Abstract of thesis entitled

An evidence-based guideline of promoting self-monitoring blood glucose (SMBG)
and self-titration insulin to promote optimal blood glucose control
for poorly glycemic controlled D.M. patients

Submitted by

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Introduction

Patients with type 2 diabetes mellitus are vulnerable to develop diabetic complications such as micro- or macro-vascular diseases which lead to higher rate of mortality and morbidity. The underlying cause is the suboptimal blood glucose control in which evidence shown 1% increase in HbA1c resulted in 10% increase in risk of developing diabetic complications (Diabetic Research Group, 1993). Traditional physician-titrated insulin is found to be insufficient to control patients’ HbA1C within an optimal range (HbA1C <7%), in which patients receive a daily fixed dose of insulin regardless of their blood glucose readings. Currently a new practice is being advocated world widely, patients have to titrate their insulin dosage according to their daily self-monitoring blood glucose readings (SMBG). Nurses are now in a vital role to teach eligible DM patients to learn this new practice in which it is scientifically proved to be effective to control their blood glucose level. SMBG together with self-titration insulin are effective tools for DM disease self-management. This dissertation provides an insight to the updated research on
SMBG and patients self-titration insulin, also work out a set of useful and practical clinical guideline for implementation of the new practice.

**Objectives:**

The objectives of the study are to (1) gather empirical evidence on the effectiveness and safeness of SMBG and insulin self-titration therapy for type 2 DM patients; and (2) to develop an evidence-based guideline for implementing SMBG and insulin self-titration therapy.

**Methods:**

A comprehensive literature search on PubMed, CINAHL, and Ovid was conducted. A total five randomized controlled trials were identified. With the use of Scottish Intercollegiate Guidelines Network (SIGN) checklist, the quality of the selected studies is critically appraised.

**Results:**

Five randomized controlled trials indicated that patients’ self-titrated insulin was shown to be safe and effective, as reflected by the greater percentage of decrease in mean fasting blood glucose level and mean HbA1c level, also larger percentage of subjects in self-titration group reached the treatment target HbA1c <7.5%. The target settings in all selected studies are out-patients DM centers. The feasibility and transferability of the literature are high. An evidence-based guideline is developed to implement the new practice in a local DM center in a Hong Kong public hospital. A pilot study plan and evaluation plan for the new intervention are also proposed.

**Conclusion**

It is recommended the practice of SMBG and insulin self-titration would be transferred into a new intervention of diabetic self-management in Hong Kong, and most DM patients would be benefited from this new practice by minimizing the risk of development of diabetic complications.
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Declaration

I declare that this dissertation represents my own work, except where due acknowledge is made, and that it has not been previously included in a thesis, dissertation or report submitted to this University or to any other institution for a degree, diploma or other qualifications.

Signed: ____________________________

Liu Yuet Kuen
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Chapter 1. Introduction

Type 2 Diabetes mellitus is well known to cause the development of long term diabetic complications such as nephropathy, retinopathy, stroke, cardiovascular disease, peripheral artery disease which lead to higher rates of mortality and morbidity among the diabetes patients (Fu et al, 2013; Chen et al, 2015). Recent studies have shown that type 2 diabetes patients participated in self-monitoring blood glucose (SMBG) and self-titrated insulin dosage lower their blood glucose level effectively (Davies et al, 2005; Chen et al, 2006; Meneghini et al, 2007; YKI-Jarvinen et al, 2007; Blonde et al 2009; Khunti et al, 2013; Silva et al 2015). Intensive insulin therapy and lower blood glucose are shown to have reduced substantially incidence of aforesaid diabetic complications (The Diabetes Control and Complications Trial and UK Diabetes Study, 1993). In this chapter, the background information of diabetes, the significance and the need of change of practice, the aims and objectives of the proposed evidence-based practice will be discussed.

1.1 Background

1.1.1 Diabetes mellitus

Diabetes mellitus is a chronic metabolic disease which characterized with high blood glucose level. It can be classified into two types: type 1 and type 2. Type 1 diabetes is mainly due to autoimmune disorder. Type 2 diabetes mellitus (Type 2 DM) originates with progressive dysfunction of beta cells of the pancreas (Meneghini et al, 2007). It is defined as “insulin resistance” causing high blood glucose level by decreased responsiveness of the insulin receptor of tissue to the effect of insulin, in turn reducing insulin secretion (Fu et al, 2013). According to the diagnostic criteria adopted by World Health Organization 2011 and also the American Diabetes Association 2010, type 2 diabetes mellitus is diagnosed when the HbA1c is persistently >6.5% DCCT or the fasting blood glucose >7mmol/L (Yu et al, 2015). Smoking, obesity, sedentary lifestyle and poor diet are also associated with the impaired blood glucose and development of diabetes disease (Coppola, 2015).
1.1.2. Use of insulin in disease management

At the early stage of disease management, most type 2 DM patients started with oral antidiabetic drugs to control their blood glucose level. However, as the disease deteriorates presented with higher blood glucose (HbA1c>7 %), even with the combination of multiple oral antidiabetic therapy, many type 2 DM patients finally need insulin to achieve optimal glycemic control (Fu et al, 2013). The importance of maintaining optimal blood glucose level (HbA1c < 7%) and intensive insulin therapy are shown to have reduced substantially incidence of DM complications such as DM retinopathy (The Diabetes Control and Complications Trial and UK Diabetes Study, 1993).

1.1.3. Physician-titrated insulin

Insulin is regarded as an effective and safe drug to control blood glucose (Vinik, 2007; Swinnen et al 2009). However, a number of researches found that many type 2 DM patients did not have their insulin dosage titrated sufficiently to achieve optimal glucose level (Blonde et al, 2009; Khunti et al, 2013). According to the guidelines set forth by the American Diabetes Association, the goal of diabetic therapy for type 2 DM patients is to reduce HbA1c to < 7% (Stolar, 2010). Many type 2 DM patients are remaining suboptimal glycemic control which made them prone to higher risk of diabetic complications (Yu, 2015). First, type 2 DM patients do not have frequent titration of insulin dosage in response to the result of the blood glucose level, since their insulin dosages are solely physician-adjusted which is regarded as time-consuming process (Meneghini et al 2007; Silva et al 2015; Harris et al 2014). The frequency of insulin titration is restrained by the frequency of clinical follow up. Second, worries of causing hypoglycemia prevented physicians from actively and frequently adjusting insulin dosage (Davies et al, 2005; Meneghini et al, 2007). Third, concerns about patients’ ability, convenience and comfort level are the possible barriers for patients’ self-titrated insulin, resulted in poor blood glucose control. Poor glycemic control indicated with HbA1c persistently higher than >8.5%,
resulted in 70% higher risk of developing diabetes-related morbidity (Stolar, 2010).

1.1.4. Success of Self-monitoring blood glucose and self-titrated insulin regime

Evidence proved that patients’ blood glucose levels were effectively controlled with self-titration insulin based on the practice of self-monitoring blood glucose level (SMBG) (Davies et al, 2005; Chen et al, 2006; Meneghini et al, 2007; YKI-Jarvinen et al, 2007; Blonde et al 2009; Khunti et al, 2013; Silva et al 2015). The reasons for the success of SMBG and patients self-titration insulin are:

(i) more frequent insulin titration schedule (daily to every 3 days titration) as the result of the daily self-monitoring of blood glucose level, and (ii) relatively higher insulin dosage used (Meneghini et al, 2007). (iii) Moreover, self-titration regimen also encouraged diabetic patients to actively participate in their disease management, resulted in better insulin compliance and thus achieved targeted glycemic level without severe incidence of hypoglycemia (Davies et al, 2005).

1.2. Significance and affirming the needs

1.2.1. Prevalence of DM in Hong Kong

According to the International Diabetes Federation 2015, more than 285 million people are suffering from type 2 DM, and this figure is expected to rise rapidly due to the aging population (Whiting et al, 2011). Diabetes rated the top tenth commonest cause of death in Hong Kong in 2014 and its crude death rate showed an increasing trend from 4.7 per 100000 population in 1991 to 5.4 per 100000 population in 2014 (International Classification of Disease, Statistics of Death Registry 2014). This disease is currently affecting one in ten people in Hong Kong. It is alarming that over 30% people with type 2 DM usually suffer from diabetes-related complications such as stroke, renal failure or cardiovascular diseases which caused heavy burden on medical care service (Chan et al, 2005).
1.2.2. Low rate of participation in self-monitoring of blood glucose

Currently, the percentage of diabetes patients performed self-monitoring blood glucose (SMBG) at home is relatively low in Hong Kong compared to those in western countries (Yin et al, 2015). Research found that (1) most diabetic patients were not aware of the importance of SMBG. In a recent local study, only 50% of the type two diabetes patients reported to have performed at least weekly self-monitoring blood glucose at home (Yin et al, 2015). None of the patients had insulin-titration by themselves. (2) Adjusting insulin dosage is driven by the health care providers which can be very time-consuming and costly in terms of healthcare utilization (Khunti et al, 2012). Even the diabetes patients have monitored their blood glucose, but they did not adjust their insulin dosage in response to their blood glucose result (Silva et al, 2015). Benefits of SMBG are not well addressed and self-titration on insulin dosage is not being practiced by type 2 DM patients.

1.2.3. The role of nurses in current practice

First, evidence suggested that type 2 DM patients had their insulin dosage titrated by physician might not provide optimal glycemic management as discussed in section 1.1.3. (Barag 2011, Khunti et al 2012). In Hong Kong, type 2 DM patients usually manage their disease at DM centers or the out-patients clinics. Nurses are responsible for teaching type 2 DM patients about routine self-monitoring blood glucose, and the insulin injection technique followed the fixed dosages prescribed by physicians. Conventionally, nurses advise the patients to follow physicians’ order and not to have self-amendment on their insulin dosage. Since insulin is often regarded as high risk drug and dosage cannot be adjusted by patients. There is worry that patients may misinterpret their blood glucose result and adjust their dosage of insulin incorrectly. When hypoglycemic episode is found (blood glucose <3.9mmol/L), patients are usually taught by nurses to withhold one daily dose of insulin. Further adjustments of the insulin dosage reply heavily on physicians at next medical follow up. Medical follow up usually takes the range of
every 4 to 6 weeks intervals depends on the patient’s disease condition. However, evidence demonstrated that conventional physician-driven insulin regime is insufficient to achieve optimal treatment targets, so a simple and safe patients-driven insulin titration programme would be beneficial (Davies et al 2005, Silva et al 2015). Numerous researches showed significant reductions in HbA1c level in patients who performed self-titration insulin due to intensive insulin titration regime in a shorter intervals and closer monitoring of the blood glucose level (Silva et al 2015; Khunti et al 2013; Hannelle et al 2007; Chen 2006). Nurses under the newly proposed patients-driven self-titration insulin regime can be educators, as well as advocators and supervisors to guide the diabetes patients to participate in the disease management.

1.2.4. Needs of new practice

Currently, patients’ self-monitoring of blood glucose and insulin self-titration are being advocated world widely i.e. UK, U.S, Canada, northern Europe, Taiwan, Brazil (Jarvinen 2007, Harris 2014, Khunti 2013). The DM disease management still has a slow move in Hong Kong. According to the press release 2012 by the Hospital Authority, the admission rate of diabetes patients increased by 43% over the 10 years and it is expected to rise as the result of the poor diabetes disease management and aging population (Press Release Hospital Authority 2012). Increasing number of diabetic patients with poor glycemic control are hospitalized in which they either displayed with severe hyperglycemia with ketoacidosis and h’stix> 30mmol/L, or severe hypoglycemia ended in coma with h’stix< 1.1 mmol/L. Daily SMBG can be used an effective tool for early detection of the extreme hypo/hyperglycemia, and thus immediate treatment can be provided before patients go into unconscious condition. It is hope that admission rate of the diabetes patients would be lower as a result of more diabetes patients participating in SMBG and self-titrated insulin regime to achieve better glycemic control.
Second, numerous studies shown that strict glycemic control have been proven to reduce the risk of micro-and macrovascular complications (Mendes 2010, Chen et al 2006, Silva et al 2015). Therefore, SMBG together with the self-titration insulin are effective tools to achieve an optimal glycemic control (Meneghini et al, 2007; Davies et al, 2005; Silva et al, 2015; Harris et al, 2014; Kennedy et al, 2006).

Third, since diabetes is a chronic illness, the success of the disease management could not be achieved without deep and continuous patients’ involvement (Ceriello, 2012). Self-care behavior is important in improving glycemic control since immediate therapeutic benefits would be provided resulting from disease self-management (Silva et al, 2015). Conventionally, multi-disciplinary care model has been used for treating diabetes patients. Physicians, diabetes specialized nurses and dietitians (sometimes includes podiatry and physiotherapists) are the main healthcare providers for management of the diabetes patients. However, better disease management also largely relies on patients’ self-managed behavior, including self-monitoring blood glucose, medication compliances, lifestyle and dietary modification which are important in minimizing the diabetic complications. In addition to the multi-disciplinary care model, patient-centered self-care management model on diabetes is found to be effective (Siminerio et al 2013). SMBG and insulin self-titration would empower patients to take active control of disease management (Silva et al 2015).

