Glycemia Management in Adults with Type 2 Diabetes

A Guide for Diabetes Educators

The Community Diabetes Education Program of Ottawa

April 2018

The Community Diabetes Education Program of Ottawa. Sponsored by Centretown Community Health Centre on behalf of The Coalition of Community Health and Resource Centres of Ottawa. Funded by The Ontario Ministry of Health and Long-term Care.Programme communautaire d'éducation sur le diabète d'Ottawa. Parrainé par le Centre de santé communautaire du Centre-ville au nom de la Coalition des centres de santé et de ressources communautaires d'Ottawa. Financé par le Ministère de la santé et des soins de longue durée d'Ontario.

Acknowledgments

Written by
Julie Maranger, RN, CDE, CCRP

Edited by
Tina Leech, RD, CDE
Janis Leiterman, RN, MPA, CDE
Nazli Parast, RN, CDE
Heather Williams, RD, CDE

Reviewed by
Nadine Church, RD, CDE
Anita Ruzansky, RD, CDE
Jennifer Stipetic, RN, CDE
Chi Van, RN, M.Sc., CDE

Formatted and reviewed by
Stéphanie Cyr, RD
Samar Milan, RD, MPH

Table of Content

Glossary

Antihyperglycemic Agent (AHA): refers to all medications used to control diabetes including oral agents, non-insulin injectable agents and insulin.

Client: is a person living with type 2 diabetes or prediabetes who is 18 years of age or older and not pregnant.

Clinical Consultant: a CDEPO Educator currently certified in Glycemia Management (GM) with demonstrated competence and confidence who is formally appointed by the Clinical Manager to approve AHA recommendations made by Educators who are not certified.

Educator: refers to all Diabetes Educators, specifically a Registered Nurse or a Registered Dietitian.

Mentee: the Educator who is developing their GM knowledge and skill.

Mentor: the Educator who is already certified in GM and is enabling the Mentee's learning journey. The Mentor is either the Clinical Manager or a Clinical Consultant.

Prescriber: the regulated health professional (e.g. Physician, Nurse Practitioner) who is accountable for prescribing AHAs for the CDEPO client.

Professional judgement: is used when providers decide what is "best" in a particular situation rather than what is "right" in some absolute sense. "Neither evidence nor clinical judgment alone is sufficient. Evidence without judgment can be applied by a technician. Judgment without evidence can be applied by a friend. But the integration of evidence and judgment is what the healthcare provider does in order to dispense the best clinical care." Hertzel Gerstein, 2012.

For abbreviations in this document please see Appendix 1.

Note: For pronouns, whenever possible, "they" will be used in place of "his / her" in order to be inclusive.

Symbols

Clinical Pearl: a clinical pearl is a recommendation or statement based on experience, expertise and judgement. It is not necessarily evidenced based and could be compared to a Grade D, Consensus recommendation in the Clinical Practice Guidelines (CPG). Clinical Pearls will be represented by the symbol opposite.

Teaching points: key points for client teaching will appear in a text box with a gradient green background as illustrated.

How to Use This Guide

Introduction

Type 2 Diabetes (T2D) can be well managed with effective collaboration between the person living with diabetes and their health care team. There are many facets to effective diabetes management and this guide will focus on managing glycemia or blood glucose (BG).

It is essential that Educators make efforts to involve the client in analyzing their BG values in order to promote self-management. Taking the time to listen to the client's day-to-day issues living with diabetes, ensures that the Educator is giving the client individualized and realistic support.

Managing glycemia is not the responsibility of any one person but of a team that can involve multiple disciplines with the client always at its center. Educators need to work collaboratively with other health care providers. Physicians and Nurse Practitioners (referred to in this guide as Prescribers) often rely on the support and recommendations of Educators to guide them in which antihyperglycemic agents (AHAs) may be most suitable for their clients.[1]

This document is a guide. Clients living with T2D are not all alike which means that managing glycemia is not solely a science but also a client-centered art.

In order to facilitate Educator learning, this guide has been organized into Learning Objectives. The content found with each learning objective is based on clinical evidence as well as clinical experience, expertise and judgment. The clinical experience, expertise and judgement will be differentiated throughout the guide by the "Clinical Pearl" symbol. In addition, some of the content contains key points that are important for clients to learn. These teaching points will be highlighted throughout the guide in a green text box.

CDEPO has developed an internal certification program to recognize Educators who have gained the knowledge and experience to make safe and effective AHA recommendations to Prescribers; these Educators are identified as "Clinical Consultants" at CDEPO and provide support to all CDEPO Educators in managing glycemia. This certification process is detailed in Chapter 6 of this guide.

Purpose

This guide is meant to support all CDEPO Educators in learning how to help clients to manage their glycemia. Taking medications or insulin to control BG is an important self-management behaviour. It is essential for Educators to recognize when clients may benefit from AHA adjustments, with or without lifestyle interventions, and to support Prescribers in making the adjustments. Educators are encouraged to use this guide even if they have not completed or are not progressing through CDEPO's internal certification process for managing glycemia.

Educator Prerequisites

In order to use this guide effectively, Educators must have an understanding of BG pattern management and experience in reviewing BG values to identify patterns and trends. In order to effectively manage glycemia, the Educator needs to *understand* all of the factors that can impact glycemia and be able to translate this knowledge into practice.

Policy

CDEPO "Policy 1-09 Glycemia Management" was created to ensure the safety of the client. It also protects the Educator and the reputation of the program by ensuring safe and effective AHA recommendations are made to Prescribers.

This policy specifies that Educators will not make AHA recommendations independently (directly or indirectly) to Prescribers if they have not been certified in glycemia management by CDEPO. Rather, they will recognize when their client's glycemia is not well controlled and review the client's case with an Educator who is certified in glycemia management (a Clinical Consultant). After the client's case is reviewed, should an AHA recommendation to a Prescriber be necessary, the Educator will make this recommendation to a Prescriber upon the approval of the Clinical Consultant.

Review

This guide will be reviewed, at a minimum, every time Diabetes Canada's Clinical Practice Guidelines (CPGs) are updated (every five years). Reviews will be done after interim pharmacological updates to these CPGs. When revisions are made to this guide, the date of the revisions will be put on the front of the guide and a summary highlighting the revisions made will be included at the beginning of the guide.

The guide will be reviewed by the CDEPO Clinical Manager and the CDEPO team of Clinical Consultants.

Learning Objectives

Each chapter in this guide represents a specific learning objective. The following details the learning objectives.

The Educator will:

1. *Identify relevant factors to assess when recommending AHAs in clients with type 2 diabetes (T2D).*
   a. Describe client factors influencing blood glucose (BG) control.
   b. Describe clinical factors to consider when recommending AHAs.

2. *Demonstrate safe, optimal oral and non-insulin injectable AHA adjustment recommendations.*
   a. Describe the purpose and use of the table titled: Oral and Non-Insulin Injectable AHA in Canada.
   b. Describe when medications are off-label versus contraindicated.
   c. Describe Oral AHAs and Non-Insulin Injectable AHAs in Canada profiles and key elements to consider in their use.
   d. Describe additional features of the individual Glucagon-like peptide-1 receptor agonists (GLP-1R) agonists.
   e. Describe how to reduce the risk of Diabetic Ketoacidosis (DKA) with Sodium-glucose co-transporter 2 (SGLT2) Inhibitors.
   f. Describe key factors when making Oral and Non-Insulin Injectable AHA adjustments.
   g. Identify examples of client profiles that may benefit from specific AHAs when adding an AHA to metformin or as monotherapy.

3. *Demonstrate safe, optimal insulin adjustment recommendations.*
   a. Describe insulin profiles.
   b. Describe initial insulin regimens including 1 and 2 insulin injections per day.
   c. Describe insulin adjustment using pattern management and which insulin to adjust for hyperglycemia and hypoglycemia.
   d. Describe basic steps for pattern management with insulin.
   e. Define intensive insulin therapy and describe key components of intensive regimens.
   f. Describe indications, methods and rationale for supplemental insulin dose adjustment – both anticipatory and compensatory.
   g. Calculate insulin:CHO ratio and use this method to determine **anticipatory** insulin dose adjustments for CHO intake; discuss anticipatory insulin dose adjustment for increased physical activity.
   h. Construct an algorithm and describe its use in making **compensatory** insulin dose adjustments.

4. *Describe, and / or demonstrate how to use the Glycemia Management Assessment Tool (GMAT) to make recommendations to a Prescriber including conferring with the Clinical Consultant and drafting a Letter to a Prescriber.*
   a. Describe purpose and how to use the GMAT to support comprehensive client assessment.

b. Describe and / or demonstrate application of the GMAT using the following client cases and drafting letters to the Prescriber:
    i. Switching from a Sulfonylurea to a Meglitinide
    ii. Adding a SGLT2 Inhibitor to Metformin and a Meglitinide
    iii. PreMix Switch to Basal Bolus Insulin
    iv. Adding an Insulin Adjustment Guide to Basal Bolus Insulin

5. *Identify Key Content of Teaching Plans for clients to self-adjust AHA in special situations.*
    a. Describe key factors when developing client teaching plans for self-adjustment of AHAs in the following special situations*:*
        i. Increased physical activity
        ii. Travel
        iii. Shift work
        iv. Illness
        v. Medical Procedures

6. *Describe the Glycemia Management Certification and Recertification Processes.*

Chapter 1: Assessment

Learning Objective 1

The Educator will identify relevant factors to assess when recommending an AHA for clients with T2D by:

a. Describing client factors influencing BG control (in adults with T2D).

b. Describing clinical factors to consider when recommending an AHA.

Client factors influencing blood glucose

Prior to making AHA recommendations to a Prescriber, a comprehensive assessment of the client must be completed. The following factors are essential components of the assessment. (Note: All of the following factors are included in the Glycemia Management Assessment Tool [GMAT] described in Chapter 4).

Year of diagnosis: T2D is a progressive disease and will likely require intensification of treatment after certain periods of time. In addition, longer duration of diabetes increases the risk for diabetes complications.

History of AHA use: This includes all past and present AHAs used by the client.

Medical orders: If already provided, medical orders regarding AHA therapy will be reviewed and initiated if they are appropriate as per Educator assessment. Follow-up assessment will determine effectiveness of the therapy.

Current medications: All of the client's prescription medications are reviewed to ensure there are no contraindications to the AHA being recommended. Over-the-counter medications including natural health products known to potentially affect BG are also relevant. Examples include high doses of salicylates as well as certain cold remedies.

Other medical conditions: All other medical conditions are reviewed to determine if there are any contraindications to an AHA being considered. Knowing these, also helps to determine the presence or risk of Cardiovascular Disease (CVD).

Hypoglycemia type, frequency and treatment: Occasional episodes of hypoglycemia do not necessarily affect overall glycemic control. However, the type and frequency of hypoglycemia can be a concern.

Types of Hypoglycemia

1. Routine hypoglycemia is defined as a BG value of less than 4.0 mmol/L with or without symptoms.

2. Pseudo-hypoglycemia refers to a client experiencing symptoms of hypoglycemia when BG values are ≥ 4.0 mmol/L. This usually occurs when BG values have been significantly elevated for some time and are falling over a relatively short period of time.[2]

3. Hypoglycemia unawareness refers to a client not experiencing the symptoms from the adrenergic response to a fall in glucose until the BG reaches lower and lower values. Clients who develop hypoglycemia unawareness do so primarily because of recurrent hypoglycemia. Recurrent hypoglycemia has been shown to reduce the glucose level that precipitates the counter-regulatory response necessary to restore euglycemia during a subsequent episode of hypoglycemia.[3]

   To restore normal response to hypoglycemia, adjustments to AHA therapy must be made to scrupulously avoid hypoglycemia. The return of hypoglycemia awareness could take up to 3 months.[2]

Treatment of hypoglycemia

"Hypoglycemia begets hyperglycemia".

Incorrect treatment of hypoglycemia is a common cause of hyperglycemia as well as persistent hypoglycemia.

It is important to assess exactly how clients treat hypoglycemia including:

- The source and quantity of fast-acting carbohydrate (CHO)
- The time between treatment and retesting BG
- Whether they wait to achieve a BG of at least 4.0 mmol/L before eating a meal or snack.

If clients are treating hypoglycemia with fast-acting CHO, and eating a snack immediately after treatment, the food will delay the absorption of the fast-acting CHO. This may prolong the hypoglycemic episode. Eating more CHO than recommended is a common error because of the anxiety associated with feeling hypoglycemic. Clients may believe that the more food they consume, the faster their BG will rise. Inform the client this may actually hinder their body's response.

Review the correct treatment for hypoglycemia.

Advise clients to contact the Educator if they have two or more episodes of hypoglycemia per week.

Teach clients that if they are experiencing frequent hypoglycemia, the calories in the treatment of hypoglycemia may contribute to weight gain.

"Treating pseudo-hypoglycemia with 15 – 20 g of CHO usually results in hyperglycemia." Through trial, the client can determine how much CHO it takes to relieve the symptoms. Recommend starting with 4-5 g of carbohydrate.

BG monitoring: In general, clients monitoring their BG can strongly rely on the accuracy of measurement values. However, various factors such as size and quality of the blood sample, extreme environmental conditions and extreme hematocrit values may distort BG values.[4] For clients on dialysis, ensure the meter is approved for use in such clients by referring to the meter manual.

Size and quality of the blood sample

Any one of the following can cause inaccurate BG values:

- Applying insufficient blood.
- Failure to dry hands after using soap and water, an alcohol swab or hand sanitizer can dilute the sample.
- Excessive squeezing of the finger can cause interstitial fluid to dilute the blood sample.
- Failure to rinse away sugary substances such as cookies can raise BG values substantially.
- Using hand wash preparations such as Alcojel can leave a sugary residue from the glycerine.
- Lotions have only a minor effect and soap has almost none.[4]

Environmental conditions

Exposure of the meter and/or test strips to extreme temperatures can affect the accuracy of BG values. Store the meter in a cool, dry place below 30°C, but do not refrigerate. When the meter is exposed to extreme temperatures, it will provide accurate BG values once it is returned to normal temperatures.

Test strips are degraded by exposure to:

- Temperatures higher than 30°C
- Light
- Humidity

Following exposure, test strips may no longer be reliable and are to be discarded.[4] (Check product monographs for exceptions.)

> To avoid exposure to light and humidity, teach clients to **not** remove strips from their storage container prematurely and to close the lid immediately after removing a strip.

Extreme hematocrit values

Many meters use intricate systems to evaluate hematocrit and correct for it, but the effect of hematocrit is complex.

The results of several studies with different glucose meters have indicated that lower-than-normal hematocrit values (<30% to <35%) result in overestimates of laboratory glucose values when glucose strip methods are used, whereas hematocrit values higher than normal (>45%) result in underestimates of laboratory values.[5]

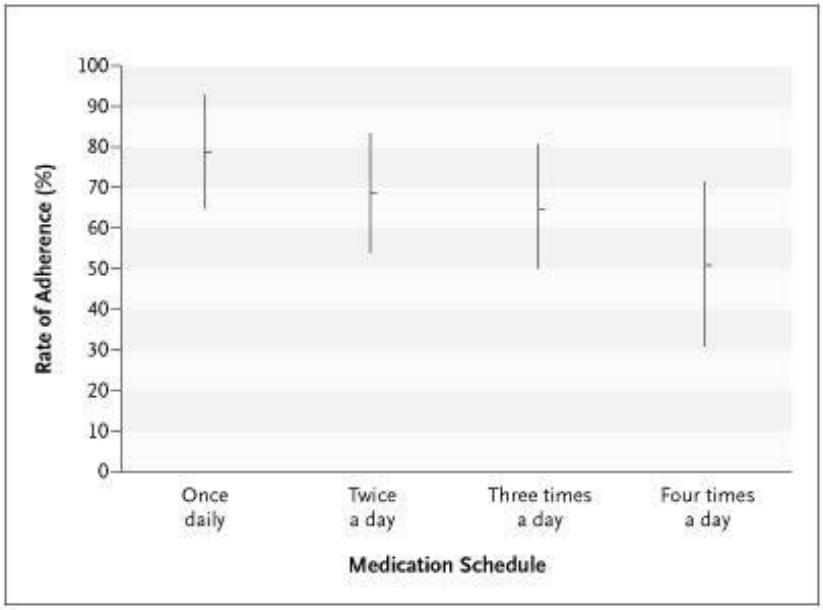
The main causes of abnormal hematocrit are anemia and severe dehydration. If meter BG values and A1C do not match, contacting the laboratory or asking the Prescriber for recent complete blood count test results may be useful.

Although consideration of these factors is required, it is essential to look at the entire situation. Adjustment to treatment must not be delayed if the overall BG values and A1C are trending upward significantly.

Medication-taking behaviour: Clients often miss prescribed medication, either intentionally or unintentionally. Reasons include forgetfulness, cost, side effects, difficulty reading labels, changing medication schedules and busy lifestyles. In addition, when clients do not understand or believe in the reason for taking the medication, there is an increased chance of non-adherence.[6]

Missed Dose Errors

Several studies have demonstrated relatively low adherence rates to taking medications as the frequency of dosing is increased.[6, 7] The following diagram is from a review article titled "Adherence to Medication" by Osterberg and Blaschke and demonstrates that the more time frames in a medication schedule, the lower the adherence rates.



Source: Osterberg, L and Blaschke, T, Adherence to Medication. NEJM 2005; 353:487-497August 4, 2005
http://www.ub.edu/farmaciaclinica/projectes/webquest/WQ1/docs/osterberg.pdf

This does not mean that Educators need to avoid suggesting medications that are to be taken at more than one time per day. There are many AHAs that are more effective when taken two or more times per day. The diagram simply reinforces the importance of getting to know the client and what medication regimen will work best for that individual.

Knowing if clients are missing doses of medications is relevant because it *may* be unsafe to make AHA adjustment recommendations if the client is not taking his/her medication consistently. For example, a client is prescribed Lantus at bedtime (hs) and gliclazide at breakfast and supper. However, they often forget the supper dose of gliclazide resulting in elevated FBG values the next day. If the Educator is unaware of the missed doses, they may recommend an increase in the dose of Lantus at hs. This would be an unsafe recommendation because it could potentially result in nocturnal hypoglycemia on nights the client does take gliclazide at supper.

Asking clients non-judgmentally how often they miss doses of medications can be done as follows as an example: "you take gliclazide twice a day. In two weeks that would be 28 doses. How many of those doses did you remember to take and how did you remember to take them?"[8]

"Medications do not work in people who do not take them."

Extra Dose Errors

Mistakenly taking extra doses of medications is less common but can also occur. Ask the client if they may have taken extra doses when there are unexplained episodes of hypoglycemia.

'Reminder packaging' refers to any assembly of medication(s), such as a pill box or dosette, blister pack, bottle or single-use container that physically incorporates a system for the day and/or time when the medication(s) are to be taken. Looking at the client's 'reminder packaging' can assist the Educator to determine if medications are being missed and how often.[9]

Medication Mix-up

Clients who take multiple types of medications can sometimes mix-up their medications particularly if they have pills that look very similar. For example, repaglinide 2 mg and Atacand 16 mg are both small, round and dark peach coloured tablets and could easily be mixed-up.

Clients who take more than one type of insulin also have reported accidentally switching their insulins. Either labelling insulin pens or using different models or colours of pens for each insulin type can help prevent this error.

Timing of medication

Asking what time clients take their medications in relation to the timing of meals/snacks and activity is important for most AHAs with respect to compliance and effectiveness. Examples include taking metformin with the meal to help prevent gastrointestinal upset; taking gliclazide before meals; taking repaglinide 1-30 minutes before a meal; and taking rapid acting insulin within 15 minutes before a meal.

In some instances, changing the timing of the AHAs can improve BG values. For example, a client taking Lantus at breakfast and suppertime whose FBG values are elevated may benefit from moving the supper dose of Lantus to hs. Educators also need to consider that some studies have shown that preprandial administration was associated with lower medication adherence compared to postprandial administration; this is particularly true if it is also associated with increased dosing frequency.[7]

Food and alcohol intake:

Food intake

Understanding the impact of food on BG is a fundamental role of the Diabetes Educator. Assessing the timing, quantity and type of CHO, protein, fat, and alcohol intake of the client is necessary to determine which AHA is best suited to the individual. Moreover, assessing the client's knowledge of which foods contain these elements is important in determining whether or not the client would be able to adjust an AHA based on food intake.

Clients may choose to either be as consistent as possible with their intake, particularly of CHO; or have a flexible intake and count CHOs. This will guide the Educator to recommend an AHA suitable for their intake. For example, if the client chooses to have a flexible intake, repaglinide may be a good option if a secretagogue is the AHA of choice. Refer to Chapter 3 and the section titled: Anticipatory insulin dose adjustments based on CHO intake.

There is limited evidence on how much CHO clients need to consume or by how insulin needs to be adjusted to prevent hypoglycemia. These will need to be individualized based on BG patterns.

Alcohol intake

Alcohol metabolism inhibits the production of glucose by the liver. The decline in hepatic glucose production can provoke hypoglycemia when alcohol is ingested in the fasting state.[10]

For clients treated by diet or AHAs that are not insulin and/or secretagogues, alcohol consumed with food does not necessarily cause hypoglycemia if the food is the equivalent of a healthy meal or snack.

For clients on insulin or secretagogues, there is a risk of delayed hypoglycemia resulting from alcohol consumed with or after the previous evening's meal.[11]

> Teach clients on insulin or secretagogues preventive actions such as consuming CHO equivalent to a healthy meal or snack and/or insulin dose adjustments and increased BG monitoring. For example, consuming crackers and cheese, or a sandwich may help to maintain BG where peanuts or chicken wings may not.

Alcohol in itself does not raise BG. However, if BG values are elevated after a situation where alcoholic beverages were consumed, the Educator needs to assess potential contributing factors such as the food intake, changes in activity, and/or adjustments to AHA that occurred when the alcohol was being consumed. Adjustments to AHA are based on the individual's BG values.

Clients also need to consider that excessive amounts of alcohol impair judgment; possibly resulting in inaccurate medication dosing or unrecognized hypoglycemia.[11] Because of its potential impact on BG, assessing the client's alcohol intake is essential and needs to be done in a non-judgmental manner.

Insulin and GLP-1R Agonists administration: There are several aspects of insulin administration that can affect BG control. Few studies address proper injection technique with GLP-1R. Pending further studies, clients using GLP-1R agonists are advised to follow the recommendations for insulin injections regarding needle length, site selection, and rotation.

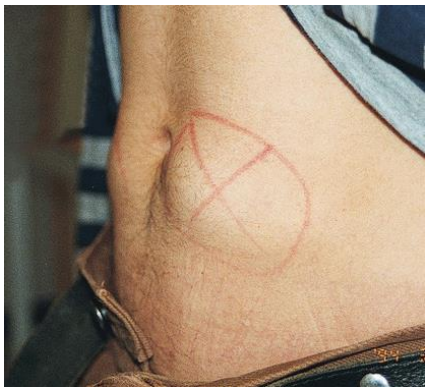
Injection site rotation

- Insulin analogues may be given at any injection site with similar uptake and action.
- Human insulins (regular, NPH, Novolin 30/70) vary substantially, with absorption being fastest from the abdomen and slowest from the buttocks. Varying between the sites with different rates of absorption can affect BG control.[12]

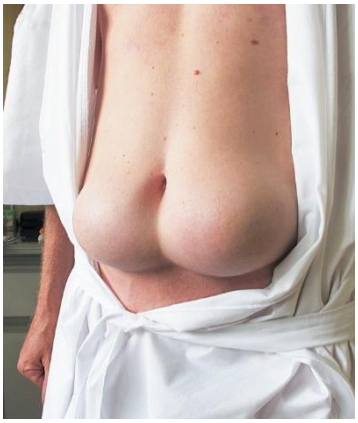
Rotating sites is essential for preventing *lipodystrophy* which can present as either lipohypertrophy or lipoatrophy.

Lipohypertrophy is an abnormal accumulation of fat underneath the surface of the skin caused by many insulin injections in the same site and/or needle re-use. It may be unsightly, mildly painful, and will change the insulin action profile. Lipohypertrophy is quite common.[12] The following pictures show two different clients with lipohypertrophy.

Lipohypertrophy:



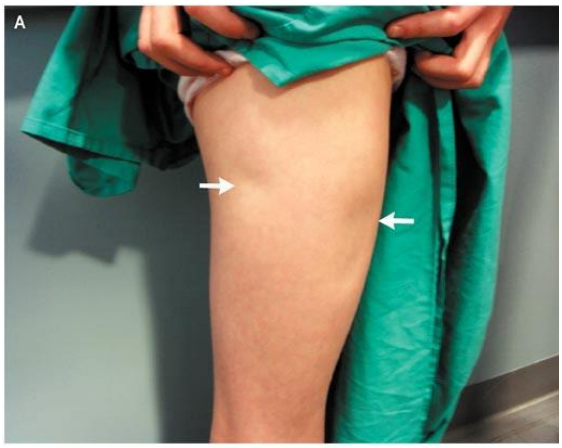
A 29-year-old man with two areas of insulin induced lipohypertrophy in the early stages.[13]



A 55-year-old man with a 31-year hx of T1D. He had injected insulin into two locations in the periumbilical region. Two discrete subcutaneous masses were palpated. Both masses were firm and pendulous.[14]

Lipoatrophy is the loss of subcutaneous fat around an injected area that clinically manifests as indenting and cratering. The mechanism of lipoatrophy is not well understood and may involve autoimmunity or local inflammation but it is relatively uncommon.[12] The following picture shows a client with lipoatrophy.

Lipoatrophy[15]:



To prevent lipodystrophy:

- Use insulin analogues whenever possible.
- Identify problems early by examining and palpating injection sites at each visit if possible; yearly at a minimum.

Teach clients to:

1. Rotate sites with each injection using
    i. an easy-to-follow rotation pattern
    ii. larger injection zones.
2. Avoid re-use of needles.
3. Inspect their injection sites. Give them 'hands on' training in how to detect lipohypertrophy and to a lesser extent lipoatrophy.
4. Avoid injecting into areas of lipodystrophy.

When changing from a lipohypertrophic injection site to a healthy site, caution clients about the risk of hypoglycemia since the insulin will be better absorbed in the new site. Advise them to reduce their insulin dose by 10% initially and monitor BG more frequently.[12]

Injection technique

Proper injection technique is essential to achieving optimal BG control and reducing BG variability. Most clients use insulin pens to administer insulin and GLP-1R. For the few clients using insulin syringes please refer to FIT Forum for Injection Technique Canada 3rd Edition 2017.

Insulin pen technique can affect BG values. It is essential to assess the following aspects of pen technique before making AHA adjustment recommendations:

i. Failing to prime the needle before the injection may result in air taking the place of insulin and reduce the expected dose.

ii. Removing the needle from the injection site too quickly can exacerbate leakage of insulin and reduce the expected dose. A small volume of leakage (a tiny bead of liquid at the injection site) can be ignored. It is almost always clinically insignificant.

iii. Using a needle that is too long can result in an intra-muscular (IM) injection. Insulin has different absorption profiles when deposited into a muscle.

iv. Reusing a needle can result in clogging of the needle and inaccurate dosing.

v. Mixing cloudy insulin improperly will result in unpredictable action times which can cause BG variability.[13]

Timing of insulin injections

The timing of basal insulin injections is kept as consistent as possible using +/- 60 minutes from the usual time as a guide. For example, if the usual time of hs insulin is 2200 hours then giving the dose sometime between 2100 and 2300 hours is ideal. It is acceptable to give the insulin earlier or later in the day for unexpected circumstances. However, changing the time frequently can result in glucose variability. When teaching clients to give insulin at hs, it is better to specify a time rather than say 'hs' as this can vary.

Ultra-rapid insulin (Fiasp) may be administered two minutes before a meal and up to 20 minutes after starting a meal, without compromising overall glycemic control or safety because its onset of action is so quick.[16]

The timing of rapid-acting insulin is ideally 0-15 minutes before the meal in most cases. It may also be given up to 15 minutes after the meal finishes in clients with gastroparesis due to delayed meal absorption.

The timing of regular insulin is ideally 30 to 45 minutes before the meal.

Allowing time for these insulins to peak helps match the insulin to the time the glucose from the meal is entering the blood stream.

Missed or extra insulin injections

Memory aids can be explored for clients who have difficulty remembering whether or not they took their insulin. Examples of aids include insulin pens with a memory, a memory aid that attaches to the pen or putting pen needles into a dosette.

> Teach clients to record missed or extra doses of insulin in their BG logs so that the Educator is aware when making dose adjustments.

Activity: Both aerobic and resistance activity can improve BG control, and a combination of both is better than either type alone.[17] However, because activity and variations in types and intensity of activity can impact BG values, Educators must assess the client's exercise/activity routine to determine its effect on their BG values.

Clients on secretagogues and/or insulin are at risk of hypoglycemia with higher than usual activity levels. This risk can last for up to 24 hours or more after the activity. To prevent hypoglycemia, clients may need to reduce their secretagogues or insulin dose before (and possibly after) exercise.[18]

Refer to Chapter 5, section titled "Developing client teaching plans for self-adjustment of AHAs in specific situations: Increased Physical Activity".

On the other hand, a major increase in glucose production can occur during brief, intense aerobic exercise as catecholamine levels rise. Hyperglycemia can result from such activity and persist for up to 1–2 hours, likely because catecholamine levels and glucose production do not return to normal immediately after the activity stops.[19]

Other: This section of the GMAT includes 'other' client factors that may influence BG control.

