	4	5

		Not at all	A little	A moderate amount	Very much	Extremely
7(F5.3)	How well are you able to concentrate?	1	2	3	4	5
8 (F16.1)	How safe do you feel in your daily life?	1	2	3	4	5
9 (F22.1)	How healthy is your physical environment?	1	2	3	4	5

The following questions ask about **how completely** you experience or were able to do certain things in the last two weeks.

		Not at all	A little	Moderately	Mostly	Completely
10 (F2.1)	Do you have enough energy for everyday life?	1	2	3	4	5
11 (F7.1)	Are you able to accept your bodily appearance?	1	2	3	4	5
12 (F18.1)	Have you enough money to meet your needs?	1	2	3	4	5
13 (F20.1)	How available to you is the information that you need in your day-to-day life?	1	2	3	4	5
14 (F21.1)	To what extent do you have the opportunity for leisure activities?	1	2	3	4	5

		Very poor	Poor	Neither	Good	Very good

				poor nor good		
15 (F9.1)	How well are you able to get around?	1	2	3	4	5

The following questions ask you to say how **good or satisfied** you have felt about various aspects of your life over the last two weeks.

		Very dissatisfied	Dissatisfied	Neither satisfied nor dissatisfied	Satisfied	Very satisfied
16 (F3.3)	How satisfied are you with your sleep?	1	2	3	4	5
17 (F10.3)	How satisfied are you with your ability to perform your daily living activities?	1	2	3	4	5
18(F12.4)	How satisfied are you with your capacity for work?	1	2	3	4	5
19 (F6.3)	How satisfied are you with yourself?	1	2	3	4	5
20(F13.3)	How satisfied are you with your personal relationships?	1	2	3	4	5
21(F15.3)	How satisfied are you with your sex life?	1	2	3	4	5
22(F14.4)	How satisfied are you with the support you get from your friends?	1	2	3	4	5
23(F17.3)	How satisfied are you with the conditions of your living place?	1	2	3	4	5
24(F19.3)	How satisfied are you with your access to health services?	1	2	3	4	5
25(F23.3)	How satisfied are you with your transport?	1	2	3	4	5

The following question refers to **how often** you have felt or experienced certain things in the last two weeks.

		Never	Seldom	Quite often	Very often	Always
26 (F8.1)	How often do you have negative feelings such as blue mood, despair, anxiety, depression?	1	2	3	4	5

Did someone help you to fill out this form?.....

How long did it take to fill this form out?.....

Do you have any comments about the assessment?

.....

.....

THANK YOU FOR YOUR HELP

Appendix 5. 15: WHOQOL-BREF questionnaire (Mandarin)

世界卫生组织生存质量测定简表（WHOQOL-BREF）

以下问题涉及您对生活质量、健康、或生活其他方面的看法。在我读出每一个问题的同时，请您做出选择。请选择最适当的答案。如果您暂时不能确定，则头脑中的第一反应往往是最正确的。

所有问题都请您按照自己的标准、愿望或自己的感觉来回答。注意所有问题都是您最近4周内的情况。

		很差	差	一般	好	很好
1.	您如何评价您的生活质量？	1	2	3	4	5

		非常不满意	不满意	一般	满意	很满意
2.	您对自己健康状况满意吗？	1	2	3	4	5

下列问题是有关您在过去4周中经历某些事情的感觉

		根本没有	有点	中等	很大	极其
3.	您因躯体疼痛而妨碍您去做需要做的事感到有多烦恼？	1	2	3	4	5
4.	您对保持日常生活的医学治疗的需求程度有多大？	1	2	3	4	5
5.	您觉得生活有乐趣吗？	1	2	3	4	5
6.	您觉得自己的生活有意义吗？	1	2	3	4	5

		根本不	有点	中等	很大	极其
7.	您能集中注意力吗？	1	2	3	4	5
8.	日常生活中您感觉安全吗？	1	2	3	4	5
9.	您的生活环境对健康好吗？	1	2	3	4	5

下列问题有关您在过去4周中做某些事情的能力。

		根本没有	有点	中等	多数有(能)	完全有(能)

10.	您有充沛的精力去应付日常生活吗？	1	2	3	4	5
11.	您认为自己的外形过得去吗？	1	2	3	4	5
12.	您有足够的钱来满足您的需要吗？	1	2	3	4	5
13.	在日常生活中，您需要的信息都能得到吗？	1	2	3	4	5
14.	您有机会进行休闲活动吗？	1	2	3	4	5

		很差	差	一般	好	很好
15.	您行动的能力如何？	1	2	3	4	5

		非常不满意	不满意	一般	满意	很满意
16.	您对自己的睡眠情况满意吗？	1	2	3	4	5
17.	您对自己做日常生活事情的能力满意吗？	1	2	3	4	5
18.	您对自己的工作能力满意吗？	1	2	3	4	5
19.	您对自己满意吗？	1	2	3	4	5
20.	您对自己的人际关系满意吗？	1	2	3	4	5
21.	您对自己的性生活满意吗？	1	2	3	4	5
22.	您对自己从朋友那里得到的支持满意吗？	1	2	3	4	5
23.	您对自己居住地的条件满意吗？	1	2	3	4	5
24.	您对您能享受到的卫生保健服务满意吗？	1	2	3	4	5
25.	您对自己的交通情况满意吗？	1	2	3	4	5

下列问题是关于您在过去4周中经历某些事情的频繁程度。

		从不	很少	有时	经常	总是
26.	您有消极感受吗？如情绪低	1	2	3	4	5

	落、绝望、焦虑、忧郁。					

您需要对以上评估进行解释吗?

_____

_____

[下列表格应在访谈结束后完成]

		领域分计算式	原始分值	转换分值	
				4-20	0-100
27.	领域 **1**	(6-Q3) + (6-Q4) + Q10 + Q15 + Q16 + Q17 + Q18 + + + + +	a. =	b:	c:
28.	领域 **2**	Q5 + Q6 + Q7 + Q11 + Q19 + (6-Q26) + + + + +	a. =	b:	c:
29.	领域 **3**	Q20 + Q21 + Q22 + +	a. =	b:	c:
30.	领域 **4**	Q8 + Q9 + Q12 + Q13 + Q14 + Q23 + Q24 + Q25 + + + + + + +	a. =	b:	c:

* 参阅操作手册, 13-15页

Curtin University

School of Pharmacy

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Webcurtin.edu.au

INFORMATION SHEET FOR PATIENTS

Development and Evaluation of a Pharmacist Diabetes Management Tool: a Mixed Methods Study

What is this study about? If you agree to participate in this study, you will be asked to sign the Participant Consent Form. You will then be allocated to either one of the two arms. Pharmacists from each centre will be given six brown envelopes labelled with unique identification numbers. Each brown envelope will contain a note which will reveal the arm you will be assigned to. This study will be conducted over 6 months. You will interviewed on questions regarding your family history, medications, medical history, lifestyle, relationship, financial and on your living environment. You will then be asked to visit the pharmacist who will dispense your medications and who will monitor your diabetes and help you to self-manage in order to keep diabetes in control. In addition, pharmacists would access your medical record to obtain information relevant to the study. You will be asked to measure your blood glucose levels every two days and blood pressure levels every month. You can do it either at home or at the pharmacy where you will be seen.