Fourth, concerning safety matters arising from self-titration insulin, a number of RCT studies proved that overall frequency of hypoglycemia was not significantly different between physician-titrated insulin group and patients-titrated insulin group. Self-titration insulin was found to be safe and effective in optimizing glucose control (Harris et al, 2014; Meneghini et al, 2007; Davies et al, 2005; Silva et al, 2015; Harris et al, 2014; Kennedy et al, 2006). Overseas studies also demonstrated that patients who undergone well-trained workshop on SMBG and
intensive workshops on blood glucose interpretation and insulin self-titration, errors that they wrongly adjusted dosage can be minimized (Khunti, 2013). Education programmes focusing on SMBG seems to be strong stimulus for behavioural change, empowering them to participate in the insulin titration treatment, resulting in better glycemic control (Silva et al, 2015). In short, there is a definite need for an evidence based guideline for poorly controlled type 2 DM patients on promoting self-monitoring blood glucose (SMBG) and self-titration insulin in order to achieve optimal glycemic control.
1.3. Research Questions, Aims and Objectives of the study

Research Questions

1. In type 2 diabetes mellitus patients, is self-monitoring blood glucose (SMBG) combined with insulin self-titration more effective than usual care (physician-led insulin titration) in achieving better glycemic control?

2. In type 2 diabetes mellitus patients, how safe is the self-monitoring blood glucose combined with insulin self-titration in comparison to usual care (physician-led insulin titration)?

Aim

To develop an evidence-based guideline of promoting self-monitoring blood glucose (SMBG) and self-titration insulin to promote optimal blood glucose control for poorly glycemic controlled type 2 DM patients in an out-patient DM center.

Objectives

1. To gather empirical evidence on the effectiveness and safeness of self-monitoring of blood glucose and insulin self-titration therapy for type 2 DM patients.

2. To develop an evidence-based guideline for implementing self-monitoring of blood glucose and insulin self-titration therapy.

3. To assess the feasibility of implementing the plan of educating type 2 DM patients on self-monitoring of blood glucose self-titration therapy in a DM center.

4. To work out an implementation plan the proposed self-monitoring of blood glucose and insulin self-titration therapy.

5. To evaluate the effectiveness and safeness of insulin self-titration therapy for type 2 DM patients.
Chapter 2 Critical Appraisal

The background of diabetes mellitus, the needs and significance of promoting patient-driven insulin self-titration based on self-monitoring blood glucose were discussed in the previous chapter. Next is to critique and synthesis relevant research findings.

2.1. Search strategies

2.1.1. Searching Method

Several searching methods were adopted to identify relevant journals. A systematic literature search via three electronic databases was completed from 1 Apr 2015 to 21 September 2015. A total of 27 relevant studies were found in PubMed (1980-2015), CINAHL (1970-2015), and Ovid (1970-2015). The journals are restricted to English or Chinese language. Years are not limited. Other search for literature found any books or journals published on the Yu Chung Keung Medical library catalogue. Additionally, the search of reference list of the available journals was performed.

2.1.2. Study Selection

Inclusion criteria

- poorly glycemic controlled type 2 DM patients with Hba1C>7% or above;
- already on insulin therapy for more than 1 year;
- absence of any DM complications such as retinopathy or renal or liver failure;
- stable mental state with the ability to participate in study protocol;
- randomised control trials were selected, and written in English or Chinese, published since 1970 onwards. The intervention must be self-monitoring blood glucose and patient’s self-titration on insulin dosage, for comparison all controls must be physician-directed insulin titration.
Exclusion criteria

- studies in which interventions other than patients’ self-titration on insulin or the control groups’ insulin therapy are not directed by physicians
- without control group for comparison are excluded.
- non-RCT studies such as observational studies are excluded.

2.1.3 Keywords

“Insulin self-titration” or “patient managed insulin” and “type 2 diabetes Mellitus” are used as the keywords of search in the electronic database. The type of journals is restricted to randomized controlled trials or evidence-based study. Appendix 1 shows the flow of search strategy.

After reviewing the abstracts and full text of all available journals that are fulfilled with the criteria of the searching keywords, a total of 5 journals are identified and reviewed to further assess its study quality and intervention effectiveness.

2.1.4 Appraisal Strategy

Scottish Intercollegiate Guidelines Network (SIGN) checklist for RCTs was used to critically evaluate and systematically review the quality of the selected articles. SIGN checklist was chosen to be the appraisal tool since SIGN appraisal tool is highly recognized for its objectivity on assessment on the content validity, methodology flaws and strengths, degree of bias and quality of the research. SIGN was publicly funded and formed by a pool of professionals who aimed to help healthcare professions develop evidence-based guidelines based on strong and valid evidence (Lowe et al, 2005). Therefore, data of the selected articles were then entered and internal validity and assessment of each study were performed according to the SIGN checklists, then quality of each article was rated from + means acceptable quality, to ++ which means high quality.
Tables of SIGNs checklists are attached in appendix 2.

2.2 Results

A total of five articles out of the searched twenty-seven articles are identified and reviewed to further assess its study quality and intervention effectiveness. The searching method presented in PRISMA flowchart is attached at appendix 1.

2.2.1. Research problem and purpose

Five articles addressed the research questions clearly (Meneghini et al, 2007; Davies et al, 2005; Silva et al, 2015; Harris et al, 2014; Kennedy et al, 2006). All these studies targeted at evaluating the effectiveness and safeness of patients self-directed insulin titration compared to that of physician-directed insulin titration. Ten relevant studies searched but three studies excluded due to the criteria are not met: those studies involved other interventions such as internet or tele-counselling or dietitian counselling. Therefore studies involved interventions other than patients’ effect are excluded.

2.2.2. Study type and level of evidence

The selected five articles are all randomized control trials (Meneghini et al, 2007; Davies et al, 2005; Silva et al, 2015; Harris et al, 2014; Kennedy et al, 2006). According to Melnyk & Fineout-Overholt’s rating system for hierarchy of evidence, randomized controlled trials are categorized as level two, which are the second strongest level of evidence (Melnyk & Fineout-Overholt, 2005). The chosen five studies carried out well-designed randomized controlled trials in which the primary data from primary clinical settings were collected. The interventions were scientifically and ethnically carried out without doing any harm to the subjects. Four researches were carried out in multi-centers, and multi-national in U.S.A., Western and Eastern Europe, South America, Asian, Middle East, Canada. Only one research was pilot study
done in a medical centre in Brazil. All research was carried out by scholars who are specialized in Diabetes and Endocrinology. Two studies were funded by Aventis and Sanofi. Sample size of the studies ranges from 23 to 5000 subjects. Outcome measures are mean reduction of HbA1c%, reduction of mean fasting plasma glucose (mmol/L), percentage of subjects reached the target HbA1c <7% or <7.5%, and the rate of hypoglycemic event.

2.2.3. Intervention

All of the studies used patients’ self-directed insulin titration strategy based on patients self-monitoring fasting blood glucose reading for titration as the intervention. The control groups were usual care as physician-directed insulin titration strategy. The main difference is the frequency of insulin titration between patients-directed and physicians-directed. Insulin used in the studies are basal, long-acting insulin which effect last for 24 hours duration and so it is injected once daily. Subjects in Meneghini’s study included both intervention and control group used le vemir as the basal insulin for daily injection. Subjects in Davies’ study, Harris’s study and Kennedy’s study used glargine. Subjects in Silva study used human protamine Hagedorn.

For duration of intervention, the intervention groups had to perform SMBG daily and regularly self-titrated their insulin dosage until follow ups (one study at 6 weeks, two studies follow up at 12 & 24 week, one at 26 weeks). As for the frequency of titration, subjects in the intervention group adjusted their insulin dose on a regular basis (two studies targeted at adjusting every 3 days, one study targeted at weekly, two studies targeted at daily adjustment). Compared with the usual care of physician-titrated insulin once only at follow ups ranging from every 4 to 6 weeks.
Quality Assessment

2.2.4 Internal validity

Quality assessment of the selected five articles is based on the criteria fulfilled under the SIGN checklist (Scottish Intercollege guidelines Network critical appraisal checklist for RCT, 2001). Internal validity refers to the research designed in randomized control, focused research question adequate concealment, blinding to investigators and subjects, subjects characteristics, sample size and drop out rate, analyzing method and outcome measures in standard and reliable ways. The quality of each study is then rated from + acceptable quality, to ++ high quality according to the completed SIGN checklists (see Appendix 2). The selected studies are rated as high quality to acceptable quality.

First, the chosen five studies carried out well-designed randomized controlled trials (Meneghini et al, 2007; Davies et al, 2005; Silva et al, 2015; Harris et al, 2014; Kennedy et al, 2006). Computerized randomization was stated in the search method in each articles, only one of them mentioned about the concealment method. Clearly focused research questions were asked in the five studies. Double binding was inapplicable since it is impossible to blind physicians as they adjusted insulin only in control groups at follow up.

Subjects were recruited in multi-centres as well as multi-national in U.S.A., Western and Eastern Europe, South America, Asian, Middle East, Canada. Only one research was pilot study done in a medical centre in Brazil. Multi-centres and multi-national RCT increased the power and generalizability of the study. Subjects mean aged ranged from 57 to 61. Background characteristics were all similar with type 2 DM, on daily insulin therapy for more than 2 years, without diabetic complications such as nephropathy, retinopathy, baseline HbA1c >8%, no major hypoglycemic events happened before. There were no significant differences in demographic characteristics between intervention and control group.
For the outcome measurement, the five articles clearly described the use of standardized measurement. All baseline and end of intervention HbA1c were taken in the laboratory. Subjects in intervention and control group used the same set of blood glucose meters with standardized platform for SMBG. Five studies addressed validity of the outcome measurements which were of highly reliable and valid in which calibrations were done in a unified and standardized way to provide accurate blood glucose readings. In addition, data and calibrations were verified under quality control system. Outcome measures are HbA1c%, mean reduction of HbA1c from baseline, mean fasting plasma glucose (mmol/L), percentage of subjects reached the target HbA1c <7% or <7.5%, and the rate of hypoglycemic event.

Sample size calculation was included in 4 studies. Number of samples in each intervention group ranged from 154 to 2529, only one pilot study with 23 subjects recruited. Drop-out rate ranged from 2.5% to 8.8% which seems as acceptable level in four studies. Only one study with drop-out rate 30% and the reasons behind were: the subjects recruited in multi-centres in the U.S., some subjects refused to follow up due to long travelling time or discontinue the study due to other disease attack e.g. ischemic attack, cerebrovascular accidents or even died. However, the effect of intervention was not affected because the calculated sample size met the targeted 1,000 subjects per group to achieve 90% power. The effect size is large which indicating the outcome measures are statistically significant and the results are analyzed with p value <0.05 (see appendix 3 table of evidence).

Source of funding were indicated in three studies (Davies et al, 2005; Harris et al 2014; Kennedy et al 2006). One of sponsors was the Sanofi-aventis, but all sponsors did not participate in carrying out the research so the results of the studies are unlikely to be affected by the sponsor organizations. The researchers are not from the sponsoring organisations, they are professors whose specialty in Medicine, Diabetes and Endocrine.
2.2.5. Overall assessment of the study

Quality rating of the study is based on internal validity. According to SIGNS (Scottish Interallelgiate guidelines Network critical appraisal checklist for RCT 2012), the quality of RCT study is classified from “0” low quality with few criteria fulfilled with design flaws, “+” acceptable quality with most criteria met with some risk of bias and conclusion might change by further studies; ++ high quality in which all or most criteria met with little or no risk of bias, conclusion unlikely to be changed by further studies. Four studies rated “++” (Meneghini et al, 2007; Davies et al, 2005; Harris et al, 2014; Kennedy et al, 2006) and one pilot study rated “+” (Silva et al, 2015) under the criteria fulfillment of the SIGNS critical appraisal checklists.

2.3 Summary and Synthesis of Finding

The findings from the selected studies demonstrated a positive effect of the patients self-directed insulin titration compared with physician titration group. The effects were measured in terms of HbA1c%, mean reduction of HbA1c from baseline, mean fasting plasma glucose (mmol/L), percentage of subjects reached the target HbA1c <7% or <7.5%, and the rate of hypoglycemic event. The findings are summarized as below.

2.3.1. Characteristics of the insulin

The insulins used in four studies were long-acting insulins such as Levemir and glargine which required patients to inject once daily. The insulin used in one study named protamine which was an intermediate-acting insulin which also acted as basal insulin, required patients to inject once daily. The long-acting or intermediate-acting insulins were chosen to be the insulin adjusted by patients in the study because of the numerous advantages: (i) prolonged duration of action resulted in lower incidence of hypoglycemic attack (Caputo et al 2015); (ii) effectively improve glycemic control presented with improve HbA1c level with good tolerability (Meneghini et al, 2009); (iii) ideal agent for poor DM control patients whose blood glucose cannot be
controlled simply by oral diabetic agents (Meneghini et al 2009). (iv) easy to use as it is supplied in pen-filled with a dose-adjustment lock at the top of the insulin pen. (v) high availability with widely used in the hospitals and out-patients clinics in N. S America, western and eastern Europe, also in South-east Asia and China.

2.3.2. Characteristics of the participants

All participants are type 2 DM patients without diabetic related complications such as retinopathy or nephropathy. Majority of them are poorly glycemic controlled with average HbA1c 8.25% to 13%. All of their blood glucose cannot be well controlled by oral diabetic agents alone, therefore long-acting or intermediate-acting insulin was injected on a daily basis aimed to achieve better glucose control.