Presence of illness or infection

Minor illnesses such as the common cold have little to no impact on BG values.

More serious illnesses and/or infection cause a stress response in the body by increasing the amount of hormones such as cortisol and epinephrine. These 'stress' hormones work against the action of insulin, which increases the body's production of glucose and leads to high BG values.[20] In these cases, AHAs may need to be increased temporarily and most often involve the addition of, or increase in, insulin.

Refer to Chapter 5, section titled "Developing client teaching plans for self-adjustment of AHAs in specific situations: Illness".

Unusual stresses

During periods of unusually significant stress, BG values may increase due to the release of stress hormones. Clients need to be aware of the effects of stress on their BG values and make a note on their BG logs so that Educators are aware when reviewing the logs. AHA adjustments may need to be made if the stressor occurs frequently or over a long period of time.

In addition, constant stress and frustration caused by long term problems with BG control can also wear clients down and cause them to neglect their diabetes care. For example, they may start to ignore their BG values or simply forget to monitor BG or they may adopt poor lifestyle habits, such as exercising less, eating more 'junk' and processed foods, drinking more alcohol, and smoking. This is sometimes referred to as diabetes distress which is something different from stress. It is very specific to diabetes and caused by feeling overwhelmed by the burden of diabetes self-management.[21]

Concomitant use of other drugs that may affect BG values

Many concomitant medications can either inhibit or potentiate the action of insulin. Examples include:

a. **Inhibitors**: thiazide diuretics, glucocorticoids, thyroid hormone[22]
b. **Potentiators**: beta blockers, MAO inhibitors, salicylates (1.5-6 g/day), marijuana[23]

When clients are initiated on such medications, their AHA regimen may need to be adjusted to compensate for the effect on BG values. This is particularly true for medications used for the long-term. For example, you may note a rise in BG values if your client is started on Chlorthalidone which is a thiazide diuretic taken for blood pressure control. Since thiazide diuretics are usually a

long-term therapy with consistent duration of action, AHAs may need to be increased. This same theory applies to clients initiating thyroid hormone therapy.

However, medications such as glucocorticoids can have a short to long-acting effect on BG values. Thus, depending on the specific glucocorticoid, the choice of AHA to either initiate or adjust becomes important.

The table below titled 'Relative potencies of glucocorticoids and duration of action' provides the action time of some of the more commonly used glucocorticoids.[24]

Relative potencies of glucocorticoids and duration of action			
Duration	**Short acting 8-12 hours**	**Intermediate acting 12-36 hours**	**Long acting 36-72 hours**
Specific gluco-corticoid	Cortisone Acetate 25 mg Hydrocortisone 20 mg	Methylprednisolone 4 mg Prednisone 5 mg Prednisolone 5 mg	Betamethasone 0.6 mg Dexamethasone 0.75 mg

Source: Liu D et al. A practical guide to the monitoring and management of complications of systemic corticosteroid therapy. *Allergy Asthma Clin Immunol*. 2013; 9:30 https://aacijournal.biomedcentral.com/articles/10.1186/1710-1492-9-30

For example, when Hydrocortisone is initiated, a client may benefit from the action of either NPH or Levemir at the time of taking the Hydrocortisone (preferably in the am and at a consistent time of day) because of their shorter duration of action.

Beta blockers can mask signs and symptoms of hypoglycemia (except sweating). They also cause some inhibition of glycogenolysis and insulin secretion. Cardioselective agents such as acebutolol, atenolol, bisoprolol or metoprolol have less of these effects but may still require a decrease in AHA therapy.

Additionally, with medications that may be taken on a short-term basis such as high dose salicylates (1.5-6 grams/day), AHAs may need to be reduced to prevent hypoglycemia. Large doses of salicylates may be used in disorders such as rheumatoid arthritis, osteoarthritis and other inflammatory or painful conditions.[23]

Marijuana increases insulin sensitivity which can lead to hypoglycemia. Clients must also consider that this substance impairs judgment, possibly resulting in inaccurate medication dosing; or increases appetite which could lead to binge eating. In addition, unregulated marijuana could be contaminated with impurities such as lead which can contribute to early-onset kidney disease.[25]

Advise clients who are on insulin and/or a secretagogue and use marijuana to eat CHO when doing so.

Clinical factors to consider when recommending an AHA

Prior to making AHA recommendations to a Prescriber, all clinical factors pertaining to the client need to be assessed. The following identifies essential components of the assessment.

Client's age:

The client's age is relevant when deciding on glycemic targets and which AHAs to recommend. The same glycemic targets apply to otherwise healthy elderly as to younger people with diabetes. However, some AHAs are not recommended in the elderly or are a preferred choice. For example, sulfonylureas are to be used with caution because the risk of severe or fatal hypoglycemia increases exponentially with age and appears to be higher with glyburide.[26] Long-acting basal analogues are associated with a lower frequency of hypoglycemia than conventional insulins in this age group.[27]

Frailty Level:

<u>If client is more than 65 years old, assess frailty level.</u>
Assessing frailty level will ensure that glucose targets and AHA regimens are suitable to the individual. Clients with moderate or more advanced frailty that have a reduced life expectancy need not undergo stringent glycemic control.

The Clinical Frailty Scale, developed by Rockwood et al, has demonstrated validity as a 7-point frailty scale that has since been modified to a 9-point frailty scale from 1 (very fit) to 9 (terminally ill), which can help to determine which clients are frail.[26]

Clinical Frailty Scale

1 Very Fit – People who are robust, active, energetic and motivated. These people commonly exercise regularly. They are among the fittest for their age.

2 Well – People who have no active disease symptoms but are less fit than category 1. Often, they exercise or are very active occasionally, e.g. seasonally.

3 Managing Well – People whose medical problems are well controlled, but are not regularly active beyond routine walking.

4 Vulnerable – While not dependent on others for daily help, often symptoms limit activities. A common complaint is being "slowed up", and/or being tired during the day.

5 Mildly Frail – These people often have more evident slowing, and need help in high order IADLs (finances, transportation, heavy housework, medications). Typically, mild frailty progressively impairs shopping and walking outside alone, meal preparation and housework.

6 Moderately Frail – People need help with all outside activities and with keeping house. Inside, they often have problems with stairs and need help with bathing and might need minimal assistance (cuing, standby) with dressing.

7 Severely Frail – Completely dependent for personal care, from whatever cause (physical or cognitive). Even so, they seem stable and not at high risk of dying (within ~ 6 months).

8 Very Severely Frail – Completely dependent, approaching the end of life. Typically, they could not recover even from a minor illness.

9 Terminally Ill – Approaching the end of life. This category applies to people with a life expectancy <6 months, who are not otherwise evidently frail.

Scoring frailty in people with dementia

The degree of frailty corresponds to the degree of dementia. Common **symptoms in mild dementia** include forgetting the details of a recent event, though still remembering the event itself, repeating the same question/story and social withdrawal.

In **moderate dementia,** recent memory is very impaired, even though they seemingly can remember their past life events well. They can do personal care with prompting.

In **severe dementia,** they cannot do personal care without help.

Current A1C and target:

For most clients with diabetes, the target A1C is less than 7.0%. However, if the current A1C is significantly elevated (i.e. near or greater than 10.0%), individualizing the target to an achievable goal as a starting point may be more realistic for some clients. Individualize the A1C target based on the client's age, duration of diabetes, risk of severe hypoglycemia, presence or absence of CVD and life expectancy.

Lower A1C levels (≤ 6.5%) may be targeted in some clients to further lower the risk of nephropathy and retinopathy, but this must be balanced against the risk of hypoglycemia. More intensive BG lowering (i.e. A1C ≤ 6.5%), may be sought in clients with a shorter duration of diabetes, no evidence of significant CVD and longer life expectancy.[28]

Higher A1C targets (7.1 - 8.5%) may be appropriate in clients with any of the following:

a) Limited life expectancy
b) High level of functional dependency
c) Extensive coronary artery disease (CAD) with high risk of ischemic events
d) Multiple comorbidities
e) History of recurrent severe hypoglycemia
f) Hypoglycemia unawareness
g) Longstanding diabetes for whom it is difficult to achieve an A1C ≤ 7.0% despite effective doses of multiple AHAs, including intensified basal-bolus insulin therapy.[29, 30]

Weight and BMI:

The clients' weight and BMI are information needed when considering an AHA's effect on body weight. Weight is also used when calculating initial doses of insulin. Weight can be measured using a scale or reported by the client. BMI is a measure of body fat based on height and weight that applies to adult men and women. Height is needed to calculate the BMI. Decades of research have shown that BMI provides a good estimate of body fat and also correlates well with important health outcomes like heart disease, diabetes, cancer, and overall mortality. To calculate the client's BMI, refer to Dietitians of Canada – BMI for Adults.

An estimated 80% to 90% of people with T2D are overweight or obese. Selecting AHA therapies that have the ability to target glycemic control and overweight/obesity simultaneously represents the ideal approach to management of T2D.[31]

Clinical CVD or multiple risk factors:

Clinical CVD is defined as heart disease due to narrowing of the blood vessels caused by atherosclerosis. Recent trials have identified AHAs that show significant CV outcome benefit in people with T2D and clinical CVD.

The Empagliflozin Cardiovascular Outcome Event Trial (**EMPAREG OUTCOME**) included participants with T2D and clinical CVD consisting of prior myocardial infarction (MI), coronary

artery disease (CAD), unstable angina (UA), cerebral vascular accident (CVA) or occlusive peripheral vascular disease (PVD). See Appendix 2.[32, 33]

The Liraglutide and Cardiovascular Outcomes in Type 2 Diabetes Trial (**LEADER**) included participants with clinical CVD (including class 2 and 3 CHF) and participants with risk factors for CVD. However, the significant CV outcome benefit was only seen in those with clinical CVD. See Appendix 3.[34]

The Canagliflozin and Cardiovascular and Renal Events in Type 2 Diabetes Trial (**CANVAS**) included participants 30 years of age or older with a history of symptomatic atherosclerotic CVD or 50 years of age or older with two or more risk factors for CVD.[35]

Clients who have had the following procedures would have underlying clinical CVD:

- Coronary Artery Bypass Graph (CABG)
- Coronary, carotid or peripheral angioplasty with or without stents
- Carotid Endarterectomy (CEA)
- Limb angioplasty, stenting, or bypass surgery
- Limb or foot amputation due to circulatory insufficiency

Because the EMPAREG OUTCOME, LEADER and CANVAS Trials showed CV outcome benefit in clients who were at high risk for CV events, the observed benefits and risks may not apply to clients at lower risk or with other forms of heart disease not considered to be 'atherosclerotic'' in nature. Examples include:

- Atrial Fibrillation
- Valvular heart disease
- Hypertrophic or Dilated (Congestive) Cardiomyopathy
- Rheumatic heart disease
- Congenital heart disease

AHAs with demonstrated CV outcome benefit are to be considered in clients with clinical CVD. Empagliflozin and liraglutide are examples of AHAs that have demonstrated benefit. The CANVAS Trial also showed that participants treated with canagliflozin had a significantly lower risk of death from CV causes, nonfatal MI, or nonfatal stroke than those who received placebo but a greater risk of amputation. The highest absolute risk of amputation occurred among participants who had a history of amputation or PVD, but the relative risk of amputation with canagliflozin as compared with placebo was similar across the subgroups.[35] Canagliflozin should be used with caution in client with PVD or other risk factors for amputation.

At this time, there is no evidence that the benefit seen with empagliflozin and canagliflozin is a class effect. However, there is a trial currently taking place that will help determine this; dapagliflozin is being evaluated for its effect on CV events in the Multicenter Trial to Evaluate the Effect of Dapagliflozin on the Incidence of Cardiovascular Events (**DECLARE**) which has an estimated end of study date of April 2019.[36]

Similarly, it is not known if the CV outcome benefit seen with liraglutide is a class effect. Trials on other GLP-1R agonists (not currently approved in Canada) showed mixed results; i.e. in a trial with lixisenatide in T2D participants who had acute coronary syndrome, CV outcome results were neutral.[37] However, the trial with semaglutide in T2D participants with established CVD or CHF did show CV outcome benefit.[38]

Renal Function:

Chronic kidney disease (CKD) is associated with decreased clearance of many AHAs and their metabolites, more so in clients with moderate (eGFR from 60 to 30) to severe (eGFR from 29 to 15) CKD. This prolongs the duration of exposure to the drug and its metabolites. The only AHAs that are truly safe in clients needing dialysis (eGFR<15) are repaglinide and insulin. Some DPP4 inhibitors and dulaglutide may be used but cautiously with close monitoring of renal function. The eGFR must be considered when selecting an AHA.[39, 40]

The most common method of estimating renal function in Canada is the eGFR, using the 4-variable MDRD (Modification of Diet in Renal Disease) equation. This equation requires the patient's age, sex, serum creatinine and race. It is automatically computed and reported by many labs whenever a serum creatinine is ordered. The MDRD eGFR performs well when the GFR is <60 mL/min. The MDRD is generally more accurate than Cockcroft-Gault, especially for overweight or obese people.[41, 42]

For most clients, the eGFR provided by an Ontario laboratory is acceptable as long as they have stable creatinine concentrations. Individuals with unstable creatinine concentrations include pregnant women; patients with very serious co-morbid conditions; and hospitalized patients, particularly those with acute renal failure. If the eGFR is not provided by the laboratory or the Prescriber, the MDRD formula can be used to calculate the eGFR. The MDRD formula is found in the following link: https://www.qxmd.com/calculate/calculator_140/mdrd-egfr

For safe use of AHAs and eGFR, refer to DC CPG table titled 'Antihyperglycemic Medications and Renal Function' for dosage adjustments with reduced eGFR.

Potential AHA BG lowering effectiveness:

The AHA's effectiveness at BG lowering must be considered in terms of both the degree of baseline hyperglycemia needing correction and any heightened concerns regarding hypoglycemia (e.g. elderly clients or those with renal or hepatic dysfunction). The relative BG and A1C lowering of the various AHA classes when added to metformin are shown in the table titled 'Oral and Non-insulin Injectable Antihyperglycemic Agents in Canada 2018' found in Appendix 5.

Potential effect (of the AHA) on body weight:

Some of the classes of AHAs are associated with weight gain, while others are weight neutral or associated with weight loss. The drug effects on body weight are to be considered in glycemia management.[43] The following table shows the positive and negative effect on weight in pounds for each class of AHA.

AHAs and their effect on body weight[50]	
Weight gain	**Weight effect (kg)**
Insulin (fast acting, NPH)	+4.0 to +5.0
TZDs	+2.5 to + 5.0
Sulfonylureas	+1.5 to +2.5
Meglitinide	+0.7 to + 1.8
Weight neutral or decrease weight	
Insulin (basal analogues, detemir, glargine)	0 to +0.4
Metformin	Neutral
Acarbose	Neutral
DPP4 inhibitors	Neutral
SGLT2 Inhibitors[44]	-2.0 to -3.0
GLP-1R agonists	-1.6 to -3.0

This does not necessarily mean that Educators must avoid suggesting medications known to contribute to weight gain for clients who are overweight or obese. However, clients must be informed that the suggested medication is known to cause weight gain and may need to reduce their caloric intake accordingly.

Contraindications:

Contraindications describe situations in which the drug must **not** be used because the risk outweighs any potential therapeutic benefit. Educators must familiarize themselves with the contraindications of the medications they are recommending. The table titled 'Oral and Non-Insulin Injectable Antihyperglycemic Agents in Canada 2018' provides information on the *key* contraindications of each class of AHA. The ideal source for all contraindications is the product monograph of each specific AHA.[45]

Client preference and affordability:

Describe the benefits and risks of each class of medication to the client when adjustment to their AHA regimen is required. Involving the client in the choice of AHA may assist with adherence.

Whether or not the client can afford the recommended AHA is an essential consideration. Assessment of private insurance, Ontario Health Insurance Program (OHIP) Plus (if <25 years old) and/or Ontario Drug Benefit (ODB) coverage (if ≥65 years old or on the Ontario Disability Support Program (ODSP) of the AHA being recommended is the first step to determining affordability. Clients may choose to pay out of pocket if they do not have insurance coverage for the AHA they prefer.

Which medications are covered by the OHIP Plus program?
For OHIP Plus coverage, certain AHAs are covered for clients under the age of 25. The link to determine if an AHA is covered is https://www.ontario.ca/page/check-medication-coverage.

Which medications are covered by the Ontario Drug Benefit program?
For ODB coverage, certain AHAs are covered for clients age 65 or more as well as clients on ODSP. The main link to the ODB formulary is https://www.formulary.health.gov.on.ca/formulary and section 68:20 Anti-diabetic Agents which contains 5 sections, each with their own link. See Appendix 4. It is important to note that ODB may not cover all doses of a particular medication.

Glycemia patterns and trends:

A BG pattern is what happens to BG values throughout the day. For example, when does it go up? When does it do down? Is it too high or too low at a consistent time of day?

A trend refers to a general direction in which something is developing or changing. For example, BG values at a particular time of day are increasing over time.

Clients do not need to be concerned about a single number that is not within the target range. If the client is repeatedly above target at the same time of day however, investigate potential contributing factors.

If the current A1C is ≥ 8.5%, aim to improve pre-prandial BG first. When the A1C is ≥ 8.5%, more than one AHA is generally required to achieve target BG ranges. It can be more effective to use submaximal doses of multiple agents, rather than one agent at its maximal dose. If one agent is being added at a time; ensure additional agents are added in a timely fashion. The goal is to achieve targets within 3 to 6 months.

As the A1C approaches target values (<7.3%), postprandial BG control assumes greater importance for further A1C reduction. The AHA that have greater efficacy at lowering postprandial BG values are acarbose, repaglinide, DPP-4 inhibitors, GLP1-R (strongest is exenatide) and rapid acting insulin.[46]

Elevated FBG values may potentially be caused by either the Somogyi Effect or the Dawn Phenomenon.

Somogyi effect or rebound hyperglycemia which is defined as hyperglycemia following a hypoglycemic episode is a theory that is well known among diabetes clinicians however, there is little scientific evidence to support it. In recent studies of clients with type 1 diabetes (T1D) using continuous glucose monitoring data, FBG was significantly lower after hypoglycemic nights when compared to non-hypoglycemic nights.[47, 48] However, anecdotally many clinicians have noted episodes of rebound hyperglycemia in their practice and corrected the problem by decreasing insulin at hs. See the clinical pearl for a direct quote on the topic from Dr. Ronald Sigal who is an endocrinologist on the Expert Committee for the DC CPG.

"The studies by Choudhary and Hoi-Hansen, with reasonably large sample sizes, make the case that the Somogyi effect, if it exists, is not common. Nevertheless, I do come across cases where I believe I am seeing it. In such cases, the morning glucoses are a mix of low and high with few in target, and the problem seems to be resolved by reducing bedtime insulin or switching from NPH to detemir or glargine." Dr. Ronald Sigal May 2017.

Dawn phenomenon is the term used to describe an abnormal early-morning increase in BG usually between 3 a.m. and 8 a.m. in people with diabetes. It is caused by hepatic glucose output and peripheral insulin resistance in the early morning. This rise is subject to large day-to-day fluctuations and can extend into the post breakfast period.

When hs BG values are in target and morning BG values are elevated, ask the client to monitor BG during the night at approximately 3 a.m. for three nights in a row to help determine if the dawn phenomenon is the cause. If the dawn phenomenon is the cause, make adjustments to the AHAs that impact the morning time frame.[49]

Conclusion

This chapter discussed client factors influencing BG control as well as clinical factors to consider when recommending AHA. As described, there are many factors that need to be taken into account before recommending an AHA to a Prescriber. Achieving the learning objectives in this chapter will help to ensure that Educators demonstrate the knowledge and skill to make comprehensive client assessments before proceeding.

The next chapter will aid Educators to learn about oral and non-insulin injectable AHA and factors to consider in order to recommend safe, optimal AHA adjustments for clients.

Chapter 2: Oral and Non-Insulin Injectable AHA Adjustment

Learning Objective 2

The Educator will demonstrate safe, optimal oral and non-insulin injectable AHA adjustment recommendations by:

a. Describing the purpose and use of the table titled: Oral and Non-Insulin Injectable AHA in Canada.

b. Describing when medications are off-label versus contraindicated.

c. Describing Oral AHAs and Non-Insulin Injectable AHAs in Canada profiles and key elements to consider in their use.

d. Describing additional features of the individual Glucagon-like peptide-1 receptor agonists (GLP-1R) agonists.

e. Describing how to reduce the risk of Diabetic Ketoacidosis (DKA) with Sodium-glucose co-transporter 2 (SGLT2) Inhibitors.

f. Describing key factors when making Oral and Non-Insulin Injectable AHA adjustments.

g. Identifying examples of client profiles that may benefit from specific AHAs when adding an AHA to metformin or as monotherapy.

Oral and Non-Insulin Injectable AHAs in Canada

The table found in Appendix 5, titled: "Oral and Non-insulin Injectable Antihyperglycemic Agents in Canada" provides a summary of the classes, generic and trade names, potential A1C lowering (when added to metformin), potential effect on body weight, recommended daily doses, and key elements of all oral and non-insulin injectable AHAs available in Canada. The table will be updated when the 'Pharmacologic Glycemic Management of Type 2 Diabetes in Adults' chapter of the DC CPGs is updated.

The key elements listed in the last column of the table are a summary of important information to assist Educators to make an AHA recommendation to a Prescriber. However, this summary is NOT an exhaustive list of elements. It is meant to be a quick reference guide. In addition to the contraindications listed in the table, the AHA must not be used if the client has allergies to the medication or its ingredients. Also, insulin is the only AHA currently approved in Canada for use in pregnancy, lactating women and children under the age of 18.

It is important to note that not all doses of a given medication are necessarily covered by ODB. For example, currently metformin 500 mg tablets are covered but 1000 mg tablets are not.

Refer also to Chapter 5, "Managing Glycemia in Special Situations" to develop client teaching plans for self-adjustment of AHA's in specific situations such as: increased physical activity, travel, shift work, illness and medical procedures.

CDEPO Educators can recommend any of the AHAs approved for use in Canada except for Thiazolidinediones (TZD) as long as they are following the CDEPO Policy on Glycemia Management Recommendations. In 2010, Health Canada imposed restrictions on the use of rosiglitazone and physicians are required to obtain consent from the client when prescribing it. "The edema, weight gain, risk of CHF, increased risk of fractures and inconsistent data regarding MI risk with rosiglitazone and bladder cancer risk with pioglitazone significantly limit the clinical utility of this drug class.".[50]

For clients who are already on a TZD, the table provides information about dosages and essential assessments for clients using this class of medication. In particular, the importance of assessing for pretibial edema cannot be overemphasized. See Appendix 3: How to assess for pretibial edema.

When medications are off-label vs contraindicated

"Off-label" use of medications requires definition. All prescription pharmaceuticals (drugs) must be approved for sale by Health Canada. When Health Canada approves a drug for sale, the approval stipulates, among other things, the population for whom the drug can be prescribed, the indication(s) the drug can treat and the dosage(s) that can be administered. The use of an approved drug beyond the criteria set out in the product's approval is referred to as "off-label" use.

Off-label prescribing is not prohibited in Canada. In fact, it is permitted so that health professionals can pursue treatment that is in the best interest of their clients. In the management of type 2 diabetes, the majority of off-label recommendations are to add an AHA that is not listed for use with other AHAs in the product monograph.[51] For example, the product monograph for gliclazide does not list its use with any other AHAs; however, it is consistently used with other AHAs in practice.[52]

What does this mean for CDEPO Educators?

At CDEPO, Educators may make off-label AHA recommendations when:

- It involves the addition of an AHA that is not listed for use with other AHAs in the product monographs

  AND
- It is commonly used in practice.

When recommending an AHA that is off-label, the CDEPO Educator uses professional judgment regarding the need to inform the Prescriber that the recommendation is off-label. The chart below provides a few examples of how the Educator may decide whether or not to include a statement in the letter to the Prescriber indicating the addition of the AHA below is off-label.

Example of AHA being recommended	**Is the AHA listed for use as per the product monograph**	**Is the recommendation commonly used in practice**	**Statement in letter to prescriber indicating the addition of the AHA is off-label**
Adding Jardiance to GlucoNorm	No	No	Yes
Splitting Lantus to BID	No	Yes	No
Adding Victoza to NovoRapid and Levemir	No	Yes	No
Splitting Diamicron MR to BID	No	Yes	No
Adding Januvia to GlucoNorm	No	No	Yes

As with all AHA recommendations, suggesting the use of off-label AHA combinations is the shared responsibility of the Educator and the Prescriber.

Oral and Non-Insulin Injectable AHA profiles and key elements to consider in their use[53]

Over the last number of years there has been a growing number of Oral and Non-Insulin Injectable AHA's available in Canada. For ease of learning and reference, these agents have been organized in a table (found in Appendix 5). The table outlines the profiles of these agents and key elements to consider in their use. As well, additional information on Rosiglitazone is found in Appendix 6 which includes the Health Canada restrictions for this agent.

The table in Appendix 5 includes the profiles of the GLP-1R agonists available in Canada. A specific table, found in Appendix 7, highlights the various GLP-1R agonists and how they differ in: dosing schedule, mixing requirement, needle size, and the possibility to cause feelings of nausea, a reduction in FBG and a reduction in PPG.

How GLP-1R Agonists work

GLP-1R agonists:

- GLP-1 is a natural hormone in the body that plays a critical role in maintaining a healthy level of glucose in the blood.
- In T2D, GLP-1 production and function are often impaired.
- GLP-1R agonists lower BG values by stimulating the release of insulin from beta cells and reducing the release of glucagon from alpha cells in response to high BG values. In addition, GLP-1R agonists slow gastric emptying.
- GLP-1R agonists reduce body weight and body fat mass through mechanisms involving increased satiety, reduced hunger and decreased energy intake.
- GLP-1R agonists are taken subcutaneously, much like insulin. They come in pre-filled pens that must be refrigerated at 2-8° C and protected from light. After first use, the pen may be stored at room temperature and must not be frozen. It cannot be used if it has frozen.[54]

Note whether the needle is included with the delivery device so that the Prescriber knows whether to provide a prescription for needles.

How to reduce the risk of DKA with SGLT2 Inhibitors [55, 56]

Rare but serious, sometimes life threatening and fatal cases of diabetic ketoacidosis (DKA) have been reported in clients on Sodium-glucose co-transporter (SGLT2) inhibitors. The incidence of DKA with SGLT2 inhibitors does not appear to exceed the low levels occurring in the general diabetes population; the risk-to-benefit ratio overwhelmingly favours continued use of SGLT2 inhibitors in T2D.

The concern with SGLT2 inhibitors is that in several of the cases of DKA, the presentation of the condition was atypical; BG values were only moderately elevated (e.g. <14.0 mmol/L). Such atypical presentation could delay diagnosis and treatment of DKA.

Clients with T2D at highest risk for DKA are those:

- With long-standing T2D with marked β-cell insufficiency
- With LADA
- Experiencing prolonged starvation
- After surgery
- With an intercurrent illness
- With excessive alcohol intake
- On very low carbohydrate/ketogenic diets

Educators and Prescribers working with clients taking SGLT2 inhibitors need to be informed of the preceding. In addition, SGLT2 inhibitors must be withheld in the following situations:

- Acute illness
- Pre-and post-bariatric surgery (until off the pre-surgery low CHO diet)
- A minimum of 24 hours before elective surgery
- Post-operatively until client is fully recovered and eating and drinking well
- Upon diagnosis of DKA.

When starting on an SGLT2 inhibitor, the risk for DKA can be reduced by teaching clients:

1. That there is a risk of DKA and the symptoms that may be signs of DKA include: difficulty breathing, nausea, vomiting, stomach pain, confusion, loss of appetite, feeling very thirsty and feeling unusual tiredness.

   If these signs occur, clients must stop taking the SGLT2 inhibitor and call their Prescriber or go to the Emergency Room. Health care professionals must assess clients for DKA immediately if these symptoms occur, regardless of the BG values, and the SGLT2 inhibitor is to be discontinued.

2. The potential risk factors that can predispose them to DKA with SGLT2 inhibitors, such as:

   - any risk of dehydration, such as with very vigorous exercise and during preparation for a colonoscopy
   - conditions leading to restricted food intake or very low carbohydrate diets
   - sudden reduction in insulin
   - increased insulin requirements due to acute illness
   - excessive alcohol use

3. When on insulin and starting a SGLT2 inhibitor that they will need to increase the frequency of BG monitoring as they may need a reduction in their insulin dose. Insulin doses must be reduced gradually and cautiously to avoid the risk of sliding toward DKA. A reduction in insulin dose is not to be regarded as a positive outcome in itself.

Steps to making Oral and Non-Insulin Injectable AHA Adjustment Recommendations

After a comprehensive assessment of all client and clinical factors that can impact glycemia (refer to Chapter 1) the following steps will help guide the AHA adjustment recommendations.

1. BG Monitoring
   - Establish BG and A1C targets with the client. Individualize!
   - Obtain a recent A1C.
   - Ask the client to monitor BG at least 2 times per day; ideally 4 times per day (ac meals and hs) during initial periods of medication adjustment. Monitoring 2-hour pc may become useful as ac and hs BG values improve.

2. Food and Activity
   - Discuss whether or not there are possible lifestyle modifications that the client is willing to make to improve BG values.

3. Taking Medication
   - Assess client's medication-taking behaviours and help the client plan how to address barriers and develop effective strategies if necessary.