Why have you been asked to take part? You are eligible to participate in this study because you fit the conditions of this study. The criteria for participations are patients with Type 2 Diabetes Mellitus whose HbA1c is more than 8% (63.9mmol/mol) and who has one or more disease conditions.

Do you have to take part? The answer is no! Participation is voluntary. You have the option of withdrawing before the study commences or discontinuing after data collection has started without penalty. If you decide not to participate, it will not affect your relationship with the pharmacist or other healthcare professionals. If you withdraw, any data collected from you up to your withdrawal will still be used for the study. Your refusal to participate or withdrawal will not affect any medical or health benefits to which you are otherwise entitled.

Will your participation in the study be kept confidential? Yes. The identity of each participant will not be revealed to other participants. Any information about your identity will not appear in the thesis or publications. Any extracts from your comments will be entirely anonymous.

What will happen to the information which you give? The data will be kept confidential for the duration of the study and up to 25 years post completion of the study. On completion of the thesis, they will be retained for a further six months and then destroyed.

What will happen to the results? The results will be presented in the thesis and publications. They will be seen by my supervisors, a second marker and the external examiner. The thesis may be read by future students in the course.

What are the possible risks to you in taking part? You may feel inconvenient as you will be visiting the pharmacist every month. It may cause some distress because consultation time may be longer compared previously.

Will I benefit from the study? This study aims to further medical knowledge and may improve future delivery of diabetes care. You will be shown how to manage your disease and correct administration of your medication. This may lead to better control of your sugar, blood pressure and cholesterol targets. This in turn will prevent diabetes related complications. You will be informed the results of this study.

Will taking part in this study cost me anything, and will I be paid? You will not be paid to take part in this study, however, your participation in this study will not cost you anything.

Who has reviewed this study? Approval must be given by the Faculty of Health and Science, Curtin University, Bentley, Western Australia before the survey takes place. Curtin University conducts research in accordance with the *National Statement on Ethical Conduct in Human Research.* Approval must also be given by Malaysian Medical Research and Ethics Committee at the Ministry of Health.

Any further queries? When you have read this information, the pharmacist will discuss it with you and address any queries you may have. If you would like to know more at any stage, please do not hesitate to contact him/her. You may also contact the researchers Shamala at shamala.ayadurai@postgrad.curtin.edu.au or Dr.Laetitia Hattingh at L.Hattingh@curtin.edu.au

Curtin University Human Research Ethics Committee (HREC) has approved this study (HR214/2015). The Malaysian Medical Research and Ethics Committee has also approved the study (NMRR-15-1831-28307). Should you wish to discuss the study with someone not directly involved, in particular, any matters concerning the conduct of the study or your rights as a participant, or you wish to make a confidential complaint, you may contact the Ethics Officer on (08) 9266 9223 or the Manager, Research Integrity on (08) 9266 7093 or email hrec@curtin.edu.au. You can also contact the Secretary, Medical Research & Ethics Committee, Ministry of Health Malaysia, at telephone number 03-2287 4032

Appendix 5. 17: Phase Three consent form for patients (English)

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Project Title: Development and Evaluation of a Pharmacist Diabetes Management Tool: a Mixed Methods Study

CONSENT FORM FOR PATIENTS

By signing below I confirm the following:

- I have been given oral and written information for the above study and have read and understood the information given.
- I have had sufficient time to consider participation in the study and have had the opportunity to ask questions and all my questions have been answered satisfactorily.
- I understand that my participation is voluntary and I can at any time free to withdraw from the study without giving a reason and this will in no way affect my future treatment. I am not taking part in any other research study at this time. I understand the risks and benefits, and I freely give my informed consent to participate under the conditions stated. I understand that I must follow the study doctor's (investigator's) instructions related to my participation in the study.
- I understand that study staff, qualified monitors and auditors, the sponsor or its affiliates, and governmental or regulatory authorities, have direct access to my medical record in order to make sure that the study is conducted correctly and the data are recorded correctly. All personal details will be treated as STRICTLY CONFIDENTIAL
- I will receive a copy of this subject information/informed consent form signed and dated to bring home.
- I agree/disagree* for my family doctor to be informed of my participation in this study.
  *(*delete which is not applicable)*

Subject:

Signature: I/C number:

Name: Date:

Investigator conducting informed consent:

Signature: I/C number:

Name: Date:

Impartial witness: *(Required if subject is illiterate and contents of participant information sheet is orally communicated to subject)*

Signature:	I/C number:
Name:	Date:

Curtin University Human Research Ethics Committee (HREC) has approved this study (HR214/2015). The Malaysian Medical Research and Ethics Committee has also approved the study (NMRR-15-1831-28307). Should you wish to discuss the study with someone not directly involved, in particular, any matters concerning the conduct of the study or your rights as a participant, or you wish to make a confidential complaint, you may contact the Ethics Officer on (08) 9266 9223 or the Manager, Research Integrity on (08) 9266 7093 or email hrec@curtin.edu.au. You can also contact the Secretary, Medical Research & Ethics Committee, Ministry of Health Malaysia, at telephone number 03-2287 4032

Appendix 5. 18: Phase Three participant information sheet (Bahasa Malaysia)

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RISALAH MAKLUMAT PESERTA

Tajuk: *Development and Evaluation of a Pharmacist Diabetes Management Tool: a Mixed Methods Study*

Apakah tujuan penyelidikan ini dilakukan? Tujuan penyelidikan ini dilakukan adalah untuk menilai suatu prosedur intervensi diabetes atau penyakit kencing manis. Fungsi prosedur intervensi diabetes adalah untuk memudahkan pegawai Farmasi memberi cadangan penambahbaikan rawatan anda berdasarkan panduan klinikal diabetes sedia ada kepada pegawai perubatan. Prosedur intervensi diabetes ini diharap membantu anda mencapai sasaran gula, darah tinggi and kolesterol anda. Penyelidikan ini diperlukan kerana diabetes adalah penyakit yang kompleks dan pelbagai faktor terlibat dalam merawat dan mencegah komplikasi penyakit tersebut. Sejumlah 120 pesakit seperti anda daripada negeri Johor di Malaysia akan menyertai penyelidikan ini. Tempoh pembabitan anda dianggarkan selama enam bulan.