2.3.3. Intervention

The intervention in the selected studies required the participants to have daily monitoring of self blood glucose by a provided glucose meter using a standardized calibration platform. The readings were documented by patients as fasting blood glucose in the log book. Based on the average fasting blood level, the patients adjusted the insulin dosage themselves according to a sliding scale every three days. One study targeted at titrating insulin on a daily basis. The sliding scale provided a safe range for patients to titrate their daily insulin. The adjustment was as simply as add or deduct one to two or three units of the basal insulin according to the fasting blood readings. The patients continued to practice on SMBG and self-titration of insulin until follow up. Compared with control group, they also practice SMBG but their insulin dosages were adjusted only by physicians at each follow up ranging every 6 to 12 weeks.

2.3.4. Effect of patients self-adjusted insulin on blood glucose level

To summarize all study findings, it is notable that intervention groups had achieved
significant result in reducing blood glucose level. Studies showed that there was 7% to 14% reduction in HbA1c in intervention group, compared with 5% to 11% reduction in HbA1c in control group. Also intervention group experienced 20% to 41.3% reduction in fasting blood glucose, compared with control group had 13% to 35% reduction in fasting blood glucose. Furthermore, studies demonstrated that more participants around 28-38% in intervention groups achieved the target HbA1c<7%, compared with that 21%-30% in control group. One study manifested that 50% participants in intervention group achieved the target HbA1c <7.5%, compared with only 8.3% in control group.

Although both intervention and control groups used the same basal insulin, the intervention group was found to have substantial reduction in HbA1c, mean fasting blood glucose, and more participants in in intervention can achieve the target blood glucose level. The reasons behind are the more frequent titration schedule (daily to every 3 days), and higher insulin doses utilized in the self titration group (Meneghini et al, 2007).

Studies have shown that more participants in intervention groups around 40% subjects achieved the target HbA1c <7%, compared with only 30% in control group maintained HbA1c <7%. The importance of maintaining optimal level HbA1c has always been stressed that diabetic patients’ HbA1c level should not exceed 7%. HbA1c is known as the glycosylated hemoglobin test which measures the glucose attached to hemoglobin. Normal HbA1c level is 4% to 6%. Diabetic patients with persistent HbA1c >6.5% have high risk of development of DM complications such as diabetic retinopathy (Yu et al 2015). Less than HbA1c 7% indicates good control of blood glucose. The patients’ self-titration insulin demonstrated to have advantageous impacts on maintaining an optimal blood glucose level.

2.3.5. Hypoglycemic events
According to the American Diabetes Association, hypoglycemia is defined as blood glucose level $\leq 70\text{mg/dL (3.9mmol/L)}$, and severe hypoglycemia is defined as blood glucose level $\leq 50\text{mg/dL (2.8mmol/L)}$ (American Diabetes Association Workgroup on Hypoglycemia, 2005). Five studies demonstrated that low rate in hypoglycemic events (0.26 to 1.2 events/patient/year) and no significant differences in hypoglycemic events between physician-titrated insulin group and patients self-titrated insulin group ($p>0.05$). It is concluded that the insulin self-titration practice provided DM patients a safe therapeutic scale of insulin dosage for adjustment. The patients can meet their treatment goals safely and effectively.

**2.3.6. Summary and Recommendations**

Five randomized controlled trials indicated that patients’ self-titrated insulin was shown to be safe and effective, as reflected by the greater percentage of decrease in mean fasting blood glucose level and mean HbA1c level, also larger percentage of subjects in self-titration group reached the treatment target HbA1c $<7\%$ or $<7.5\%$ as discussed above. Maintaining an optimal level of blood glucose is crucial to the type 2 DM patients, since many researches have shown that intensive glycemic control reduced the risk of microvascular complications and cardiovascular disease (Benhalima et al, 2010). Persistent hyperglycemia is associated with strokes, acute cardiovascular events, retinopathy, and renal disease. With 1% increase in HbA1c level, studies shown there was 40% increase in risk of coronary heart disease, 16% increase in risk of cardiovascular death, and 26% increase in risk of death (Benhalima et al, 2010). It is revealed that with the achieved HbA1c level 6%-7%, there was 20% reduction in diabetes related morbidity, 10% reduction in diabetes related mortality and 10% reduction in microvascular disease respectively (Benhalima et al, 2010). It is recommended that the treatment goal is to achieve the level of HbA1c $<7\%$ or $<7.5\%$. Therefore, tight glycemic control is necessary for type 2 diabetes patients.
For poorly controlled type 2 DM patients, their HbA1c are as high as above 8.5% in which oral antidiabetic drugs such as diamicron or metformin are not enough to maintain an optimal control of blood glucose. According to the guidelines set forth by the American Diabetes Association, the goal of diabetic therapy for type 2 DM patients is to reduce HbA1c to < 7% (Stolar, 2010). Long-acting insulin is usually added into the daily glycemic control. Even the patients have daily basal insulin injection, their blood glucose level always fluctuates and a fixed dose of insulin is insufficient to meet the treatment goal. Therefore, it is recommended that nurses at the out-patient clinic teach diabetic patients to perform SMBG at home in order to titrate their insulin dosage according to their blood glucose reading.

The selected studies consistently displayed that basal insulin titrated in a small adjustment at shorter intervals significantly reduced the blood glucose level with low rate of hypoglycemia event. The studies with large sample size (approximate 400 to 2000 subjects) increase the generalizability of the study. Low drop-out rate and large effect size increase the power of the study and results of reduction in blood glucose level displayed with significant level p<0.05. The significant differences proved that the patients-titrated insulin is more effective compared to physician-driven group.

As a conclusion, it is recommended that the poorly glycemic controlled type 2 DM patients can be referred to the DM clinic. An evidence-based guideline on SMBG and self-titrated insulin are set up for disease management, with provided insulin titration scale endorsed by physicians the patients can adjust their basal insulin daily according to their blood glucose reading. Nurses at the DM clinic are responsible for teaching diabetic patients about SMBG and insulin self-titration. With the provided safe therapeutic titration scale, patients can actively and frequently adjust their insulin for better glycemic control. SMBG enables patients to perform daily monitoring of their blood glucose level and make them more aware of their disease condition. Patients-driven
insulin self-titration empowers diabetes patients to take active control of disease management. The nurses who act as educators, as well as assessors and supervisors, facilitate the patients to have better management of their disease, in turn the risk of development of diabetic complications would be reduced.
Chapter 3 Translation and Application

In the previous chapter, self-monitoring blood glucose (SMBG) combined with patients’ self-titration insulin is shown by randomized controlled studies to be effective tools for glycemic control for type 2 DM patients. Implementation potential of a protocol for aforesaid interventions in terms of transferability, feasibility and cost-benefit ratio will be discussed in this chapter.

Aim of the proposed intervention

To develop an evidence-based guideline for the implementation of self-monitoring blood glucose (SMBG) and insulin self-titration for poor glycemic control type 2 DM patients in an out-patient DM center.

3.1 Transferability

3.1.1. Target setting

The target setting is a diabetic center in a public hospital under management of Hospital Authority in Hong Kong. It is an out-patient center run by a team of medical officers specialized in endocrinology, and nursing staff including two nursing specialists, three advanced practice nurses, and four registered nurses. The DM center serves out-patients and in-patients. When patients are newly diagnosed with type 2 DM, or poor glycemic control presented with extreme hyperglycemia or hypoglycemia required admission, the medical officers will make referrals of these patients to the D.M center for further disease self-management. Approximate ten patients are seen by the nurses at the center daily. Scope of service includes giving advice on diabetes self-management, insulin skills consolidation and diabetic drugs education.

The target settings of the reviewed RCTs were out-patient centers which provided primary care for type 2 DM poor glycemic controlled patients. Intervention included delivery of
educational package of SMBG combined with patients’ self-titration insulin, it shown effective in reducing average HbA1c and fasting blood glucose level for poor glycemic control diabetic patients in Western and Asian countries. All selected studies were conducted in multi-centers in U.S.A., Western and Eastern Europe, South America, Asia, Middle East, Canada (Meneghini et al, 2007; Davies et al, 2005; Harris et al, 2014; Kennedy et al, 2006). Only one research was pilot study done in a medical center in Brazil (Silva et al, 2015). The proposed intervention is appropriate for the out-patient center in Hong Kong since all reviewed studies involved out-patient centers care.

3.1.2. Clients

The target clients for the proposed intervention are adult patients who aged 18 or above, diagnosed with type 2 DM with poor glycemic control (HbA1c ≥ 8%), already on insulin therapy for more than two years. According to the guidelines of American Diabetes Association, type 2 DM patients who have HbA1c ≥ 8% are considered as poor glycemic control (American Diabetes Association, 2015). The clients must be orientated and conscious, and independent of activity of daily living, able to read and write without hearing or eyes problems, also able to communicate in Cantonese or English without mental retardation or psychotic diseases. They must not have any diabetic-related complications such as retinopathy or nephropathy occurred before which possibly affect the blood glucose readings or glomerular filtration rate.

Background characteristics of the target participants of the RCTs were all similar. They were all type 2 DM patients, conscious and orientated, aged 18 or above without DM related complications. Majority of them are poorly glycemic controlled with average HbA1c 8.25% to 13%. They were skillful and on daily insulin therapy for more than 2 years, no related complications no major hypoglycemic events happened before. All of their blood glucose could not be well controlled by oral diabetic agents, therefore a long-acting or intermediate-acting
insulin was injected on a daily basis aimed to achieve better glucose control. Intervention of SMBG combined with insulin self-titration showed effective in reducing Hba1c and fasting blood glucose level in these participants. Therefore, it is applicable to apply the same intervention to local patients with similar characteristics.

3.1.3. Transferability of the interventions

The interventions of the selected studies are transferrable and applicable to local out-patients center in Hong Kong because similar out-patients setting and target patients with similar characteristics are found. Although limited local research has been done on the intervention of SMBG and insulin self-titration in Hong Kong, it is believed that the effects of such intervention is transferrable from the reviewed RCTs to local setting. Since results of the studies showing greater percentage of patients in intervention groups maintained optimal blood glucose level (Hba1c≤7%) were drawn from five large scale randomized controlled studies from multi-centers and multi-nations, the selected RCTs are the second highest level of evidence, examined with high to acceptable quality (Melnyk & Fineout-Overholt, 2005). With similar settings and patients with similar background, it is regarded the interventions are highly transferrable and applicable to local type 2 DM patients with poor glycemic control in a local diabetic center.

3.1.3.i. Philosophy of care

According to the Hospital Authority annual report 2011-12, a holistic philosophy of care was adopted to promote a healthy community by providing high quality service to patients, its mission stated clearly as “helping people stay healthy” which empowers patients to regain their health by offering them with support in forms of treatment, encouragement and motivation. The vision of the DM center also emphasizes the importance of patients’ empowerment on disease self-management. Its mission is to help diabetic patients better management their blood glucose
by diabetic knowledge consolidation, insulin technique and SMBG refreshment, exercise and diet modification, and risk factor management.

In addition, the Hospital Authority Head Office now advocated “getting evidence into practice” in which evidence-based practice has been being applied in the management of clinical practice (Effective Health Care 1999). The philosophy of the care of the primary care clinics in the reviewed studies was similar. The clinics encouraged patients’ self-management of their disease by providing them with professional medical advice and treatment. The ultimate goal of the primary centers is to reduce in-patient admission rate and reduce undesirable complications due to the poor management of the diabetes. Therefore, the intervention is appropriate to be applied in the DM center under the similar philosophy of care.

3.1.3.ii. Sufficient number of patients benefited from the intervention

According to the figures of the Hospital Authority, the in-patient admission rate of the diabetic patients has increased by 43% over the past ten years, and the death rate of diabetic related complications have increased by 206% (Press release Hospital Authority, 2002). This alarming figure showed rapid rise in the prevalence of the disease. In a recent local large scale study, (i) one in six diabetic patients (n=15,196) was found to have developed chronic kidney disease, and up to 40% diabetic patients already have albuminuria as a result of sub-optimal glycemic control. (ii) Around 36% of the diabetic patients were unable to achieve HbA1c <7%, and amongst 26% of them were more likely to have retinopathy and cardiovascular disease (Luk A.O. et al, 2015). They are the high risk group who usually require emergency admission to manage diabetic-related complications such as stroke, renal failure. In addition, approximate one in ten patients was admitted to the medical department due to severe hypoglycemia or hyperglycemia arising from poor diabetic management (Wong C.K.H et al, 2015). It is estimated annually 720 diabetic patients will be benefited from the protocol. They constituted 30% of
these high risk diabetic patients would be benefited from improved HbA1c control under the proposed intervention, and thus re-admission rate to emergency department and hospitalization would be expected to reduce by 30%. It is foreseeable that improvement in HbA1c control by 1% would lead to 20% reductions in diabetic-related complications that lead to reductions in hospitalization utilization. Therefore, there is sufficient number of diabetic patients would be benefited from the practice of SMBG and insulin self-titration in the hope that the incidence rate and in-patients’ admission rate would be reduced as a result of improved disease self-management.

Moreover, the direct medical expenditure spent on each type 2 diabetic patient’s hospitalization is at least US $9200 per head per admission (Wong C.K.H et al, 2015). It is hoped that the direct medical cost would be reduced substantially by 30% as a result of improved HbA1c control and reduced diabetic complications events. The medical expenditure spent on managing in-patients diabetes would also be reduced (that will be discussed in 3.3).