4. Pattern Management

   Definitions:

   Pattern Management: Making adjustments to AHAs based on BG patterns and trends is referred to as pattern management. It is a systematic approach to identifying patterns and trends within BG data and then taking appropriate action based upon those results.[57]

   Pattern: What happens to BG throughout the day? For example: When does it go up? When does it go down? Is it too high or too low at a consistent time of day?

   Trend: A general direction in which something is developing or changing. For example: BG at a particular time of day is increasing over time.

   - Make adjustments to AHAs (non-insulin and insulin) based on BG patterns and trends, not on a single BG value.

   - When initiating pattern management, ask the clients to be as consistent **as possible** in their schedule, CHO intake, and activity level for a defined period of time until a pattern can be seen. Consistency may pose a challenge for some clients; Educators need to individualize recommendations.

- If the client decides to take immediate action to correct an out-of-target BG value, teach them to record the action. For example, clients may adjust for a high BG level by being more active or eating less food. Similarly, if the BG level is low, clients may choose to reduce or even omit their medication. The Educator making AHA adjustment recommendations needs to be aware of these actions.

> Teach a client to determine which time of day to look at in order to assess a BG trend by asking the question 'when is this medication going to have an impact'? For example, the lunchtime repaglinide dose is based on the ac supper BG trend.

5. Consider the following pharmacological management guidelines prior to making an AHA adjustment recommendation: [50]

    - If A1C is < 8.5%, lifestyle management may be used initially. If BG targets are not achieved within 3 months of lifestyle management, an AHA should be initiated.

    - Unless contraindicated, metformin remains the initial agent of choice. Metformin may be used at the time of diagnosis, in conjunction with lifestyle management.

    - Timely adjustments to, and/or additions of AHAs should be made to attain target A1C within 3 to 6 months.

    - In clients with marked hyperglycemia (A1C > 8.5%), AHAs are initiated concomitantly with lifestyle management, and consideration should be given to initiating combination therapy with 2 agents.

    - Start by adjusting one AHA at a time. However, when adding or increasing an AHA, prepare for the possibility of needing to adjust the current therapy to prevent hypoglycemia.

    - Consider that the use of combinations of submaximal doses of AHA produces more rapid and improved BG control compared to monotherapy with maximal dose of 1 agent.

    - In clients with clinical CVD, the addition of a SGLT2 inhibitor or a GLP-1R agonist with demonstrated CV outcome benefit should be considered providing there are no reasons to not use these classes.

6. Involve the client in the decision making in AHA selection by presenting the benefits and risks of the AHAs being considered.

Examples of client profiles that may benefit from specific AHAs when adding an AHA to metformin or as monotherapy

In a client who:

1. **Is overweight and 2-hour pc BG values are elevated, DPP4 Inhibitor** may be a good choice. The use of a DPP4 Inhibitor in combination with metformin has the advantages of:
   - being weight neutral
   - targeting postprandial BG values
   - not being likely to cause hypoglycemia
   - metformin and all of the current DPP4 Inhibitors are available in combination drugs.[58]

2. **Is overweight and does not have any contraindications to SGLT2 Inhibitors**, medications from this class can potentially contribute to weight loss.[45]

3. **Is obese and does not have any contraindications to GLP-1R agonists,** medications from this class can potentially contribute to significant weight loss.[55]

4. **Has irregular meal or activity patterns**, a meglitinide may be a good choice because it offers flexible dietary patterns and dosing regimens. Adding a GLP-1R agonist may be a good choice because of its mechanism of action which is to stimulate the production of insulin in response to glycemic load.

5. **Finds once-a-day medication regimens more suitable** and a sulfonylurea is the medication of choice; the use of Glumetza and Diamicron MR are a good combination.

6. **Has clinical CVD**, an AHA with demonstrated CV outcome benefit will be considered to reduce the risk of major CV events.

7. **Is elderly with a frailty scale of 5 and a target A1C of < 8.5%** (current A1C 9.0%), choosing an AHA with minimal risk of hypoglycemia such as DPP-4 inhibitor may be a good choice. If the current A1C was > 9.5%, choosing an AHA with minimal risk of hypoglycemia and a higher potential for A1C lowering such as a GLP-1R agonist may be a good choice.

   In addition to the client factors, the BG patterns and trends need to be considered when deciding which AHA to add to metformin. Examples follow.

Example #1 - Your client is on metformin 1000 mg at breakfast and at supper and presents with the BG record below. He is 60 years of age, A1C is 7.6%, BMI is 27, eGFR is 72 mL/min/1.73m^2 and there is no known CVD.

Breakfast	Lunch	Supper	Hs	0300	Comments
6.2	9.0	10.0	7.0		
4.1	7.9	9.9	9.0		Ate out for supper
7.0	8.9	8.8	7.6		
5.6	8.8				

In this case, the pattern shows ac lunch and supper BG values are elevated (highlighted in yellow); some of the hs numbers are elevated; and FBG values are in target. Because only the daytime BG values are elevated, the addition of gliclazide 80 mg in the morning may be a good choice or if he prefers to have some flexibility with his CHO intake; repaglinide ac meals is another option.

Gliclazide has a duration of action of 12-18 hours; the action of repaglinide peaks at 1 hour and is completely eliminated within approximately 4 hours. Consequently, neither medication is likely to cause nocturnal hypoglycemia in this client.

Example #2 - Your client takes metformin 500 mg at breakfast and 500 mg at supper because she cannot tolerate full dose. She presents with the BG record below. She is 72 years of age with a frailty level of 2, A1C is 8.9%, BMI is 37, eGFR is 68 mL/min/1.73m^2 and she has a history of CHF.

Breakfast	Lunch	Supper	Hs	0300	Comments
9.0	6.8	7.8	7.0		
7.6	4.4	8.0	9.8		
8.9	7.0	7.6	7.6		
8.5	5.1				

In this case, the pattern shows FBG and supper BG values are elevated (highlighted in yellow) as are some of the hs values. Pre-lunch BG values are in target. The addition of empagliflozin is an appropriate choice for this client because empagliflozin has:

1. A demonstrated CV outcome benefit in clients with CHF.
2. A strong impact on FBG and may lower values by 1.2-1.5 mmol/L with minimal risk of hypoglycemia when added to metformin.
3. The added benefit of potentially causing weight loss and this client's BMI is 37.[32]

Conclusion

This chapter discussed oral and non-insulin injectable AHAs as outlined in the most current DC CPG and key considerations in their use. Agents are continually being approved for use in Canada and it is the responsibility of the Educator to stay current. Off-label use of AHAs has been distinguished from contraindications to use. Factors relevant to making AHA adjustments and client characteristics suggesting benefit from particular classes of AHAs have been reviewed.

The next chapter will aid Educators to learn about insulin and how to make safe, optimal insulin adjustment recommendations.

Chapter 3: Insulin Adjustment

Learning Objective 3

The Educator will demonstrate safe, optimal insulin adjustment recommendations by:

a. Describing insulin profiles.

b. Describing initial insulin regimens including one and two insulin injections per day.

c. Describing insulin adjustment using pattern management and which insulin to adjust for preventing and/or managing hyperglycemia and hypoglycemia.

d. Describing basic steps for pattern management with insulin.

e. Defining intensive insulin therapy and describing key components of intensive regimens.

f. Describing indications, methods and rationale for supplemental insulin dose adjustment – both anticipatory and compensatory.

g. Calculating insulin:CHO ratio and using this method to determine **anticipatory** insulin dose adjustments for CHO intake; and discussing anticipatory insulin dose adjustment for increased physical activity.

h. Constructing an algorithm and describing its use in making **compensatory** insulin dose adjustments.

Insulin profiles

The insulin action profiles described in Appendix 8 are a guide as the action times can vary from client to client. NPH and regular insulin (including combinations) have the most variability whereas insulin analogues may be more predictable. The individual response to insulin is best determined by the client's BG patterns and trends.[59]

Insulin regimens involving one (1) and two (2) insulin injections per day

Insulin regimens are tailored to the individual's goals, lifestyle and ability for self-management. Which type of insulin and regimen used is based on the assessment of client factors influencing BG control and clinical factors to consider when recommending the insulin. Initially, insulin regimens in T2D typically involve one and two injections per day. Three and four injections of insulin regimens are included in the intensive insulin therapy section of this guide.

One (1) Injection per Day

Examples of regimens:

1. Intermediate-acting insulin pre-breakfast or at hs*
2. Long-acting or ultra-long acting insulin analogue in am, at supper or at hs
3. Premixed insulin pre-breakfast or pre-supper

hs is used in the literature as the bedtime timeframe for taking insulin. However, bedtime may vary from one night to the next. Advise clients to be as consistent with the timing of this injection as possible.

Key elements in adjusting one injection of insulin per day

- One injection per day is indicated in T2D only and typically is used in combination therapy with other AHAs.

- A starting dose of 0.1-0.3 U/kg or 10 U of intermediate or long-acting analogue insulin at hs and titrating 1U per day until morning BG target is met are common ways of initiating insulin.[60, 61]

For clients with a BMI <26, a starting dose of 0.1 U per kg of intermediate insulin or long-acting analogue may be safer, especially in the elderly.

- The recommended minimum is once daily FBG monitoring when starting basal insulin.

- When using one injection of premixed insulin[62], a starting dose of 10 U or 0.1 U per kg either at breakfast or supper can be used. Clients who may benefit from the addition of a premixed insulin versus basal insulin include those:
    a. With an A1C > 8.5%

b. With higher postprandial BG values (difference between preprandial and postprandial >3mmol/L)
c. Who are less capable or willing to perform several measurements of BG per day
d. Who are able to eat regularly and fairly consistently

- It is *not recommended* to increase insulin if two episodes of hypoglycemia in one week or any nocturnal hypoglycemia occurs.

- The recommended starting dose of Toujeo[63] in insulin naïve clients is 0.2 units per kg once daily.

- When switching from once daily intermediate-acting insulin to once daily long-acting insulin analogue, the initial dose remains the same. For very large doses, consider decreasing initial dose by 20%. However, when switching to glargine 300 U/ml (Toujeo) or detemir, most clients will require a higher total daily dose (TDD) than the original dose of intermediate insulin.

- When switching from twice-daily basal insulins to once-daily Toujeo, the recommended initial Toujeo dose is 80% of the TDD of basal insulin that is being discontinued.

> Important: When using insulins that have greater than 100 U/ml concentrations, clients must be taught to never use an insulin syringe to draw insulin out of the cartridges; examples include Toujeo and Humalog 200 U/ml. This could result in serious overdoses of insulin.

- The recommended starting dose of degludec (Tresiba)[64] in insulin naïve clients is 10 U once daily.

- When switching to degludec from once-daily long or intermediate-acting insulin, the initial dose remains the same.

- When switching from twice daily long or intermediate-acting insulin it is recommended that the dose of degludec be reduced by 20% to lower the risk of hypoglycemia.

- When switching from twice daily intermediate-acting insulin to a once daily long-acting insulin analogue (glargine or detemir), the initial TDD is decreased by 20%.

When deciding on which long-acting basal insulin analogue to use, based on a systematic review done by SG Swinnen et al., there are very few statistically significant differences between detemir and glargine. Overall, pooling of the four studies used in the review resulted in:

- The difference in A1C between the two treatment groups was not statistically significant, although glargine was associated with slightly lower fasting plasma glucose.
- The difference in overall nocturnal and severe hypoglycemia when comparing insulin detemir to insulin glargine was not statistically significant.

- Insulin detemir was associated with statistically significant relatively small reduction of weight gain.
- Treatment with insulin glargine resulted in a lower daily basal insulin dose and a lower number of injection site reactions.[65]

Two (2) Injections per Day

Examples of regimens:

1. Premixed insulin before breakfast and before supper

2. Intermediate-acting insulin or long-acting analogue *plus* one injection of rapid acting insulin to either the main meal or breakfast - starting dose of rapid acting insulin is 2 to 4 U

3. Intermediate acting insulin in am and at hs

4. Long-acting insulin analogue in am and either at supper or hs

Key elements in adjusting two injections of insulin per day

- Two injections per day are primarily indicated in T2D and are typically used in combination therapy with other AHAs.

- A minimum of twice daily BG monitoring is recommended to safely titrate two injections of insulin per day.

- When switching from once daily intermediate-acting or long-acting insulin analogue to twice daily, the initial TDD remains the same.

- In the previous examples of regimens, numbers 1 and 2 involve the addition of prandial insulin. When the TDD exceeds 0.5 U per kg per day the need for prandial insulin becomes more likely. This is especially true as it approaches 1 unit per kg per day.[66]

- Premixed insulin may be started:
  - With 5-10 U twice daily and titrate dose by 1 to 2 U in one or both injections every 2-3 days.

    OR
  - Using a TDD of 0.1 U per kg and split of 2/3 of TDD in am and 1/3 at supper.

- When switching from twice daily NPH or Levemir to once-daily Toujeo, the recommended starting Toujeo dose is 80% of the TDD of basal insulin that is being discontinued.[63]

- When switching from twice daily long or intermediate-acting insulin to once daily Tresiba, it is recommended that the dose of Tresiba is reduced by 20% to lower risk of hypoglycemia.[64]

Insulin adjustment using pattern management and which insulin to adjust for hyperglycemia and hypoglycemia

- As with non-insulin AHA adjustments, pattern management is used to initiate or make adjustments to insulin. To best determine patterns of BG values, the client is asked to be as consistent as possible in their schedule, CHO intake, and activity level for a period of time.

- BG values, or a pattern of values, are a reflection of insulin taken in the past. To make the correction, an adjustment needs to be made in the insulin dose that was taken before the time of the pattern.

- If a pattern is seen at a particular time of day, the insulin impacting that time frame is adjusted. Which dose is adjusted depends on the time of the pattern and on the insulin regimen. Refer to the following table titled 'Which insulin to adjust for hyperglycemia and hypoglycemia'.

Which insulin to adjust for hyperglycemia and hypoglycemia

For BG values consistently out of target, adjust the most responsible insulin dose by up to 10% of the dose being adjusted. (If BG >14 mmol/L across the day, consider 20%) (> = greater than; < = less than).

Hyperglycemia	Hypoglycemia
Before breakfast: • If FBG is >7 and < 10 mmol/L, increase hs (or evening) intermediate or long-acting. • If BG is > 10 mmol/L, check BG at 0300. • If 0300 BG is high, increase hs (or evening) intermediate or long-acting. • If 0300 BG is low, decrease hs (or evening) intermediate or long-acting. *2 hours after breakfast:* • Increase breakfast rapid-acting.	*Before breakfast:* • If 0300 low, decrease hs (or evening) intermediate or long-acting. *Before breakfast:* • Decrease hs (or evening) intermediate or long-acting or AM long-acting. *2 hours after breakfast:* • Decrease breakfast rapid-acting.
Before lunch: • Increase morning rapid-acting. *2 hours after lunch:* • Increase lunch rapid-acting.	*Before lunch:* • Decrease morning rapid-acting. *2 hours after lunch:* • Decrease lunch rapid-acting.
Before supper: • Increase lunch rapid-acting or morning intermediate or long-acting. *2 hours after supper:* • Increase supper rapid-acting.	*Before supper:* • Decrease lunch rapid-acting or morning intermediate or long-acting. *2 hours after supper:* • Decrease supper rapid-acting.
Before bed: • Increase supper rapid-acting.	*Before bed:* • Decrease supper rapid-acting.

2. Establish target BG values with the client.

3. Ensure a plan for reasonably consistent CHO intake and activity level is in place with what the client's usual lifestyle entails while dose adjustments are being made.

4. Have client monitor BG ac meals and hs as initial insulin adjustments are made on pre-meal values.

5. Have the client keep a record of BG values, CHO intake (either by counting CHO or indicating an approximate quantity) and insulin doses. Clients may use the "CDEPO Blood Glucose, CHO & Insulin Record" (Appendix 9) or "Carbohydrate Counting Assessment – Blood Glucose and Food Record" (Appendix 10) or a record of their choice. The important thing is that they keep an accurate record.

6. For adjustments to rapid-acting analogues, 2-hour pc meals monitoring will help fine-tune mealtime insulin doses. Only consider this once the A1C is closer to target (7.3%).

7. Assess patterns or trends of BG values over 2 to 3 days.

8. Identify insulin action that influences a particular pattern.

9. If both hypoglycemia and hyperglycemia are present, adjust for hypoglycemia first.

10. Adjust most responsible insulin by 10 to 20% of the dose being adjusted.

11. If all BG values are comparably elevated, start with adjusting the insulin taken at the timeframe prior to the highest BG pattern.

12. In some cases, it may be appropriate to adjust more than one insulin simultaneously. For example, if hs and am BG values are elevated, adjustment of both the hs long-acting insulin and supper rapid-acting insulin may be needed. Increasing the supper rapid-acting insulin will decrease the hs BG. With a lower hs BG value, the hs long-acting insulin may need to be reduced to prevent hypoglycemia.

13. Re-evaluate BG values in 3 days. Advise the client to call sooner if they are experiencing frequent hypoglycemia or have other concerns.

14. Ensure client understands rationale for all dose adjustments and that they agree to make the change. If appropriate, teach the client to make self-adjustments to insulin and provide an Insulin Dose Adjustment Guide.

15. Follow-up intervals may lengthen as BG values reach target and/or the client becomes proficient at adjusting his/her own insulin.

Examples of insulin adjustments based on pattern management

Example #1 - Client A is on one injection of intermediate or long-acting insulin at 2200 and presents with the BG values recorded below.

Breakfast	Lunch	Supper	Hs	0300	Comments
12.1	9.0	7.8	7.0	10.2	
11.9	7.6	6.0	9.8		
7.2	8.9	8.8	7.6	9.0	
10.2	8.5				

In this case, all of the BG values before breakfast are elevated as are the 0300 values. An increase in the insulin at 2200 is needed.

Example #2 - Client B is on 2 injections of insulin detemir, one at breakfast and the other at 2200 and presents with the BG values recorded below.

Breakfast	Lunch	Supper	Hs	0300	Comments
11.1	9.0	7.8	7.0	3.9	
14.9	7.6	6.0	9.8		
8.2	8.9	8.8	7.6	3.5	
13.2	8.5				

In this case, all of the BG values before breakfast are elevated however, the 0300 values are low. A decrease in the insulin detemir taken at 2200 is needed.

Example #3 - Client C is on Humalog Mix25 at breakfast and at supper and presents with the BG values recorded below.

Breakfast	Lunch	Supper	Hs	0300	Comments
6.2	9.0	7.8	7.0		
4.1	7.6	9.0	9.8		
7.0	8.9	8.8	7.6		
5.6	8.5				

In this case, lunch and supper BG values are elevated. An increase in the Humalog Mix25 taken at breakfast is needed.

Example #4 - Client D is on Novolin 30/70 at breakfast and supper and presents with the BG values recorded below.

Breakfast	Lunch	Supper	Hs	0300	Comments
5.0	7.0	7.8	4.2	3.5	
14.1	12.0	6.0	9.8		
7.0	6.7	5.8	4.6	3.9	
10.2	8.7				

In this case, breakfast BG values are erratic and 0300 values are low. This is a common problem with Novolin 30/70 insulin because the peak action time of NPH in the supper dose is during the night.

- A first step may be to try decreasing the supper Novolin 30/70.

- If the first step is not effective and the client prefers to maintain a 2-injection regimen, then switching to Humalog Mix25 or NovoMix 30 may result in less night-time hypoglycemia. Premixed insulin analogues **do not have 2 distinct peaks.** Once absorbed, the time of action corresponds to the rapid onset of action, and the duration of action corresponds to the intermediate insulin component. The peak of action is unimodal, corresponding to the maximum effect of rapid insulin, and it is steep with a slow decline.[67]

- If neither of the above are effective, this client would likely benefit from discontinuing Novolin 30/70 and switching to rapid-acting insulin at breakfast and supper and intermediate or long-acting insulin at hs.

Key components of intensive insulin therapy and intensive regimens

- Clients with T2D may benefit from moving on to intensive insulin therapy particularly if they have variable BG values due to varying meal times/content, varying levels of activity, frequent hypoglycemia or hypoglycemia unawareness.

- Intensive insulin therapy describes insulin regimens that are designed to mimic physiologic insulin.

- Safe and effective implementation of intensive insulin therapy requires that the client is willing and able to participate actively in treatment and problem solving and that they are supported by a diabetes care team.

- When deciding whether or not to recommend a client start intensive insulin therapy, the Educator must assess the client's ability to manage their diabetes with all the complexity of basal-bolus treatment (multiple daily injections and multiple daily BG monitoring).

- Deciding which client will benefit from the more complex basal-bolus regimen and will be able to comply with its demands involves complex and important clinical judgment.[68, 69, 70]

- Key elements to implementing intensive insulin therapy include:
  - 3 to 4 injections per day insulin regimen (or use of an insulin pump which will not be discussed in this guide).
  - Frequent BG monitoring is needed; if A1C is > 8.5%, ac and hs BG monitoring may suffice.
  - When A1C is closer to target (approximately 7.3%), BG monitoring ac as well as 2-hour pc and hs is recommended for the first 1-2 weeks.
  - Self-adjustments of insulin doses to variations in BG values, food intake, and activity.
  - Frequent contact between the client and diabetes care team.

Three (3) Injection Times per Day

Examples of regimens:

1. Rapid-acting insulin plus intermediate-acting insulin before breakfast and rapid-acting insulin before supper and intermediate-acting insulin at hs

2. Rapid-acting insulin before supper and long-acting insulin analogue at breakfast and hs

3. Three injection insulin regimens plus metformin may or may not be used in combination therapy with other AHAs. Thus, the starting TDD ranges from 0.3 to 0.5U per kilogram depending on which other AHAs are in place.

Four (4) Injection Times per Day Multiple Daily Injections (MDI)

Examples of regimens:

1. Rapid-acting insulin before breakfast, lunch and supper and long-acting insulin at hs

2. Rapid-acting insulin before breakfast, lunch and supper and long-acting insulin in am

3. Calculate TDD of insulin at 0.3 to 0.5U per kg; in T2D, usual TDD is 40% basal and 60% bolus (divided 20% per meal).

Consider a basal/bolus split of 50/50 or 60/40 especially in clients with a BMI >30.

Bolus doses may also be distributed as follows:

- ***15 to 25% TDD ac breakfast***
- ***10 to 20% TDD ac lunch***
- ***15 to 20% TDD ac supper***

Once pattern management has been established, supplemental doses of insulin can be added as either anticipatory or compensatory doses. Supplemental doses are temporary insulin adjustments to the rapid-acting insulin dose to compensate for hyperglycemia or hypoglycemia. Supplemental doses can be additional insulin added to the usual dose. A decrease in the usual dose may be needed to for hypoglycemia.

Indications, methods and rationale for supplemental insulin dose adjustment

Supplemental insulin dose adjustments have various names in the literature. In this guide, the terms anticipatory and compensatory insulin dose adjustments will be used.[71, 72]

1. **Anticipatory:** Adjustment based on CHO intake or planned exercise/physical activity.

2. **Compensatory:** Adjustment to correct for an immediate high or low BG value.

Anticipatory insulin dose adjustments based on CHO intake and planned physical activity

Based on CHO intake:

- CHO counting combined with calculating the insulin to CHO ratio (*insulin*:CHO) is the most common method used for making anticipatory dose adjustments for planned changes in CHO intake.

- With *insulin*:CHO ratios, clients learn to adjust the dose of rapid-acting insulin according to how much CHO is in their meal or snack. This allows for more "flexible insulin therapy" and is one of the many benefits of using MDI. Insulin to CHO ratios vary from client to client and may be different from meal to meal in the same client.

- Before calculating *insulin*:CHO ratios with a client, it is important to assess the client's ability to count CHO using different tools (examples include the Diabetes Food Guide (DFG), CHO counting books, apps, and labels). CHO counting books and labels are usually more accurate than the DFG because the latter provides approximate CHO quantities. For example, the DFG indicates that 1 slice of bread contains 15g of CHO and this can vary substantially. However, for some clients, the DFG may still be appropriate to use. Also, the tools that a client decides to use for CHO counting may need to be assessed by the Educator to ensure they provide accurate information.

- Encourage clients to record food intake by measuring portion sizes so that CHO counting accuracy can be assessed. Suggest using scales and measuring cups on a temporary basis to improve accuracy of the count.

- It may be helpful to review how to count CHO in vegetables, condiments and homemade recipes which may be overlooked when people first learn how to count CHOs.
- A client may be very interested in using *insulin:CHO* ratios to allow for varied CHO intake once ratios are determined. However, when determining *insulin:CHO* ratios, the client is asked to maintain a reasonably consistent CHO intake as it will help to establish the ratio per meal more accurately. This can be challenging for clients and they may not be successful in being completely consistent. One method of providing safe starting *insulin:CHO* ratios while preventing hypoglycemia is to choose higher more conservative *insulin:CHO* ratios than calculated. For example, the Educator calculates that the client's breakfast ratio is 1U:5g but chooses to start with 1U:6g carb to prevent hypoglycemia. Ratios can then be adjusted based on future BG patterns.

- Ask clients to record their CHO intake, BG values and insulin doses on the Carbohydrate Counting Assessment, Blood Glucose and Food Record or an equivalent form.

- The effectiveness of the *insulin:CHO* ratio is best verified by 2-hour pc testing.

- A common initial *insulin:CHO* ratio in T1D is 1U of insulin to 10 or 15g CHO.

This ratio is usually not sufficient for clients with T2D because of insulin resistance.

In clients with T2D, more insulin is often needed therefore much smaller <u>insulin:CHO</u> ratios are required. Ratios could be as low as 1U:1g.

- All ratios are adjusted to the client's BG patterns and trends.

To calculate the *insulin*:CHO ratio, divide the *<u>total g of CHO in the meal</u>* by the number of units of insulin to be taken to get to target

$$\frac{\textbf{\# g of CHO/meal}}{\textbf{\# U of insulin}} = \textbf{ratio}$$

Example:
Mr. C. usually consumes 50g of CHO at supper and has determined that he requires 8U of rapid-acting insulin to achieve target BG values 2 hours pc and at hs.
His insulin:CHO ratio is calculated as follows:

$\frac{50 \text{ g CHO}}{8 \text{ U insulin}}$ = 6.25 g/U (round to 6g) (round down when < 0.50 and round up when > 0.50)

- His *insulin:CHO* ratio for supper is 1U:6g CHO.

- You had previously calculated his breakfast ratio to be 1U:5g and lunch ratio to be 1U:6g.

- You also calculated his Insulin Sensitivity Factor (ISF) to be 2 mmol/L per U of insulin (described later in this chapter).

- You complete an Insulin Dose Adjustment Guide (Appendix 11) which summarizes his insulin regimen as follows:

Insulin Dose Adjustment Guide Name: Mr. C. Date: dd/mm/yyyy					
Blood Glucose Reading	**Background Insulin _____**	**Rapid-Acting Insulin: NovoRapid**			**Background Insulin Lantus**
		Breakfast	**Lunch**	**Supper**	
<2.9*		-2	-2	-2	
<3.9*		-1	-1	-1	
4-7	0	1U:5g	1U:6g	1U:6g	20
7.1-9.0		+1	+1	+1	
9.1-11.0		+2	+2	+2	
11.1-13.0		+3	+3	+3	
13.1-15.0		+4	+4	+4	
15.1-17.0		+5	+5	+5	
>17.0		+6	+6	+6	

Based on planned physical activity

Clients may need to make anticipatory dose adjustment to their insulin for exercise/increased physical activity. When increased physical activity is planned, reducing insulin doses helps to reduce the risk of hypoglycemia. Refer to Chapter 5, section titled "Developing client teaching plans for self-adjustment of AHAs in specific situations: Increased Physical Activity".

Compensatory insulin dose adjustments: Construct an algorithm and describe its use

Algorithms are developed to guide a client in making compensatory insulin dose adjustments. Although short-acting insulin may be used when compensatory insulin is used, rapid-acting insulin is the insulin of choice.

Algorithms vary according to actual insulin requirements by each individual client, but some basic principles to remember when constructing and using an algorithm include the following:

- Consider the client's willingness and ability to supplement for BG out of target range.
- Consider how sensitive the client is to rapid-acting insulin; sensitivity to insulin varies from person to person and using an Insulin Sensitivity Factor **(ISF)** is a method to determine algorithm increments. Note, in some literature, ISF may be referred to as a correction factor.

- Sensitivity to insulin can vary throughout the day; clients with T2D are often less sensitive to insulin in the morning hours and need more insulin at that time.

Determining Insulin Sensitivity Factor (ISF)

- ISF estimates the point drop of BG in mmol/L per U of rapid-acting insulin.
- ISF is calculated by dividing the TDD into 100 when using rapid-acting insulin.
- ISF provides only an estimated starting point. **It will need to be individualized and modified based on the client's BG values.**

- To calculate the initial ISF when using rapid-acting insulin, the following formula is used:

$$\textbf{ISF} = \frac{\textbf{100}}{\textbf{TDD}}$$

Example:

Mr. C. is taking 20U of Lantus at hs and 15U NovoRapid at breakfast, 5U at lunch and 10U at suppertime; **TDD is 50U.**

$$\textbf{ISF} = \frac{\textbf{100}}{\textbf{50}} = \textbf{2 mmol/L per unit of insulin}$$

This means 1U of rapid-acting insulin will potentially lower Mr. C's BG by 2 mmol/L. When constructing his algorithm, the BG in Mr. C's **Insulin Dose Adjustment Guide** will range by 2 mmol/L increments.