Apakah yang terjadi sekiranya saya bersetuju untuk menyertai penyelidikan ini?

Jika anda bersetuju, anda akan diminta untuk menandatangani borang persetujuan/keizinan peserta. Pegawai farmasi anda akan membuka satu sampul surat yang mengandungi arahan berkenaan kumpulan yang anda bakal diperuntukkan. Anda akan dimasukkan ke kumpulan A atau Kumpulan B. Anda perlu rakamkan sendiri bacaan pada meter glukosa dan bacaan pada meter tekanan darah. Anda boleh rakamkan di rumah atau di Farmasi di mana kajian dikendalikan. Kekerapan rakaman ini adalah setiap hari atau sekali dalam dua hari untuk meter glukosa dan sekali sebulan untuk rakaman meter tekanan darah. Anda diminta membuat lawatan susulan ke Farmasi setiap bulan sekali atau seperti diarahkan pegawai farmasi untuk tempoh enam bulan. Pegawai farmasi akan membantu anda mencapai sasaran gula, darah tinggi dan juga kolesterol. Seterusnya ini akan mencegah kerosakkan tisu dan organ seperti jantung, buah pinggang dan sistem saraf.

Kenapakah anda dijemput untuk menyertai penyelidikan ini? Anda telah dijemput untuk menyertai penyelidikan ini kerana anda memenuhi syarat kajian. Syaratnya adalah pesakit kencing manis yang mempunyai bacaan HbA1c lebih daripada 8% (63.9mmol/mol) dan mempunyai satu atau lebih penyakit selain kencing manis.

Perlukah anda menyertai penyelidikan ini? Penyertaan anda dalam penyelidikan ini adalah secara sukarela. Anda tidak perlu menyertai penyelidikan ini jika anda tidak mahu. Anda juga mempunyai hak untuk tidak menjawab mana-mana soalan yang anda tidak mahu jawab. Anda juga boleh menarik diri daripada penyelidikan ini pada bila-bila masa sahaja. Jika anda menarik diri, segala maklumat yang telah diperolehi sebelum anda menarik diri tetap akan digunakan dalam penyelidikan ini. Jika anda tidak mahu menyertai ataupun menarik diri dari penyelidikan ini, tindakan anda tidak akan menjejaskan segala hak dan keistimewaan perubatan kesihatan yang selayaknya anda terima.

Adakah maklumat perubatan saya akan dirahsiakan? Segala maklumat anda yang diperolehi dalam penyelidikan ini akan disimpan dan dikendalikan secara sulit untuk tempoh 25 tahun, bersesuaian dengan peraturan-peraturan dan/ atau undang-undang yang

berkenaan. Sekiranya hasil penyelidikan ini diterbitkan atau dibentangkan kepada orang ramai, identiti anda tidak akan didedahkan tanpa kebenaran anda terlebih dahulu. Pihak-pihak tertentu seperti individu yang terlibat dalam penyelidikan dan rawatan perubatan anda, boleh memeriksa dan membuat salinan laporan perubatan anda jika berkenaan dan diperlukan.

Apakah akan terjadi kepada hasil daripada kajian ini? Hasil daripada kajian ini akan dibentangkan dalam thesis and mungkin di terbitkan. Hasil kajian ini juga akan dibaca oleh penyelia saya dan para penuntut yang lain.

Apakah risiko menyertai penyelidikan ini? Oleh kerana anda perlu datang ke Jabatan Farmasi sekali setiap bulan, ia mungkin menyusahkan anda. Anda mungkin rasa tertekan kerana tempoh konsultasi dengan pegawai Farmasi mungkin lebih lama jika dibandingkan sebelum ini.

Apakah manfaatnya saya menyertai kajian ini? Kajian ini akan memberi manfaat kepada anda dari segi pengambilan, pengurusan dan penyimpanan ubat yang betul. Anda juga akan didedahkan tentang risiko penyakit diabetes dan bagaimana untuk mencegah kerosakkan tisu dan organ anda. Segala maklumat yang diperolehi daripada penyelidikan ini akan dapat membantu dalam penambahbaikan kaedah rawatan peserta lain yang menghidap penyakit yang sama dengan anda. Keputusan kajian ini akan dimaklumkan kepada anda setelah tamat kajian ini.

Perlukah saya membayar untuk menyertai kajian ini? Anda tidak akan dibayar untuk menyertai kajian ini walaubagaimanapun penyertaan anda dalam kajian ini adalah percuma dan tidak melibatkan apa-apa kos kewangan.

Siapakah yang telah menyemak dan meluluskan kajian ini? Kelulusan perlu diperolehi dari *Faculty of Health and Science, Curtin University, Bentley, Western Australia* sebelum kajian ini dimulakan. Kelulusan juga diperlukan dari Jawatankuasa etika & penyelidikan perubatan, Kementerian Kesihatan Malaysia.

Siapakah yang perlu saya hubungi sekiranya saya mempunyai sebarang pertanyaan? Anda boleh menghubungi Pegawai Farmasi penyelidikan ini di Klinik Kesihatan anda, atau Pn. Shamala Ayadurai, shamala.ayadurai@postgrad.curtin.edu.au sekiranya anda mempunyai sebarang pertanyaan mengenai kajian ini. Jika anda mempunyai sebarang pertanyaan berkaitan dengan hak-hak anda sebagai peserta dalam penyelidikan ini, sila hubungi: Setiausaha, Jawatankuasa Etika & Penyelidikan Perubatan, Kementerian Kesihatan Malaysia, melalui talian telefon 03-2287 4032.