3.2. Feasibility

3.2.1. Organizational culture towards evidence-based practice

The proposed protocol is feasible to be applied in the DM center with the support of the medical department. First, the stakeholders involved are the nurses in the DM center, Nurse Consultants, Chief of Service, Department of Operational managers, and ward manger. They are always supportive to evidence-based practice. Forums and literature sharing on evidence-based practice are regularly held and nursing colleague are always invited to attend. Organizational culture promote a positive and supportive attitude towards evidence-based practice. For example, another evidence-based protocol related to nurse-initiated defibrillation has been endorsed and already in practice in the medical unit the past two years. Therefore, good presentations of the strong evidence of the RCTs findings related to the evidence-based practice to the stakeholders are essential to gain their support and endorsement. “Empowering diabetic patients on disease
self-management” is always the vision of the center, which is consistent with the objective of the proposed protocol that emphasizes on patients’ self-monitoring blood glucose, and advocates them to adopt a proactive approach to manage their disease.

3.2.2.i. Nursing aspects: freedom in implementation

The reviewed studies consistently shown SMBG and insulin self-titration is safe and effective for patients for glycemic control. Nurses at the diabetic center have received professional trainings on diabetic management, they have the autonomy of deciding the eligible patients who are suitable for the intervention, and when to start and under what situation to end the intervention. Job satisfaction among nurses will be enhanced in terms of reducing admissions of patients due to poor glycemic control and diabetic complications. Studies demonstrated that nurses who devoted in the patient’s diabetic education with high work autonomy showed greater job satisfaction (Wu, S.F. et al, 2014).

3.2.2.ii. Nursing aspects: Potential friction and staff trainings

Concerning the manpower and workload involved in the proposed projects, there may be potential friction among nursing staff related to learning new protocol and teaching diabetic patients on titrating insulin. No extra staff is needed. Workload is expected to increase slightly during the preparation and implementation period. Additional time for training is a concern for nurses. Therefore, a step-down approach started with the nursing consultants can be a good start. The two nursing consultants can be the project leaders. A simple and easy-to-follow protocol is suggested (in later chapter). Three training sessions (one hour each) is needed. Recognition and rewards such as CNE points and certificate on entitling “project facilitators” giving credits to nurses who join the in-service training sessions can enhance staff involvement and compliance. Acknowledgment on nursing autonomy on patients’ education and insulin adjustment promote a positive image to the professionalism of nurses and enhance the recognition of nursing specialists’
3.2.2. iii. Nursing aspects: interference with current staff function

The intervention of SMBG combined with insulin self-titration may interfere with staff function. Currently, educating those poor glycemic control diabetic patients on disease management and blood glucose monitoring is the responsibility of nurses at the center. Approximate ten patients are seen by nurses at the center daily. In addition to patient’s education, nurses under the protocol have to select eligible patients for insulin self-titration. It is estimated three patients are selected daily to follow the protocol, and nurses have to deliver the education package on insulin self-titration. Individualized patients’ education may consume extra time and work. Thus a simple insulin titration schedule is suggested (as in appendix 5) to help staff compliance.

3.2.3. Medical aspects: cooperation with the physicians

It is expected that physicians would be in favor of the patient’s insulin self-titration. First, the protocol may help reduce in-patients admission rate due to severe hyperglycemia and hypoglycemia or diabetic complication. Second, patients’ self-titration insulin is proved by evidence to be safe. There is strong belief that diabetic patients are responsible for their disease self-management. Third, previously a nurse-directed insulin sliding scale for hyperglycemia was endorsed by the Medical C.O.S. and is still being used for in-patients medical units. It is expected patients’ self-titration insulin would be supported and endorsed by physicians. Fourth, protocols initiated by nursing specialists are always upheld in the medical unit.

3.2.4. Availability of the facilities and equipment

Third, facilities such as seminar rooms are free to use, and resources on educational package for demonstrations are easy to be retrieved in the center. Resources for patients
education includes lancets and testing strips required for daily SMBG are already available. Eligible patients who are selected to follow the insulin self-titration protocol are suggested to purchase their own lancets and strips which cost only $5 per day and it is affordable for patients. For those who are on CSSA, these are the consumable items that can be reimbursed.

3.2.5. Measuring tools for clinical evaluation

Evaluation includes objective data showing baseline and end of intervention HbA1c were taken in the laboratory. Log books recorded on daily fasting blood glucose level and daily dose of insulin titrated. Selected patients are suggested to use the same set of blood glucose meters with standardized platform for SMBG. Five studies already addressed previously that using a standardized platform with calibration to obtain accurate blood glucose readings is highly reliable. In addition, data and calibrations were verified by nurses. Subjective data are also collected via questionnaire at the end of intervention includes patients’ satisfaction and convenience and comfortableness on insulin self-titration.

3.3. Cost-benefit ratio

3.3.1. Risk of maintaining current practice

Currently, insulin titration is directed by physicians at each medical follow-up that usually takes 6-8 weeks intervals. The infrequent insulin titration caused lots of problems: First, due to medical inertia and infrequent medical follow up schedule, insulins were seldom titrated sufficiently control their blood glucose which often leads to hyperglycemia (Silva and Bosco, 2015; Meneghini L. et al, 2007). Patients with severe hyperglycemia require hospitalization to further titrate their insulin, which is avoidable under the proposed protocol of patients’ self-titrated insulin. Each hospital stay for each diabetic patient caused at least US $9,200 includes diabetic complications management, admissions to intensive care unit due to ketoacidosis coma (Wong C.K.H et al, 2015). The cost will increase 1.3 fold if both macro- and microvascular
complications coexists (Fung S.C. et al 2015). This potential medical burden arises from poor glycemic management.

Second, functional loss due to diabetic complications such as diabetic foot required amputation required extra hospital stay which costs at least US$ 5922 per persons (Yam H.K. et al, 2010). Loss of limbs and the development of diabetic foot ischemia are avoidable under good glycemic control. According to the UK prospective study, HbA1c>7% is regarded as suboptimal blood glucose control, every 1% increase in mean HbA1c would increase by 14% risk of diabetic related mortality and increase by 9.9% cardiovascular heart disease (Fung S.C., 2015).

3.3.2. Potential benefits of the evidence-based protocol

The reviewed studies proved that insulin is safe and effective drug to manage blood glucose, and there was no risk of implementing patients’ SMBG combined with self-titration insulin. Benefits shown substantial reduced in mean HbA1c and mean fasting glucose without increase events of severe hypoglycemia. Nurses at the diabetic center can always have the autonomy to select the eligible candidate to start with the new practice. Improved patients’ outcome as shown as improved HbA1c level and the average blood glucose is well under control would give nurses greatest satisfaction, as a result reducing in-patient admission rate and complication rate.

When extreme hyperglycemia with h’stix >27.8 mmom/L, or symptomatic hyperglycemia such as ketoacidosis usually requires inpatient treatment, this can be avoidable under the evidence-based intervention. In turn, the hospital cost spends on managing diabetic patients can be reduced due to better disease management. The annual cost for treating type 2 DM patients in HK took up 6.4% of the total expenditure of the total healthcare sector (Fung S.C et al, 2015). With increasing prevalence of DM complications, the cost is expected to rise substantially. It is expected that diabetes is a chronic disease which patients can manage their disease in a more
effective way.

3.3.3. Cost and benefit ratio of the proposed intervention

The cost of the intervention include manpower for pre-preparation and implementation, nurses training sessions, notes and printing costs of log books and educational package for patients for self-titration insulin, equipment such as lancets and glucose testing strips,

The two nursing consultants can be the project leaders. Preparation work can be done during the office hours. A six-month period of preparation is shown in the Ghatt chart as attached appendix 6. Three in-service trainings sessions related to the protocol are provided for the nurses during working hours. Each session takes 1 hour and can be held in the conference room which is free of charge in the center. Notes for nurses are photocopied and cost around one hundred for the whole course. Printing of educational packages and logbooks is estimated around one thousand dollars. Extra purchase of lancets and glucose testing strips for demonstration costs around two thousands. Patients who practice SMBG and self-titration insulin have to self-pay $5 per day for the consumable items, the cost which is affordable to be approximate $150 per months, or patients on CSSA can also apply for reimbursement for the consumable items.

Good glycemic control can reduce patients’ episodes of severe hyperglycemia and in turn reduce hospital admission which cost US$423 per persons per day and they usually stay for 3 to 5 days (Yam H.K. et al, 2010).

Detailed of the calculations of the cost-benefit ratio can be seen at appendix 4. The total cost of the proposed intervention for a 36-weeks period, targets 160 out-patients with type 2 diabetes is estimated HK$34,000. The potential benefits saved in monetary is HK$3,366,000.
It is said that the proposed intervention would provide greater benefit to type 2 DM patients, as well as improve patients disease self-management and in turn provide greatest satisfaction to the nurses working in the diabetic center, also the cost saved include reducing admission rate and reduce the risk of diabetic complication which could save valuable human life and that is valuable.
Chapter 4 Evidence-Based Practice Guidelines

The reviewed studies showed strong evidence of reducing HbA1c level by patients’ self-titration insulin according to the result of SMBG. Therefore, evidence-based guidelines are suggested to standardize the intervention for the type 2 DM patients.

4.1. Name of the guideline

‘Evidence based guidelines of promoting self-monitoring blood glucose (SMBG) and self-titration insulin to promote optimal blood glucose control for poorly glycemic controlled DM patients’.

4.2. Aim and Objectives of the guideline

The guidelines aims to assist nurses in promoting self-monitoring blood glucose and self-titration insulin for poorly glycemic controlled type 2 DM patients in order to achieve optimal blood glucose level.

The objectives of guidelines are to (i) provide simplified insulin self-titration strategies according to the result of the SMBG, (ii) and to promote patients to adopt a proactive approach in managing their blood glucose.

4.3. Target clients

The target clients aged 18 or above, who are diagnosed with type 2 DM already on insulin therapy for more than 2 year, have poor glycemic control with HbA1c> 8%. The clients should be alert and conscious, mental state stable without hearing problems, and without diabetic complications such as retinopathy or renal or liver failure, not on steroid therapy. Gender is not limited, pregnant clients are excluded.
4.4. Intended users

Nurses who work in the diabetic center includes RNs, APNs, NS, at least 1 year of experience in giving diabetic education to type 2 DM patients.

4.5. Recommendations

Recommendations are listed on appendix 5 and the grades of recommendations are based on Scottish Intercollegiate Guidelines Network, 2011 (see appendix 7 & 8 for the grading system)
Chapter 5 Implementation plan

This chapter aims to describe the communication plan, pilot study plan and evaluation plan for the proposed SMBG and self-titrated insulin intervention for type 2 DM patients. A pilot study plan is essential for further adjustment and improvements to the proposed intervention.

5.1. Communication plan

A comprehensive communication plan is vital to ensure all healthcare staff to achieve the goals of the project. Interventions bring changes to the usual practice and “innovation can improve the quality of care delivery and it depends on effective management and communication” (MacPhee, 2007). The communication plan begins with identifying who to communicate with. Stakeholders involve the staff who will be affected by the proposed intervention in the DM center, users as well as the clients. Different levels of stakeholders are identified as below:

1. Managerial level: Chief of Service, Departmental Operational Manager, Ward Manager
2. Operational level: Medical officers, Nurse Specialists, Advanced Practice Nurses, nurses at the DM center
3. Clerical staff
4. Clients: type 2 DM patients

5.1.1. Setting up of a Task Force

A task force/working group should be set up to promote and implement the intervention and also participate in the communication workflow. Strategic goals of the project should be presented at the meeting. The task force should be compositied of two RNs, two nursing consultants who can be project leaders, one medical officer can be the advisor throughout the project. The task force is responsible for project presentation and delivery of the message regarding the project. Since nurses consultants are the leaders of the nursing network, they
“provide informational support, as well as emotional support to the frontline nurses, and also can help building trust and enhance nurses’ commitment to the workplace” (Macphee, 2007). They are the ideal project leaders to start off the project. The registered nurses can take part in communication with different parties, and presentation of the project with photos or posters displaying different stages of project. Dissemination of the progress of the project is to be done by the task force via a kick-off event, a post in the hospital newsletter, posters and internal emails.

Making changes to the usual practice is not easy, so good communication must be built up between service providers and users. Effective communication characterizes with “two ways, open, and face-to-face communication” (Enriquez et al., 2001). According to the Kanter’s empowerment model, “power and authority provide access to support, information and resources people need to function successfully” (Macphee, 2007). Therefore, “A step-down approach” is adopted in the communication plan. It starts with obtaining agreement and consensus among managerial level, and then communicates downward among operational level. With the support and agreement from the managerial level, resources and manpower can be retrieved easily to promote the intervention.

5.1.2. Managerial level

A presentation of the proposed intervention to the COS, DOM, WM is the first step to obtain their agreement and support. Since they are the resources distributer and the proposed project need funding and manpower to run, so they are the first party to approve the project. Without their approval, the project cannot be started off. In addition, they are the representatives of the Medical department to support the value and mission of the DM center, which is to “helping people stay healthy” which empowers patients to regain their health by offering them with support in forms of treatment, encouragement and motivation.
5.1.3. **Operational level: nursing aspects**

After seeking approval from the managerial level, next is to communicate with the operational level to gain their support and advice. Since NS and APNs are the well experienced nurses in the DM specialty, their opinions and comments to the proposed intervention are valuable in contributing to the success of the project. They are also the task force and leaders to firstly implement the intervention. Their participation is vital in formulating intervention guidelines, resources planning, monitoring performance of frontlines staff in implementing the intervention, evaluate the effectiveness of the intervention, liaising with intended clients.