Insulin Dose Adjustment Guide		**Name: Mr. C.**		**Date: dd/mm/yyyy**	
Blood Glucose Reading	**Background Insulin _____**	**Rapid-Acting Insulin: NovoRapid**			**Background Insulin Lantus**
		Breakfast	**Lunch**	**Supper**	
<2.9*		-2	-2	-2	
<3.9*		-1	-1	-1	
4-7	0	15	5	10	20
7.1-9.0		+1	+1	+1	
9.1-11.0		+2	+2	+2	
11.1-13.0		+3	+3	+3	
13.1-15.0		+4	+4	+4	
15.1-17.0		+5	+5	+5	
>17.0		+6	+6	+6	

***start by treating hypoglycemia**

Additional Clinical Pearls:

1) ***Considerations for large doses of basal insulin (TDD doses of >2 U/kg)***

- High-volume injections are uncomfortable and have increased potential for injection-site adverse reactions such as bruising; this can possibly lead to reduced adherence with insulin injections. In addition, very large volumes of insulin may have different pharmacokinetic properties.

- Toujeo is a formulation of insulin glargine that delivers the same number of units as glargine 100 U/ml, but in one-third the injection volume. Pharmacokinetic/pharmacodynamics studies have shown that, after injection, Toujeo is released more gradually from the subcutaneous tissue than glargine 100 U/ml, giving a more constant profile with a prolonged duration of action beyond 24 hours.[73]

- In the literature and product monograph, glargine is described as once daily basal insulin. However, in clients on larger doses of this insulin, splitting the dose to morning and evening can be more comfortable and effective; and result in less hypoglycemia. Examples of ways to do this include splitting the current TDD of insulin between am and hs or adding a small am dose to the existing hs dose. The TDD does not necessarily need to be evenly split (i.e. 50:50) but rather based on the individual BG patterns.

2) ***Split doses of Amaryl and Diamicron MR***

- In the literature and product monographs, Amaryl and Diamicron MR are described as once daily medications. However, splitting the dose to morning and evening can result in less hypoglycemia and be more effective particularly if morning BG values are elevated. Diamicron MR 30 mg tablets cannot be split because the extended release action is no longer predictable. Diamicron MR 60 mg tablets are scored and can be split.

3) ***Essential assessments specific to the client on a TZD***

The Educator will:

- Assess for pretibial edema; at a minimum quarterly and every visit if dosages have been adjusted.

- Ask about shortness of breath with minimal exertion. If present, assess for additional symptoms of CHF such as fatigue, increased urination, or difficulty sleeping in a lying position.

- Contact the client's Prescriber if edema and shortness of breath with minimal exertion are reported as this may represent a medical emergency.

4) ***Effective strategies for introducing acarbose***

- "Acarbose reduces A1C and postprandial BG values, improves insulin sensitivity and is **not** associated with weight gain. Acarbose has no serious side effects and with all of these positive metabolic effects, why is it not being used more frequently? The response to this question is, "The unpleasant side effects of flatulence and abdominal discomfort cause clients to stop the drug." In turn, this has caused Prescribers to shy away from its use.

- When a recommendation to initiate acarbose is made, the following approach increases the client's ability to tolerate the drug:
    a. Be positive about the benefits listed previously, in particular that it is not associated with weight gain and in some cases, clients experience weight loss.
    b. Inform the client of the **possible** unpleasant side effects (not all clients will experience flatulence and abdominal discomfort). Be sure to explain that if these side effects occur, in most people, they will likely diminish in time.
    c. The table below was developed by Dr. JF Yale as a strategy for titrating acarbose in clients who experience moderate gastrointestinal side effects.

Initiating acarbose (Glucobay), in 50 mg tablets[74] **Name:**					
	Start Date	**Dosage/day**	**Dosage in mg**		
			AM	**Lunch**	**Dinner**
Weeks 1-4		25	0	0	25
Weeks 5-8		50	25	0	25
Weeks 9-12		75	25	25	25
Weeks 13-16		100	25	25	50
Weeks 17-20		125	50	25	50
Weeks 21-24		150	50	50	50

Conclusion

This chapter discussed the insulins currently available in Canada and how to use them with clients to maximize their effectiveness. This included description of insulin action profiles, pattern management, and how to make supplemental insulin dose adjustments.

You should now feel comfortable assessing the client; helping the client learn how to manage their BG optimally with either AHAs or insulin and AHAs; and supporting Prescribers to initiate and or make adjustments to AHA and insulin management of clients that has the best interests and the preferences of the client at heart.

The next chapter will introduce you to a tool that helps you to put everything into practice, from assessing the client to making recommendations to a Prescriber. It will also provide you with opportunities to practice using knowledge you have gained from these first three chapters.

Chapter 4: Glycemia Management Assessment Tool (GMAT)

Learning Objective 4

The Educator will identify relevant factors to assess when recommending an AHA for clients with T2D by:

a. Describing the purpose and how to use the Glycemia Management Assessment Tool to support comprehensive client assessment.

b. Describing and / or demonstrating application of the GMAT using the following client cases and drafting letters to the Prescriber:

   i. Switching from a Sulfonylurea to a Meglitinide

   ii. Adding a SGLT2 Inhibitor to Metformin and a Meglitinide

   iii. Switching PreMix to Basal Bolus Insulin

   iv. Adding an Insulin Adjustment Guide to Basal Bolus Insulin

Using the GMAT to support comprehensive client assessment

The "Glycemia Management Assessment Tool" (GMAT) is a tool meant to assist the Educator to gather essential information for a comprehensive assessment prior to making an AHA recommendation to a Prescriber. It includes both 'client factors' affecting glycemic control and 'clinical factors' to consider when choosing an AHA best suited to the individual.

How and when to use the tool:

1. Educators who are not certified in glycemia management will use this tool when reviewing a client's case with a Clinical Consultant. The Educator may choose to complete the tool OR use it as a check-list when discussing the case.

2. Clinical Consultants may use the tool as a checklist for making sure all factors have been considered before making an AHA recommendation to a Prescriber.

3. During the glycemia management certification process, the GMAT will assist both the Mentee and the Mentor to review client cases in a structured and comprehensive manner.

a. The Mentee may choose to:
    i. fill-out the tool ***but this will not be a requirement.***
    ii. use it as a checklist or 'cheat sheet' to prepare for discussing a case with the Mentor.
b. The Mentor may choose to:
    i. use the tool for taking notes during a discussion with a Mentee ***but this will not be a requirement.***
    ii. use it as a checklist to ensure the Mentee has addressed all factors affecting glycemia.

The GMAT and the abbreviated descriptions of what to include in the tool are found on the pages following this description. The GMAT will be available as a document for Educators to use in practice with the abbreviated descriptions on the back of the printed version.

Glycemia Management Assessment Tool	**Date of last client visit:**
Year of Diagnosis, History of AHA use and Medical Orders:	
Current medications:	**Other medical conditions:**
Client factors influencing BG control:	
Hypoglycemia frequency & treatment:	**BG monitoring:**
Medication-taking behaviours:	**Food & alcohol intake:**
Insulin and GLP-1R administration:	**Activity:**
Other:	

Clinical factors to consider when recommending the AHA: _____

Client's age: **If > 65, include frailty level:**	**A1C:** **Date:** **Target:**	**Weight:** **BMI:**
Evidence of Clinical CVD or multiple risk factors:		
Renal function: Serum Creatinine eGFR		
Potential AHA BG lowering effectiveness: (select one) ↓ or ↓↓ or ↓↓ ↓		**Potential effect on body weight:** (select one) significant wt loss - wt loss - wt neutral – wt gain
Contraindications:		**Client preferences and affordability:**
Glycemia patterns & trends:		

Current BG records and insulin doses (if applicable) or attach a copy of client's BG records

Date	Breakfast		Lunch		Supper		Bedtime	Night	Comments
	ac	pc	ac	pc	ac	pc			

Prior to completing the assessment and making recommendations, be sure you have considered all relevant client and clinical factors. The Clinical Consultant will want to discuss the following with you:

1. What BG patterns and trends do you identify in the BG record?
2. How might client behaviours influence the success of 1 strategy over another? Use the AADE-7 behaviours framework.
3. What do you need to review or include in a client teaching plan prior to recommending adjustment to the client's AHAs?
4. What potential recommendation(s) could you make to this client's Prescriber?
5. What is your rationale for the recommendation(s)?

How & When to Use the Glycemia Management Assessment Tool (GMAT)

1. CDEPO Educators who are not certified in glycemia management will use this tool when reviewing a client's case with a Clinical Consultant. It can be completed in advance OR used as a check-list to cue practice and consultation.
2. CDEPO Clinical Consultants can use the tool to review client cases in a structured & comprehensive manner prior to approving a Mentee's recommendations to a Prescriber.

Glycemia Management Assessment Tool	**Date of last client visit:**
Year of Diagnosis, History of AHA use & Medical Orders: include year or estimated year of Dx, all previous & current AHAs; and medical orders if applicable.	
Current medications: all prescription & over-the-counter meds.	**Other medical conditions:** all other medical conditions
Client factors influencing BG control:	
Hypoglycemia frequency & treatment: BG value when S/S, number of episodes in last 14 days & time of occurrence. Be specific with all aspects of treatment of hypoglycemia.	**BG monitoring:** type & age of meter; technique; frequency of testing; & meter care.
Medication-taking behaviours: any missed or extra doses; timing of each medication; method used to remember to take meds as prescribed.	**Food & alcohol intake:** info pertinent to BG control i.e. CHO intake, knowledge regarding CHO content of meals / snacks; # of alcoholic drinks per week; consumed with food or not.
Insulin & GLP-1R administration: injection sites & technique; timing of, missed & extra doses; & storage of insulin or GLP-1R.	**Activity:** type, timing & intensity of activity; method of preventing activity induced hypoglycemia**.**
Other: dawn phenomenon; illness and /or infection; unusual stresses; other drugs that may affect BG values	

Clinical factors to consider when recommending the AHA: include which AHAs you are considering for this client		
Client's age: include age **If > 65, include frailty level:** as per the Clinical Frailty Scale	**A1C:** value of most current & date **Target:** individualized target	**Weight:** actual or reported in kg or lbs **BMI:** calculated BMI
Evidence of Clinical CVD or multiple risk factors: clinical CVD i.e. hx of CAD, MI, CABG, CHF, angina, TIA, CVA, PVD. Risk factors i.e. ↑BP, ↑lipids, uncontrolled diabetes, obesity, family hx, smoking, inactivity, & unhealthy eating & alcohol intake. **Renal function:** Serum Creatinine: value from lab or Prescriber eGFR: value from lab, Prescriber or calculate with MDRD		
Potential AHA BG lowering effectiveness: (select one) ↓ or ↓↓ or ↓↓ ↓		**Potential effect on body weight:** (select one) significant wt loss - wt loss - wt neutral – wt gain
Contraindications: must be 'none' or the AHA must not be used.		**Client preferences & affordability:** why client chose the AHA & how they will pay.
Glycemia patterns & trends: frequency & time of ↓ or ↑BG values; trends of ↓ or ↑BG values		

Current BG values & insulin doses (if applicable) or attach a copy of client's BG records

Date	Breakfast		Lunch		Supper		Bedtime	Night	Comments
	ac	pc	ac	pc	ac	pc			

Prior to completing the assessment & making recommendations, be sure you have considered all relevant client & clinical factors. The Clinical Consultant will want to discuss the following:

1. What BG patterns & trends do you identify in the BG record?
2. How might client behaviours influence the success of 1 strategy over another? Use the AADE-7 behaviours framework.
3. What do you need to review or include in a client teaching plan prior to recommending adjustment to the client's AHAs?
4. What potential recommendation(s) could you make to this client's Prescriber?
5. What is your rationale for the recommendation(s)?

*Once the Educator has gathered all of the assessment data, th*e questions at the end of the GMAT are meant to encourage them to take time for critical thinking and to reflect on what else they might need to hear from the client to ensure *client-centred* recommendations.

1. What BG patterns and trends do you identify in the BG record?
    a. Identify the most relevant BG patterns and trends you note in the client's BG record.
    b. Which one should be addressed first?

2. How might client behaviours influence the success of 1 strategy over another? Use the AADE-7 behaviours framework.
    a. Do you have information, for example about other diagnoses or living circumstances, which could be relevant to your recommendations?

3. What do you need to review or include in a client teaching plan prior to recommending adjustment to the client's AHAs?
    a. Are there client behaviours needing further clarification or education regarding how modifications may improve BG control?

4. What potential recommendation(s) could you make to this client's Prescriber?
    a. List all of the recommendations you plan to make to the Prescriber as you would include them in the Letter to the Prescriber.

5. What is your rationale for the recommendation(s)?
    a. The rationale for the recommendation will include all pertinent aspects of the client factors influencing BG control and clinical factors to consider when recommending the AHA involved.
    b. The rationale will structure the assessment section of your letter to the Prescriber.

Using the GMAT in reviewing four client cases

This section presents four clients cases each with a completed GMAT, including documentation of other relevant client issues, and a letter making recommendations to the Prescriber. Each case can be read to gain familiarity with how the GMAT is used; but the Mentee may learn more by using the cases to practice preparing to consult with a Mentor. For this reason, the first GMAT of each case is completed only as far as the BG record. The completed GMAT follows later in the case presentation.

For those wishing to pursue more active learning:

1. *Read the case as presented on the GMAT.*
2. *Identify BG patterns and trends in the BG record.*
3. *Answer the questions in the bottom box to the best of your ability.*
4. *Read the answers to the first 3 questions (where you will gather more information about the case).*
5. *Provide your potential recommendations for AHA adjustments and rationale.*
6. *Check this against the answers to questions 4 and 5.*
7. *Review the completed GMAT.*
8. *Draft a letter to the Prescriber using the template found in Appendix 12.*
9. *Check your letter against the enclosed letter to the Prescriber.*

Glycemia Management Assessment Tool — Date of last client visit: March 9, 2016

Year of Diagnosis, History of AHA use and Medical Orders: Diagnosed T2D in 2003. On metformin since diagnosis and Januvia for 3 years. Started on Diamicron MR 30 mg 3 months ago but was having several episodes of hypoglycemia so he started to split tablets in half. No orders from physician.

Current medications:	ASA 81mg daily	**Other medical conditions:**	Schizophrenia
Januvia 100 mg daily	Metoprolol 50 mg daily		Depression
Metformin 1000 mg twice daily	Ramipril 10 mg daily		Hypertension
Diamicron 30 mg MR daily	Risperdal 3 mg daily		Hyperlipidemia
	Fluvoxamine 150 mg daily		

Assessment of client factors influencing BG control

Frequency of hypoglycemia & treatment: Was having frequent episodes, now approximately 1 to 2 per week. Does not drive. Uses chocolate bars because he likes them.

BG monitoring: Technique is good, checks BG 1 to 2 times per day and when having episodes of hypoglycemia. Meter is 6 months old.

Medication-taking behaviours: Takes medication daily and reports does not miss them. Due to frequent hypoglycemia, he decided to split his Diamicron MR 30 mg tablets in half not knowing this is not recommended for this drug.

Food and alcohol intake: Has 2 meals per day and snacks in between. Does not eat regularly or consistently. Has a Mars bar as his hs snack and does not wish to eliminate this from his diet because he enjoys it and he believes it helps him with stress relief. No alcohol.

Insulin and GLP-1R administration: Not Applicable (N/A)

Activity: Walks daily 30 to 90 minutes usually in the am.

Clinical factors to consider when recommending the AHA: Repaglinide

Client's age: 53 If > 65, include frailty level: N/A	**A1C:** 7.8% **Date:** Feb 2016 **Target:** < 7.0%	**Weight:** 195 lbs **BMI:** 27.19

Evidence of Clinical CVD or multiple risk factors: no known clinical CVD; hyperlipidemia & hypertension; does not smoke.
Renal function: SeCr is 103 umol/L eGFR is 71

Potential AHA effectiveness of lowering BG: (select one)
↓ or [↓↓] or ↓↓ ↓

Potential effect on body weight: (select one)
significant wt loss – wt loss – [wt gain] – wt neutral

Contraindications: None

Client preferences and affordability: Client willing to try repaglinide and it can be covered by ODB.

Glycemia patterns & trends:

Current BG values and insulin doses (if applicable) or attach a copy of client's blood glucose records

DATE	Breakfast		Lunch		Supper		Bedtime	Night	Comments
	ac	pc	ac	pc	ac	pc			
Mar 3/16	8.5				8.7				
Mar 4/16	8.3				8.6				
Mar 5/16	9.1				9.2		6.3		
Mar 6/16	9.7				7.6				
Mar 7/16	8.2				10.1				
Mar 8/16	6.6						8.3		
Mar 9/16	8.6								

Prior to completing the assessment and making recommendations, be sure you have considered all relevant client and clinical factors. The Clinical Consultant will want to discuss the following:

1. What BG patterns and trends do you identify in the BG record?
2. How might client behaviours influence the success of 1 strategy over another? Use the AADE-7 behaviours framework.
3. What do you need to review or include in a client teaching plan prior to recommending adjustment to the client's AHAs?
4. What potential AHA recommendations could you make to this client's Prescriber?
5. What is your rationale for the recommendation?

Discussion re Client Case Switching from a Sulfonylurea to Meglitinide

1. **What BG patterns and trends do you identify in the BG record?**
   a. Most BG values are above target.

   b. Occasionally in target.

   c. Was having frequent hypoglycemia but now only having a 1 to 2 per week; none in the last week.

2. **How might client behaviours influence the success of 1 strategy over another? Use the AADE-7 behaviours framework.**
   a. Solving Problems:
      i. What is the status of his schizophrenia and how will it affect his ability to take multiple doses of medications as well as make self-adjustments to doses?
      ii. Does he know the correct treatment of hypoglycemia but chooses chocolate which is not recommended? Does he carry a source of fast acting carbohydrate at all times?

   b. Taking Medications:
      i. How long has he been splitting his Diamicron MR?
      ii. How does he ensure medications are not missed?

3. **What do you need to review or include in a client teaching plan prior to recommending adjustment to the client's AHAs?**
   a. Solving Problems:
      i. "Compared to those with diabetes only, individuals with diabetes and mental health concerns have decreased participation in diabetes self-care, a decreased quality of life, increased functional impairment, increased risk of diabetes complications."[75] Discuss whether or not the client thinks his schizophrenia will affect his ability to manage frequent medication dosing and making self-adjustments to a medication such as repaglinide/ GlucoNorm. The Educator determines this client's schizophrenia is well controlled with his current treatments and does not feel it will be a factor in his ability to take GlucoNorm as directed. He reports being very diligent with taking his medication correctly and agrees to working with the Educator to learn to make self-adjustments.

         Teach the client that the recommendation of starting repaglinide 0.5 mg ac meals is just a starting point and he may need different doses at each meal. He should not take any repaglinide if he skips a meal or his meal does not contain carbohydrate.

      ii. He states he forgot that chocolate was not recommended to treat hypoglycemia and agreed to switch to using DEX4 tablets.

   b. Taking Medications: He reports he has been splitting his Diamicron MR for 1 month now.
      i. Teach the client that splitting Diamicron 30 MR is not recommended because the extended action of the drug is affected and it becomes unpredictable. It is best for him to contact his Prescriber, Pharmacist or Educator before making changes to

medications such as this one. If not able to reach a Health Care Provider in a timely manner and hypoglycemia persists, temporarily discontinue the drug.

ii. He reports that his routine for ensuring he remembers his medications is to put out all of the morning pills and take them after testing his FBG; then put his pm medications in a small bowl on the kitchen counter where he sees them as he prepares supper.

4. What potential AHA recommendations could you make to this client's Prescriber?

a. Discontinue Diamicron MR.

b. Start repaglinide 0.5 mg at each meal and if needed, with snacks.

c. Assist and teach client to titrate repaglinide by 0.5 mg at appropriate meals and/or snacks every 1 to 2 weeks until ac next meal BG < 7.0 mmol/L and pc BG are 5 to 10.0 mmol/L; up to a maximum dose of 4 mg per meal and 16 mg per day.

5. What is your rationale for the recommendation(s)?

a. BG values are mainly above target as is the February 2016 A1C of 7.8%.

b. Client was having frequent episodes of hypoglycemia when taking lowest available dose of Diamicron MR so he decided to split his tablets in half not knowing this is not recommended for Diamicron MR 30 mg tablets.

c. He does not eat regularly or consistently and because of this repaglinide may be a better option as it allows for flexibility in timing and carbohydrate content of meals.

d. He is eligible for Ontario Drug Benefit through the Ontario Disability Support Program. However, repaglinide is not covered by ODB unless the physician completes a 'Request for an Unlisted Drug Product – Exceptional Access Program (EAP)' form. Educator will partially complete an EAP form and attach it to the letter to the Prescriber.

Completed GMAT for Client Case Switching from a Sulfonylurea to Meglitinide

Glycemia Management Assessment Tool **Date of last client visit: March 9, 2016**

Year of Diagnosis, History of AHA use and Medical Orders: Diagnosed T2D in 2003. On metformin since diagnosis and Januvia for 3 years. Started on Diamicron MR 30 mg 3 months ago but was having several episodes of hypoglycemia so he started to split tablets in half. No orders from physician.

Current medications:	ASA 81mg daily	**Other medical conditions:**	Schizophrenia
Januvia 100 mg daily	Metoprolol 50 mg daily		Depression
Metformin 1000 mg twice daily	Ramipril 10 mg daily		Hypertension
Diamicron 30 mg MR daily	Risperdal 3 mg daily		Hyperlipidemia
	Fluvoxamine 150 mg daily		

Assessment of client factors influencing BG control:

Frequency of hypoglycemia & treatment: Was having frequent episodes, now approximately 0 to 2 per week. Does not drive. Uses chocolate bars because he likes them.	**BG monitoring:** Technique is good, checks BG 1 to 2 times per day and when having episodes of hypoglycemia. Meter is 6 months old.
Medication-taking behaviours: Takes medication daily and reports does not miss them. Due to frequent hypoglycemia, he decided to split his Diamicron MR 30 mg tablets in half not knowing this is not recommended for drug.	**Food and alcohol intake:** Has 2 meals per day and snacks in between. Does not eat regularly or consistently. Has a Mars bar as his hs snack and does not wish to eliminate this from his diet because he enjoys it and he believes it helps him with stress relief. No alcohol.
Insulin and GLP-1R administration: N/A	**Activity:** Walks daily 30 to 90 minutes usually in the am.

Clinical factors to consider when recommending the AHA: repaglinide

Client's age: 53 If > 65, include frailty level: N/A	**A1C:** 7.8% **Date:** Feb 2016 **Target:** < 7.0%	**Weight:** 195 lbs **BMI:** 27.19

Evidence of Clinical CVD or multiple risk factors: no known clinical CVD; hyperlipidemia & hypertension; does not smoke.
Renal function: SeCr is 103 umol/L eGFR is 71

Potential AHA effectiveness of lowering BG: (select one) ↓ or [↓↓] or ↓↓ ↓	**Potential effect on body weight:** (select one) significant wt loss – wt loss – [wt gain] – wt neutral
Contraindications: None	**Client preferences and affordability:** Client willing to try repaglinide and it can be covered by ODB.

Glycemia patterns & trends: Most BG values are above target; 2 values in target & no hypos in last week; was having frequent hypos but reports now only having a 0-2/week.

Current BG values and insulin doses (if applicable) or attach a copy of client's blood glucose records

DATE	Breakfast		Lunch		Supper		Bedtime	Night	Comments
	ac	pc	ac	pc	ac	pc			
Mar 3/16	8.5				8.7				
Mar 4/16	8.3				8.6				
Mar 5/16	9.1				9.2		6.3		
Mar 6/16	9.7				7.6				
Mar 7/16	8.2				10.1				
Mar 8/16	6.6						8.3		
Mar 9/16	8.6								

Assessment: BG values are mainly above target as is the February 2016 A1C of 7.8%. Client was having frequent episodes of hypoglycemia when taking lowest available dose of Diamicron MR so he decided to split his tablets in half not knowing this is not recommended for Diamicron MR 30 mg tablets. He does not eat regularly or consistently and because of this, repaglinide may be a better option as it allows for flexibility in timing and carbohydrate content of meals. He is eligible for Ontario Drug Benefit through the Ontario Disability Support Program. However, repaglinide is not covered by ODB unless the physician completes a 'Request for an Unlisted Drug Product – Exceptional Access Program (EAP)' form; see attached partially completed EAP form.

Educator's recommendation(s):

1. Discontinue Diamicron MR.
2. Start repaglinide 0.5 mg at each meal and if needed, with snacks.
3. Assist and teach client to titrate repaglinide by 0.5 mg at meals and/or snacks every 1 to 2 weeks until ac next meal BG < 7.0mmol/L and pc BG are 5 to 10.0 mmol/L; up to a maximum dose of 4 mg per meal and 16 mg per day.

The Community Diabetes Education Program of Ottawa
Le programme communautaire d'éducation sur le diabète d'Ottawa

Date: March 10, 2016
Physician name: Dr. Sam Apple
Fax number: 613-613-6136

Re: Joe Lee
DOB: Feb 14, 1963

Dear Dr. Apple,
Your client has been followed at CDEPO since March of 2015 and was last seen on March 9, 2016. Since starting on Diamicron MR 30 mg daily 3 months ago, he has been having frequent episodes of hypoglycemia.

Current antihyperglycemic medications: (as per referral form)
Januvia 100 mg daily
Metformin 500 mg 2 tabs twice daily
Diamicron MR 30 mg daily

BG values: March 3-9, 2016 FBG range 6.6 to 9.7; BG ac supper range 7.6 to 10.1; 2 BGs at hs 6.3 and 8.3 mmol/L.

Assessment: BG values are mainly above target as is the February 2016 A1C of 7.8%. Client was having frequent episodes of hypoglycemia when taking lowest available dose of Diamicron MR so he decided to split his tablets in half not knowing this is not recommended for Diamicron MR 30 mg tablets. He does not eat regularly or consistently and because of this repaglinide may be a better option as it allows for flexibility in timing and carbohydrate content of meals. He is eligible for Ontario Drug Benefit through the Ontario Disability Support Program. However, repaglinide is not covered by ODB unless the physician completes a 'Request for an Unlisted Drug Product – Exceptional Access Program (EAP)' form; see attached partially completed EAP form.

Suggestions for changes to antihyperglycemic medications:
1. Discontinue Diamicron MR.
2. Start repaglinide 0.5 mg at each meal and if needed, with snacks.
3. Assist & teach client to titrate repaglinide by 0.5 mg at meals / snacks every 1 to 2 weeks until ac next meal BG < 7.0 mmol/L & pc BG are 5 to 10.0 mmol/L; up to a maximum dose of 4 mg per meal & 16 mg per day.

Please sign below if you agree with the suggestions above and submit the EAP form to the Ministry of Health. Return this letter by fax to (name) at (fax #).

Otherwise indicate alternate orders: _____. By returning this order to me, I will follow-up with the client to support him in making the changes.

Physician: _____ Signature: _____ Date: _____

This form was completed by a Certified Diabetes Educator who is also certified in Glycemia Management.

Next appointment:

If you wish to discuss this case further please contact:

Name and signature of Educator:

Ontario Ministry of Health and Long-Term Care

Drug Programs Delivery Branch
5700 Young Street 3rd floor

Request for an Unlisted Drug Product
Exceptional Access Program (EAP)

Please fax completed form and/or any additional relevant information to 416 327-7526 or toll-free 1 866 811-9908; or send to Drug Programs Delivery Branch (DPDB), 3rd floor, 5700 Yonge Street, Toronto ON M2M 4K5. For copies of this and other EAP forms, please visit http://www.health.gov.on.ca/en/public/forms/odb_fm.aspx

The Ministry of Health and Long-Term Care (the "ministry") considers requests for coverage of drug products not listed in the Ontario Drug Benefit Formulary under Section 16 of the *Ontario Drug Benefit Act*. This form is intended to facilitate requests for drugs under the Exceptional Access Program. The ministry may request additional documentation to support the request. Please ensure that all appropriate information for each section is provided to avoid delays.

Section 1 – Prescriber Information

First name	Initial	Last name
John	C	Apple

Mailing Address

Street no.	Street name
22	First Street

City	Postal code
Ottawa	K1K 0K0

Fax no.	Telephone no.
(613) 333-3333	(613) 333-3332

Section 2 – Patient Information

First name	Initial	Last name
Joe		Lee

Health Number: 999999999

Date of birth *(yyyy/mm/dd)*: 1956/11/12

☒ **New request** ☐ **Renewal of existing EAP approval** *(specify EAP#)* _____ – _____

Section 3 – Drug Requested

Requested drug product	DIN
repaglinide	02239924

Strength / Dosage form	Frequency of administration
0.5 mg-4 mg	ac meals and snacks

Expected start date	Duration of therapy
March 2017	indefinitely

Section 4 – Diagnosis and Reason for Use

Diagnosis for which the drug is requested:
type 2 diabetes

Reason for use over formulary alternatives:
Client was experiencing hypoglycemia when taking Diamicron MR and hyperglycemia without; please see attached BG values.