Curtin University Human Research Ethics Committee (HREC) has approved this study (HR214/2015). The Malaysian Medical Research and Ethics Committee has also approved the study (NMRR-15-1831-28307). Should you wish to discuss the study with someone not directly involved, in particular, any matters concerning the conduct of the study or your rights as a participant, or you wish to make a confidential complaint, you may contact the Ethics Officer on (08) 9266 9223 or the Manager, Research Integrity on (08) 9266 7093 or email hrec@curtin.edu.au. You can also contact the Secretary, Medical Research & Ethics Committee, Ministry of Health Malaysia, at telephone number 03-2287 4032

Appendix 5. 19: Phase Three participant consent form (Bahasa Malaysia)

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Tajuk Penyelidikan: ***Development and Evaluation of a Pharmacist Diabetes Management Tool: a Mixed Methods Study***

BORANG PERSETUJUAN/ KEIZINAN PESERTA

Dengan menandatangani di bawah, saya mengesahkan bahawa :

- Saya telah diberi maklumat tentang penyelidikan di atas secara lisan dan bertulis and saya telah membaca dan memahami segala maklumat yang diberikan dalam risalah ini.
- Saya telah diberikan masa yang secukupnya untuk mempertimbangkan penyertaan saya dalam penyelidikan ini dan telah diberi peluang untuk bertanyakan soalan dan semua persoalan saya telah dijawab dengan sempurna dan memuaskan.
- Saya juga faham bahawa penyertaan saya adalah secara sukarela dan pada bila-bila masa saya bebas menarik diri daripada penyelidikan ini tanpa harus memberi sebarang alasan dan ianya sama sekali tidak akan menjejaskan rawatan perubatan saya pada masa akan datang. Saya tidak mengambil bahagian dalam mana-mana penyelidikan lain pada masa ini. Saya juga memahami tentang risiko dan manfaat penyelidikan ini dan saya secara sukarela memberi persetujuan untuk menyertai penyelidikan ini di bawah syarat-syarat yang telah dinyatakan di atas. Saya faham saya harus mematuhi nasihat dan arahan yang berkaitan dengan penyertaan saya dalam penyelidikan ini daripada Pegawai Farmasi penyelidikan (penyelidik) .
- Saya faham bahawa kakitangan penyelidikan, pemantau dan juruaudit terlatih , dan pihak berkuasa kerajaan atau undang-undang, mempunyai akses langsung dan boleh menyemak laporan perubatan saya bagi memastikan penyelidikan ini dijalankan dengan betul dan data direkodkan dengan betul. Segala maklumat dan data peribadi akan dianggap sebagai SULIT.
- Saya akan menerima satu salinan 'Risalah Maklumat Peserta dan Borang Persetujuan atau Keizinan Peserta' yang telah lengkap dengan tarikh dan tandatangan untuk dibawa pulang ke rumah.
- Saya bersetuju/ tidak bersetuju* untuk doktor yang merawat keluarga saya diberitahu tentang penyertaan saya dalam penyelidikan ini.
  *(*Potong mana yang tidak berkenaan)*

Subjek :

Tandatangan: Nombor K/P:

Nama: Tarikh :

Penyelidik yang mengendalikan proses menandatangani borang keizinan:

Tandatangan: Nombor K/P:

Nama: Tarikh :

Saksi tidak-berpihak/adil: *(Diperlukan; jika subjek adalah buta huruf dan kandungan risalah maklumat peserta disampaikan secara lisan kepada subjek)*

Tandatangan: Nombor K/P:

Nama: Tarikh :

Curtin University Human Research Ethics Committee (HREC) has approved this study (HR214/2015). The Malaysian Medical Research and Ethics Committee has also approved the study (NMRR-15-1831-28307). Should you wish to discuss the study with someone not directly involved, in particular, any matters concerning the conduct of the study or your rights as a participant, or you wish to make a confidential complaint, you may contact the Ethics Officer on (08) 9266 9223 or the Manager, Research Integrity on (08) 9266 7093 or email hrec@curtin.edu.au. You can also contact the Secretary, Medical Research & Ethics Committee, Ministry of Health Malaysia, at telephone number 03-2287 4032

Appendix 5. 20: 8- items modified Morisky medication adherence scale (English)

8-items Modified Morisky Medication Adherence Scale

No.	Questions	Yes (Y) No(N) (Please circle)											
		Visit 1		Visit 2		Visit 3		Visit 4		Visit 5		Visit 6	
1.	Do you sometimes forget to take your pill?	Y=0	N=1	Y=0	N=1	Y=0	N=1	Y=0	N=1	Y=0	N=1	Y=0	N=1
2.	People sometimes miss taking medications for reasons other than forgetting. Thinking over the past two weeks, were there any days when you did not take your medicine?	Y=0	N=1	Y=0	N=1	Y=0	N=1	Y=0	N=1	Y=0	N=1	Y=0	N=1
3.	Have you ever cut back or stopped taking your medication without telling your doctor because you felt worse when you took it?	Y=0	N=1	Y=0	N=1	Y=0	N=1	Y=0	N=1	Y=0	N=1	Y=0	N=1
4.	When you travel or leave home, do you sometimes forget to bring along your medications?	Y=0	N=1	Y=0	N=1	Y=0	N=1	Y=0	N=1	Y=0	N=1	Y=0	N=1
5.	Did you take your medicine yesterday?	Y=1	N=0	Y=1	N=0	Y=1	N=0	Y=1	N=0	Y=1	N=0	Y=1	N=0
6.	When you feel like your disease is under control, do you sometimes stop taking your medicine?	Y=0	N=1	Y=0	N=1	Y=0	N=1	Y=0	N=1	Y=0	N=1	Y=0	N=1
7.	Taking medicine every day is a real inconvenience for some people. Do you ever get hassled about sticking to your treatment plan?	Y=0	N=1	Y=0	N=1	Y=0	N=1	Y=0	N=1	Y=0	N=1	Y=0	N=1
8.	How often do you have difficulty remembering to take all your medication?												
	Never/Rarely	1		1		1		1		1		1	
	Once in while	0.75		0.75		0.75		0.75		0.75		0.75	
	Sometimes	0.5		0.5		0.5		0.5		0.5		0.5	
	Usually	0.25		0.25		0.25		0.25		0.25		0.25	
	All the time	0		0		0		0		0		0	
Score	**Total score**												
	Low adherence=<6; Medium adherence=(6 to <8); High adherence=8	___ /8		___ /8		___ /8		___ /8		___ /8		___ /8	

Appendix 5. 21: 8-items modified Morisky medication adherence scale (Bahasa Malaysia)