5.1.4. **Medical aspects**

Besides, the proposed intervention also needs the support and acknowledgment of the medical officers. The medical officers should be acknowledged of the proposed intervention since the treatment given to those patients for self-adjusted insulin is different from the physician-titrated insulin regime. Medical officers should be well informed of which eligible patients participating in the project. Therefore, meeting with the medical officers is important in discussing: (i) how to prevent complications such as hypoglycemia arising from the proposed intervention; (ii) clarify the principles of patients-titrated insulin protocol and minimize misconceptions, (iii) help monitor the effectiveness of the intervention during medical follow-up.

5.1.5. **Clerical staff**

A briefing will be held to all clerical staff at the DM center include the protocol guidelines and the workflow and proper document/forms of the project. They are responsible for contacting eligible patients for nurse clinic follow up.
5.1.6. **Target clients**

Target clients will be recruited at the DM nurse clinic follow-up. Eligible clients who are aged 18 or above, diagnosed with type 2 DM with HbA1c >8% already on insulin therapy for more than two years without any DM complications, will be screened and recruited by the nurses at the DM clinic. Information sheet will be given and consent has to be signed by the participants. The intervention will be explained by the nurses in details. A two-hours educational workshops with examination on insulin technique and insulin dosage titration will be held in order to ensure the selected clients are capable of performing insulin self-titration. A time line is suggested (see appendix 8).

5.2. **Pilot Study plan**

A pilot study plan is essential to explore the feasibility and applicability of the proposed intervention. It is a small scale study to detect any flaws of the intervention which might need modification after the pilot study.

5.2.1. **The objectives of the pilot study plan include:**

(i) The feasibility of the workflow of the project
(ii) The level of acceptance and comments towards the implementation of intervention from frontline users (nurses at DM clinic)
(iii) Collect feedback from nurses who attended the training sessions
(iv) Evaluate the recruitment process of eligible clients
(v) Refine the clinical guidelines after the pilot study
(vi) Evaluate the effectiveness of the educational workshops for clients and collect their feedback on the intervention
(vii) Detect any unexpected outcome or complications arising from the intervention
(viii) Appreciate the assessment tools
5.2.2. Setting and participants

The pilot study should be tested in the DM center. Eligible participants will be recruited, as mentioned earlier type 2 DM patients who aged 18 or above with poorly glycemic control, HbA1c >8% already on insulin therapy for more than two years without any DM complications or mental or psychiatry problems, will be recruited.

5.2.3. Target sample size and duration of the pilot study

The target sample size is expected to be sixteen participants. The whole pilot study will last for one month. The first week will be the recruitment week, educational week will last for one week, intervention will last for two weeks, and outcome measurement and evaluation will be conducted at the last week.

5.2.4. Workflow and Intervention

The Week 1 is the recruitment period. Sixteen eligible participants will be screened and interviewed by the nurses at the nurses clinic follow-up. Information sheets regarding the SMBG and patients’ self-titrated insulin will be given to and the advantages and risk of intervention will be explained by the nurses. Consents should be signed before attending the educational classes. In addition, baseline characteristics include age, sex, past medical history, occupation, dietary history, dosage of daily insulin being used, blood pressure, also blood taking of baseline HbA1C will be taken for baseline measurement.

Week 2 is educational and training period. Eligible participants have to attend a two-sessions educational classes in which each class will last for one hour on two consecutive days. The educational class will serve various aims:

i) Consolidate the skills of self-monitoring of blood glucose and insulin injection technique

ii) Introduce the innovative intervention i.e. patients performing in insulin self-titrated based on
the result of the SMBG, and insulin titration scale;

iii) Provides ways of seeking advice and problem-solving when encountering problems of insulin self-titration

iv) Examine on their skills and knowledge on SMBG and insulin self-titration by a written and practical examination

When the subjects pass the examination, they are seen as capable of participating in the study. Each subject will be delivered with a free set of standardized glucose meter and a bottle of glucose testing strips and a logbook recording daily SMBG result and daily dosage of insulin injected. The Week 3 & 4 is the intervention weeks, the subject will perform daily SMBG and insulin self-titration. For any enquiries arising from the self-titration, the mobile numbers (for work) of two Nurse Consultants can be contacted. At week 5, subjects will be asked to attend the nurse clinic follow-up to collect the end-of-intervention blood taking of HbA1C, blood pressure and comments of the subjects towards the intervention, includes the easiness to use and level of comfort regarding the intervention.

5.2.5. Outcome measures

The outcome of this pilot study is to test the feasibility of patients’ insulin self-titration. Its applicability, feasibility and level of safety are all included in the analysis of result of the study. Measurements composed of fasting blood glucose, HbA1C level, and incidence of hypoglycemic event with h’stix < 3.9mmol/L, frequency of SMBG and accuracy of insulin self-titration according to the insulin-titration scale.
5.2.6. Feedback from staff and clients

Qualitative method is also adopted to analyze the comments arising from the new protocol after the pilot study period. One focus group interviews with nursing staff will be conducted and collect their feedback. Questionnaires will be distributed to the clients at the end of the study. Questions for the clients will be analyzed in a five-point Likert scale ranging from 1 representing strongly disagree to 5 strongly agree, type of questions includes:

For clients:
1. I found the insulin self-titration scale is easy to understand and to use.
2. I feel comfortable to participate in daily self-monitoring blood glucose.
3. I think insulin self-titration is an effective tool to better control my blood glucose level.
4. I feel more concerned about my blood glucose level after starting the insulin self-titration.
5. I would like to continue insulin self-titration regime.

5.3. Evaluation plan

Evaluation targets at analyzing the effectiveness of the proposed intervention whether or not patients’ self-titration insulin is determined as effective and safe in lowering blood glucose level. The evaluation helps to refine the intervention in order to achieve better patients’ outcomes in terms of safeness, effectiveness and comfortness.

5.3.1. Duration and timeline for evaluation

It is proposed the intervention period would last for 36 weeks. Evaluation will be conducted by the task force group within 24 weeks after the intervention. The result will be presented at the DM committee quarterly meeting. A detailed report will be posted at the hospital research website. A proposed timeline for the preparation, implementation and evaluation of innovation is attached in the appendix 6.
5.3.2. Identify outcomes

Two major outcomes are identified in the evaluation: Clients’ outcomes and users (nurses) outcomes. Both quantitative data and qualitative data are analyzed.

Clients’ outcomes can be classified into primary and secondary outcomes. Primary outcomes aims to measure the change of blood glucose level which include fasting blood glucose level (mmol/L) and the drop in HbA1C level (%). Baseline measurements of HbA1C and fasting blood glucose will be obtained when clients agreed to participate in the self-titration regime. Pre-test and post-test of the change in blood glucose level will be compared the differences between before starting patients insulin self-titration and after the intervention. The intervention period would last for 36 weeks. At the end of the intervention period, patients’ blood tests will be taken for analysis. The results of the literature reported that there was a greater reduction in mean blood glucose level in the intervention group. With effective use and titration of insulin, more subjects will reach the target HbA1C level <7.5%. It is expected the clients can achieve similar results with greater extent of drop in mean blood glucose level in order to minimize the risk of developing DM complications.

Secondary outcome is to measure the safeness of the intervention. The incidence of hypoglycemic events (≤3.9mmol/L) will be recorded by patients in the daily h’stix logbook. As patients have to titrate their daily insulin dosage according to the titration scale, and also based on the result of their blood glucose reading. Daily SMBG and daily insulin dosage used are all recorded. The result of literature revealed there is no significant increase in hypoglycemic events between pre- and post- intervention. It is also expected the local eligible type 2 DM patients can titrate their insulin safely.

Users outcome refers to the protocol users, that is the nurses at the DM centre. They are
responsible of recruiting eligible DM patients to adopt new intervention in order to achieve better blood glucose level. They also have to conduct educational classes to teach patients how to follow and titrate their insulin dosage according to the result of the SMBG. Trouble-shooting skills will be discussed at the classes. At the end of the intervention period, quantitative data in forms of questionnaires with 5 point Likert scale will be distributed to the nurses to collect their satisfaction level. Besides, focus group interviews will be conducted to collect qualitative data including nurses’ comments towards the new intervention.

5.3.3. Sample size and method

Convenience sampling will be adopted as eligible patients at the DM centre follow-up will be recruited by nurses to follow the new intervention. Demographic characteristics of the eligible patients will be analyzed to fully meet the inclusion criteria: aged 18 or above, poor glycemic control with HbA1C >8% already on insulin therapy for more than two years without any DM complications, absence of psychiatric problems or mental disability. Similar background characteristics are needed to ensure the change of blood glucose level is merely due to the intervention effect.

Sample size is calculated to ensure the generalizability of the result. Paired t-test is used to analyze the changes of blood glucose level and incidence of hypoglycemic events before and after the intervention. According to the previous literature, a small effect size <0.5 is estimated. The significance level is set as p<0.05 with 80% power, the attribution rate is 8.75%, at least 160 subjects should be recruited. A sample size is 160 will be recruited for the intervention. The recruitment period will last for three months. A suggested time-line is included in appendix 6.
5.4. Basis for implementation

After 24 weeks of intervention, evaluation will be conducted to see the effectiveness and safeness of the intervention. The innovation will be fully implemented under the following basis.

Based on the evaluation results, criteria need to meet with to continue the intervention:

(i) At least eighty per cent of the clients have reduction in the mean blood glucose level in terms of fasting blood glucose level (mmol/L) and HbA1C level (%) compared with pre-intervention baseline data;

(ii) Provided that no significant increase in severe hypoglycemic events with h’stix <3.4 mmol/L;

(iii) No overloading the nursing staff at the DM center in terms of workload and overtime period;

(iv) At least eighty per cent of clients feeling satisfied and comfortable with the intervention, considering that the titration scale is easy to follow and use;

(v) At least eighty per cent of the staff is satisfied with the new protocol and agree to continue the intervention;

(vi) The running cost is not over budgeting for 20% than estimated amount.

6. Conclusion

This chapter discusses the implementation plan and evaluation plan of the proposed innovation. Detailed analysis of the objective data and subjective data are included in the evaluation in order to evaluate the clients’ outcomes and users’ outcomes. It is expected that the collected data and comments will be useful in amending an applicable and user-friendly evidence-based guideline for nurses to help patients titrate their insulin in a safe and effective way.
Appendix 1 PRISMA Flow Diagram

Note:
1. Electronic database used: PubMed, CINAHL, and Ovid
2. YU Chung Kung Medical library collections of journals and books
3. Journals that no full text available
4. Reasons for excluded: not RCTs design, the control is not physician-managed insulin titration
### APPENDIX 2: Quality Assessment

#### Table of Critical Appraisal (SIGN for RCT)  Study 1


Guideline topic: Self-titration blood glucose and self-adjusted insulin improve glycemic control

Key Question no: 2

Reviewer: LIU, Yuet Kuen

<table>
<thead>
<tr>
<th>Citation</th>
<th>Meneghini et al, 2007</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Section 1: Internal Validity</strong></td>
<td></td>
</tr>
<tr>
<td>1.1 clearly-focused question</td>
<td>Yes</td>
</tr>
<tr>
<td>1.2 Appropriate to carry out a RCT</td>
<td>Yes</td>
</tr>
<tr>
<td>1.3. adequate concealment method</td>
<td>Can’t say</td>
</tr>
<tr>
<td>1.4. blinding about treatment</td>
<td>Yes</td>
</tr>
<tr>
<td>1.5. treatment and control group are similar</td>
<td>Yes</td>
</tr>
<tr>
<td>1.6 only difference is the treatment</td>
<td>Yes</td>
</tr>
<tr>
<td>1.7 outcomes are measured in a standard, valid and reliable way</td>
<td>Yes</td>
</tr>
</tbody>
</table>
### APPENDIX 2: Quality Assessment

<table>
<thead>
<tr>
<th><strong>1.8 percentage of drop out</strong></th>
<th>low</th>
<th>9% (&lt;20% is considered acceptable)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>1.9 Intention to treat analysis</strong></td>
<td>Yes</td>
<td>Clearly stated applied intention to treat principle</td>
</tr>
<tr>
<td><strong>1.10 study carried out more than one site</strong></td>
<td>Yes</td>
<td>Multi-centres in the U.S.A.</td>
</tr>
</tbody>
</table>

### Section 2: Overall Assessment of the study

<table>
<thead>
<tr>
<th><strong>2.1 how well to minimise bias</strong></th>
<th>High++</th>
<th>Majority of criterion met and RCTs is adopted in the study.</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>2.2 evaluation of the methodology used and statistical power of the study</strong></td>
<td>RCT was used as the research design, this design is the most reliable and of higher hierarchy of evidence. Subjects characteristics were similar. The overall effect is due to intervention only. Sample size is large with 5604 subjects recruited from multi centres. A same size of 2000 patients per group was calculated to achieve 85% power. 96% confidence interval and p value was provided for measurement of difference in A1C change. Large sample size increased the power of the study.</td>
<td></td>
</tr>
<tr>
<td><strong>2.3 results applicable to patients targeted by this guideline</strong></td>
<td>Yes</td>
<td>Applicable in other type2 DM insulin required patients who are able to follow self-titration insulin protocol, also applicable in other countries and other races.</td>
</tr>
<tr>
<td><strong>2.4. summarize</strong></td>
<td>Self-titrating insulin dose combined with SMB facilitated effective insulin therapy to meet target treatment goals. The study showed greater effectiveness in glycemic control in intervention group than conventional treatment with no increase in hypoglycemic incidence. My comments on this study: Well-conducted RCT study with low risk of bias. Large sample size in multicentres presented with strong power of the study. Results were convincing and statistically significant as major outcomes presented with p-value &lt;0.05, which meant intervention made changes. Higher percentages of subjects in intervention group achieved greater reduction in A1C (p&lt;0.025). To a large extent, it is feasible to apply the study in out-patients unit for DM patients for better management of blood glucose and to reach the therapeutic targets.</td>
<td></td>
</tr>
</tbody>
</table>
APPENDIX 2: Quality Assessment