If the patient is currently taking the requested product, please provide start date & objective evidence of its efficacy:

Section 5 – Current and / or Previous Medications

a) Please provide details of alternatives *(listed drugs and/or non-drug therapy)* tried for this condition:

Name of drug *(indicate if currently or previously taken)*	Dosage	Approximate timeframe of therapy	Reason(s) why formulary alternatives are not appropriate
Diamicron MR ☒ current ☐ previous	30 mg	3 months	caused frequent hypoglycemia at lowest dose
☐ current ☐ previous			

b) Provide patient's concomitant drug therapies for other conditions:
Metformin 1000 mg twice daily; Januvia 100 mg daily; ASA 81 mg daily, Metoprolol 50 mg daily, Ramipril 10 mg daily, Risperdal 3 mg daily, Fluvoxamine 150 mg daily

Section 6 – Clinical Information

Please provide relevant medical data *(e.g. culture and sensitivity reports, serum drug levels, laboratory results):*
February 2016 A1C was 7.8%

The information on this form is collected under the authority of the *Personal Health Information Protection Act*, 2004, S.O. 2004, c.3, Sched. A (PHIPA) and Section 13 of the *Ontario Drug Benefit Act*, R.S.O. 1990c.O.10 and will be used in accordance with PHIPA, as set out in the Ministry of Health and Long–Term Care "Statement of Information Practices", which may be accessed at www.health.gov.on.ca. If you have any questions about the collection or use of this information, call the Ontario Drug Benefit (ODB) Help Desk at 1 800 668–6641 or contact the Director, Drug Programs Delivery Branch (DPDB), Ministry of Health and Long-Term Care, 3rd floor, 5700 Yonge St., Toronto ON M2M 4K5.

Prescriber signature *(mandatory)*	CPSO number	Date
JApple	22222	March 10, 2016

Glycemia Management Assessment Tool — Date of last client visit: August 19, 2016

Year of Diagnosis, History of AHA use and Medical Orders: Diagnosed with T2D in 2007. In 2015, GlucoNorm added to Metformin resulting in a decrease in A1C. MD now referred client back for follow-up as A1C increased from 7.4% Dec 2015 to 8.2% Aug 2016.

Current medications:		**Other medical conditions:**
Metformin 1000 mg tabs twice daily	Cipralex 20 mg daily	Coronary Artery Disease, CABG 2014
GlucoNorm 1 mg (1-2-2-x) ac meals	Lipitor 20 mg daily	Depression, Obstructive Sleep Apnea (C-pap)
	Altace 10 mg twice daily	Hyperlipidemia, hypertension

Assessment of client factors influencing glycemic control:

Hypoglycemia frequency & treatment: Client has had 1-2 episodes of hypoglycemia since staring GlucoNorm in 2015; none x 1 month. Carries dextrose tablets with her and follows correct procedure including retesting BG 15 minutes after treatment.

BG monitoring: Good technique as demonstrated in office, new BG meter in 2015. BG monitoring 1-2 times per day so it is difficult to assess BG patterns.

Medication-taking behaviours: Client reports she takes all medications as prescribed, missed doses are rare. She is unable to adjust GlucoNorm doses.

Food and alcohol intake: Has irregular meal timing and size, and this is not something she is interested in changing. Has already made positive changes to her diet by reducing portions and trying to have 3/5 food groups per meal. Aims for 30 to 45 g CHO per meal but CHO intake varies. No alcohol intake.

Insulin and GLP-1R administration: N/A

Activity: Recently added aqua fit and group exercise classes, attends for 1 hour at least 3 times per week. Has office job, mostly sitting at work.

Clinical factors to consider when recommending the AHA: SGLT2 Inhibitor - Jardiance

Client's age: 59 If > 65, include frailty level: N/A	**A1C:** 8.2% **Date:** August 2016 **Target: <** 7.0%	**Weight:** 127.2 kg has been stable for last year **BMI:** 50.3

Evidence of Clinical CVD or multiple risk factors: CAD & CABG. In addition to diabetes, risk factors for CVD include hyperlipidemia, hypertension and morbid obesity. No know family history of CVD and has never smoked.
Renal function: SeCr is 73 (Aug/2016) eGFR is 78

Potential AHA effectiveness of lowering BG: (select one)
↓ or [↓↓] or ↓↓ ↓

Potential effect on body weight: (select one)
significant wt loss – [wt loss] – wt gain – wt neutral

Contraindications: None

Client preferences and affordability: After review of general info about AHAs, client prefers to try adding empagliflozin instead of increasing GlucoNorm doses due to possible weight loss and its cardiovascular outcome benefit. Client has 100% drug insurance.

Glycemia patterns & trends:

Current BG values and insulin doses (if applicable) or attach a copy of client's blood glucose records

DATE	Breakfast		Lunch		Supper		Bedtime	Night	**Comments**
	ac	**pc**	**ac**	**pc**	**ac**	**pc**			
Aug 11/16	12.0		8.8						
Aug 12	9.0				10.0				
Aug 13	8.0								
Aug 15	8.3								
Aug 17			8.3						
Aug 18	8.4								
Aug 19	10.6								

Prior to completing the assessment and making recommendations, be sure you have considered all relevant client and clinical factors. The Clinical Consultant will want to discuss the following:

1. What BG patterns and trends do you identify in the BG record?
2. How might client behaviours influence the success of 1 strategy over another? Use the AADE-7 behaviours framework.
3. What do you need to review or include in a client teaching plan prior to recommending adjustment to the client's AHAs?
4. What potential recommendations could you make to this client's Prescriber?
5. What is your rationale for the recommendation?

Discussion regarding Client Case Adding a SGLT2 Inhibitor to Metformin and a Meglitinide

1. **What BG patterns and trends do you identify in the BG record?**
    a. All BG values are above target.
    b. No hypoglycemia for one month.
    c. BG monitoring is infrequent.

2. **How might client behaviours influence the success of 1 strategy over another? Use the AADE-7 behaviours framework.**
    a. Reducing Risks: Client has Coronary Artery Disease and had a CABG in 2014 thus, is at higher risk for major cardiovascular events. Is she aware of this?
    b. Medication-Taking: How does she ensure she remembers all doses of medications?
    c. Being Active: Has she noted any effect of the Aqua Fitness on her BG values?
    d. Monitoring: Is she willing to increase BG monitoring for 3 to 4 weeks after staring new AHA?

3. **What do you need to review or include in a client teaching plan prior to recommending adjustment to the client's AHAs?**
    a. Reducing Risks: Since this client has clinical CVD as evidenced by having Coronary Artery Disease and had CABG, an AHA with demonstrated CV outcome benefit would be the best choice to reduce the risk of major CV events. Current evidence for such agents includes empagliflozin (Jardiance) and liraglutide (Victoza).
    b. Medication-Taking: Client reports using a dosette for all of her medications which is highly recommended when dosing frequency is ≥ 2 times per day. She fills her dosette herself every Sunday. Ask client to bring her dosette to all appointments with the Educator.
    c. Being Active: Client states she has not noted any effect of her recently added activities on her BG. Teach the client to work at monitoring her BG before and after her exercise sessions especially with the addition of another AHA.
    d. Monitoring: Teach the client that the addition of another AHA may lead to increased frequency of hypoglycemia and she would benefit from increasing the frequency of BG monitoring for at least 3 to 4 weeks after starting a new agent.

4. **What potential recommendations could you make to this client's Prescriber?**
    a. Start Jardiance 10 mg daily; increase to 25 mg daily if hyperglycemia persists after 2 to3 weeks.
    b. If needed, reduce GlucoNorm by 0.5 mg at meals and/or snacks every 1to 2 weeks based on BG values.

5. **What is your rationale for the recommendation(s)?**
    a. All BG values are above target and last A1C in August 2016 was also above target at 8.2%. Client has made as many positive changes to lifestyle as she is presently able.
    b. She would benefit from the addition of another antihyperglycemic agent to get to target. She prefers to add a drug that may contribute to weight loss such as Jardiance. In addition, Jardiance has demonstrated cardiovascular outcome benefit in clients with clinical CVD.
    c. With the addition of Jardiance, and as her BG values decrease, she may also need to decrease her doses of GlucoNorm.

Glycemia Management Assessment Tool — Date of last client visit: August 19, 2016

Year of Diagnosis, History of AHA use and Medical Orders: Diagnosed with T2D in 2007. In 2015, GlucoNorm added to metformin resulting in a decrease in A1C. MD now referred client back for follow-up as A1C increased from 7.4% Dec 2015 to 8.2% Aug 2016.

Current medications:	Cipralex 20 mg daily	**Other medical conditions:**	Coronary Artery Disease, CABG 2014
Metformin 1000 mg tabs twice daily	Lipitor 20 mg daily		Depression, Obstructive Sleep Apnea (C-pap)
GlucoNorm 1 mg (1-2-2-x) ac meals	Altace 10 mg twice daily		Hyperlipidemia, hypertension

Assessment of client factors influencing glycemic control:

Hypoglycemia frequency & treatment: Client has had 1 to 2 episodes of hypoglycemia since staring GlucoNorm in 2015; none recently. Carries dextrose tablets with her and follows correct procedure including retesting BG 15 minutes after treatment.

BG monitoring: Good technique as demonstrated in office, new BG meter in 2015. BG monitoring 1 to 2 times per day so it is difficult to assess BG patterns.

Medication-taking behaviours: Client reports she takes all medications as prescribed, missed doses are rare. She is unable to adjust GlucoNorm doses.

Food and alcohol intake: Has irregular meal timing and size, and this is not something she is interested in changing. Has already made positive changes to her diet by reducing portions and trying to have 3/5 food groups per meal. Aims for 30 to 45 g CHO per meal but CHO intake varies. No alcohol intake.

Insulin and GLP-1R administration: N/A

Activity: Recently added aqua fit and group exercise classes, attends for 1 hour at least 3 times per week. Has office job, mostly sitting at work.

Clinical factors to consider when recommending the AHA: SGLT2 Inhibitor - Jardiance

Client's age: 59 If > 65, include frailty level: N/A	**A1C:** 8.2% **Date:** August 2016 **Target: <** 7.0%	**Weight:** 127.2 kg has been stable for last year **BMI:** 50.3

Evidence of Clinical CVD or multiple risk factors: CAD & CABG. In addition to diabetes, risk factors for CVD include hyperlipidemia, hypertension and morbid obesity. No know family history of CVD and has never smoked.
Renal function: SeCr is 73 (Aug/2016) eGFR is 78

Potential AHA effectiveness of lowering BG: (select one)
↓ or [↓↓] or ↓↓ ↓

Potential effect on body weight: (select one)
significant wt loss – [wt loss] – wt gain – wt neutral

Contraindications: None

Client preferences and affordability: After review of general info about AHAs, client prefers to try adding empagliflozin instead of increasing GlucoNorm doses due to possible weight loss and its CV outcome benefit. Has 100% drug insurance.

Glycemia patterns & trends: All BG values above target; no hypoglycemia x 1 month; infrequent testing.

Current BG values and insulin doses (if applicable) or attach a copy of client's blood glucose records

DATE	Breakfast		Lunch		Supper		Bedtime	Night	Comments
	ac	**pc**	**ac**	**pc**	**ac**	**pc**			
Aug 11/16	12.0		8.8						
Aug 12	9.0				10.0				
Aug 13	8.0								
Aug 15	8.3								
Aug 17			8.3						
Aug 18	8.4								
Aug 19	10.6								

Assessment: All BG values are above target and last August 2016 A1C was also above target at 8.2%. Client has made as many positive changes to lifestyle as she is presently able. She would benefit from the addition of another antihyperglycemic agent to get to target. She prefers to add a drug that may contribute to weight loss such as Jardiance. In addition, Jardiance has demonstrated cardiovascular outcome benefit in client with clinical CVD. With the addition of Jardiance, and as her BG values decrease, she may also need to decrease her doses of GlucoNorm.

Educator's recommendation(s):
1. Start Jardiance 10 mg daily; increase to 25 mg daily if hyperglycemia persists after 2 to 3 weeks.
2. If needed, reduce GlucoNorm by 0.5 mg at meals and/or snacks every 1 to 2 weeks based on BG values.

Letter to Prescriber re Client Case Adding a SGLT2 Inhibitor to Metformin and a Meglitinide

The Community Diabetes Education Program of Ottawa
Le programme communautaire d'éducation sur le diabète d'Ottawa

Date: August 20, 2016
Physician name: Dr. John Smith
Fax number: 613-613-6136

Re: Jane Doe
DOB: August 1, 1957

Dear Dr. Smith,

Thank you for referring your client to our program because of a recent increase in her A1C.

Current antihyperglycemic medications: (as reported by client)
Metformin 1000 mg twice daily
GlucoNorm 1 mg – 1 tab with breakfast, 2 tabs with lunch and 2 tabs with supper

BG values: August 11-19, 2016 FBG range 8.0 to 12.0 (6 readings); 2 BG ac lunch of 8.3 and 8.8; 1 BG ac supper of 10.0 mmol/L.

Assessment: All BG values are above target and August 2016 A1C was also above target at 8.2%. Client has made as many positive changes to lifestyle as she is presently able. She would benefit from the addition of another antihyperglycemic agent to get to target. She prefers to add a drug that may contribute to weight loss such as Jardiance. In addition, Jardiance has demonstrated cardiovascular outcome benefit in clients with clinical cardiovascular disease. With the addition of Jardiance, and as her BG values decrease, she may also need to decrease her doses of GlucoNorm.

Suggestions for changes to antihyperglycemic medications:

1. Start Jardiance 10 mg daily; increase to 25 mg daily if hyperglycemia persists after 2 to3 weeks.
2. If needed, reduce GlucoNorm by 0.5 mg at meals/snacks every 1 to 2 weeks based on BG values.

Please sign below if you agree with the suggestions above and **return by fax to (name) at (fax no.).**

Otherwise indicate alternate orders: _____. By returning this order to me, I will follow-up with the client to support her in making the changes.

Physician: _____ Signature: _____ Date: _____

This form was completed by a Certified Diabetes Educator who is also certified in Glycemia Management.

Next appointment:

If you wish to discuss this case further please contact:

Name and signature of Educator:

B.c Client Case PreMix Switch to Basal Bolus Insulin

Glycemia Management Assessment Tool **Date of last client visit: September 9, 2016**

Year of Diagnosis, History of AHA use and Medical Orders: Diagnosed with T2D in 1994. At initial visit, was on NPH morning and hs and metformin 1000 mg twice daily. Due to poor glycemic control and hypoglycemia, NPH was d/c and NovoMix 30 38 U at breakfast and 26 U at supper was initiated in May 2016. No current orders from Prescriber at time of visit.

Current medications:	Zocor 40 mg daily	**Other medical conditions:**	COPD
NovoMix 30 (38-X-26-X)	Flovent and Ventolin		Glaucoma
Metformin 1000 mg twice daily			Hypercholesterolemia

Assessment of client factors influencing BG control:

Frequency of hypoglycemia & treatment: No recent hypoglycemia. Has treated symptoms of hypoglycemia with 2 teaspoons of honey in the past. Reports symptoms of blurry vision when BG is low.	**BG monitoring:** Technique reviewed in office and is well done; monitors 3-4x/day; BG meter is 2 years old. Is willing to test ac meals and hs.
Medication taking behaviours: Reports not missing her medication or insulin.	**Food and alcohol intake:** Often snacks between meals and in the evening. CHO content of her 3 meals and snacks are variable, except is consistent at breakfast and lunch has the lowest amount of CHO. Is not interested in carbohydrate counting but understands which foods contain carbohydrate. No alcohol.
Insulin GLP-1R administration: Primarily uses abdomen and sites are well rotated. No evidence of lipodystrophy noted. Uses a FlexPen with good technique as demonstrated by client in office.	**Activity:** Does all of her own house work and is actively involved in the community. Goes on day trips and church events. No scheduled exercise.

Clinical factors to consider when recommending the AHA: Basal Bolus Insulin

Client's age: 75 If >65, include frailty level: Level 3 - manages well; lives with her husband.	**A1C:** 9.5% **Date:** Aug 8, 2016 **Target:** 8.5%	**Weight:** 136 lbs **BMI:** 29

Evidence of Clinical CVD or multiple risk factors: No known CVD and risk factors are uncontrolled diabetes and hypercholesterolemia

Renal function: SeCr is 76 umol/L eGFR is 64

Potential AHA effectiveness of lowering BG: (select one) ↓ or [↓↓] or ↓↓ ↓	**Potential effect on body weight:** (select one) significant wt loss - wt loss - [wt gain] - wt neutral
Contraindications: none	**Client preferences and affordability:** Willing to inject 4 times per day. Insulin covered by ODB, no private insurance.

Glycemia patterns & trends:

Current BG values and insulin doses (if applicable) or attach a copy of client's blood glucose records:

DATE	Breakfast		Lunch		Supper		Bedtime	Night	Comments
	ac	**pc**	**ac**	**pc**	**ac**	**pc**			
Sept.3	4.2				11.0	16.0	12.0		
Sept.4	6.8				10.0		11.0		
Sept.5	5.8		8.0	13.2		14.0	8.0		
Sept.6	8.1	13.3			7.0	12.7			
Sept.7	6.2				8.0	12.7			
Sept.8	7.5	11.0			8.0	17.1			

Prior to completing the assessment and making recommendations, be sure you have considered all relevant client and clinical factors. The Clinical Consultant will want to discuss the following:

1. What BG patterns and trends do you identify in the BG record?
2. How might client behaviours influence the success of 1 strategy over another? Use the AADE-7 behaviours framework.
3. What do you need to review or include in a client teaching plan prior to recommending adjustment to the client's AHAs?
4. What potential recommendations could you make to this client's Prescriber?
5. What is your rationale for the recommendation?

Discussion re Client Case PreMix Switch to Basal Bolus Insulin

1. **What BG patterns and trends do you identify in the BG record?**
    a. FBG in target ≤ 8.0 mmol/L
    b. Elevated pc supper and hs BG values
    c. Rarely tests ac lunch.
2. **How might client behaviours influence the success of 1 strategy over another? Use the AADE-7 behaviours framework.**
    a. Healthy Eating: Since this client often has snacks between meals and in the evening, are her elevated ac supper BG values potentially due to snacking? If yes, is she snacking because she either feels hypoglycemic or to prevent hypoglycemia?
    b. Problem Solving: She uses honey to treat hypoglycemia – what does she carry with her at all times? What does she have with her at the visit?
    c. Medication-Taking: How does this client ensure she is not missing medications? Is she consistently taking her NovoMix 30 at supper?
3. **What do you need to review or include in a client teaching plan prior to recommending adjustment to the client's AHAs?**
    a. Healthy Eating: She reports that her snacks are taken primarily mid-morning and at hs therefore, her elevated ac supper BG values are not likely due to snacking. Teach the client to make a note in the comments section of her BG log sheet when she has a snack containing CHO. She does not think she is snacking due to hypoglycemia or to prevent hypoglycemia.
    b. Problem Solving: When hypoglycemia is infrequent, clients often stop carrying a source of rapid acting CHO at all times as was the case with this client. Reinforce the importance of always carrying fast acting CHO and ask at each visit what she has with her.
    c. Medication-Taking: She reports using a dosette which is highly recommended when dosing frequency is ≥ 2 times per day. Her dosette shows she is taking her Metformin approximately 90% of the time which is very good. She reports she occasionally took her NovoMix 30 at hs because she was so used to taking her NPH at that time. Ask her to document her insulin doses as she takes them and not by recall. Reinforce the need for her to document if she forgot a dose of insulin or took later than usual so that adjustments can be made accordingly.
4. **What potential AHA recommendations could you make to this client's Prescriber?**
    a. Discontinue NovoMix 30.
    b. Start Lantus 35 U hs; titrate by 1 to 2 U every 3 days until FBG ≤ 8.0 mmol/L.

c. Start NovoRapid with meals containing carbohydrate 8-4-8-X U; titrate by 1 to 2 U every 2 to 3 days until ac meals ≤ 8.0 mmol/L and 2-hour pc meals 5.0 to10.0 mmol/L.

d. Phone follow-up every 2 to 3 days for 2 to 3 weeks for adjustments to NovoRapid & Lantus as per titration orders.

5. What is your rationale for the recommendation(s)?
For this case, also include how you calculated the doses of basal/bolus insulin.

a. Presents with significant postprandial hyperglycemia based on recent A1C of 9.5% and elevated BG values.

b. She is inconsistent with the timing and CHO content of her meals and is not prepared to change.

c. She is a fully functional elderly client and has no known complications of diabetes despite the long duration of her disease. In the elderly, basal bolus regimens can result in excellent glycemic control with reduced glycemic variability, as well as good safety and patient satisfaction.

d. She has agreed to increase the frequency of BG monitoring to ac meals and hs (and when feeling unwell).

The doses of insulin were calculated as follows:

Her current TDD is 64 U of insulin. Since her A1C is so high, her starting TDD of basal-bolus will only be reduced by 10% as follows:

a. 64 U x 0.10 = 6.4 rounded to 6 U. 64-6= 58 U. New TDD will be 58 U.

b. Basal insulin will be 60% of TDD at 35 U.

c. Bolus will be 40% of TDD at approximately 23 U = 8-4-8-X since breakfast is consistently 65 g of CHO, lunch is only 30 g and supper vary but not usually less than 60 to 65 g.

d. Lantus will be started at hs to try to maintain her current FBG trend.

Completed GMAT Client Case PreMix Switch to Basal Bolus Insulin

Glycemia Management Assessment Tool **Date of last client visit: September 9, 2016**

Year of Diagnosis, History of AHA use and Medical Orders: Diagnosed with T2D in 1994. At initial visit, was on NPH morning and hs and metformin 1000 mg twice daily. Due to poor glycemic control and hypoglycemia, NPH was d/c and NovoMix 30 38 Us at breakfast and 26 Us at supper was initiated in May 2016. No current orders from Prescriber at time of visit.

Current medications: Zocor 40 mg daily NovoMix 30 (38-X-26-X) Flovent and Ventolin Metformin 1000 mg twice daily	**Other medical conditions:** COPD Glaucoma Hypercholesterolemia

Assessment of client factors influencing BG control:

Frequency of hypoglycemia & treatment: No recent hypoglycemia. Has treated symptoms of hypoglycemia with 2 teaspoons of honey in the past. Reports symptoms of blurry vision when BG is low.	**BG monitoring:** Technique reviewed in office and is well done; monitors 3-4x/day; BG meter is 2 years old. Is willing to test ac meals and hs.
Medication-taking behaviours: Reports not missing her medication or insulin.	**Food and alcohol intake:** Often snacks between meals and in the evening. CHO content of her 3 meals and snacks are variable, except is consistent at breakfast and lunch has the lowest amount of CHO. Is not interested in carbohydrate counting but understands which foods contain carbohydrate. No alcohol.
Insulin GLP-1R administration: Primarily uses abdomen and sites are well rotated. No lipodystrophy noted. Uses a FlexPen with good technique as demonstrated by client in office.	**Activity:** Does all of her own house work and is actively involved in the community. Goes on day trips and (church) events. No scheduled exercise.

Clinical factors to consider when recommending the AHA: Basal Bolus Insulin

Client's age: 75 If > 65, include frailty level: Level 3 - manages well; lives with her husband.	**A1C:** 9.5% **Date:** Aug 8, 2016 **Target:** 8.5%	**Weight:** 136 lbs **BMI:** 29

Evidence of Clinical CVD or multiple risk factors: No known CVD and risk factors are uncontrolled diabetes and hypercholesterolemia
Renal function: SeCr is 76 umol/L eGFR is 64

Potential AHA effectiveness of lowering BG: (select one) ↓ or [↓↓] or ↓↓ ↓	**Potential effect on body weight:** (select one) significant wt loss - wt loss - [wt gain] - wt neutral
Contraindications: none	**Client preferences and affordability:** Willing to inject 4 times per day. Insulin covered by ODB, no private insurance.

Glycemia patterns & trends: FBGs in target ≤ 8.0 mmol/L; elevated pc S & hs BG values; rarely tests ac L.

Current BG values and insulin doses (if applicable) or attach a copy of client's blood glucose records

DATE	Breakfast		Lunch		Supper		Bedtime	Night	Comments
	ac	**pc**	**ac**	**pc**	**ac**	**pc**			
Sept.3	4.2				11.0	16.0	12.0		
Sept.4	6.8				10.0		11.0		
Sept.5	5.8		8.0	13.2		14.0	8.0		
Sept.6	8.1	13.3			7.0	12.7			
Sept.7	6.2				8.0	12.7			
Sept.8	7.5	11.0			8.0	17.1			

Assessment: Presents with significant postprandial hyperglycemia based on recent A1C of 9.5% and elevated BG values.
She is inconsistent with the timing and CHO content of her meals and is not prepared to change. She is a fully functional elderly client and has no known complications of diabetes despite the long duration of her disease. In the elderly, basal bolus regimens can result in excellent glycemic control with reduced glycemic variability, as well as good safety and patient satisfaction. She has agreed to increase the frequency of BG monitoring to ac meals and hs (and when feeling unwell).

Educator's recommendation(s):

1. Discontinue NovoMix 30.
2. Start Lantus 35 U hs; titrate by 1-2 U every 3 days as until FBG < 8.0 mmol/L.
3. Start NovoRapid with meals containing carbohydrate 8-4-8-X U; titrate by 1 to 2 U every 2 to 3 days until ac next meal < 8.0 and 2-hour pc meals 5.0 to 10.0 mmol/L.
4. Telephone follow-up every 2 to 3 days for 2 to 3 weeks to make adjustments to the NovoRapid & Lantus as per titration orders.

The Community Diabetes Education Program of Ottawa
Le programme communautaire d'éducation sur le diabète d'Ottawa

Date: September 10, 2016
Physician name: Dr. K. Clarke
Fax number: 613-613-6136

Re: Lois Lane
DOB: September 1st, 1941

Dear Dr. Clarke,
Since starting on NovoMix 30 in July 2015, your client's glycemic control has deteriorated as is evidenced by her recent A1C on August 8, 2016 of 9.5%.

Current antihyperglycemic medications: (as reported by client)
Metformin 1000 mg twice daily
NovoMix 30 38 U in the morning and 26 U at supper

BG values: September 3 to 8, 2016 – see attached blood glucose log.

Assessment: Presents with significant postprandial hyperglycemia based on recent A1C of 9.5% and elevated BG values. She is inconsistent with the timing and carbohydrate content of her meals and is not prepared to change. She is a fully functional elderly client and has no known complications of diabetes despite the long duration of her disease. In the elderly, basal bolus regimens can result in excellent glycemic control with reduced glycemic variability, as well as good safety and patient satisfaction. She has agreed to increase the frequency of BG monitoring to ac meals & hs (and when feeling unwell).

Suggestions for changes to antihyperglycemic medications:

1. Discontinue NovoMix 30.
2. Start Lantus 35 U hs; titrate by 1 to 2 U every 3 days until FBG $\leq$ 8.0 mmol/L.
3. Start NovoRapid with meals containing carbohydrate 8-4-8-X U; titrate by 1 to 2 U every 2 to 3 days until ac meals $\leq$ 8.0 and 2-hour pc meals 5.0 to 10.0 mmol/L.
4. Phone follow-up every 2 to 3 days for 2 to 3 weeks for adjustments to NovoRapid & Lantus as per titration orders.

Please sign below if you agree with the suggestions above and **return by fax to (name) at (fax no.)**.

Otherwise indicate alternate orders: _____. By returning this order to me, I will follow-up with the client to support her in making the changes.

Physician: _____ Signature: _____ Date: _____

This form was completed by a Certified Diabetes Educator in consultation with a CDE who is also certified in Glycemia Management.

Next appointment:

If you wish to discuss this case further please contact:

Name and signature of Educator:

B.d. Client Case Adding an Insulin Dose Adjustment Guide to Basal Bolus Insulin

Glycemia Management Assessment Tool **Date of last client visit: September 19, 2016**

Year of Diagnosis, History of AHA use and Medical Orders: Diagnosed with T2D in 1983. Janumet and Lantus started 3 years ago. Recently started on NovoRapid insulin by her GP; he has been slowly increasing the NovoRapid. Today was her initial assessment at CDEPO.

Current medications:	Candesartan 32 mg daily	**Other medical conditions:**	Hypertension
Janumet 1000 mg/50 mg twice daily	Celexa 40 mg daily		Anxiety, Depression
Lantus 120 Us at hs			Obstructive Sleep Apnea (on CPAP)
NovoRapid 16 Us at each meal.			Parkinson's disease

Assessment of client factors influencing glycemic control:

Hypoglycemia frequency & treatment: No history of hypoglycemia but is knowledgeable re signs and symptoms. Describes appropriate treatment and carries Dextrose tablets. Had them in her purse today.	**BG monitoring:** Was removing BG test strips from the bottle and keeping some in her purse. Reviewed that test strips must be kept in the original bottle or this will affect the accuracy of her BG values. Her meter is approximately one year old.
Medication-taking behaviours: Client reports missing 3 out of 14 supper doses of Janumet in past 2 weeks.	**Food and alcohol intake:** Has 3 meals per day. Timing of meals can vary but tries to make sure to at least have 4 hours between meals. Her CHO intake varies especially at supper and has occasional supper meals with little to no CHO. Does not think it is realistic for her to make changes to her food intake at this time. No alcohol intake.
Insulin and GLP-1R administration: Uses a Lantus SoloStar pen & NovoRapid FlexTouch pen which she finds easiest to use because of her Parkinson's disease. Technique reviewed, good except abdomen has two areas showing evidence of lipohypertrophy. Agreed to avoid these areas & rotate injections to other sites.	**Activity:** Is currently not very active, not a priority for her right now.