8-items Modified Morisky Medication Adherence Scale: Versi Bahasa Malaysia

No.	Soalan	Ya (Y) Tidak (N) (Sila bulatkan pada jawapan berkenaan)											
		Lawatan 1		Lawatan ke-2		Lawatan ke-3		Lawatan ke-4		Lawatan ke-5		Lawatan ke-6	
1.	Pernahkan anda terlupa untuk mengambil ubat anda?	Y=0	N=1	Y=0	N=1	Y=0	N=1	Y=0	N=1	Y=0	N=1	Y=0	N=1
2.	Selain terlupa, terdapat juga alasan-alasan lain yang menyebabkan pesakit tidak dapat atau terlepas mengambil ubat mereka. Sejak dua minggu yang lepas, pernahkah anda terlepas atau tidak dapat mengambil ubatan anda?	Y=0	N=1	Y=0	N=1	Y=0	N=1	Y=0	N=1	Y=0	N=1	Y=0	N=1
3.	Adakah anda pernah berhenti atau mengurangkan pengambilan ubat tanpa memberitahu doktor terlebih dahulu jika anda mendapati ubat itu memberi kesan yang tidak diingini selepas menggunakannya?	Y=0	N=1	Y=0	N=1	Y=0	N=1	Y=0	N=1	Y=0	N=1	Y=0	N=1
4.	Apabila anda melancong atau keluar dari rumah, pernahkan anda terlupa untuk membawa bersama ubat anda?	Y=0	N=1	Y=0	N=1	Y=0	N=1	Y=0	N=1	Y=0	N=1	Y=0	N=1
5.	Adakah anda mengambil ubat anda semalam?	Y=1	N=0	Y=1	N=0	Y=1	N=0	Y=1	N=0	Y=1	N=0	Y=1	N=0
6.	Apabila anda merasakan penyakit anda terkawal, adakah kadang kala anda akan berhenti mengambil ubat?	Y=0	N=1	Y=0	N=1	Y=0	N=1	Y=0	N=1	Y=0	N=1	Y=0	N=1
7.	Pengambilan ubat setiap hari menyebabkan kesulitan terhadap sesetengah pesakit. Pernahkan anda mengalami kesulitan untuk mengikuti jadual pengambilan ubatan anda?	Y=0	N=1	Y=0	N=1	Y=0	N=1	Y=0	N=1	Y=0	N=1	Y=0	N=1
8.	Berapa kerapkah anda mengalami kesukaran dalam mengingati pengambilan semua ubat anda?												
	Tidak pernah	1		1		1		1		1		1	
	Jarang-jarang	0.75		0.75		0.75		0.75		0.75		0.75	
	Kadang-kadang	0.5		0.5		0.5		0.5		0.5		0.5	
	Selalu/sering kali	0.25		0.25		0.25		0.25		0.25		0.25	
	Sepanjang masa	0		0		0		0		0		0	

Appendix 5. 22: Naranjo adverse drug reaction probability scale

Naranjo Adverse Drug Reaction Probability Scale

No	Questions	Yes	No	Do not know
1.	Are there previous *conclusive* reports on this reaction?	+1	0	0
2.	Did the adverse event occur after the suspected drug was administered?	+2	-1	0
3.	Did the adverse reaction improve when the drug was discontinued or a *specific* antagonist was administered?	+1	0	0
4.	Did the adverse reaction reappear when the drug was readministered?	+2	-1	0
5.	Are there alternative causes (other than the drug) that could have on their own caused the reaction?	-1	+2	0
6.	Did the reaction reappear when a placebo was given?	-1	+1	0
7.	Was the blood detected in the blood (or other fluids) in concentrations known to be toxic?	+1	0	0
8.	Was the reaction more severe when the dose was increased or less severe when the dose was decreased?	+1	0	0
9.	Did the patient have a similar reaction to the same or similar drugs in *any* previous exposure?	+1	0	0
10.	Was the adverse event confirmed by any objective evidence?	+1	0	0
	Definite=>9; Probable=5 to 8; Possible=1 to 4; Doubtful = 0			

The Naranjo adverse drug reaction (ADR) probability scale. The Naranjo criteria classify the probability that an adverse event is related to drug therapy based on a list of weighted questions, which examine factors such as the temporal association of drug administration and event occurrence, alternative causes for the event, drug levels, dose – response relationships and previous patient experience with the medication. The ADR is assigned to a probability category from the total score as follows: *definite* if the overall score is 9 or greater, *probable* for a score of 5-8, *possible* for 1-4 and *doubtful* if the score is 0. The Naranjo criteria do not take into account drug-drug interactions. Drugs are evaluated individually for causality, and points deducted if another factor may have resulted in the adverse event, thereby weakening the causal association.

Ref: Naranjo CA et al. A method for estimating the probability of adverse drug reactions. Clin Pharmacol Ther 1981; 30: 239245.

Appendix 5. 23: Data collection form

Data collection form

1. Demographic Data					
Visit No:					
IC/DOB:					
Gender:	☐F			☐M	
Race:	☐M	☐I		☐C	☐OTHERS
Family History of Diabetes:	☐Y			☐N	
Drug Allergies:	☐Y			☐N	
No. of Comorbidities. Specify....					

2. Medication Adherence Data	
8 items modified Morisky medication adherence scale (0-8)	
Framingham risk score	

3. Lab Data	
HbA1C	
LDL	
TG	
Creatinine	
No of hypoglycaemia like symptoms during the past 4 weeks	

4.Drug Profile					
Lipid Lowering drugs	☐Statin		☐Gemfibrozil		☐Ezetimibe
Antihypertensive drugs	☐ACEI	☐ARB	☐BetaBlocker	☐AlphaBlocker	☐Diuretic ☐CCB
Antiplatelet drugs		☐Aspirin	☐Clopidogrel		
Insulin	☐Rapid	☐Short	☐Intermediate	☐Long	☐Pre-Mixed
Oral hypoglycaemic agents	☐Biguanides	☐Sulfonylureas ☐Thiazolidinediones	☐Acarbose ☐GLPagonist	☐SGLT-2inhibitor ☐DPPIVinhibitor	
Other Medications	Specify:				
Non-prescription drugs (eg traditional, herbal drugs)	☐Y			☐N	
	Specify:				

5. Adverse Drug Reaction Detected			
Naranjo score (0-13)	Drug Involved	Visit Number	Description (eg. rashes, itchiness, swollen face, difficulty breathing etc.)