Table of Critical Appraisal (SIGN for RCT)  
Study 2


Guideline topic: Self-titration blood glucose and self-adjusted insulin improve glycemic control

Key Question no: 2
Reviewer: LIU, Yuet Kuen

<table>
<thead>
<tr>
<th>Citation</th>
<th>Davies et al, 2007</th>
</tr>
</thead>
</table>

**Section1: Internal Validity**

<table>
<thead>
<tr>
<th>1.1 clearly-focused question</th>
<th>Yes</th>
<th>To compare the effectiveness and safety of two algorithms (patient self-adjusted treatment vs conventional treatment by physician-adjusted insulin) in terms of hypoglycemic incidence and effectiveness of glycemic control (HbA1C and FBG).</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.2 Appropriate to carry out a RCT</td>
<td>Yes</td>
<td>5033 type 2 DM patients were electronically randomized by computer control group: insulin dosage was adjusted by physicians weekly Intervention group: self-adjust their insulin doses every 3 days based on the average three self-measured fasting blood glucose according to specific protocol</td>
</tr>
<tr>
<td>-----------------------------</td>
<td>-----</td>
<td>---------------------------------------------------------------------------------</td>
</tr>
<tr>
<td>1.3. adequate concealment method</td>
<td>Can’t say</td>
<td>Not mentioned</td>
</tr>
<tr>
<td>1.4. blinding about treatment</td>
<td>Yes</td>
<td>Impossible to blind subjects and physicians as the intervention group have to learn SMBG and self-adjusted insulin dosage. Physicians titrated the insulin dose only in control group.</td>
</tr>
<tr>
<td>-----------------------------</td>
<td>-----</td>
<td>---------------------------------------------------------------------------------</td>
</tr>
<tr>
<td>1.5. treatment and control group are similar</td>
<td>Yes</td>
<td>Subjects characteristics were similar, all were T2DM with poor glycemic control and they all never had systematic DM education conducted before the study. Differences in outcome were mainly due to intervention effect not due to individual difference. This would increase the power of evidence.</td>
</tr>
<tr>
<td>-----------------------------</td>
<td>-----</td>
<td>---------------------------------------------------------------------------------</td>
</tr>
<tr>
<td>1.6 only difference is the treatment</td>
<td>Yes</td>
<td>Both control group and intervention group used the same insulin but only intervention group had self-adjusted insulin dose according to the result of SMBG. Control group insulin dosage adjusted by physician only.</td>
</tr>
<tr>
<td>-----------------------------</td>
<td>-----</td>
<td>---------------------------------------------------------------------------------</td>
</tr>
<tr>
<td>1.7 outcomes are measured in a standard, valid and reliable way</td>
<td>Yes</td>
<td>All subjects received standard glucose meters that using a standardized platform. All subjects used the same insulin glargine. Blood samples were drawn for baseline A1C, and fasting blood by the same laboratories. A DCCT standard method with a documented quality controlled system was adopted.</td>
</tr>
<tr>
<td>-----------------------------</td>
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<td>---------------------------------------------------------------------------------</td>
</tr>
<tr>
<td>1.8 percentage of drop out</td>
<td>low</td>
<td>2.5% (&lt;20% is considered acceptable)</td>
</tr>
</tbody>
</table>

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APPENDIX 2: Quality Assessment

<table>
<thead>
<tr>
<th>1.9. Intention to treat analysis</th>
<th>Yes</th>
<th>Clearly stated applied intention to treat principle</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.10 study carried out more than one site</td>
<td>Yes</td>
<td>Multi-centres and multinational in western and Eastern Europe, South America, Asia, Middle East, Africa</td>
</tr>
</tbody>
</table>

**Section 2: Overall Assessment of the study**

<table>
<thead>
<tr>
<th>2.1 how well to minimise bias</th>
<th>High++</th>
<th>Majority of criterion met and RCTs is adopted in the study.</th>
</tr>
</thead>
<tbody>
<tr>
<td>2.2 evaluation of the methodology used and statistical power of the study, the overall effect is due to intervention</td>
<td>Yes</td>
<td>RCT was used as the research design, this design is the most reliable and of higher hierarchy of evidence. Subjects characteristics were similar. The overall effect is due to intervention only. Sample size is large with 5033 subjects recruited from multi centres and multi-national. A same size of 2216 patients per group was calculated to achieve 90% power. 95% confidence interval and p value was provided for measurement of difference in A1C change. Large sample size increased the power of the study.</td>
</tr>
<tr>
<td>2.3 results applicable to patients targeted by this guideline</td>
<td>Yes</td>
<td>Applicable in other type2 DM insulin required patients who are able to follow self-titration insulin protocol, also applicable in other countries and other races.</td>
</tr>
<tr>
<td>2.4 summarize</td>
<td></td>
<td>Subjects in intervention group showed greater reduction in HbA1C and FBG than conventional treatment with minimal incidence of hypoglycemic. My comments on this study: Well-conducted RCT study with low risk of bias. Large sample size in multi-centres and multi-national presented with strong power of the study. Results were convincing and statistically significant as major outcomes presented with p-value &lt;0.05, which meant intervention made changes. Higher percentages of subjects in intervention group achieved greater reduction in A1C (p&lt;0.025). To a large extent, it is feasible to apply the study in out-patients unit for type 2 DM patients for better management of blood glucose and to reach the therapeutic targets.</td>
</tr>
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APPENDIX 2: Quality Assessment

Table of Critical Appraisal (SIGN for RCT)  
Journal 3


Guideline topic: Self-monitoring blood glucose and self-adjusted insulin improve glycemic control

Key Question no: 2  
Reviewer: LIU, Yuet Kuen

<table>
<thead>
<tr>
<th>Citation</th>
<th>Silva and Bosco (2015)</th>
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<tr>
<td>Section1: Internal Validity</td>
<td></td>
</tr>
<tr>
<td>1.1 clearly-focused question</td>
<td>Yes</td>
</tr>
<tr>
<td>1.2 Appropriate to carry out a RCT</td>
<td>Yes</td>
</tr>
<tr>
<td>1.3. adequate concealment method</td>
<td>Can’t say</td>
</tr>
<tr>
<td>1.4. blinding about treatment</td>
<td>Yes</td>
</tr>
<tr>
<td>1.5. treatment and control group are similar</td>
<td>Yes</td>
</tr>
<tr>
<td>1.6 only difference is the treatment</td>
<td>Yes</td>
</tr>
<tr>
<td>1.7 outcomes are measured in a standard,</td>
<td>Yes</td>
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</table>
### APPENDIX 2: Quality Assessment

<table>
<thead>
<tr>
<th>Valid and reliable way</th>
<th>drawn for baseline A1C, and fasting blood by the same laboratories. The A1C analysis was certified by the National Glycohemoglobin Standardized Program.</th>
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<tbody>
<tr>
<td>1.8 percentage of drop out</td>
<td>low 3.8% (&lt;20% is considered acceptable)</td>
</tr>
<tr>
<td>1.9 Intention to treat analysis</td>
<td>Yes Clearly stated applied intention to treat principle</td>
</tr>
<tr>
<td>1.10 study carried out more than one site</td>
<td>No one medical centre in Brazil</td>
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#### Section 2: Overall Assessment of the study

<table>
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<th>2.1 how well to minimise bias</th>
<th>acceptable+ Majority of criterion met and RCTs is adopted in the study.</th>
</tr>
</thead>
<tbody>
<tr>
<td>2.2 evaluation of the methodology used and statistical power of the study, the overall effect is due to intervention</td>
<td>Yes RCT was used as the research design, this design is the most reliable and of higher hierarchy of evidence. Single binding applied and subjects characteristics were similar. The overall effect is due to intervention only. However, the sample size is small where only 23 subjects were recruited in the study. Power of the study is not strong as this is a pilot study with only one centre. Effect size is medium. Result represented clearly in p-value with outcome p&lt;0.05, also present in percentage, s.d..</td>
</tr>
<tr>
<td>2.3 results applicable to patients targeted by this guideline</td>
<td>Yes Applicable in other type2 DM insulin required patients who are able to follow self-titration insulin protocol, also applicable in other countries and other races.</td>
</tr>
<tr>
<td>2.4 summarize</td>
<td>The study showed more subjects in intervention group achieved treatment target HbA1C&lt;7.5% than control group with no increase in hypoglycemic incidence. My comments on this study: Well-conducted RCT study with low risk of bias. Results are presented statistically in a clear way. Results were convincing and statistically significant as majority of outcomes presented with p-value &lt;0.05, which meant intervention made changes. Higher percentages of subjects in intervention group achieved an A1C near target targets (p&lt;0.028). It is feasible to apply the study in out-patients unit for DM patients for better monitoring of self-blood glucose and to reach their therapeutic targets. More subjects from multi-centres can be recruited. Larger sample size on randomized controlled studies are needed to increase the power of the study.</td>
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# APPENDIX 2: Quality Assessment

**Table of Critical Appraisal (SIGN for RCT)  Journal 4**


Guideline topic: Self-titration blood glucose and self-adjusted insulin improve glycemic control

Key Question no: 2

Reviewer: LIU, Yuet Kuen

<table>
<thead>
<tr>
<th>Citation</th>
<th>Harries et al, 2007</th>
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## Section1: Internal Validity

<table>
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<tr>
<th>1.1 clearly-focused question</th>
<th>Yes</th>
<th>To compare the effectiveness and safety of two algorithms (patient self-adjusted treatment vs conventional treatment by physician-adjusted insulin) in terms of hypoglycemic incidence and effectiveness of glycemic control (HbA1C and FBG).</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.2 Appropriate to carry out a RCT</td>
<td>Yes</td>
<td>316 type 2 DM patients in 47 medical centres in Canada were electronically randomized by computer control group: insulin dosage was adjusted by physicians weekly Intervention group: self-adjust their insulin doses every 3 days based on the average three self-measured fasting blood glucose according to specific protocol</td>
</tr>
<tr>
<td>1.3. adequate concealment method</td>
<td>Yes</td>
<td>Using concealed allocation</td>
</tr>
<tr>
<td>1.4. blinding about treatment</td>
<td>Yes</td>
<td>Impossible to blind subjects and physicians as the intervention group have to learn SMBG and self-adjusted insulin dosage. Physicians titrated the insulin dose only in control group.</td>
</tr>
<tr>
<td>1.5. treatment and control group are similar</td>
<td>Yes</td>
<td>Subjects characteristics were similar, all were T2DM with poor glycemic control and they all never had systematic DM education conducted before the study. Differences in outcome were mainly due to intervention effect not due to individual difference. This would increase the power of evidence.</td>
</tr>
<tr>
<td>1.6 only difference is the treatment</td>
<td>Yes</td>
<td>Both control group and intervention group used the same insulin but only intervention group had self-adjusted insulin dose according to the result of SMBG. Control group insulin dosage adjusted by physician only.</td>
</tr>
<tr>
<td>1.7 outcomes are measured in a standard, valid and reliable way</td>
<td>Yes</td>
<td>All subjects received standard glucose meters that using a standardized platform. All subjects used the same insulin glargine. Blood samples were drawn for baseline A1C, and fasting blood by the same laboratories. A DCCT standard method with a documented quality controlled system was adopted.</td>
</tr>
<tr>
<td>1.8 percentage of drop</td>
<td>Low</td>
<td>8.8% (&lt;20% is considered acceptable)</td>
</tr>
</tbody>
</table>
**APPENDIX 2: Quality Assessment**

<table>
<thead>
<tr>
<th>Section</th>
<th>Question</th>
<th>Rating</th>
<th>Reason</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.9.</td>
<td>Intention to treat analysis</td>
<td>Yes</td>
<td>Clearly stated applied intention to treat principle</td>
</tr>
<tr>
<td>1.10</td>
<td>study carried out more than one site</td>
<td>Yes</td>
<td>Multi-centres in Canada</td>
</tr>
<tr>
<td>Section 2:</td>
<td>Overall Assessment of the study</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2.1</td>
<td>how well to minimise bias</td>
<td>High++</td>
<td>Majority of criterion met and RCTs is adopted in the study.</td>
</tr>
<tr>
<td>2.2</td>
<td>evaluation of the methodology used and statistical power of the study, the overall effect is due to intervention</td>
<td>Yes</td>
<td>RCT was used as the research design, this design is the most reliable and of higher hierarchy of evidence. Subjects characteristics were similar. The overall effect is due to intervention only. Sample size is sufficient with 320 subjects recruited from multi-centres. A sample size of 160 patients per group was calculated to achieve 80% power. 95% confidence interval and p value was provided for measurement of difference in A1C change.</td>
</tr>
<tr>
<td>2.3</td>
<td>results applicable to patients targeted by this guideline</td>
<td>Yes</td>
<td>Applicable in other type2 DM insulin required patients who are able to follow self-titration insulin protocol, also applicable in other countries and other races.</td>
</tr>
<tr>
<td>2.4</td>
<td>summarize</td>
<td></td>
<td>Subjects in intervention group showed more aggression in titrating insulin and this result in greater reduction in HbA1C and FBG than conventional treatment with minimal incidence of hypoglycemic. My comments on this study: Well-conducted RCT study with low risk of bias. Sufficient sample size in multi-centres presented with strong power of the study. Results were convincing and statistically significant as major outcomes presented with p-value &lt;0.05, which meant intervention made changes. Higher percentages of subjects in intervention group achieved targeted A1C&lt;7% (p&lt;0.01). To a large extent, it is feasible to apply the study in out-patients unit for type 2 DM patients for better management of blood glucose and to reach the therapeutic targets.</td>
</tr>
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### APPENDIX 2: Quality Assessment