Clinical factors to consider when recommending the AHA: Using an Insulin Adjustment Guide

Client's age: 65 If > 65, include frailty level: Level 3 - manages well despite trembling from Parkinson's Disease	**A1C:** 11.5% **Date:** August 2016 **Target:** < 8.0% initially	**Weight:** 230 lbs **BMI:** 40

Evidence of Clinical CVD or multiple risk factors: No known CVD. Risk factors: duration of & uncontrolled diabetes, hypertension, morbid obesity

Renal function: SeCr is 70 eGFR is 100

Potential AHA effectiveness of lowering BG: (select one) ↓ or ↓↓ or [↓↓↓]	**Potential effect on body weight:** (select one) significant wt loss - wt loss – [wt gain] – wt neutral
Contraindications: None	**Client preferences and affordability:** Has 100% drug insurance. She is most interested in adjusting her insulin doses.

Glycemia patterns & trends:

Current BG values and insulin doses (if applicable) or attach a copy of client's BG records

DATE	Breakfast		Lunch		Supper		Bedtime	Night	Comments
	ac	**pc**	**ac**	**pc**	**ac**	**pc**			
Sept 15/ 16	13.9		12.9		12.3				
Sept 16	10.3		12.7		17.6				
Sept 17	14.3		15.2		17.5				
Sept 18	13.0		10.9		13.7				

Prior to completing the assessment and making recommendations, be sure you have considered all relevant client and clinical factors. The Clinical Consultant will want to discuss the following:

1. What BG patterns and trends do you identify in the BG record?
2. How might client behaviours influence the success of 1 strategy over another? Use the AADE-7 behaviours framework.
3. What do you need to review or include in a client teaching plan prior to recommending adjustment to the client's AHAs?
4. What potential AHA recommendations could you make to this client's Prescriber?
5. What is your rationale for the recommendation?

Discussion re Client Case Adding an Insulin Dose Adjustment Guide to Basal Bolus Insulin

1. **What BG patterns and trends do you identify in the BG record?**
   a. All BG values are above target; the accuracy of some of her results may have been affected by storing testing strips incorrectly however, her BG values match her A1C of 11.5%.

   b. No history of hypoglycemia. This client's A1C and the fact she has not had any hypoglycemia at all indicate she definitely needs an increase in AHA and this must not be delayed.

   c. No hs BG values.

2. **How might client behaviours influence the success of 1 strategy over another? Use the AADE-7 behaviours framework**.
   a. Healthy Eating: She is willing to work at keeping her CHO at meals fairly consistent for at least a week as the Insulin Adjustment Guide is being developed. How are her CHO counting skills and what resources will she use?

   b. Reducing Risks: Is this client aware of her risk factors for CVD especially because of the duration of her diabetes (33 years) and significant level of hyperglycemia?

   c. Medication Taking:
      i. How will she work at remembering to take her supper dose of Janumet?
      ii. Is she comfortable following an Insulin Dose Adjustment Guide?

3. **What do you need to review or include in a client teaching plan prior to recommending adjustment to the client's AHAs?**
   a. Healthy Eating: Client is open to keeping the CHO content of meals as consistent as possible for at least a week as she understands how inconsistencies make it difficult to determine base doses of NovoRapid at meals. She states she can easily be consistent at breakfast and lunch because she already has foods she eats most of the time at these meals. For example, at breakfast, she agreed to having 2 toasts with protein and either an apple or an orange. The supper meal will be her biggest challenge as she has not counted carbohydrate in her meals in the past but understands which foods contain CHO. Provide her with some CHO counting resources.

   b. Reducing Risks: Since this client has had type 2 diabetes for over 30 years and despite multiple antihyperglycemic therapies her A1C is 11.5%, you set a target A1C with her of <8.0%. According to the 2013 CDA CPG "Individualized and higher A1C targets may be indicated in older type 2 patients with longer duration of diabetes, established CV risk factors, and/or without A1C reduction despite treatment intensification." In this case, not only will an A1C target of <8.0% be more realistic and achievable than <7.0%, it will be less discouraging for her to try to achieve. Teach the client that every 1% reduction in A1C helps to reduce her risk of diabetes complications.

   c. Medication Taking: i. She finds the supper dose of Janumet challenging to remember because she is so busy getting supper ready. The order from the physician is to take the Janumet twice daily therefore, it is reasonable to advise her to take the second dose of Janumet at hs at the same time she takes her hs Lantus.

i. Insulin Dose Adjustment Guide: You review an example of an Insulin Dose Adjustment Guide and the client is able to tell you what dose she would take base on a given blood glucose level.

ii. You calculate her ISF=100/ 168 (TDD). The calculated ISF is 1U:0.6mmol/L. However, you decide to be more conservative and start with a ISF of 1U:2mmol/L and develop the Insulin Dose Adjustment Guide below:

Insulin Dose Adjustment Guide **Name: June Grant** **Date: Sept 19, 2016**					
Blood Glucose Reading	**Basal Insulin:**	**Rapid-Acting Insulin: NovoRapid**			**Basal Insulin:**
		Breakfast	**Lunch**	**Supper**	
<2.9*		-2	-2	-2	
<3.9*		-1	-1	-1	
4-7	None in am	16	16	16	Lantus 120 U at hs
7.1-9.0		+1	+1	+1	
9.1-11.0		+2	+2	+2	
11.1-13.0		+3	+3	+3	
13.1-15.0		+4	+4	+4	
15.1-17.0		+5	+5	+5	
>17.0		+6	+6	+6	

4. What potential AHA recommendations could you make to this client's Prescriber?

a. Continue Lantus 120 U at hs and NovoRapid (NR) 16 U as base dose for each meal but add a ISF of 1U:2mmol/L when premeal BG is > 7.0 mmol/L.

b. Plan is to start with adding an ISF of 1U:2mmol/L first and then adjust base doses of NR and/or Lantus as needed using the following titration orders:

i. Titrate NR doses at meals by 1 to 2 U every 2 days until BG ac the next meal is < 7 mmol/L.

ii. Titrate Lantus by 4 to 6 U every 3 days until FBG is < 7.0 mmol/L.

5. What is your rationale for the recommendation(s)?

a. All of client's BG values are above target and A1C is significantly elevated at 11.5%.

b. Client is motivated to improve her BG; she would like to make self-adjustments to her insulin.

c. She is now taking a TDD of 168 U with a ratio of 71% basal to 29% bolus insulin and may benefit from taking closer to 60% basal/40% bolus split given the degree of her hyperglycemia. Because she is on a high TDD of insulin, the calculated ISF is quite low at 0.6 mmol/L. To be more conservative, an ISF of 1 U:2 mmol/L will be used as a starting point for her to be able to adjust her doses of NovoRapid based on her BG values.

d. She has agreed to try to be as consistent as possible with the carbohydrate content of her meals for one week and to monitor her BG ac meals and hs in order to evaluate all of her meal boluses.

Completed GMAT Client Case Adding an Insulin Dose Adjustment Guide to Basal Bolus Insulin

Glycemia Management Assessment Tool — Date of last client visit: September 19, 2016

Year of Diagnosis, History of AHA use and Medical Orders: Diagnosed with T2D in 1983. Janumet and Lantus started 3 years ago. Recently started on NovoRapid insulin by her GP; he has been slowly increasing her rapid insulin doses. Today was her initial assessment at CDEPO.

Current medications: Janumet 1000 mg/50 mg twice daily Lantus 120 Us at hs NovoRapid 16 Us at each meal.	Candesartan 32 mg daily Celexa 40 mg daily	**Other medical conditions:**	Hypertension Anxiety, Depression Obstructive Sleep Apnea (on CPAP) Parkinson's disease

Assessment of client factors influencing glycemic control:

Hypoglycemia frequency & treatment: No history of hypoglycemia but is knowledgeable re signs and symptoms. Describes appropriate treatment and carries Dextrose tablets. Had them in her purse today.	**BG monitoring:** Was removing BG test strips from the bottle and keeping some in her purse. Reviewed that test strips must be kept in the original bottle or this will affect the accuracy of her BG values. Her meter is approximately one year old.
Medication-taking behaviours: Client reports missing 3 out of 14 supper doses of Janumet in past 2 weeks.	**Food and alcohol intake:** Has 3 meals per day. Timing of meals can vary but tries to make sure to at least have 4 hours between meals. Her CHO intake varies especially at supper and has occasional supper meals with little to no CHO. Does not think it is realistic for her to make changes to her food intake at this time. No alcohol intake.
Insulin and GLP-1R administration: Uses a Lantus SoloStar pen & NovoRapid FlexTouch pen which she finds easiest to use because of her Parkinson's disease. Technique reviewed, good except abdomen has two areas with evidence of lipohypertrophy. Agreed to avoid these areas & rotate injections to other sites.	**Activity:** Is currently not very active, not a priority for her right now.

Clinical factors to consider when recommending the AHA: Using an Insulin Adjustment Guide

Client's age: 65 If >65, include Clinical Frailty Level: Level 3; manages well despite trembling from Parkinson's Disease	**A1C:** 11.5% **Date:** August 2016 **Target:** < 8.0% initially	**Weight:** 230 lbs **BMI:** 40

Evidence of Clinical CVD or multiple risk factors: No known CVD. Risk factors: duration of & uncontrolled diabetes, hypertension, morbid obesity

Renal function: SeCr is 70 eGFR is 100

Potential AHA effectiveness of lowering BG: (select one) ↓ or ↓↓ or **[↓↓↓]**	**Potential effect on body weight:** (select one) significant wt loss - wt loss – [wt gain] – wt neutral
Contraindications: None	**Client preferences and affordability:** Has 100% drug insurance. She is most interested in adjusting her insulin doses.

Glycemia patterns & trends: all BG values above target; no hx of hypoglycemia; no hs BG values

Current BG values and insulin doses (if applicable) or attach a copy of client's BG records

DATE	Breakfast		Lunch		Supper		Bedtime	Night	Comments
	ac	**pc**	**ac**	**pc**	**ac**	**pc**			
Sept 15/ 16	13.9		12.9		12.3				
Sept 16	10.3		12.7		17.6				
Sept 17	14.3		15.2		17.5				
Sept 18	13.0		10.9		13.7				

Assessment: All of client's BG values are above target and A1C is significantly elevated at 11.5%. Client is motivated to improve her BG, and she would like to make self-adjustments to her insulin. She is now taking a TDD of 168 U with a ratio of 71% basal to 29% bolus insulin and may benefit from taking closer to 60% basal/40% bolus split given the degree of her hyperglycemia. Because she is on such a high TDD of insulin, an ISF of 1U:2 mmol/L is a starting point for her to be able to adjust her doses of NovoRapid based on her BG values. She has agreed to try to be as consistent as possible with the carbohydrate content of her meals for one week and to monitor her BG ac meals and hs in order to evaluate all of her meal boluses.

Educator's recommendation(s):

1. Continue Lantus 120 U at hs and NovoRapid (NR) 16 U as base dose for each meal but add an ISF of 1U:2 mmol/L when premeal BG is > 7.
2. Plan is to start with #1 first and then adjust base doses of NR and/or Lantus as needed using the following titration orders:
    a. Titrate NR doses at meals by 1 to 2 U every 2 days until BG ac the next meal is <7 mmol/L.
    b. Titrate Lantus by 4 to 6 U every 3 days until FBG is < 7 mmol/L.

Letter to Prescriber Client Case Adding an Insulin Dose Adjustment Guide to Basal Bolus Insulin

The Community Diabetes Education Program of Ottawa
Le programme communautaire d'éducation sur le diabète d'Ottawa

Date: September 20, 2016
Physician name: Dr. Paul Smith
Fax number: 613-613-6136

Re: June Grant
DOB: August 30, 1951

Dear Dr. Smith,
Your client had her initial assessment today at the CDEPO. Given the degree of hyperglycemia as is evidenced in her A1C of 11.5% (August 2016), I am writing to suggest some changes to her insulin.

Current antihyperglycemic medications: (as per referral form)
Janumet 1000 mg/50 mg twice daily
Lantus 120 U at hs
NovoRapid 16 U at each meal

BG values: September 15 to 19, 2016 her pre-meal BG values range 10.3 to 17.6 mmol/L.

Assessment: All of client's BG values are above target and A1C is significantly elevated at 11.5%. Client is motivated to improve her BG, and she would like to make self-adjustments to her insulin. She is now taking a TDD of 168 U with a ratio of 71% basal to 29% bolus insulin and may benefit from taking closer to 60% basal/40% bolus split given the degree of her hyperglycemia. Because she is on a high TDD of insulin, the calculated ISF is quite low at 0.6 U. To be more conservative, an insulin sensitivity factor (ISF) of 1U:2mmol/L will be used as a starting point for her to be able to adjust her doses of NovoRapid based on her BG values. She has agreed to try to be as consistent as possible with the carbohydrate content of her meals for one week and to monitor her BG ac meals and hs in order to evaluate all of her meal boluses.

Suggestions for changes to antihyperglycemic medications:

1. Continue Lantus 120 U at hs and NovoRapid (NR) 16 U as base dose for each meal but add an ISF of 1U:2mmol/L when premeal BG is > 7.0 mmol/L.
2. Plan is to start with adding an ISF of 1U:2mmol/L first and then adjust base doses of NR and/or Lantus as needed using the following titration orders:
    i. Titrate NR doses at meals by 1 to 2 U every 2 days until BG ac the next meal is < 7.0 mmol/L.
    ii. Titrate Lantus by 4 to 6 U every 3 days until FBG is < 7.0 mmol/L.

Please sign below if you agree with the suggestions above and **return by fax to (name) at (fax no.)**.
Otherwise indicate alternate orders: _____. By returning this order to me, I will follow-up with the client to support her in making the changes.

Physician: _____ Signature: _____ Date: _____

This form was completed by a Certified Diabetes Educator in consultation with the Clinical Manager.

Next appointment:

If you wish to discuss this case further please contact:

Name and signature of Educator:

Conclusion

This chapter introduced you to a tool that cues your practice to ensure comprehensive client assessment prior to making recommendations to adjust AHAs and/or insulin. It also provided case studies of client scenarios to help you practice applying your knowledge from Chapters 1, 2, and 3. It is this kind of practice which will help you to develop expertise to safely and confidently manage glycemia.

The next chapter will introduce you to five specific situations you need to consider when teaching clients glycemia self-management.

Chapter 5: Managing Glycemia in Special Situations

Learning Objective 5

The Educator will identify relevant factors to assess when recommending an Antihyperglycemic Agent for clients with T2D by:

A. Describing key factors when developing client teaching plans for self-adjustment of AHAs in the following special situations*:*
   i. Increased physical activity
   ii. Travel
   iii. Shift work
   iv. Illness
   v. Medical Procedures

Developing client teaching plans for self-adjustment of AHAs in specific situations

Increased Physical Activity

- In clients whose diabetes is controlled by lifestyle and/or AHAs that do not increase insulin levels, the risk of developing hypoglycemia during increased physical activity is minimal, and most will not need to monitor their BG values or be required to supplement with CHO for exercise lasting less than 1 hour.[76]

- For clients on insulin and/or insulin secretagogues, hypoglycemia resulting from increased physical activity needs to be considered and adjustments may be needed especially if the activity is greater than 1 hour in duration and of moderate to high intensity.

- BG monitoring before, during (if longer than 1 hour) and after physical activity will help determine individual response. BG monitoring before and after physical activity is used to determine the appropriate adjustments for the next time the activity is done. BG monitoring during a prolonged activity is used to prevent hypoglycemia.

- Increased BG monitoring and choosing a safe time to exercise (for example following a meal) may be sufficient to prevent hypoglycemia especially if the activity is of low intensity.

The individual response to exercise can vary and the adjustments to the client's regimen are best determined by their BG trends.

- If hypoglycemia is experienced with physical activity, decreasing the dose of insulin/secretagogue peaking at the time of the activity (versus adding food) is recommended (particularly if the client is overweight).

- Late onset hypoglycemia may occur after moderate to high intensity physical activity; a decrease in the hs intermediate-acting or long-acting insulin may be required. This is best determined by BG monitoring at bedtime and during the night to prevent nocturnal hypoglycemia.

For planned physical activity, clients on one or two injections of insulin:

- Adjustments may not be needed, particularly if the physical activity is of low intensity.
- However, if needed, adjustments may be made as follows:
    - Low intensity decrease by 10%
    - Moderate intensity decrease by 20%
    - High intensity decrease by 30-40%
- When moderate to high intensity physical activity is planned for the next day (e.g. hiking, cross country skiing, cycling), a decrease in the dose of intermediate-acting or long-acting morning and/or hs dose may assist in preventing hypoglycemia.

For clients on an MDI regimen:

- MDI regimens provide the most flexibility for participating in physical activity.
- When a client engages in a *new* physical activity, the rapid-acting insulin that is going to peak during the physical activity is reduced by up to 50%.
- Fifty percent is a starting point. The next time the client engages in the same physical activity, the insulin dose will be adjusted based on BG values during and/or after the activity.

For clients on secretagogues:

- Adjustments may not be needed, particularly if the activity is of low intensity.
- For clients who participate in moderate to high intensity physical activity, repaglinide offers the most flexibility due to its short duration of action. If hypoglycemia is experienced with increased physical activity, the client may try decreasing the dose of repaglinide peaking at the time of the activity by 0.5 to 1 mg at a time, depending on the usual dose.
- For clients on longer acting secretagogues participating in moderate to high intensity physical activity, additional CHO may need to be consumed. The actual amount of CHO will be dependent on time of the activity, its duration and intensity, and BG values.

For unplanned physical activity of moderate to high intensity in clients on insulin or an insulin secretagogue:

- Additional CHO may need to be consumed. If the client has taken their usual doses of AHA therapy and pre-physical activity BG is <5.5 mmol/L, approximately 15 to 30 g CHO can be ingested before the activity. The actual amount of CHO will be dependent on the AHA, activity duration, activity intensity, and BG values.[76]

Example of insulin adjustment for exercise in a client on 3 insulin injections:

Your client Jane tells you she will be starting to attend an exercise class of moderate intensity three times a week from 1000 to 1100 hours (Monday, Wednesday and Friday). She takes the following insulin doses:

- **Before breakfast Lantus 15 U and Humalog 12 U**
- **Before supper Humalog 12 U**
- **Before bed Lantus 40 U**

The insulin peaking during her exercise class is the breakfast Humalog.

For her first few classes, you advise her to reduce her morning Humalog by 50% from 12 U to 6 U.

After attending 3 classes and reducing her morning Humalog as instructed, Jane calls you to report the following BG values.

	Breakfast	Lunch	Supper	Hs	0300	Comments
Mon	5.2	7.9	7.8	4.2		Ex. class
Tues	10.1	5.0	6.0	9.8		
Wed	7.0	9.7	5.8	5.6	5.0	Ex. class
Thurs	8.2	6.7	7.7	9.0		
Fri	6.5	8.0				Ex. class

Based on her BG pattern, you suggest she change to reducing her morning Humalog by 30% since her pre-lunch BG values are elevated on the days she attends her classes.

12 U x 0.30 = 3.6 rounded to 4 U; 12 – 4 U = 8 U.

Jane will now take 15 U Lantus and 8 U Humalog before breakfast on the mornings she exercises. Future BG values will be needed to further fine-tune her adjustments.

Travel

- Oral and non-insulin injectable AHAs typically do not require adjustment for travel. Clients can take their usual medications when traveling and continue to monitor their BG values.

- Ensure all clients receive CDEPO handout “Tips for Travel” (Appendix 13) and a travel letter.

- For clients on insulin, travel involving less than a 3-hour time zone difference does not require insulin dose adjustments. Clients should monitor BG regularly and take insulin according to their Insulin Dose Adjustment Guide.

- To determine the number of time zones travelled, click on the link below and enter the time of departure and destination city. http://www.thetimezoneconverter.com

- For travel involving a time zone difference of 3 or more hours, insulin adjustments may be needed. Because there are so many possible variations in time zone differences, the

individual client's treatment plan and travel plans will all factor in the final adjustments to AHA.

There are several methods of adjusting insulin for travel. The two methods of adjusting insulin doses for travel presented below are meant to be used as guides when clients are travelling through 3 or more time zones. The formulas may not be suitable for all situations particularly, if clients are travelling through a very high number of time zones. Educators will need to use clinical judgment when advising on how much clients should reduce or increase their insulin.

Method 1: the table below provides basic guidelines for calculating insulin adjustments based on direction of travel through 3 or more time zones.

Insulin adjustments for Travel ≥ 3-hour Time Zone Difference		
Eastbound – day is shorter e.g. Canada to Europe		
Insulin Regimen	**Day of Departure**	**Day of Arrival**
Once daily premix in am	Usual doses	Usual doses
One injection intermediate or long-acting analogue	Give 2/3 of dose	Resume usual dose
Premix or intermediate or long-acting analogue BID	Give 2/3 of evening/hs dose	Resume usual dose
MDI	Give 2/3 of hs basal dose and use Insulin Adjustment Guide	Resume usual dose
Westbound – day is longer e.g. Europe to Canada		
Once daily or BID premix	Usual doses	Usual doses or add 1/3 to evening dose based on BG
MDI	Usual doses	Usual doses and use Insulin Adjustment Guide

Method 2: the following suggestions provide a formula for calculating insulin dose adjustments based on the number of time zone changes and which direction the client is travelling.

Travelling East through 3 or more time zones (≥ 3 hours):

- When flying east, the day will be shorter; therefore, less intermediate-acting insulin or long-acting insulin analogue may be required on the day of travel.

- When flying east, decrease the intermediate-acting insulin or long-acting insulin analogue by hours lost in the day using the following formula:

Usual dose of basal - (usual dose of basal x # hours lost/24) = New dose

- The night of arrival, resume usual dose of basal insulin.

Examples:

1. John is travelling from Ottawa to Munich, Germany and takes a TDD of 40 U of Lantus at hs. The flight leaves at 2200 and he will lose 6 hours because it is 6 hours later than Eastern Standard Time (EST)
To determine the insulin adjustment for his travel day: **Usual hs basal – (usual dose x # hours lost/24) = New dose**
40 U Lantus – (40 U x 6/24) = 40 – 10 = 30 U taken at hs evening of departure

2. Jane is travelling from Halifax to London, England and takes 36 U of Lantus in am and 34 U at hs for a TDD of 70 U. The flight leaves at 1200 and she will lose 4 hours because it is 4 hours later than Atlantic Standard Time (AST).
Usual morning basal – (usual dose x # hours lost/24) = New dose
36 U Lantus – (36 x 4/24) = 36 – 6 = 30 U taken morning of departure
Whether or not dose of hs Lantus is reduced is based on BG monitoring.

Travelling West through 3 or more time zones (≥ 3 hours):

- When flying west, the day will be longer; therefore, more intermediate-acting insulin or long-acting insulin analogue may be required on the day of travel.

Usual dose + (usual dose of basal x # hours gained/24) = New dose

Example:

3. Chris is travelling from Halifax to Vancouver and takes 40 U of Lantus at hs. The flight leaves at 1700 and he will gain 4 hours because it is 4 hours earlier than AST.
Usual hs basal + (usual dose x # hours gained/24) = New dose
40 U of Lantus + (40 U x 4/24) = 40 + 6.7 rounded to 7 = 47 U of Lantus at hs day of arrival

- In this case the client may chose not to add the supplemental insulin and base adjustments on BG patterns and trends.

Shift Work

Day to evening shifts:

- For the client working day to evening shifts, no adjustment is usually needed to AHAs. An exception would be if the work involves moderate to high intensity activity. If this is the case, the recommendations in the increased physical activity section of this guide would be followed.

Day to night shifts:

- For the client working frequent rotating shifts including nights, the night shift is the biggest challenge. Regimens that allow for adjustments to relatively short time intervals help reduce BG variability. In cases where an insulin secretagogue or insulin must be used, repaglinide and MDI insulin regimens offer the most flexibility and are the preferred AHAs for these clients. Shift work involving night shifts is a situation where individualization of the plan based on the AHA regimen, hours of work, type of activity at work and BG patterns and trends cannot be overemphasized. The following suggestions are meant as a guide only.

For clients on Oral AHAs:

- AHAs that are not insulin secretagogues or insulin usually do not need to be adjusted for night shifts.
- The timing of insulin secretagogues will likely need to be adjusted. The use of short acting secretagogues such as repaglinide is preferred.
- If longer acting secretagogues are used, the following are important considerations when making the switch from days to nights:
    - the change in the timing of meals will determine the change in timing of the secretagogue
    - the change in the timing of activity level particularly if the work is physical in nature
    - frequent BG monitoring is recommended to determine the effect on the individual client's BG values of switching from days to nights.

For clients on insulin:

- For clients working night shift, the greatest stability with BG control is obtained from a once-a-day long-acting insulin analogue given at the same time each day with rapid-acting insulin given before meals. Initially frequent BG monitoring will be needed to determine if dose adjustments are necessary in addition to the adjustment in timing of the AHAs.

For clients on one injection of intermediate or long-acting insulin regimens:

- No adjustment of insulin dose is typically needed especially with long-acting insulin.
- These clients may also be taking an insulin secretagogue and the timing will need to be adjusted to changes in meal times.

For clients on two injections per day regimens:

- Clients on 2 injections of basal insulin who work 3 different shifts, may benefit from the following shift work plan to adjust for days at work and days off. This plan can be used as a **"starting point and will need individualization using clinical judgment."**

Morning Dose = A; Evening Dose = B

Shift	Morning	Evening
Days	Dose A	Dose B
Evenings	Dose A	Dose B
Going on Nights	Dose A	Dose A
Nights	Dose B	Dose A
1st Day Off Nights	Dose B	Dose B

Example:

John takes Levemir 20 U in am and 30 U at hs		
Shift	**Morning**	**Evening**
Days	Levemir 20 U	Levemir 30 U
Evenings	Levemir 20 U	Levemir 30 U
Going on Nights	Levemir 20 U	Levemir 20 U
Nights	Levemir 30 U*	Levemir 20 U
1st Day Off	Levemir 30 U*	Levemir 30 U

*dose may need to be reduced based on activity level at work and am BG value

For clients on three or four injections per day regimens:

- MDI regimens offer the most flexibility for shift work. In this instance, the client continues use of the individualized Insulin Dose Adjustment Guide but the timing of rapid-acting insulin will change to coincide with changing meal times.

- If the type of work during the night is of moderate to high intensity activity, initially, the dose of basal insulin at hs may need to be reduced by 20 to 30%. Frequent BG monitoring will assist in determining what percentage can be used successfully.

Illness

The literature on illness and T2D focuses on critically ill or hospitalized clients. Publications in peer reviewed journals regarding the management of minor illnesses in T2D, like a cold or flu, are non-existent.

"In most people with stable diabetes, minor illnesses are not a big deal. Clients should be able to weather a cold or flulike problem without too much difficulty. The real issue is recognizing when things are getting to be more than they can safely handle at home and when to contact a health care provider". (Dr. Jack Merendino, endocrinologist and co-author of 'The Best Life Guide to Managing Diabetes and Pre-Diabetes' 2009).[77]

- Ensure all clients receive and review the CDEPO handout 'What to Do When You're Sick' (Appendix 14); it provides general recommendations.

- Clients should know that if they are unable maintain hydration, they need to seek medical attention.

- BG should be monitored every 4 to 5 hours (at usual monitoring times, ac meals and hs snack, even if not eating) as well as at 0300 (as long as significant hyperglycemia is present).

- Educators should ask what remedies for a cough or cold the client is taking as they may have an impact on BG values.

- DKA can occur in anyone with diabetes but it is rare in people with TD2. SGLT2 inhibitors pose a risk for DKA in clients with T2D who are ill and not able to eat or drink. If the client has a cold or minor illness and is still able to eat and drink normally, the risk is minimal.

- If the illness is causing an **increase in BG values clients can make adjustments to their AHAs as follow:**

For clients on one injection of insulin:

- If hyperglycemia persists for > 2 days, increase intermediate or long-acting insulin by 10%.

For clients on two injections of premixed insulin:

- If hyperglycemia persists for > 2 days, increase morning dose of premixed insulin by 10%.

For clients on an MDI regimen:

- Take usual basal insulin.
- Use correction doses of rapid-acting insulin as per the client's Insulin Dose Adjustment Guide.

For clients on Oral and Non-Insulin Injectable AHAs:

- If the client is ill but **still able to eat and drink normally**, they can take Oral and Non-Insulin Injectable AHAs as usual.

- Several classes of medications commonly used in people with diabetes can reduce kidney function during periods of intercurrent illness. They will need to be withheld when clients are unwell to the point of not being able to eat and drink normally, in particular when they develop significant dehydration due to reduced oral intake or excessive losses due to vomiting or diarrhea. [78]

- If dehydration is present, the client must seek medical assistance. Until such time that the client has consulted with a Prescriber, Educators can advise clients to withhold metformin, sulfonylureas and SGLT2 inhibitors.

Medical Procedures

Modifying Insulin Regimens in clients with T2D undergoing a Colonoscopy		
	Usual Insulin regimen	**Modification**
Day of preparation before the colonoscopy	Pre-supper premix or hs intermediate or long-acting insulin	Take 70% of usual dose. E.g. client takes: 1. 30 U NovoMix 30 at supper. 30 U x 0.7 = 21 U 2. 50 U Lantus hs. 50 U x 0.7 = 35 U
	Regimens that include rapid-acting insulin before meals	Take usual doses and replace usual CHO intake with fluids containing CHO.
Day of the colonoscopy	One injection of intermediate or long-acting in the morning	Take 50 to 70% of usual dose.
	Two injections of premix morning and evening	Take 50% of usual dose in the morning and resume usual dose in the evening.
	Regimens that include rapid-acting insulin before meals	Do not take rapid acting insulin the morning of the test. Take usual rapid acting insulin when able to eat.
	One injection of intermediate or long-acting insulin in the evening	Take usual dose.
These are general guidelines adapted from the 'Strategies for Managing Special Situations in the Patient with T2D'.[79]		

- The modifications included in the table above can be adapted to other medical procedures or surgery where the client needs to be on clear fluids the day before, and/or fast the evening before and the morning of the procedure. E.g. bowel or stomach surgery.