6. Pharmacist compliance to Diabetes Guidelines		
Factor	**Indicator**	**Please tick (/)**
Statin	1. Achieve targets: LDL<2.6 mmol/L, TG<1.7 mmol/L.	
	2. Statin initiation in patients with CVD	
	3. Statin initiation in patients **> 40 years** old without CVD	
Insulin/Glycaemic control	1. Insulin initiation if glycaemic control not achieved despite being on two or more oral hypoglycaemic agents	
	2. Management of hypoglycaemia	
	3. Self-monitoring of blood glucose Malaysia	
	4. Initiate/continue metformin if not contraindicated	
Blood pressure	1. BP target: ≤135/75	
	2. ACEI/ARB initiation in patients with/without microalbuminuria /proteinuria	
	3. Reduce sodium intake (<2400mg sodium/day; 6g/1 teaspoon/day)	
	4. Take one or more antihypertensive at bedtime	
Lifestyle	1. Exercise: 30 mins walking (or equivalent) 5 or more days/week (total ≥150 min/week)	
	2. Weight loss: Caucasian (BMI< 25 kg/m2), Asian (BMI ≤ 23 kg/m2)	
	3. Smoking cessation	
	4. Waist circumference: Caucasian (<94 cm in men,<80 cm in women, Asian (≤90 cm in men,≤80cm in women)	
	5. Alcohol intake: ≤2 standard drinks (20 g) per day for men	
	6. Management of stress & diabetes related distress	
	7. Foot care	
	8. Diet advice using plate model	
	9. Annual eye assessment	
	10. Address sleep hygiene	
Education	1. Knowledge & understanding of medicine	
	2. Medicine storage	
	3. Medication optimisation during fasting month for Muslims and other religious arms	
Cardiovascular Risk	1. Aspirin therapy as secondary prevention in those with diabetes with history of CVD	

6. Pharmacist compliance to Diabetes Guidelines		
Factor	**Indicator**	**Please tick (/)**
	2. Use of Framingham risk calculator to calculate CVD risk and educate patients	
	3. Aspirin therapy (75mg-162mg/day) as primary prevention to decrease CVD risk (10 year risk>10%, Framingham) (patients >65 years old)	

Medication	**Medicine Related Problems**	**No. of problems**
	1.Unnecessary Drug Therapy	
	2.Needs Additional Drug Therapy	
	3.Ineffective Drug	
	4.Dosage Too Low	
	5.Adverse Drug Reaction	
	6.Dosage Too High	
	7.Non-adherence	

Medication	**Causes of Nonadherence**		
	8. Cannot Afford Drug Product	☐Y	☐N
	9. Does Not Understand Instructions	☐Y	☐N
	10. Patient Prefers Not To Take	☐Y	☐N
	11. Patient Forgets To Take	☐Y	☐N
	12. Drug Product Not Available	☐Y	☐N
	13. Cannot Swallow or Administer Drug	☐Y	☐N

Medication	**Collaboration with Patient: Interventions to Resolve Non adherence Problems**		
	14. Patient education to clarify instructions and remove barriers	☐Y	☐N
	15. Reinitiated drug therapy	☐Y	☐N
	16. Changed product	☐Y	☐N
	17. Initiated monitoring plan	☐Y	☐N
	18. Provided patient with a pill reminder device	☐Y	☐N
	19. Discontinued drug therapy	☐Y	☐N

Medication	**Collaboration with doctor: Interventions to Resolve Non adherence**	**No.interventions**
	20. Changed Drug Product	
	21. Reinitiated Drug Therapy	
	22. Discontinued Drug Therapy	
	23. Changed Dosage	
	24. Initiated Monitoring Plan	
	25. Not resolvable	
	26. Add drug	

Appendix 5. 24: Simpler™ tool hand-out for Phase Three pharmacists

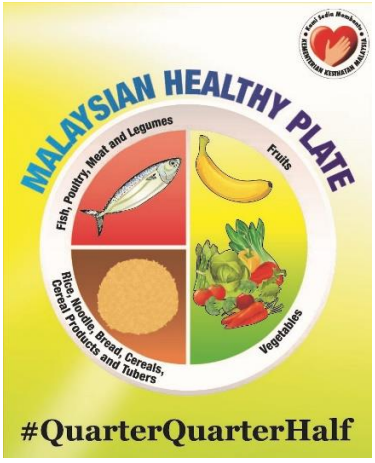
Simpler™ Pharmacist Diabetes Management Tool (page 1)

S=Statin	• **Statin** initiation in patients with CVD • Achieve targets: **LDL<2.6 mmol/L**, **TG<1.7 mmol/L**. • Statin initiation in patients **> 40 years** old without CVD
I=Insulin/Glycaemic control	• **Insulin** initiation if glycaemic control not achieved despite being on two or more oral hypoglycaemic agents • Target of **HbA1c ≤ 7% (53mmol/mol)** if no other complications • Management of **hypoglycaemia** • **Self-monitoring** of blood glucose Malaysia (4.4-6.1 mmol/L fasting); Malaysia CPG (4.4-8 mmol/L-2h postprandial) • Aim a difference of -1% for **HbA1c** if above target • Initiate/continue **metformin** if not contraindicated
M=Medication	• Assess **medicine related problems** • Review medication adherence using 8-items modified **Morisky** medication adherence scale
P=Blood Pressure	• BP target: **≤135/75** • **ACEI/ARB** initiation in patients with/without microalbuminuria /proteinuria • **Reduce sodium** intake (<2400mg sodium/day; 6g/1 teaspoon/day) • One or more antihypertensive medicine to be taken at **bedtime**
L=Lifestyle	• **Exercise:** 30 mins walking (or equivalent) 5 or more days/week (total ≥150 min/week) • **Weight loss**: Caucasian (BMI< 25 kg/m2), Asian (BMI ≤ 23 kg/m2) • **Smoking cessation** • **Waist circumference**:Caucasian (<94 cm in men,<80 cm in women, Asian (**≤90 cm in men,≤80cm in women**) • **Alcohol** intake: ≤2 standard drinks (20 g) per day for men & women • Management of **stress** & diabetes related distress • **Erectile dysfunction**: recommend PDE-5 inhibitor as first line therapy for male patients • **Foot care** • Diet advice using **plate model** • Annual **eye** assessment • Address **sleep** hygiene
E=Education	• **Knowledge** & **understanding** of medicine • Medicine **storage** • Medication optimisation during **fasting** month for Muslims and other religious arms
R=Cardiovascular Risk	• **Aspirin** therapy as secondary prevention in those with diabetes with history of CVD • Use of **Framingham risk calculator** to calculate CVD risk and educate patients • Aspirin therapy (75mg-162mg/day) as primary prevention to decrease CVD risk (10 year risk>10%, Framingham) (patients **>65 years** old)