**Table of Critical Appraisal (SIGN for RCT)  
Journal 5**

<table>
<thead>
<tr>
<th>Citation</th>
<th>Kennedy et al, 2007</th>
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#### Section1: Internal Validity

| 1.1 clearly-focused question | Yes | To compare the effectiveness and safety of two algorithms (patient self-adjusted active titration vs usual treatment by physician-adjusted insulin) in terms of hypoglycemic incidence and effectiveness of glycemic control (HbA1C and FBG). |
| 1.2 Appropriate to carry out a RCT | Yes | 3948 type 2 DM patients in multi- medical centres in the U.S. were electronically randomized by computer. Control group: insulin dosage was adjusted by physicians every 6 weeks. Intervention group: self-adjust their insulin doses titrated weekly based on the average three self-measured fasting blood glucose according to specific protocol. |
| 1.3. adequate concealment method | Can’t say | Not mentioned |
| 1.4. blinding about treatment | Yes | Impossible to blind subjects and physicians as the intervention group have to learn SMBG and self-adjusted insulin dosage. Physicians titrated the insulin dose only in control group. |
| 1.5. treatment and control group are similar | Yes | Subjects characteristics were similar, all were T2DM with poor glycemic control and they all never had systematic DM education conducted before the study. Differences in outcome were mainly due to intervention effect not due to individual difference. This would increase the power of evidence. |
| 1.6 only difference is the treatment | Yes | Both control group and intervention group used the same insulin but only intervention group had self-adjusted insulin dose according to the result of SMBG. Control group insulin dosage adjusted by physician only. |
| 1.7 outcomes are measured in a standard, valid and reliable way | Yes | All subjects received standard glucose meters. All subjects used the same insulin glargine. Blood samples were drawn for baseline A1C, and fasting blood by the same laboratories. |
| 1.8 percentage of drop out | high | 30% |
### APPENDIX 2: Quality Assessment

<table>
<thead>
<tr>
<th>1.9. Intention to treat analysis</th>
<th>Yes</th>
<th>Clearly stated applied intention to treat principle</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.10 study carried out more than one site</td>
<td>Yes</td>
<td>2164 multi-centres in the U.S.</td>
</tr>
</tbody>
</table>

**Section 2:** Overall Assessment of the study

<table>
<thead>
<tr>
<th>2.1 how well to minimise bias</th>
<th>High++</th>
<th>Majority of criterion met and RCTs is adopted in the study.</th>
</tr>
</thead>
<tbody>
<tr>
<td>2.2 evaluation of the methodology used and statistical power of the study, the overall effect is due to intervention</td>
<td>Yes</td>
<td>RCT was used as the research design, this design is the most reliable and of higher hierarchy of evidence. Subjects characteristics were similar. The overall effect is due to intervention only. Large sample size is with 2600 subjects recruited from multi-centres. A sample size of 1300 patients per group was calculated to achieve 90% power. 95% confidence interval and p value was provided for measurement of difference in A1C change. The only problem is high drop out rate.</td>
</tr>
<tr>
<td>2.3 results applicable to patients targeted by this guideline</td>
<td>Yes</td>
<td>Applicable in other type2 DM insulin required patients who are able to follow self-titration insulin protocol, also applicable in other countries and other races.</td>
</tr>
<tr>
<td>2.4. summarize</td>
<td></td>
<td>Subjects in active titration intervention group showed more reduction in HbA1C than usual treatment by physician titrated insulin every 6 week with minimal incidence of hypoglycemic. My comments on this study: Well-conducted RCT study with low risk of bias. Sufficient sample size in multi-centres presented with strong power of the study. Results were convincing and statistically significant as major outcomes presented with p-value &lt;0.05, which meant intervention made changes. Higher percentages of subjects in intervention group achieved targeted A1C&lt;7% (p&lt;0.01). To a large extent, it is feasible to apply the study in out-patients unit for type 2 DM patients for better management of blood glucose and to reach the therapeutic targets.</td>
</tr>
</tbody>
</table>
### Appendix 3: Table of Evidence. RCT study 1

<table>
<thead>
<tr>
<th>Bibliography</th>
<th>Study type</th>
<th>Level of evidence</th>
<th>Subject Characteristics</th>
<th>Intervention</th>
<th>Control</th>
<th>Lengths of follow up</th>
<th>Outcome measures</th>
<th>Effect size (IG-CG)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Meneghini et al, 2007</td>
<td>RCT</td>
<td>II</td>
<td>1 live in U.S.A</td>
<td>daily SMBG</td>
<td>standard-of-care insulin titrated by physician at follow up</td>
<td>At 26 weeks</td>
<td>% reduction in mean fasting plasma glucose (mmol/L)</td>
<td>(9.7-7.8)/9.7<em>100% -(9.7-8.4)/9.7</em>100% = 19.6%-13.4% = +6.2%</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>2 mean age:58</td>
<td>insulin self-titration</td>
<td></td>
<td></td>
<td>% reduction in HbA1C % (mean change from baseline)</td>
<td>(8.5-7.9)/8.5<em>100% -(8.5-8.0)/8.5</em>100% =7.1%-5% +=2.1%(p&lt;0.0001)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>3 type 2 D.M., no other DM complications such as retinopathy</td>
<td>adjusted every 3 days by patients</td>
<td></td>
<td></td>
<td>% of subject reach HbA1C&lt;7% without hypoglycemia</td>
<td>21%-18%+=3%</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>4 B.M.I. 33.8 kg/m2</td>
<td>aFBG&lt;4.4mmol/L=3U</td>
<td></td>
<td></td>
<td>Rate of hypoglycemic event (events/patient/year)</td>
<td>0.26-0.2 =0.06(p=0.23)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>5 mean A1c 8.5%</td>
<td>aFBG 4.4-6.1mmol/L=no change</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>6 on daily insulin therapy</td>
<td>aFBG&gt;6.1 mmol/L=+3U</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>7 not on steroid, other drugs like beta blockers, monoamine oxidase inhibitors that interfere glucose metabolism</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

n=2409 (drop out 224)

n=2416 (drop out=221)

aFBG=average fasting blood glucose

General comment: Patients driven insulin titration achieved significant improvement in glycemic control with minimal risk of hypoglycemia
### Appendix 3: Table of Evidence. RCT study 2

<table>
<thead>
<tr>
<th>Bibliography</th>
<th>Study type</th>
<th>Level of evidence</th>
<th>Subject Characteristics</th>
<th>Intervention</th>
<th>Control</th>
<th>Lengths of follow up</th>
<th>Outcome measures</th>
<th>Effect size (IG-CG)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Davies et al, 2005</td>
<td>RCT</td>
<td>II</td>
<td>West &amp; East Europe, South America, Asia, Middle East, Africa</td>
<td>daily SMBG</td>
<td>standard-of-care insulin titrated by physician at follow up</td>
<td>at 12 &amp; 24 week</td>
<td>% reduction in fasting plasma glucose (mmol/L)</td>
<td>(9.4-6.0)/9.4<em>100% - (9.4-6.3)/9.4</em>100%</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>mean age: 57.5</td>
<td>self-manged insulin titration adjusted every 3 days by patient</td>
<td></td>
<td></td>
<td>% reduction in HbA1C % (mean change from baseline)</td>
<td>36%-32% = +4%</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>type 2 D.M., no other DM complications</td>
<td>aFBG&gt;5.5 and &lt;6.6mmol/L = 0U</td>
<td></td>
<td></td>
<td>= 13.4%-11% = +2.4% (p&lt;0.001)</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>B.M.I. 29kg/m2</td>
<td>aFBG&gt;6.7 and &lt;7.8mmol = +2U</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>mean A1c 8.9%</td>
<td>aFBG&gt;7.8 and &lt;10mmol/L = +2U</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>on daily insulin therapy</td>
<td>aFBG&gt;10mmol/L = +2U</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>no acute or chronic metabolic disease, no liver or renal disease</td>
<td>n=2529 (drop out 61)</td>
<td>n=2504 (drop out=65)</td>
<td></td>
<td>% of subject reached target HbA1C&lt;7% without hypoglycemia</td>
<td>30%-26% = +4%(p=0.004)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Rate of hypoglycemic event (events/patient/year)</td>
<td>1.1-0.9=0.2%</td>
</tr>
</tbody>
</table>

aFBG = average fasting blood glucose

General comment: A simple patients-driven insulin titration algorithm achieved significantly improved glycemic control with low rate of hypoglycemia
## Appendix 3: Table of Evidence. RCT study 3

<table>
<thead>
<tr>
<th>Bibliography</th>
<th>Study type</th>
<th>Level of evidence</th>
<th>Subject Characteristics</th>
<th>Intervention</th>
<th>Control</th>
<th>Lengths of follow up</th>
<th>Outcome measures</th>
<th>Effect size (IG-CG)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Silva et al., 2015</td>
<td>RCT</td>
<td>II</td>
<td>1 live in Brazil</td>
<td>daily SMBG</td>
<td>standard-of-care insulin titrated by physician at follow up</td>
<td>at 12 week</td>
<td>% reduction in Hba1C % (mean change from baseline)</td>
<td>(9.0-8.0)/9<em>100% - (9.6-9.0)/9.6</em>100% = 11.1%-6.25% = +4.85% (p=0.006)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>2 mean age: 57.7</td>
<td>Self-manged insulin titration</td>
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<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>3 type 2 D.M., no other DM complications</td>
<td>adjusted weekly by patient</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>4 B.M.I 29.3kg/m2</td>
<td>aFPG &lt;5 mmol/L = -1U</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>5 mean A1c 9.3%</td>
<td>aFPG 5-7.2mmol/L = No adjust</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>6 on daily insulin therapy</td>
<td>aFPG &gt;7.2 mmol/L = +2U</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>7 no severe hypoglycemic events happened before</td>
<td>n=11 (drop out 1)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

- aFPG=average fasting plasma glucose
- General comment: SMBG combined with patients’ self-titration insulin can safely improve glycemic control. More portion of subjects in intervention group reached optimal Hba1C level.
### Appendix 3: Table of Evidence.  RCT study 4

<table>
<thead>
<tr>
<th>Bibliography</th>
<th>Study type</th>
<th>Level of evidence</th>
<th>Subject Characteristics</th>
<th>Intervention</th>
<th>Control</th>
<th>Lengths of follow up</th>
<th>Outcome measures</th>
<th>Effect size (IG-CG)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Harris et al, 2014</td>
<td>RCT</td>
<td>II</td>
<td>1 live in Canada</td>
<td>daily SMBG</td>
<td>standard-of-care</td>
<td>at 24 week</td>
<td>% reduction in Hba1%</td>
<td>(10.4-9.6)/10.4*100%</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>2 mean age:60.4</td>
<td>Self-manged insulin titration</td>
<td>insulin titrated</td>
<td>(mean change from baseline)</td>
<td>% = 7.6%-6.6% =+1%</td>
<td>(p&lt;0.05)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>3 type 2 D.M.</td>
<td>adjusted daily by patient</td>
<td>by physician at follow up</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>4 B.M.I 34.2kg/m2</td>
<td>aFPG &lt; or =5.5 mmol/L=0U</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>5 mean A1c 8.25%</td>
<td>aFPG &gt;5.5mmol/L=+1U</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>6 on daily insulin therapy</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>7 no severe hypoglycemic events happened before</td>
<td>n=154 (drop out 10)</td>
<td>n=162 (drop out 18)</td>
<td>% of subject reached the target Hba1C &lt;7 %</td>
<td>28.4%-21.2% =+7.2%</td>
<td>(p=0.01)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Rate of hypoglycemic event (events/patient/year)</td>
<td>7.1-6.2=0.9</td>
<td>(p=0.5)</td>
</tr>
</tbody>
</table>

aFPG=average fasting plasma glucose

General comment: Patient titrated insulin resulted in greater reduction in levels of HbA1C without differences in change of hypoglycemic events.
### Appendix 3: Table of Evidence. RCT study 5