- For clients on oral and non-insulin injectable AHAs, the Prescriber is responsible for advising clients on which medications need to be withheld in the days prior to surgery and the day of surgery. The following general guidelines apply:

Guideline for pre-operative adjustment of Oral and Non-Insulin Injectable AHAs[80]		
Metformin	D/C a minimum of 24 hours before surgery and for a minimum of 48 hours post-operatively.	Check kidney function before resuming.
Acarbose	D/C day of surgery & until client has resumed eating.	They have no effect in the fasting state.
Sulfonylureas and meglitinides	D/C day of surgery & until client has resumed eating.	Insulin may be used post-operatively until client is able to eat normally.
TZD	D/C day of surgery.	May cause fluid retention in the postoperative phase.
GLP-1R agonists	D/C day of surgery and postoperatively until bowel sounds are present.	They slow gastric motility and may delay restoration of proper gastrointestinal function during recovery.
DPP-4 inhibitors	Take as usual.	Their effect will be diminished in the client who is NPO.
SGLT2 inhibitors	D/C day prior and day of surgery as well as postoperatively until client is metabolically stable and no longer at risk for dehydration.	Monitor for signs and symptoms of DKA even if BG is less than 14 mmol/L.

Tests involving IV Iodinated Contrast:

- Metformin is temporarily discontinued in clients undergoing radiologic studies involving IV administration of iodinated contrast materials, because use of such products may result in acute alteration of renal function. Examples of such tests include IV urogram, IV cholangiography, angiography, and CT scans.

- Metformin is withheld on the day of the procedure and for 48 hours after the procedure. It can be re-started after renal function has been re-evaluated and found to be normal.[81]

Conclusion

An important aspect of glycemia management is optimizing client self-management. This chapter discussed important considerations when developing teaching plans for specific client situations such as increased physical activity or shift work.

This chapter brings to a close the clinical practice aspects of glycemia management. The next chapter will outline the certification and recertification processes at CDEPO.

Chapter 6: Glycemia Management Certification Process

Learning Objective 6

The Educator will describe the Glycemia Management Certification and Recertification Processes.

What is the CDEPO Process for Certification in Glycemia Management?

The CDEPO certification for glycemia management process is an Educator's learning journey towards making independent AHA recommendations to Prescribers. It builds on the Educator's competence in fundamental diabetes management & adult education skills, including the initiation of insulin therapy.

The Educator gains knowledge & experience in making AHA adjustment recommendations throughout the certification process and under the guidance of a Mentor. The certification process involves a series of activities that enhance the Educator's knowledge & skills for making optimal AHA recommendations.

Once the Educator has completed the certification process, they will be able to independently make AHA adjustment recommendations to Prescribers. The length of time needed to complete this certification process is individualized based on the Educator's learning needs.

The learning journey for certification in glycemia management is outlined in a diagram following this narrative description.

Prerequisites

Prior to entering the glycemia management certification learning journey, the Educator will have completed the following:

- Achieved CDEPO Certification in Insulin Initiation.
- Achieved Certified Diabetes Educator (CDE) status.
- Obtained clinical experience in promoting optimal BG control by assessing the client factors affecting glycemia; and teaching clients about lifestyle modifications as well as insulin initiation.
- Participated in several guided/mentored AHA recommendations (for example, contacting a Clinical Consultant when a client's glycemia is not well controlled and discussing options for AHA adjustment). Mentors include the Clinical Manager and/or a Clinical Consultant.

Approval for Certification Process

Once the prerequisites have been met, the Educator & Clinical Manager determine the Educator's readiness to enter into the Glycemia Management Certification Process. When both parties agree, the Educator becomes a Mentee who will work towards developing competency in making independent, safe and effective AHA recommendations to Prescribers.

Glycemia Management Certification Process

- **Read and use** the CDEPO Guide for Glycemia Management of Adults with Type 2 Diabetes 2018.

- **Attend** the Oral & Non-insulin Injectable AHA & the Insulin Adjustment learning sessions.

- **Document competency** (Appendix 15) in all of the topics listed on the 'Oral & Non-insulin Injectable Competency Skills Checklist (CSC)' & the 'Insulin Adjustment CSC' as determined by the Mentor(s) throughout the process.

    - The purpose of the **CSC** is to ensure that the Mentee has gained the key knowledge & skills needed to make AHA recommendations. This is assessed through discussions between the Mentee and Mentor regarding their client cases. It is the responsibility of the Mentee to have the Mentor sign off on competencies once they have been met.

    - The Mentor(s) provides a brief summary or comment on the experience & dates/initials the CSC as the knowledge & skills are acquired.

    - The Mentee and Mentor(s) will co-sign the CSC once the Mentor(s) has determined that all competencies have been demonstrated.

- **Practice making AHA Recommendations to Prescribers** in consultation with the Mentor(s). The step by step process is as follows:

  The Mentee will work with the Mentor(s) to:
    a. observe the Mentor(s) making recommendations
    b. make recommendations jointly with the Mentor(s)
    c. make their own recommendations with Mentor(s) approval.

- **Document experiences** of making their own AHA recommendations with Mentor(s) approval, on the AHA Adjustment Recommendations Experience Record(s).

- The purpose of the **Experience Record** (see Appendix 16) is to track whether the Mentee has had the opportunity to apply their knowledge with clients in a variety of situations and a range of complexities. It is the responsibility of the Mentee to keep track of these approved recommendations.

Present experiences to the Clinical Manager.

- The purpose of the "experience presentations" is to demonstrate that the Mentee has gained the skills to competently and confidently make AHA adjustment recommendations.

- When the Mentee has a record of several experiences, the Mentee arranges a Glycemia Management Case Review meeting with the Clinical Manager to discuss the Experience Record.

- At Glycemia Management Case Review meetings, the Mentee will verbally present each recommendation on the Experience Record to the Clinical Manager who will ensure that it meets the following expectations:

- The Mentee is able to articulate all aspects of the case in a manner that demonstrates overall understanding of the client case

- All elements of the GMAT have been assessed or there is appropriate rationale as to why elements were omitted

- The documentation needed for the recommendation is complete and clear and reflective of the GMAT

- An order was obtained prior to implementation of the recommendation (assuming that the Prescriber responded and agreed with the recommendation)

- If the preceding expectations are met, the Clinical Manager is responsible for signing each experience on the Experience Record(s).

- The Clinical Manager will provide a written report to the Mentee (using the Glycemia Management Case Review form in Appendix 17) following the Case Review Meeting, which includes an "expectations moving forward" section. If these expectations are not met in the next Case Review, the Clinical Manager will not approve the experiences and will not sign the Experience Record.

- Several Case Review meetings will be required until the Mentee has a total of 10 Oral and Non-Insulin Injectable recommendation experiences and a total of 15 Insulin Adjustment Recommendation experiences signed off by the Clinical Manager. At least 5 of the 15 insulin experiences must be intensive insulin regimen experiences.

- **Have a Practice Review** by the Clinical Manager.

  - The purpose of the practice review is for the Mentee to demonstrate sound knowledge and knowledge application of glycemia management with clients.

  - The Clinical Manager will observe the Mentee's clinical practice with a minimum of 2 clients (not necessarily where AHA recommendations are being made to Prescribers but ideally where glycemia is being managed).

  - Verbal feedback will be given to the Educator immediately following the observations. Written feedback will be given to the Mentee after the Clinical Manager has reviewed the Mentee's documentation in the EHR.

Certification Exams

- The purpose of the Certification Exams is for the Mentee to demonstrate knowledge of AHAs & the ability to make safe & effective glycemia management recommendations to Prescribers. The exams are based on the Learning Objectives found in this guide.

- As the final step to the certification process, the Mentee will write 2 exams:
  1. Oral & Non-Insulin AHA Recommendations exam
  2. Insulin Adjustment Recommendations exam

- The exams may be written one at a time or simultaneously as per the Mentee's choice & Clinical Manager's discretion.

- The exams will be supervised by the Clinical Manager or designate at one of the CDEPO locations on a pre-arranged day.

- Exam questions are weighted based on complexity of the question. The passing score for each exam is set at 80%.

    - The Clinical Manager will review the completed exams with the Mentee & give the Mentee the opportunity to expand on their answers verbally. The Clinical Manager will provide feedback on the responses and grade the exam using an Answer Guide.

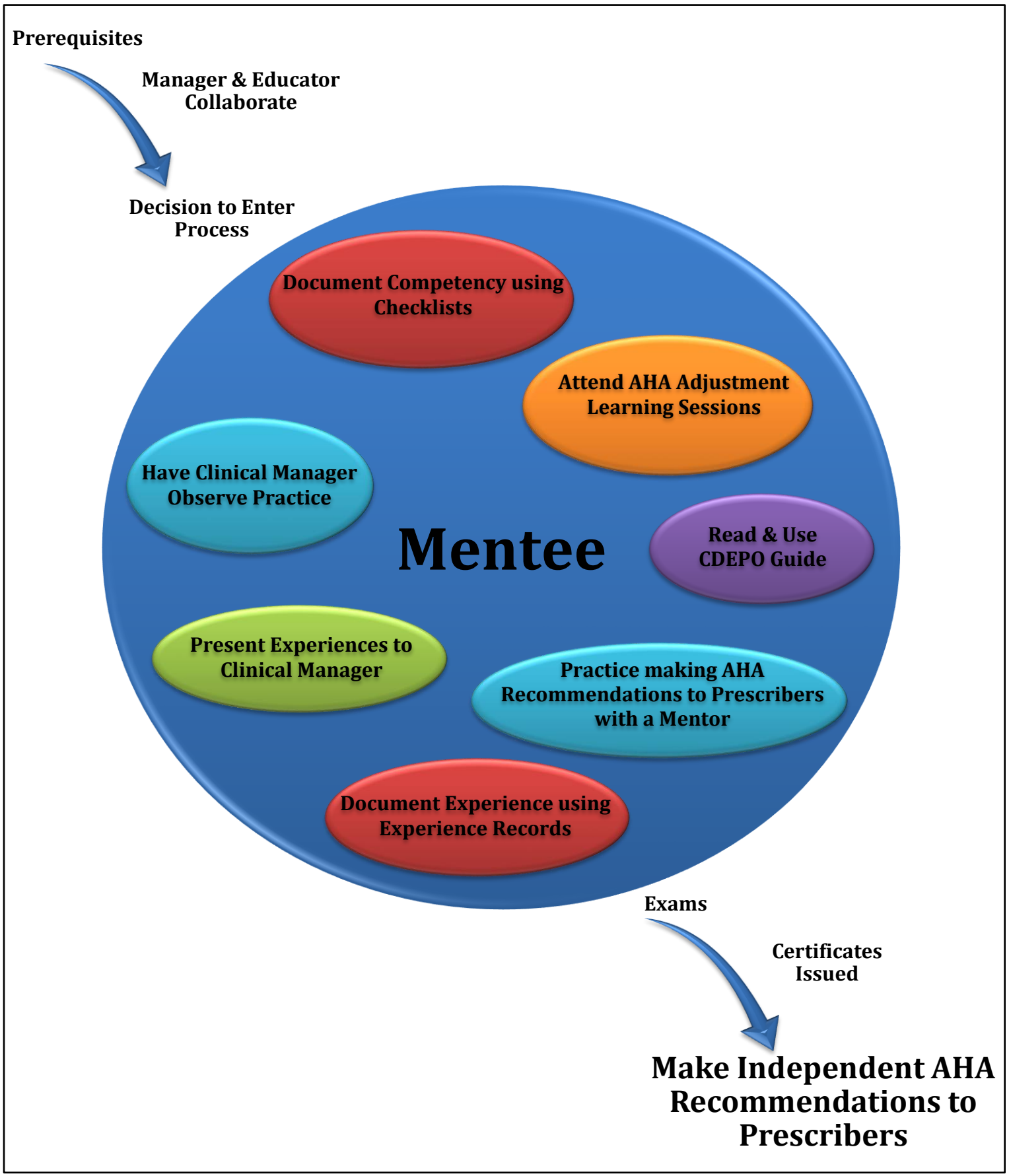
    - If the Mentee does not achieve a score of 80%, the Mentee will discuss a learning plan with the Clinical Manager in order to continue to build competence in specific areas of deficiency. The exam may be taken again once further learning has been demonstrated.

- The Mentee will not be provided with a copy of the exam.

Successful Glycemia Management Certification

CDEPO Mentees who successfully complete the certification process & pass the exams will be issued Certificates of Glycemia Management by the Clinical Manager. The Mentee may then begin to make independent AHA recommendations to Prescribers.

The Community Diabetes Program of Ottawa
Process for Educator Certification in Glycemia Management



Recertification in Glycemia Management:

Recertification in Glycemia Management is necessary because diabetes management is constantly evolving & new learning is a continuous process grounded in experience. The recertification process will provide the Clinical Manager with evidence that the Educator has gained up to date knowledge & skills needed to continue to make independent AHA recommendations to Prescribers.

Recertification will take place every 5 years from the date of the initial certification. It is the Educator's responsibility to ensure certification in Glycemia Management is maintained in order to be able to continue to make AHA adjustment recommendations independently.

To achieve Glycemia Management Recertification, the Educator will demonstrate competence through both knowledge gained and practical experience. The Educator will have some choices in how they demonstrate these competencies.

Knowledge - the Educator will:

Attend a minimum of 5 education sessions regarding different AHA therapy & maintain a record of the sessions on the Recertification in Glycemia Management Record.

and

Read a minimum of 10 articles from peer reviewed journals regarding AHA therapy & maintain a record.

OR

Write a Recertification in Glycemia Management exam and achieve a score of 80%.

Practical Experience – the Educator will:

Present in person to the Clinical Manager, a minimum of 4 client experiences in making AHA recommendations to Prescribers.

OR

Present 2 client experiences in making AHA recommendations to Prescribers to a colleague (will be a Clinical Consultant chosen by the Educator but approved by the Clinical Manager); and present a minimum of 2 cases to the Clinical Manager.

The Glycemia Management Recertification Record will be used to document the preceding activities (next page). Once all of the activities have been completed, the Educator will meet with the Clinical Manager for a final review of the Glycemia Management Recertification Record. If successful, the Clinical Manager will issue a new certificate of Certification in Glycemia Management.

CDEPO Recertification in Glycemia Management Record

AHA Education Session title & presenter	Date	Key learning
1.		
2.		
3.		
4.		
5.		
Articles re AHA Therapy & source	**Date read**	**Key learning**
1.		
2.		
3.		
4.		
5.		
6.		
7.		
8.		
9.		
10.		
Recertification exam (if chosen by Educator)	**Date**	**Grade**
Client Case Presentations (clients EHR number)	**Date**	**Clinical Manager/Clinical Consultant Signature**
1.		
2.		
3.		
4.		

The Educator has successfully completed the CDEPO Recertification in Glycemia Management process.

Clinical Manager Signature **DATE**

Appendices

Appendix 1: Abbreviations

A	
AADE	American Association of Diabetes Educators
A1C	glycosylated hemoglobin
ac	before meals
AHA	Antihyperglycemic Agent(s)
B	
B	breakfast
BG	Blood glucose
BID	twice daily
BMI	Body Mass Index
C	
CDA	Canadian Diabetes Association
DC	Diabetes Canada
CDE	Certified Diabetes Educator
CHO	Carbohydrate
CDEPO	Community Diabetes Education Program of Ottawa
CPG	Clinical Practice Guidelines
CKD	Chronic Kidney Disease
CPAP	Continuous Positive Airway Pressure
CSC	Competency Skills Checklist
CV	Cardiovascular
CVD	Cardiovascular Disease
D	
D/C	discontinue
Diamicron MR	Diamicron extended release (also gliclazide MR)
DKA	diabetic ketoacidosis
DOB	date of birth
DPP-4	dipeptidyl peptidase 4
dula	dulaglutide; Trulicity
E	
EAP	Exceptional Access Program
eGFR	Estimated glomerular filtration rate
EHR	Electronic Health Record
ER	Emergency Room
exe	exenatide
exeQW	exenatide QW
G	
G or g	gram(s)
GLP-1	glucagon-like peptide -1
GLP-1R	glucagon-like peptide-1 receptor agonist
GMAT	Glycemia Management Assessment Tool
H	
hs	evening or at bedtime
hx	history

I	
ICU	Intensive Care Unit
IM	intra-muscular
ISF	insulin sensitivity factor
K	
kg	kilogram
L	
L	lunch
LADA	Latent Autoimmune Diabetes in Adults
lira	liraglutide
M	
Max	maximum
mcg	micrograms
MDI	multiple daily injections
MDRD	Modification of Diet in Renal Disease
metformin ER	metformin extended release
mg	milligrams
ml	milliliter
mmol/L	millimoles per liter
N	
N/A	not applicable
NPO	nothing by mouth
NR	NovoRapid insulin
O	
ODSP	Ontario Disability Support Program
ODB	Ontario Drug Benefit Program
P	
pc	after meals
Q	
QW	once a week
S	
S	supper
SGLT2	Sodium/glucose cotransporter 2
T	
T1D	type 1 diabetes
T2D	type 2 diabetes
TDD	total daily dose
TID	three times daily
TZD	Thiazolidinediones
U	
U	Unit(s)
umol/L	micromole per liter
W	
wt	weight
X	
Xigduo XR	dapagliflozin and metformin extended release

Appendix 2: EMPAREG OUTCOME and LEADER Trials

Clinical Cardiovascular Disease based on the EMPAREG OUTCOME and LEADER Trials

Participants with clinical CVD included in the **EMPAREG OUTOME Trial** had a hx of:[82]

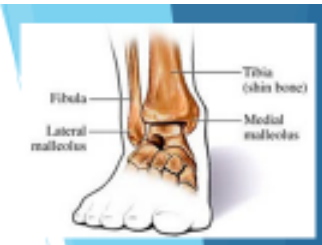
- MI
- Evidence of multi-vessel CAD i.e. in ≥ 2 major coronary arteries or the left main coronary artery, documented by any of the following:
    - Presence of significant stenosis: ≥ 50% luminal narrowing during angiography
    - Revascularization (coronary angioplasty ± stent or coronary artery bypass graft)
    - The combination of revascularization in one major coronary artery and significant stenosis (≥ 50% luminal narrowing) in another major coronary artery
- Evidence of single-vessel coronary artery disease, ≥ 50% luminal narrowing during angiography (coronary or multi-slice computed tomography) not subsequently successfully revascularized, with at least 1 of the following:
    - A positive non-invasive stress test for ischemia
    - Hospital discharge for unstable angina ≤ 12 months prior to consent
    - Unstable angina
- Stroke (ischemic or hemorrhagic)
- Occlusive peripheral artery disease documented by any of the following:
    - Limb angioplasty, stenting, or bypass surgery
    - Limb or foot amputation due to circulatory insufficiency
    - Evidence of significant peripheral artery stenosis (> 50% on angiography, or > 50% or hemodynamically significant via non-invasive methods) in 1 limb
    - Ankle brachial index < 0.9 in ≥ 1 ankle

Participants with clinical CVD included in the **LEADER Trial** had a hx of:[83]

- MI
- Stroke or TIA
- Coronary, carotid or peripheral arterial revascularization
- > 50% Stenosis of coronary, carotid, or lower extremity arteries
- Symptomatic CHD documented by positive exercise stress test or any cardiac imaging or unstable angina with ECG changes
- Asymptomatic cardiac ischemia documented by positive nuclear imaging test, exercise test or dobutamine stress echo
- Chronic heart failure NYHA class II-III

Appendix 3: How to Assess for Pretibial Edema

Assessing for pre-tibial edema
(adapted from procedure used in ACCORD trial 2001-2014)



1. Place index 10 cm above lateral malleolus and press down for 5 seconds. If pitting is noted, move to the dorsum of the foot and as far up the lower leg as the pitting is present.
2. Grade as follows:

Grading pitting edema	What does the extremity look like?	Depth and duration of pitting	Informing the Prescriber
1+	No visible change in shape	2 mm or less pit, disappears rapidly	Include in letter.
2+	No marked change in shape	2-5 mm pit, usually gone in 10-15 secs	Include in letter.
3+	Noticeably edematous	5-10 mm pit, may persist for 1 min	Include in letter. Call Prescriber; leave message if needed.
4+	Very swollen and distorted	>10 mm pit, may persist for >2 mins	Include in letter. Speak with Prescriber stat especially if also SOB.*

***If unable to speak with Prescriber, send client to emergency.**

<u>Important note</u>: if the client is experiencing pitting edema in combination with shortness of breath with minimal exertion, the physician must be notified <u>immediately</u>.

Appendix 4: Medications covered by the OHIP Plus and Ontario Drug Benefit (ODB) program

For OHIP Plus coverage, the following link provides information regarding which AHAs are covered for clients under the age of 25. (effective January 1, 2018)
https://www.ontario.ca/page/check-medication-coverage

For ODB coverage, the following links provide information regarding which AHAs are covered for clients age 65 or more as well as clients on ODSP. The main link to the ODB formulary is https://www.formulary.health.gov.on.ca/formulary and section 68:20 Anti-diabetic Agents which contains these 5 sections, each with their own link:

1. **Oral agents:**
   https://www.formulary.health.gov.on.ca/formulary/results.xhtml?class=682002000

2. **Rapid Insulins:**
   https://www.formulary.health.gov.on.ca/formulary/results.xhtml?class=682010000

3. **Intermediate Insulins:**
   https://www.formulary.health.gov.on.ca/formulary/results.xhtml?class=682012000

4. **Long Acting Insulins:**
   https://www.formulary.health.gov.on.ca/formulary/results.xhtml?class=682014000

5. **Premixed Insulins:**
   https://www.formulary.health.gov.on.ca/formulary/results.xhtml?class=682016000

It is important to note that not all doses of a given medication are necessarily covered by ODB.

Appendix 5: Oral and Non-Insulin Injectable Antihyperglycemic Agents in Canada 2018

***Class* Generic/ Trade Name**	**Potential: A1C lowering and effect on weight**	**Recommended Daily Dose**	**Key Elements**
Alpha-glucosidase inhibitor acarbose/ Glucobay	0.6% ↓ Wt. neutral	**Start dose**: Week 1: 25-50 mg daily Week 2-3: 25-50 mg BID Week 3-4: 25-50 mg TID Max dose = 100 mg TID	1. Unlikely to cause hypoglycemia with monotherapy. 2. Side effects may include flatulence and abdominal discomfort; dose related and may diminish with time. 3. Taken with the first bite of meal; meal contains CHO. 4. Evaluate response using 2-hour pc blood glucose. 5. If taken in combination with sulfonylureas or insulin, appropriate treatment for hypoglycemia: milk, honey and oral glucose (dextrose tablets). Do not treat with sucrose. 6. Refer to DC CPG table titled 'Antihyperglycemic Medications and Renal Function' for dosage adjustments in reduced eGFR. 7. ***Contraindicated*** in intestinal problems.
Biguanide metformin/ Glucophage	1.0-1.5% ↓↓ Wt. neutral	**Start dose:** 250-500 mg daily and titrate upwards. Usual dose 850-1000 mg twice daily. Max dose is 2500 mg daily.	1. Unlikely to cause hypoglycemia with monotherapy. 2. Side effects may include metallic taste in mouth, epigastric discomfort, nausea, vomiting, diarrhea and anorexia. Most are transient and controlled by taking with food and reducing the dose. 3. Discontinue in severe infections, trauma or surgery, severe dehydration or acidosis of any kind. 4. Refer to DC CPG table titled 'Antihyperglycemic Medications and Renal Function' for dosage adjustments in reduced eGFR. 5. ***Contraindicated*** in acute or chronic excessive alcohol intake, severe liver disease or eGFR< 30 mL/min/1.73m^2.
metformin ER / Glumetza		**Start dose:** 500 mg once daily (extended release); max dose 2000 mg daily.	
DPP-4 Inhibitors alogliptin/ Nesina	0.7% ↓↓ Wt. neutral	**Start dose**: 6.5 mg daily. Max dose is 25 mg daily.	1. Unlikely to cause hypoglycemia with monotherapy. 2. Side effects may include upper respiratory infection, headache and gastric upset. Rare cases of severe joint pain. 3. Avoid in clients with heart failure. 4. Refer to DC CPG table titled 'Antihyperglycemic Medications and Renal Function' for dosage adjustments in reduced eGFR. 5. ***Contraindicated*** in severe liver disease, alcoholism, pancreatitis, gallstones, and hypertriglyceridemia.
linagliptin/ Trajenta		**Start dose**: 5 mg daily. Max dose is 5 mg daily.	
saxagliptin/ Onglyza		**Start dose**: 2.5 mg daily. Max dose 5 mg daily.	
sitagliptin/ Januvia		**Start dose:** 25 mg daily. Max dose 100 mg daily.	
GLP-1R Agonists **(non-insulin injectables)** dulaglutide/ Trulicity	1.0-1.5% ↓↓ to ↓↓↓ (up to 1.9% with exeQW) Wt. loss with exe; Significant wt. loss (up to ≥3.0 kg) lira, dula and exeQW.	**Start dose**: 0.75 mg once weekly. Max dose 1.5 mg weekly.	1. Unlikely to cause hypoglycemia with monotherapy. 2. Side effects may include nausea, vomiting and diarrhea; rare cases of pancreatitis and parafollicular cell hyperplasia. Rare cases of acute gallstone disease. 3. Caution with heart rhythm disturbance. 4. Liraglutide demonstrated CV outcome benefit and reduced progression of nephropathy in clients with clinical CVD. 5. Refer to DC CPG table titled 'Antihyperglycemic Medications and Renal Function' for dosage adjustments in reduced eGFR. Rare cases of acute gallstone disease. 6. *Contraindicated* with personal/ family history of medullary thyroid cancer, multiple endocrine neoplasia syndrome type 2.
exenatide/ Byetta		**Start dose**: 5 mcg twice daily. Max dose is 10 mcg twice daily.	
exenatide QW/ Bydureon		**Start dose**: 2 mg weekly. Max dose 2 mg weekly.	
liraglutide/ Victoza		**Start dose**: 0.6 mg daily Max dose 1.8 mg daily.	
lixisenatide/ Adlyxine		Start dose: 10 mcg daily. Max dose: 20 mcg daily.	

Class Generic/ Trade Name	Potential: A1C lowering and effect on weight	Recommended Daily Dose	Key Elements
Insulin Secretagogues			
Meglitinide repaglinide/ GlucoNorm	0.7% ↓↓ Wt. gain	**Start dose:** 0.5-4 mg with meals/snacks. Max dose per meal/snack 4mg. Max dose 16 mg daily.	1. Risk of hypoglycemia minimal to moderate. 2. Side effects may include abdominal pain, diarrhea, vomiting, constipation, nausea and elevated liver enzymes. 3. Taken 1- 30 minutes before meal containing CHO; if meal is skipped, dose is skipped. 4. Doses can be adjusted to CHO content of meals. 5. ***Contraindicated*** with clopidogrel (Plavix) and gemfibrozil (Lopid) and in severe liver disease.
Sulfonylureas gliclazide/ Diamicron	0.8% ↓↓ Wt. gain	**Start dose:** 40-80 mg; doses>160 mg, split into BID. Max dose 320 mg daily.	1. Risk of hypoglycemia minimal to moderate with gliclazide, moderate risk with glimepiride, and significant risk with glyburide; glyburide poses the highest risk in the elderly. 2. Side effects may include nausea, epigastric fullness and heart burn; may diminish as dose is reduced. 3. Do not split Diamicron MR 30 mg tabs; do not crush any dose of Diamicron® MR. 4. Refer to DC CPG table titled 'Antihyperglycemic Medications and Renal Function' for dosage adjustments in reduced eGFR. 5. ***Contraindicated*** *in s*evere liver impairment.
gliclazide MR/ Diamicron MR (extended release)		**Start dose**: 30 mg daily. Max dose 120mg daily.	
glimepiride/ Amaryl		**Start dose:** 1-2 mg daily. Max dose 8 mg daily.	
glyburide/ Diabeta		**Start dose:** 2.5 mg daily; titrate up to 10 mg BID. Max dose 20 mg daily.	
SGLT2 Inhibitors canagliflozin/ Invokana	0.7-1.0% ↓↓ to ↓↓↓ Wt. loss	**Start dose**: 100mg daily. Maximum dose 300 mg.	1. Unlikely to cause hypoglycemia as monotherapy. 2. Side effects may include urinary tract infections and genital infections, hypotension - caution with concomitant loop diuretics, hyperkalemia, rise in LDL-C and HDL-C, decrease in bone density and increased risk of fractures. 3. In clients with clinical CVD, CV outcome benefit, reduced progression of nephropathy and reduction in CHF hospitalisations with empagliflozin and canagliflozin. 4. Increased risk of amputations and fractures with canagliflozin. Use with caution in clients at risk for amputations. 5. Rare diabetic ketoacidosis cases have been reported (may occur with euglycemia or mild hyperglycemia). 6. Refer to DC CPG table titled 'Antihyperglycemic Medications and Renal Function' for dosage adjustments in reduced eGFR. 7. ***Contraindications:*** dapagliflozin if history of or active bladder cancer.
dapagliflozin/ Forxiga		**Start dose**: 5 mg daily. Maximum dose 10 mg.	
empagliflozin/ Jardiance		**Start dose**: 10 mg daily. Maximum dose 25 mg.	
Thiazolidinediones **(TZD)** pioglitazone/ Actos	0.8% ↓↓ Wt. gain	**Start dose:** 15-30 mg daily. Max dose 45 mg daily.	1. Unlikely to cause hypoglycemia in monotherapy. 2. Side effects may include edema, worsening of heart failure, weight gain, macular edema, and ovulation in previously anovulatory women. 3. **Monitor for symptoms of CHF as can cause fluid retention.** 4. Increased risk of bone fracture and with pioglitazone, increased risk of bladder cancer. 5. Rosiglitazone not recommended in ischemic heart disease. 6. Refer to DC CPG table titled 'Antihyperglycemic Medications and Renal Function' for dosage adjustments in reduced eGFR. 7. Triple therapy with TZD is not approved in Canada. 8. ***Contraindicated with insulin,*** CHF, severe hepatic impairment and osteoporosis.
rosiglitazone/ Avandia **(See Appendix 6 for Health Canada Restrictions)**		**Start dose:** 2-4 mg daily or BID. If inadequate response after 8-12 weeks, increase to 8 mg daily or 4 mg BID.	