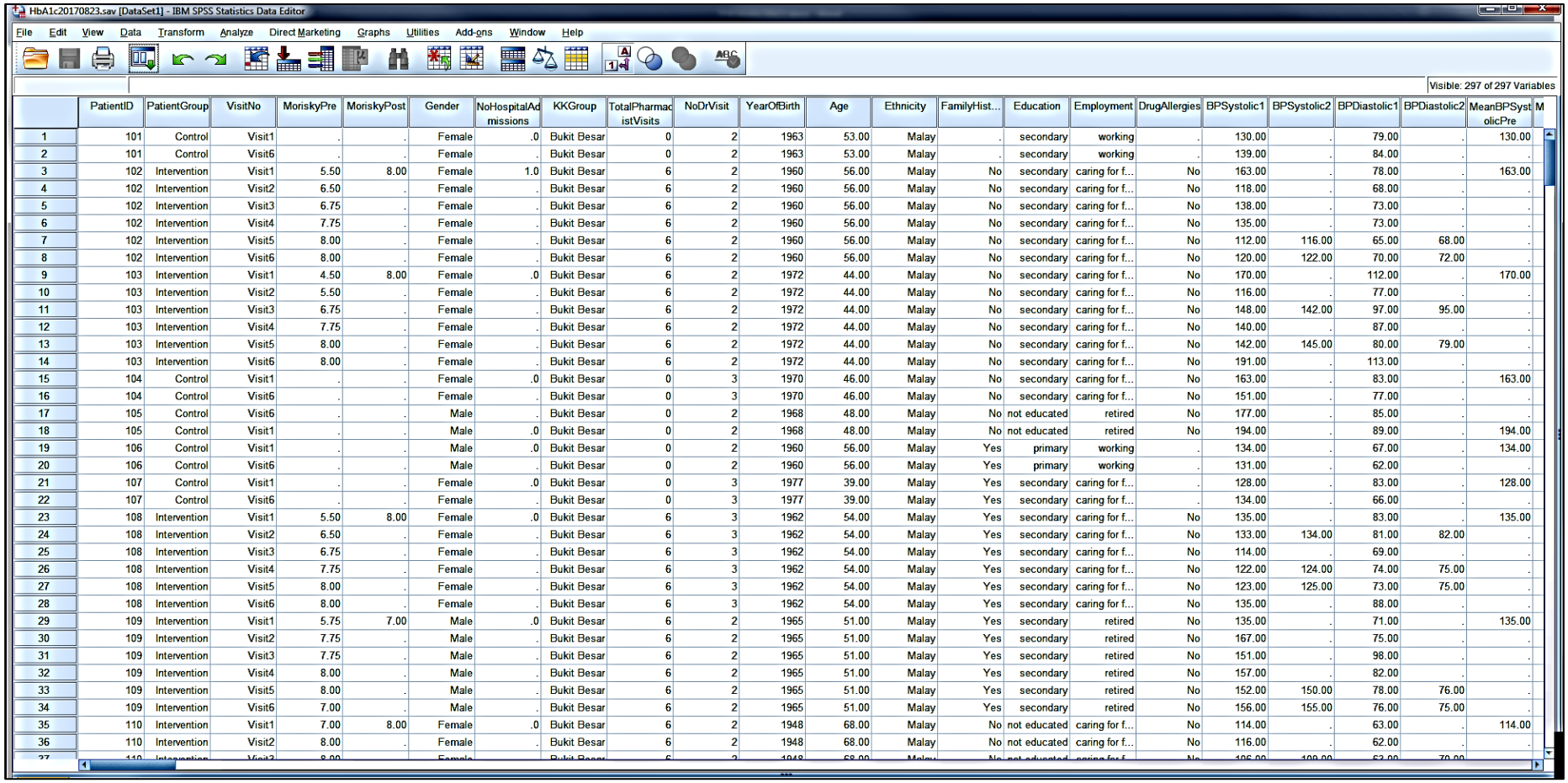
8-items Modified Morisky Medication Adherence Scale (page 2)

No.	Questions	Yes/No (Please circle)	
1.	Do you sometimes forget to take your pill?	Y=0	N=1
2.	People sometimes miss taking medications for reasons other than forgetting. Thinking over the past two weeks, were there any days when you did not take your medicine?	Y=0	N=1
3.	Have you ever cut back or stopped taking your medication without telling your doctor because you felt worse when you took it?	Y=0	N=1
4.	When you travel or leave home, do you sometimes forget to bring along your medications?	Y=0	N=1
5.	Did you take your medicine yesterday?	Y=1	N=0
6.	When you feel like your disease is under control, do you sometimes stop taking your medicine?	Y=0	N=1
7.	Taking medicine every day is a real inconvenience for some people. Do you ever get hassled about sticking to your treatment plan?	Y=0	N=1
8.	How often do you have difficulty remembering to take all your medication?	Never/Rarely	1
		Once in while	0.75
		Sometimes	0.5
		Usually	0.25
		All the time	0
Score	Low adherence=<6; Medium adherence=(6 to <8); High adherence=8	Total	___ /8

Plate Model



Appendix 5. 25: Excerpt of SPSS data set for Phase Three data



HbA1c20170823.sav [DataSet1] - IBM SPSS Statistics Data Editor

File Edit View Data Transform Analyze Direct Marketing Graphs Utilities Add-ons Window Help