<table>
<thead>
<tr>
<th>Bibliography</th>
<th>Study type</th>
<th>Level of evidence</th>
<th>Subject Characteristics</th>
<th>Intervention</th>
<th>Control</th>
<th>Lengths of follow up</th>
<th>Outcome measures</th>
<th>Effect size (IG-CG)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Kennedy et al, 2006</td>
<td>RCT</td>
<td>II</td>
<td>1 live in US</td>
<td>daily SMBG</td>
<td>standard-of-care insulin titrated by physician at follow up</td>
<td>at 6,12 &amp; 24 week</td>
<td>% reduction in Hba1C % (mean change from baseline)</td>
<td>(10.3-8.8)/10.3*100</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>2 mean age: 57</td>
<td>Self-manged insulin titration</td>
<td></td>
<td></td>
<td>%-(10.2-8.9)/10.2*100</td>
<td>%</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>3 type 2 D.M., no other DM complications</td>
<td>adjusted weekly by patient</td>
<td></td>
<td></td>
<td>% of subject reached the target Hba1C&lt;7% without hypoglycemia</td>
<td>38%-30%= +8%</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>4 B.M.I 34.3kg/m2</td>
<td>aFPG &lt; or≈5.5mmol/L= no change</td>
<td></td>
<td></td>
<td>% reduction in fasting plasma glucose (mmol/L)</td>
<td>(11.6-6.8)/11.6*100</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>5 mean A1c 13.3%</td>
<td>aFPG 5.6-6.6mmol/L=0-2U</td>
<td></td>
<td></td>
<td>Rate of hypoglycemic event (events/patient/year)</td>
<td>6.0-3.7=2.3(p&lt;0.05)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>6 on daily insulin therapy</td>
<td>aFPG 6.7-7.7mmol/L=+2U</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>7 no severe hypoglycemic events happened before</td>
<td>aFPG 7.8-8.8mmol/L=+4U</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>8 no acute or chronic metabolic disease, no liver or renal disease</td>
<td>aFPG 8.9-10mmol/L=+6U</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>n=1973(drop out 607)</td>
<td>n=1975 (drop out 612)</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

aFPG=average fasting plasma glucose

General comment: Active patients-titrated insulin and SMBG resulted in significant improvements in glycemic control, greater portion achieved treatment target.
### Appendix 4: Cost benefit ratio of the proposed intervention

**Target participants:** 160 persons

<table>
<thead>
<tr>
<th>Items of cost (HK$)</th>
<th>Benefits in monetary items (HK$)</th>
</tr>
</thead>
</table>
| **1. Staff training cost**  
3 trainings sessions (1 hour each), one NS responsible | **1. Hospital cost**  
- Uncontrolled hyperglycemia  
- Diabetic complications (diabetic foot amputation, cardiovascular disease, nephropathy) |
| $350 \times 3 = $1,050 | $3300 \times 3 \times 60 = $594,000  
$4620 \times 60 \times 10 = $2,772,000 |
| **2. Manpower for preparation**  
Existing NS x 2 as projects leaders | **Hidden benefit**  
Patients reduced risk of complications |
| 40 hours x 2 x $350 = $28,000 | Estimated to be reduced by 20% of risk with 1% reduction in HbA1c |
| **3. Printing cost**  
Notes for trainings  
Educational packages and logbooks for patients | |
| $100  
$1,000 | $1,100 |
| **4. Lancets and glucose testing strips for education**  
Patients SMBG and self-titration insulin | |
| Total $5 each lancet and strips) = $2000  
Patients self-paid ($5 each day) x 30 days = $150 x 9 months = $1,350 | |
| **5. Stationery** | |
| $500 | |
| **6. Venue (conference room)** | free |
| **7. Data analysis (by computers and excel)** | free |
| **Total (cost of intervention)** | **Total (benefits saved)** |
| $34,000 | $3,366,000 |
Appendix 5

An evidence-based guideline of promoting self-monitoring blood glucose (SMBG) and self-titration insulin to promote optimal blood glucose control for poorly glycemic controlled D.M. patients

Recommendation 1 (grade A)
1. Assessment should be done on eligible patients for baseline measurements
   Baseline measurements include HbA1C and fasting blood glucose level, dosages of insulin being used daily, episodes of hyperglycemia (h’stix > 16mmol/L) or hypoglycemia (h’stix <3.9mmol/L), body mass index.

Supporting evidence
- The baseline A1C and FPG values reflected overall glycaemia control (Meneghini L. et al, 2007) (1+)
- Efficacy assessments were based on the laboratory A1C values and fasting blood glucose (Kennedy L et al, 2006) (1+)

Recommendation 2 (grade A)
2. Type 2 D.M. patients with poor glycemic control are suggested to use insulin despite of oral anti-diabetic drugs to control their blood glucose level (HbA1C <7%).

Supporting evidence
- Good glycemic control in type 2 diabetes patients is associated with reduced risk of diabetes complications (Davies M. et al, 2005) (1+)
- The American Diabetes Association (ADA) recommended A1C goal of <7% (Meneghini L. et al, 2007) (1+)
- The Diabetes Control and Complications Trial and UK prospective Diabetes study have shown that lower A1C levels substantially reduce the incidence of long-term complications in type 2 diabetes patients (Meneghini L. et al, 2007) (1+)

Recommendation 3 (grade A)
3. Self-monitoring blood glucose (SMBG) should combine with insulin self-titration are useful tools for improving glycemic control. Patients are suggested to have daily SMBG on their fasting glucose, and insulin dosage is titrated according to the result of the SMBG.

Supporting evidence
- SMBG combined with patients self-adjusted dosing algorithm achieved significant improvements in glycemic control with minimal risk of hypoglycemia (Meneghini L. et al, 2007) (1+)
- The approach of using a self-directed titration algorithm based on the result of fasting plasma glycose is safe and increase the likelihood of achieving the target level of HbA1C (Blonde L et al, 2009) (1+)
- Patients achieved a lower fasting plasma glucose because of more frequent titration schedule (Meneghini L. et al, 2007) (1+)

**Recommendation 4 (grade A)**

4. Long-acting insulin is suggested to be self-titrated daily.

Supporting evidence
- Long acting insulin have 24 hours duration of action without pronounced peak, less likely to induce severe hypoglycemia (Davies M. et al, 2005) (1+)
- Low risk of hypoglycemia for patients titrating long acting basal insulin (Blonde L et al, 2009) (1+)

**Recommendation 5 (grade A)**

5. Daily Insulin titration algorithm suggested as below.

<table>
<thead>
<tr>
<th>Fasting blood glucose</th>
<th>Increase in daily basal insulin</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;3.9 mmol/L</td>
<td>withhold daily insulin once</td>
</tr>
<tr>
<td>4 – 7 mmol/L</td>
<td>0 unit</td>
</tr>
<tr>
<td>7.1 – 7.8 mmol/L</td>
<td>+2 units</td>
</tr>
<tr>
<td>7.8 - &gt;10 mmol/L</td>
<td>+2 units</td>
</tr>
</tbody>
</table>

Supporting evidence
- The reduction in fasting blood glucose and HbA1c was greater with the patient adjusted insulin algorithm (Davies M. et al, 2005) (1+)
- At week 12 and 14, the fasting blood glucose was close to 6.7mmol/L with low incidence of severe hypoglycemia, by using this titration regimen, it can facilitate patients participate in their treatment management (Davies M. et al, 2005) (1+)
- The use of insulin self-titration facilitated empowerment of patients, it resulted in substantial reductions of HbA1c in patients with type 2 diabetes using a patient-directed insulin titration algorithm. (Blonde L. et al, 2009) (1+)

**Recommendations 6 (grade B)**

6. A structured education program for training eligible patients on SMBG and insulin self-titration has to be delivered. Information about glycemic control has to be provided and allow patients to make appropriate adjustments to their insulin dose.
Supporting evidence
- Patients participated actively in the learning process, SMBG and blood glucose values were discussed in depth with patients so they could make changes in insulin dose (Silva and Bosco, 2015) (1-)
- A constructed education package for SMBG could improve glycemic control in subjects with type 2 diabetes (Chen H.S. et al, 2008) (1+)
- Education is important for type 2 diabetes patients (Meneghini L. et al, 2007) (1+)

Recommendations 7 (grade B)
7. Results of the daily SMBG should be recorded daily in a logbook by patients.

Supporting evidence
- The insulin dosage used, frequency of SMBG and frequency of hypoglycemia were assessed by reviewing the patients’ logbooks. (Silva and Bosco, 2015) (1-)
- Results of SMBG and hypoglycemic and adverse events were recorded and confirmed by a documented glucose value (Harris S. et al, 2014) (1+)

Recommendations 8 (grade B)
8. Clinic visit should be arranged at week 6 for monitoring the performance of patients’ self-titration insulin. End point HbA1c and fasting blood glucose should be taken at the follow up to monitor the efficacy of the patients’ adjusted insulin.

Supporting evidence
- Objective measurements should be HbA1c, hypoglycemic events, fasting glucose can be obtained at the follow up (Davies M. et al, 2005) (1+)
- Improvements in HbA1c can be obtained at follow up and early monitoring the effect of SMBG and patients self-adjusted insulin (Silva and Bosco, 2015) (1+)

Recommendations 9 (grade B)
9. Dosage of oral antidiabetic drugs should be made unchanged.

Supporting evidence
- Improvements in glycemic control with insulin titrated therapy can be evaluated, given the oral antidiabetic drugs remained unchanged. (Meneghini L. et al, 2007) (1+)
- Titration only made to insulin but not for oral antidiabetic drugs in order to evaluate the effect of frequent insulin titration (Kennedy L. et al, 2006) (1+)
Appendix 6. Gantt chart for implementing self-monitoring blood glucose (SMBG) and insulin self-titration for poor glycemic control type 2 D.M. patients in an out-patient DM center.

<table>
<thead>
<tr>
<th>Tasks</th>
<th>Months</th>
</tr>
</thead>
<tbody>
<tr>
<td>Meeting with ward manager, medical COS, and DOM to seek approval and funding</td>
<td>1</td>
</tr>
<tr>
<td>Set up a project team</td>
<td>2</td>
</tr>
<tr>
<td>Meeting with medical consultants and NS (diabetic) to see advice for the protocol</td>
<td>3</td>
</tr>
<tr>
<td>Develop nurse-led protocol and guidelines on SMBG and self-titration. Seek approval for the proposed protocol</td>
<td>4</td>
</tr>
<tr>
<td>Powerpoint presentation to medical doctors, nurses at DM centre</td>
<td>5</td>
</tr>
<tr>
<td>Training programmes for nurses at D.M. center</td>
<td>6</td>
</tr>
<tr>
<td>Pilot trial program (4 weeks testing period)</td>
<td>7</td>
</tr>
<tr>
<td>Gather advice and feedback, refine the titration protocol</td>
<td>8</td>
</tr>
<tr>
<td>Briefing the updated insulin self-titration protocol to nurses and doctors</td>
<td>9</td>
</tr>
<tr>
<td>Recruitment of patients &amp; Training period</td>
<td>10</td>
</tr>
<tr>
<td>Implementation of the insulin self-titration protocol (36 weeks)</td>
<td>11</td>
</tr>
<tr>
<td>Project Evaluation</td>
<td>12</td>
</tr>
<tr>
<td>Presentation of outcomes</td>
<td>13</td>
</tr>
<tr>
<td>Meeting to discuss the continuity of the innovation</td>
<td>14</td>
</tr>
</tbody>
</table>
### Appendix 7  Level of evidence (Scottish Intercollegiate Guidelines Network, 2011)

<table>
<thead>
<tr>
<th>Level</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>1++</td>
<td>High quality meta-analyses, systematic reviews of RCTs, or RCTs with a very low risk of bias</td>
</tr>
<tr>
<td>1+</td>
<td>Well-conducted meta-analyses, systematic reviews, or RCTs with a low risk of bias</td>
</tr>
<tr>
<td>1-</td>
<td>Meta-analyses, systematic reviews, or RCTs with a high risk of bias</td>
</tr>
</tbody>
</table>
| 2++   | High quality systematic reviews of case control or cohort or studies  
      | High quality case control or cohort studies with a very low risk of confounding or bias and a high probability that the relationship is causal |
| 2+    | Well-conducted case control or cohort studies with a low risk of confounding or bias and a moderate probability that the relationship is causal |
| 2-    | Case control or cohort studies with a high risk of confounding or bias and a significant risk that the relationship is not causal |
| 3     | Non-analytic studies, e.g. case reports, case series |
| 4     | Expert opinion |
## Appendix 8  Grades of Recommendations (Scottish Intercollegiate Guidelines Network, 2011)

| A | ● At least one meta-analysis, systematic review, or RCT rated as 1++, and directly applicable to the target population; or  
  ● A body of evidence consisting principally of studies rated as 1+, directly applicable to the target population, and demonstrating overall consistency of results |
|---|---|
| B | ● A body of evidence including studies rated as 2++, directly applicable to the target population, and demonstrating overall consistency of results; or  
  ● Extrapolated evidence from studies rated as 1++ or 1+ |
| C | ● A body of evidence including studies rated as 2+, directly applicable to the target population and demonstrating overall consistency of results; or  
  ● Extrapolated evidence from studies rated as 2++ |
| D | ● Evidence level 3 or 4; or  
  ● Extrapolated evidence from studies rated as 2+ |
REFERENCE


Kennedy L., Herman, W., Strange, P., Harris, A., Impact of active versus usual algorithmic titration of basal insulin and point-of-care versus laboratory measurement of HbA1c on glycemic control in patients with type 2 diabetes. Diabetes Care 29:1 1-8


Siminerio S., Ruppert KM., Gabby RA.(2013) Who can provide diabetes self management support in primary care? Finding from a randomized controlled trial. The Diabetes Educator 39:5 705-713