Visible: 297 of 297 Variables

	PatientID	PatientGroup	VisitNo	MoriskyPre	MoriskyPost	Gender	NoHospitalAdmissions	KKGroup	TotalPharmacistVisits	NoDrVisit	YearOfBirth	Age	Ethnicity	FamilyHist...	Education	Employment	DrugAllergies	BPSystolic1	BPSystolic2	BPDiastolic1	BPDiastolic2	MeanBPSystolicPre	M
1	101	Control	Visit1	.	.	Female	.0	Bukit Besar	0	2	1963	53.00	Malay	.	secondary	working	.	130.00	.	79.00	.	130.00	
2	101	Control	Visit6	.	.	Female	.	Bukit Besar	0	2	1963	53.00	Malay	.	secondary	working	.	139.00	.	84.00	.	.	
3	102	Intervention	Visit1	5.50	8.00	Female	1.0	Bukit Besar	6	2	1960	56.00	Malay	No	secondary	caring for f...	No	163.00	.	78.00	.	163.00	
4	102	Intervention	Visit2	6.50	.	Female	.	Bukit Besar	6	2	1960	56.00	Malay	No	secondary	caring for f...	No	118.00	.	68.00	.	.	
5	102	Intervention	Visit3	6.75	.	Female	.	Bukit Besar	6	2	1960	56.00	Malay	No	secondary	caring for f...	No	138.00	.	73.00	.	.	
6	102	Intervention	Visit4	7.75	.	Female	.	Bukit Besar	6	2	1960	56.00	Malay	No	secondary	caring for f...	No	135.00	.	73.00	.	.	
7	102	Intervention	Visit5	8.00	.	Female	.	Bukit Besar	6	2	1960	56.00	Malay	No	secondary	caring for f...	No	112.00	116.00	65.00	68.00	.	
8	102	Intervention	Visit6	8.00	.	Female	.	Bukit Besar	6	2	1960	56.00	Malay	No	secondary	caring for f...	No	120.00	122.00	70.00	72.00	.	
9	103	Intervention	Visit1	4.50	8.00	Female	.0	Bukit Besar	6	2	1972	44.00	Malay	No	secondary	caring for f...	No	170.00	.	112.00	.	170.00	
10	103	Intervention	Visit2	5.50	.	Female	.	Bukit Besar	6	2	1972	44.00	Malay	No	secondary	caring for f...	No	116.00	.	77.00	.	.	
11	103	Intervention	Visit3	6.75	.	Female	.	Bukit Besar	6	2	1972	44.00	Malay	No	secondary	caring for f...	No	148.00	142.00	97.00	95.00	.	
12	103	Intervention	Visit4	7.75	.	Female	.	Bukit Besar	6	2	1972	44.00	Malay	No	secondary	caring for f...	No	140.00	.	87.00	.	.	
13	103	Intervention	Visit5	8.00	.	Female	.	Bukit Besar	6	2	1972	44.00	Malay	No	secondary	caring for f...	No	142.00	145.00	80.00	79.00	.	
14	103	Intervention	Visit6	8.00	.	Female	.	Bukit Besar	6	2	1972	44.00	Malay	No	secondary	caring for f...	No	191.00	.	113.00	.	.	
15	104	Control	Visit1	.	.	Female	.0	Bukit Besar	0	3	1970	46.00	Malay	No	secondary	caring for f...	No	163.00	.	83.00	.	163.00	
16	104	Control	Visit6	.	.	Female	.	Bukit Besar	0	3	1970	46.00	Malay	No	secondary	caring for f...	No	151.00	.	77.00	.	.	
17	105	Control	Visit6	.	.	Male	.	Bukit Besar	0	2	1968	48.00	Malay	No	not educated	retired	No	177.00	.	85.00	.	.	
18	105	Control	Visit1	.	.	Male	.0	Bukit Besar	0	2	1968	48.00	Malay	No	not educated	retired	No	194.00	.	89.00	.	194.00	
19	106	Control	Visit1	.	.	Male	.0	Bukit Besar	0	2	1960	56.00	Malay	Yes	primary	working	.	134.00	.	67.00	.	134.00	
20	106	Control	Visit6	.	.	Male	.	Bukit Besar	0	2	1960	56.00	Malay	Yes	primary	working	.	131.00	.	62.00	.	.	
21	107	Control	Visit1	.	.	Female	.0	Bukit Besar	0	3	1977	39.00	Malay	Yes	secondary	caring for f...	.	128.00	.	83.00	.	128.00	
22	107	Control	Visit6	.	.	Female	.	Bukit Besar	0	3	1977	39.00	Malay	Yes	secondary	caring for f...	.	134.00	.	66.00	.	.	
23	108	Intervention	Visit1	5.50	8.00	Female	.0	Bukit Besar	6	3	1962	54.00	Malay	Yes	secondary	caring for f...	No	135.00	.	83.00	.	135.00	
24	108	Intervention	Visit2	6.50	.	Female	.	Bukit Besar	6	3	1962	54.00	Malay	Yes	secondary	caring for f...	No	133.00	134.00	81.00	82.00	.	
25	108	Intervention	Visit3	6.75	.	Female	.	Bukit Besar	6	3	1962	54.00	Malay	Yes	secondary	caring for f...	No	114.00	.	69.00	.	.	
26	108	Intervention	Visit4	7.75	.	Female	.	Bukit Besar	6	3	1962	54.00	Malay	Yes	secondary	caring for f...	No	122.00	124.00	74.00	75.00	.	
27	108	Intervention	Visit5	8.00	.	Female	.	Bukit Besar	6	3	1962	54.00	Malay	Yes	secondary	caring for f...	No	123.00	125.00	73.00	75.00	.	
28	108	Intervention	Visit6	8.00	.	Female	.	Bukit Besar	6	3	1962	54.00	Malay	Yes	secondary	caring for f...	No	135.00	.	88.00	.	.	
29	109	Intervention	Visit1	5.75	7.00	Male	.0	Bukit Besar	6	2	1965	51.00	Malay	Yes	secondary	retired	No	135.00	.	71.00	.	135.00	
30	109	Intervention	Visit2	7.75	.	Male	.	Bukit Besar	6	2	1965	51.00	Malay	Yes	secondary	retired	No	167.00	.	75.00	.	.	
31	109	Intervention	Visit3	7.75	.	Male	.	Bukit Besar	6	2	1965	51.00	Malay	Yes	secondary	retired	No	151.00	.	98.00	.	.	
32	109	Intervention	Visit4	8.00	.	Male	.	Bukit Besar	6	2	1965	51.00	Malay	Yes	secondary	retired	No	157.00	.	82.00	.	.	
33	109	Intervention	Visit5	8.00	.	Male	.	Bukit Besar	6	2	1965	51.00	Malay	Yes	secondary	retired	No	152.00	150.00	78.00	76.00	.	
34	109	Intervention	Visit6	7.00	.	Male	.	Bukit Besar	6	2	1965	51.00	Malay	Yes	secondary	retired	No	156.00	155.00	76.00	75.00	.	
35	110	Intervention	Visit1	7.00	8.00	Female	.0	Bukit Besar	6	2	1948	68.00	Malay	No	not educated	caring for f...	No	114.00	.	63.00	.	114.00	
36	110	Intervention	Visit2	8.00	.	Female	.	Bukit Besar	6	2	1948	68.00	Malay	No	not educated	caring for f...	No	116.00	.	62.00	.	.	

Appendix 5. 26: Baseline characteristics of patients who completed two visits

Table: The baseline characteristics of the six patients who only completed two visits

Characteristics	**SC (n=6)**
Mean age(years)	55.7 (SD=8.1)
Existing family history of diabetes	3 (50%)
Gender	
Female	5 (83.3%)
Male	1 (16.7%)
Ethnic origin	
[a]*Melayu*	5 (83.3%)
Chinese	0
Indian	1 (16.7%)
Comorbidities	
Hypertension	5(83.3%)
*CVD	1(16.7%)
CKD	1(16.7%)
Highest education level	
Primary	2 (33.3%)
Secondary	2 (33.3%)
Pre university	1 (16.7%)
Not educated	1 (16.7%)
Current employment	
Caring for family	3 (50.0%)
Working	2 (33.3%))
Unemployed	1 (16.7%)