In order to keep the '***Oral and Non-Insulin Injectable Antihyperglycemic Agents in Canada 2018***' table to an easy to use one-page guide, combination agents have not been included in the table. For combination agents, the key elements for each class are to be considered.

Combination AHAs		
Generic names/ trade name	**Doses**	**Key elements**
alogliptin & metformin/ Kazano	12.5 mg & 500 mg Tab	Refer to Biguanide and DPP4 Inhibitors
	12.5 mg & 850 mg Tab	
	12.5 mg & 1000 mg Tab	
canagliflozin & metformin / Invokamet	50 mg & 500 mg Tab	Refer to Biguanide and SGLT2 Inhibitors
	50 mg & 1000 mg Tab	
	150 mg & 500 mg Tab	
	150 mg & 1000 mg Tab	
dapagliflozin & metformin/ Xigduo	5 mg & 850 mg Tab	
	5 mg & 1000 mg Tab	
dapagliflozin & metformin ER/ Xigduo XR	5 mg & 500 gm ER Tab	
	5 mg & 1000 mg ER Tab	
	10 mg & 500 mg ER Tab	
	10 mg & 1000 mg ER Tab	
empagliflozin & metformin/ Synjardy	5 mg & 500 mg Tab	
	5 mg & 850 mg Tab	
	5 mg & 1000 mg Tab	
	12.5 mg & 500 mg Tab	
	12.5 mg & 850 mg Tab	
	12.5 mg & 1000 mg Tab	
linagliptin & metformin/ Jentadueto	2.5 mg & 500 mg Tab	Refer to Biguanide and DPP4 Inhibitors
	2.5 mg & 850 mg Tab	
	2.5 mg & 1000 mg Tab	
rosiglitazone & metformin/ Avandamet	2 mg & 500 mg Tab	Refer to Biguanide and TZD
	2 mg & 1000 mg Tab	
	4 mg & 500 mg Tab	
	4 mg &1000 mg tab	
saxagliptin & metformin/ Komboglyze	2.5 mg & 500 mg Tab	Refer to Biguanide and DPP4 Inhibitors
	2.5 mg & 850 mg Tab	
	2.5mg & 1000 mg Tab	
sitagliptin & metformin/ Janumet	50 mg & 500 mg Tab	
	50 mg & 850 mg Tab	
	50 mg & 1000 mg Tab	
sitagliptin & metformin ER/ Janumet XR	50 mg & 500 mg ER Tab	

The link below shows a table summarizing research studies involving each of the AHAs:
http://www.rxfiles.ca/rxfiles/uploads/documents/Diabetes-Agents-Outcomes-Comparison-Summary-Table.pdf

Appendix 6: Summary of Health Canada restrictions for rosiglitazone (Nov 18, 2010)

- Rosiglitazone is now indicated only in people with T2D when all other OAA have not lowered blood glucose enough or are not appropriate.

- Before starting or renewing a prescription for rosiglitazone physicians will complete the PATIENT INFORMED CONSENT PROCESS.
    - In this process, physicians will:
        - Discuss other diabetes treatment options and the benefits and risks of rosiglitazone therapy with patients
        - Ask patients to read the Consumer Information for AVANDIA®, AVANDAMET® or AVANDARYL®
        - Ask patients to read and sign a form (see Informed Consent Form at the end of this Public Communication) indicating that the patient understands the heart-related risks of the medication and has discussed other options to treat their diabetes with their doctor (Consumer Information and Informed Consent Form are also available electronically, See Below).

- Rosiglitazone is not approved for use alone (i.e., as a "monotherapy"), unless metformin is inappropriate.

- Rosiglitazone is not recommended for use as part of a "triple therapy" (i.e., in combination with the diabetes drugs metformin and sulfonylurea).

- Rosiglitazone is not approved for use with insulin.

- **Rosiglitazone can be used in combination therapy as follows:**
    - In combination with metformin; or
    - When metformin is contraindicated or not tolerated, in combination with a sulfonylurea.

The complete version of the restriction can be found at http://www.healthycanadians.gc.ca/recall-alert-rappel-avis/hc-sc/2010/14591a-eng.php

Appendix 7: GLP-1R agonists available in Canada 2018

GLP-1R Agonists Dosing and other information							
Generic (trade name) and Dosing	**eGFR** $mL/min/1.73m^2$	**Mixing**	**Needle size**	**Needles included**	**Nausea**	**↓ FBG**	**↓PPG**
dulaglutide (Trulicity) **0.75-1.5mg QW**	Caution eGFR <30	No	29-gauge, 5 mm	Yes, part of device	8-28%	strong	modest
exenatide (Byetta) **5-10 mcg BID**	Caution eGFR 30-50 **Contraindicated <30**	No	Optional choice	No	33-57%	modest	strong
exenatide extended release (Bydureon) **2 mg QW**	Caution eGFR 30-50 **Contraindicated <30**	Yes 80 times	23-gauge, 7 mm	Yes	9-26%	strong	modest
liraglutide (Victoza) **0.6-1.8 mg Once daily**	Not recommended eGFR <50	No	Optional choice	No	10-47%	strong	Modest
lixisenatide (Adlyxine) **10-20 mcg 1hr ac once daily**	Not recommended eGFR <30	No	Optional choice	No	9-25%	Modest	Modest

Appendix 8: Profiles of types of insulin available in Canada 2018

Profiles of types of insulin available in Canada 2018			
Insulin types (trade name)	Onset	Peak	Duration
Prandial (bolus) insulin			
Ultra-rapid-acting analogue (clear) ➢ aspart (Fiasp)	4 min	30-90 min	3-5 hours
Rapid-acting analogues (clear) ➢ aspart (NovoRapid) ➢ lispro 100 U/ml (Humalog U-100) ➢ lispro 200 U/ml (Humalog U-200) ➢ glulisine (Apidra)	9-20 min 10-15 min 10-15 min 10-15 min	1-1.5 hours 1-2 hours 1-2 hours 1-1.5 hours	3-5 hours 3.5-4.75 hours 3.5-4.75 hours 3.5-5 hours
Short-acting regular insulin (clear) ➢ Humulin-R ➢ Novolin®ge Toronto ➢ Entuzity (U-500)	30 min 15 min	2-3 hours 4-8 hours	6.5 hours 17-24 hours
Basal insulins			
Intermediate-acting (cloudy) ➢ Humulin-N ➢ Novolin®ge NPH	1-3 hours	5-8 hours	Up to 18 hours
Long-acting basal insulin analogues (clear) ➢ detemir (Levemir) ➢ glargine 100 U/ml (Lantus or Basaglar) ➢ glargine 300 U/ml (Toujeo)	1.5 hours 6 hours	Not applicable as they are peakless	detemir 16-24 hours glargine 24 hours >30 hours
Ultra-long-acting basal insulin analogues (clear) ➢ degludec U-100 (TRESIBA U-100) ➢ degludec U-200 (TRESIBA U-200)		Not applicable as they are peakless	Up to 42 hours (half life approximately 25 hours)
Premixed insulins			
Premixed regular insulin – NPH (cloudy) ➢ Humulin 30/70 ➢ Novolin®ge 30/70, 40/60, 50/50	30/70 = 30% regular and 70% NPH insulin 40/60 = 40% regular and 60% NPH insulin 50/50 = 50% regular and 50% NPH insulin		
Premixed insulin analogues (cloudy) ➢ Biphasic insulin aspart (NovoMix 30) ➢ Insulin lispro/lispro protamine (Humalog Mix25 and Mix50)	NovoMix 30 = 30% aspart and 70% aspart protamine Humalog Mix25 = 25% lispro and 75% lispro protamine Humalog Mix50 = 50% lispro and 50% lispro protamine		

The insulin action profiles in the preceding table are a guide as the action times can vary from client to client. NPH and regular insulin (including combinations) have the most variability whereas insulin analogues may be more predictable. The individual response to insulin is best determined by the client's BG patterns and trends.[84]

Appendix 9: CDEPO Blood Glucose, CHO & Insulin Record

Blood Glucose, CHO & Insulin Record

Name: _____
EHR#_____

Basal Insulin: Meal Insulin: Insulin Sensitivity Factor:

Diabetes Medications:

DATE	**BREAKFAST ___:___**				**LUNCH ___:___**				**SUPPER ___:___**				**EVENING**	**COMMENTS**
	BG Before	Carb (g)	Ins.	BG After	BG Before	Carb (g)	Ins.	BG After	BG Before	Carb (g)	Ins.	BG After		

Appendix 10: Carbohydrate Counting Assessment Blood Glucose and Food Record

Carbohydrate Counting Assessment Blood Glucose and Food Record

EHR #: _____ Name: _____

Date	**Breakfast**			**Lunch**			**Supper**			**Hs**	**Snacks (include time eaten)**	**Comments (include physical activity)**
	BG Before	Insulin (Us)	BG After	BG Before	Insulin (Us)	BG After	BG Before	Insulin (Us)	BG After	BG		
Food			Carbs (g)			Carbs (g)			Carbs (g)			
Date	**Breakfast**			**Lunch**			**Supper**			**Hs**	**Snacks (include time eaten)**	**Comments (include physical activity)**
	BG Before	Insulin (Us)	BG After	BG Before	Insulin (Us)	BG After	BG Before	Insulin (Us)	BG After	BG		
Food			Carbs (g)			Carbs (g)			Carbs (g)			

Appendix 11: Insulin Dose Adjustment Guide

Insulin Dose Adjustment Guide

Name: _____ **Date: _____**

Blood Glucose Reading	**Background Insulin _____**	**Rapid-Acting Insulin: _____**			**Background Insulin _____**
		Breakfast	**Lunch**	**Supper**	
		+	+	+	
		+	+	+	
		+	+	+	
		+	+	+	
		+	+	+	
		+	+	+	

Appendix 12: CDEPO Template Letter to Prescriber When Making AHA Recommendations

Date: _____
Physician name:
Fax number:

Re: Client's name
DOB: Client's DOB

Dear Dr._____,

Write a brief statement regarding main concern/issue(s) or purpose of letter.

Current antihyperglycemic medications: (as per referral form or client report)

1.
2.
3.

BG values: date of BGs provided here _____ OR
See attached Blood Glucose Logs.

Assessment:

Suggestions for changes to antihyperglycemic medications:

1.
2.
3.

Please sign below if you agree with the suggestions above and **return this letter by fax to (name) at (fax #).**

Otherwise indicate alternate orders: _____. By returning this order to me, I will follow-up with the client to support him/her in making the changes.

Physician: _____ Signature: _____ Date: _____

This form was completed by a Certified Diabetes Educator in consultation with the Clinical Manager; Certified Diabetes Educator who is also certified in Glycemia Management; or in consultation with a Certified Diabetes Educator who is also certified in Glycemia Management.

Next appointment:

If you wish to discuss this case further please contact:

Name and signature of Educator:

Appendix 13: CDEPO Handout Tips for Travel

Tips for Travel

Getting ready to go

Visit Your Health Care Provider	Visit Your Pharmacist
Ask: • Are vaccinations up to date? • For a travel letter from your Health Care Provider • What to do if you get sick or dehydrated	• Get a list of your current medications • Make sure you have enough for trip • Ensure you have enough supplies (lancets, strips, batteries, medications)

Get your blood glucose as close to target as possible before your trip.
Visit your Diabetes Educator if you want help.

Preparing for your trip

- Diabetes medications
- Blood glucose meter & supplies
- List of contacts (family member, doctor, pharmacist, diabetes educator)
- Fast acting carbohydrate to treat low BG
- Snack to cover missed or late meals
- Water
- Sunscreen and bug repellent
- Medication for nausea and diarrhea
- Comfortable walking shoes

When travelling with others

- Tell them you have diabetes
- Tell them why regular meal times and exercise are important for you
- Know the daily vacation schedule so you can plan ahead

Wear diabetes identification such as a Medical Alert ID or carry a wallet card.
Be sure to have travel insurance.

Appendix 14: CDEPO What to Do When You're Sick Client Handout

What to Do When You're Sick

Being sick is not fun. When you have diabetes, it can be serious.

When you are sick your blood glucose (BG) will likely go up even if you are not eating. **Check your BG every four hours –** more often if it is too high or too low.

When you cannot eat or keep food down, you might think it makes sense to stop your diabetes medications. That's not true! **Keep taking your diabetes medications.**

It is easy to get **dehydrated** from vomiting, diarrhea, fever and high BG.
Drink lots of water and fluids.

IMPORTANT:
Some medications can affect your kidneys if you become dehydrated.

- Ask your Health Care Provider which medications to stop taking
- Do not take over-the-counter medication unless your pharmacist says it is safe

If you cannot eat your regular meals and snacks, try some of the following:

- Grains & starches: soda crackers, rice, toast, rice cakes, noodle soup
- Milk & Alternatives: yogurt, ice cream, frozen yogurt
- Fruits: apple sauce, apple juice, orange juice, banana
- Other: Jell-O, Ginger Ale*, Gatorade*, Glucerna, hot tea with 1 tablespoon honey and lemon, cough candies, popsicle

***Have drinks with sugar in them (not sugar-free)** if you are using them to replace meals or snacks.

If you don't know what to do, call your Health Care Provider or Diabetes Educator. We can help.

Appendix 15: Competency Skills Checklists for Certification

Oral & Non-Insulin Injectable AHA Adjustment Recommendations

Competency Skills Checklist

Name of Mentee: _____ **Date started: _____**

Oral & Non-insulin Injectable AHA Adjustment Topics	Date & mentor sign-off	Comments
Identify assessment of client factors influencing glycemic control.		
Describe the purpose of the 'Oral & Non-insulin Injectable AHA* in Canada 2018' table & its use. (*in this document, AHA refers to Oral & Non-insulin Injectable AHA).		
Describe which AHAs can be recommended by CDEPO Educators & off-label use of medications.		
Describe the use of AHAs in decreased renal function & calculate eGFR using the MDRD.		
Describe Oral & Non-Insulin Injectable AHA profiles of agents in Canada 2018.		
Describe the assessment of clinical factors when selecting a specific AHA.		
List key elements to consider when recommending AHAs.		
Describe how to reduce the risk of DKA with SGLT2 Inhibitors.		
Describe considerations when making AHA adjustment recommendations including pattern management.		
Provide examples of adding a second AHA to metformin.		
Describe Health Canada Restrictions with rosiglitazone.		
Perform or describe assessment for pretibial edema.		

Assess client BG records & provide recommendations with rationale for AHA adjustments.		
Demonstrate or explain AHA adjustment recommendations for increased activity, travel, shift work, illness & medical procedures.		
Demonstrate AHA adjustments recommendations based on BG patterns, and client & clinical factors in CDEPO clients.		
Document accurately in the clients' EHR.		
Write letters to obtain Prescriber orders for AHA adjustments that have been approved by a Mentor.		
Ensure adequate follow-up with client once Prescriber's orders are received.		

(Name of Mentor) _____ certifies that _____ (name of Mentee) is knowledgeable regarding the preceding topics on oral and non-insulin injectable AHA adjustments recommendations.

_____ _____ _____

Signature of Mentor Signature of Mentee Date

_____ _____

Signature of Clinical Manager Date

Insulin Adjustment Recommendations
(Competency Skills Checklist)

Name of Mentee: _____ **Date started: _____**

Insulin Adjustment Topics	Date & Mentor sign-off	Comments
Identify assessment of client factors influencing glycemic control.		
Describe insulin profiles.		
Describe insulin regimens.		
Describe the assessment of clinical factors when selecting a specific type of insulin regimen.		
Describe the concept of adjusting insulin using pattern management.		
Describe the steps to pattern management.		
Discuss which insulin to adjust for hyperglycemia & hypoglycemia for the various time frames.		
Assess client BG records & identify patterns.		
Explain important considerations when working with insulin.		
Define intensive insulin therapy & describe key elements to implementation.		
Identify clients who may benefit from intensive insulin therapy regimens.		
Identify indications for supplemental insulin doses.		
Describe 2 types of supplemental insulin doses: compensatory & anticipatory.		
Calculate ISF & construct algorithms.		

Demonstrate making insulin adjustment recommendations based on insulin to CHO ratios.		
Demonstrate making or describe insulin adjustment recommendations for increased activity, travel, shift work & medical procedures.		
Demonstrate insulin adjustment recommendations based on BG patterns in CDEPO clients.		
Demonstrate insulin adjustments based on algorithms in CDEPO clients.		
Document accurately in the clients' HER.		
Write letters to obtain Prescriber orders for AHA adjustments that have been approved by a Mentor.		
Ensure adequate follow-up with client once Prescriber's orders are received.		

(Name of Mentor) _____ certifies that _____ (name of Mentee) is knowledgeable regarding the preceding topics on insulin adjustment recommendations.

_____ _____ _____

Signature of Mentor Signature of Mentee Date

_____ _____

Signature of Clinical Manager Date

Appendix 16: Experience Record for Certification

AHA Recommendations Experience Record

Name of Mentee_____ **Date started _____**

Oral and Non-Insulin Injectable Adjustments Recommendations:

Date	Client EHR#	Adjustments recommended	Signature of Clinical Manager
1.			
2.			
3.			
4.			
5.			
6.			
7.			
8.			
9.			
10.			

Insulin Adjustment Recommendations (5 of which are intensive insulin):

Date	Client EHR#	Adjustment(s) recommended	Signature of Clinical Manager
1.			
2.			
3.			
4.			
5.			
6.			
7.			
8.			

Continuation: Insulin Adjustment Recommendations (5 of which are intensive insulin):

9.			
10.			
11.			
12.			
13.			
14.			
15.			

Practice Review of Client Visits (a minimum of two satisfactory client visits):

Date	Client EHR#	Clinical Manager comments	Signature of Clinical Manager
1.			
2.			
3.			
4.			
5.			

I, (the Clinical Manager) _____ certify that _____ (name of Mentee) is able to make safe and effective AHA recommendations.

_____ _____ _____

Signature of Clinical Manager Signature of Mentee Date

Appendix 17: Glycemia Management Case Review Form

The Community Diabetes Education Program of Ottawa
Le programme communautaire d'éducation sur le diabète d'Ottawa

Glycemia Management Certification

Case Review Feedback Form

Meeting Date: **Location:** **Educator:**

Prepared by: Clinical Manager

Overall Summary

Notes on the specific client cases reviewed are included here; may include what worked well and what didn't work well in making the AHA recommendation.

Expectations Moving Forward

Notes on what the Mentee may need to learn or skills that may need to improve prior to the next client case review session with the Clinical Manager.

Plan:

This may include specifics on learning opportunities for the Mentee that are specific to achieving certification in glycemia management.

This will include upcoming dates for client case review sessions, exams etc. pertaining to glycemia management certification

I acknowledge that I have read and understand the above information and I have received a copy.

_____ _____
Signature of Mentee Signature of Clinical Manager

_____ _____
Date Date

References

[1] Furler J et al. Supporting insulin initiation in type 2 diabetes in primary care: results of the Stepping Up pragmatic cluster randomised controlled clinical trial. BMJ 2017; 356: j783: 1-10. http://www.bmj.com/content/bmj/356/bmj.j783.full.pdf

[2] Seaquist E et al. Hypoglycemia and Diabetes: A Report of a Workgroup of the American Diabetes Association and The Endocrine Society. Diabetes Care 2013; 36 (5): 1384–1395. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3631867

[3] Martin-Timon I et al. Mechanisms of hypoglycemia unawareness and implications in diabetic patients World J Diabetes 2015; 6 (7): 912–926. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4499525/

[4] Erbach M et al. Interferences and Limitations in Blood Glucose Self-Testing: An Overview of the Current Knowledge. J Diabetes Sci Technology 2016; 10 (5): 1161-1168. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5032951/

[5] Ramljak S et al. Hematocrit Interference of Blood Glucose Meters for Patient Self-Measurement. J Diabetes Sci Technology 2013; 7 (1): 179-189. http://journals.sagepub.com/doi/pdf/10.1177/193229681300700123

[6] Osterberg L and Blaschke T. Adherence to Medication. NEJM 2005; 353: 487-497. http://www.ub.edu/farmaciaclinica/projectes/webquest/WQ1/docs/osterberg.pdf

[7] Koyanagi K et al. Prescription Factors Associated with Medication Non-adherence in Japan Assessed from Leftover Drugs in the SETSUYAKU-BAG Campaign: Focus on Oral Antidiabetic Drugs. Front Pharmacol 2016; article 12: 1-9. https://doi.org/10.3389/fphar.2016.00212

[8] Zongo A et al. Predictive Validity of Self-Reported Measures of Adherence to Noninsulin Antidiabetes Medication against Control of Glycated Hemoglobin Levels. Can J Diabetes 2016; 40 (1): 58-65. http://www.canadianjournalofdiabetes.com/article/S1499-2671(15)00497-9/pdf

[9] Boeni F et al. Effect of drug reminder packaging on medication adherence: a systematic review revealing research gaps. Systematic Reviews 2014; 3 (29): 1-15. http://www.systematicreviewsjournal.com/content/3/1/29

[10] Shai I et al. Glycemic Effects of Moderate Alcohol Intake among Patients with Type 2 Diabetes: A Multicenter, Randomized, Clinical Intervention Trial. Diabetes Care 2007; 30 (12): 3011-3016. http://care.diabetesjournals.org/content/diacare/30/12/3011.full.pdf

[11] Pietraszek A, Gregersen S, Hermansen K. Alcohol and type 2 diabetes. A review. Nutr Metab Cardiovasc Dis 2010; 20: 366e75 http://www.sciencedirect.com/science/article/pii/S0939475310001067 abstract only; full text available for purchase.

[12] Frid et al. New Insulin Delivery Recommendations. Mayo Clin Proc. Sept 2016; 91 (9): 1231-1255. http://ac.els-cdn.com/S0025619616303214/1-s2.0-S0025619616303214-main.pdf?_tid=e6aa2454-581e-11e7-97f4-00000aacb360&acdnat=1498227720_95492e9f56dca75cdbcd55f3ebd55f3f

[13] FIT Forum for Injection Technique Canada, Recommendations for Best Practice in Injection Technique (3nd Ed). http://www.fit4diabetes.com/files/2314/8777/6632/FIT_Recommendations_3rd_Edition_2017.pdf

[14] Images in Clinical Medicine. Insulin Induced Lipohypertrophy. NEJM 2012; 366:e9. http://www.nejm.org/doi/full/10.1056/NEJMicm1101527#t=article

[15] Images in Clinical Medicine. Injection Site Lipoatrophy NEJM 2009; 361:e41. http://www.nejm.org/doi/full/10.1056/NEJMicm0808275#t=article

[16] Fiasp insulin product monograph. February 2, 2017. http://www.novonordisk.ca/content/dam/Canada/AFFILIATE/www-novonordisk-ca/OurProducts/PDF/fiasp-product-monograph.pdf

[17] Sigal RJ et al. Effects of Aerobic Training, Resistance Training, or Both on Glycemic Control in Type 2 Diabetes A Randomized Trial. Ann Intern Med 2007; 147 (6): 357-369. http://annals.org/aim/article/736439/effects-aerobic-training-resistance-training-both-glycemic-control-type-2

[18] Larose J, Sigal RJ, et al. Associations between physical fitness and HbA_{1c} in type 2 diabetes mellitus. Diabetologia 2011; 54: 93-102. https://link.springer.com/article/10.1007%2Fs00125-010-1941-3

[19] Colberg S, Sigal RJ, et al. Exercise and type 2 diabetes. Diabetes Care 2010; 33 (12): e147–e167. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2992225

[20] McAllister D et al. Stress Hyperglycemia in Hospitalized Patients and Their 3-Year Risk of Diabetes: A Scottish Retrospective Cohort Study. PLOS Medicine 2014; 11 (8): e1001708. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4138030/pdf/pmed.1001708.pdf

[21] Boon-How C et al. Diabetes-Related Distress, Depression and Distress-Depression among Adults with Type 2 Diabetes Mellitus in Malaysia. PLOS ONE open access internet journal March 22, 2016: 1–16. http://journals.plos.org/plosone/article/file?id=10.1371/journal.pone.0152095&type=printable

[22] Rehman A et al. Drug-Induced Glucose Alterations Part 2: Drug-Induced Hyperglycemia. Diabetes Spectrum 2011; 24 (4): 234–238. http://spectrum.diabetesjournals.org/content/diaspect/24/4/234.full.pdf

[23] Vues M et al. Drug-Induced Glucose Alterations Part 1: Drug-Induced Hypoglycemia. Diabetes Spectrum 2011; 24 (3): 171–177. http://spectrum.diabetesjournals.org/content/diaspect/24/3/171.full.pdf

[24] Liu D et al. A practical guide to the monitoring and management of complications of systemic corticosteroid therapy. Allergy Asthma Clin Immunol 2013; 9-30: 1-25. https://aacijournal.biomedcentral.com/articles/10.1186/1710-1492-9-30

[25] Penner E et al. The Impact of Marijuana Use on Glucose, Insulin and Insulin Resistance among US Adults. American Journal of Medicine 2013; 126 (7): 583-589. http://www.amjmed.com/article/S0002-9343(13)00200-3/pdf

[26] Meneilly G et al. Diabetes Canada 2018 Clinical Practice Guidelines for the Prevention and Management of Diabetes in Canada: Diabetes in Older People. Can J Diabetes 2018; 42 (Suppl 1): S283-295. https://www.sciencedirect.com/science/article/pii/S1499267117308316

[27] Papa E et al. Therapeutic options for elderly diabetic subjects: open label, randomized clinical trial of insulin glargine added to oral antidiabetic drugs versus increased dosage of oral antidiabetic drugs. Acta Diabetologia 2008; 45 (1): 53–59. https://www.ncbi.nlm.nih.gov/pubmed/18180864 (link to abstract only, PDF not available)

[28] The ADVANCE Collaborative Group. Intensive blood glucose control and vascular outcomes in patients with type 2 diabetes. NEJM 2008; 358 (24): 2560–2572. http://www.nejm.org/doi/pdf/10.1056/NEJMoa0802987

[29] Calles-Escandón J et al. Effect of intensive compared with standard glycemia treatment strategies on mortality by baseline subgroup characteristics: The Action to Control Cardiovascular Risk in Diabetes (ACCORD) trial. Diabetes Care 2010; 33 (4): 721–727. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2845012/pdf/zdc721.pdf

[30] Riddle M et al. Epidemiologic Relationships between A1C and All-Cause Mortality during a Median 3.4-Year Follow-up of Glycemic Treatment in the ACCORD Trial. Diabetes Care 2010; 33 (5): 983-990. http://care.diabetesjournals.org/content/diacare/33/5/983.full.pdf

[31] Van Gaal L and Scheen A. Weight Management in Type 2 Diabetes: Current and Emerging Approaches to Treatment. Diabetes Care 2015; 38 (6): 1161–1172. http://care.diabetesjournals.org/content/38/6/1161.full-text.pdf

[32] Zinman B et al. Empagliflozin, Cardiovascular Outcomes, and Mortality in Type 2 Diabetes. NEJM 2015; 373 (22): 2117–2128. http://www.nejm.org/doi/pdf/10.1056/NEJMoa1504720

[33] Canadian Agency for Drugs and Technologies in Health (CADTH). Empagliflozin - Indication: Prevention of Cardiovascular Mortality in Type 2 Diabetes Mellitus. Oct 2016: 1–6. https://www.cadth.ca/sites/default/files/cdr/complete/SR0488_complete_Jardiance-Oct-28-16.pdf

[34] Marso SP et al. Liraglutide and Cardiovascular Outcomes in Type 2 Diabetes. NEJM 2016; 375 (4): 311-322. https://www.nejm.org/doi/pdf/10.1056/NEJMoa1603827

[35] Neal B et al. Canagliflozin and Cardiovascular and Renal Events in Type 2 Diabetes. NEJM 2017; 377 (7): 1-14. https://www.nejm.org/doi/pdf/10.1056/NEJMoa1611925

[36] Multicenter Trial to Evaluate the Effect of Dapagliflozin on the Incidence of Cardiovascular Events (DECLARE-TIMI58). Clinical Trials.gov. 2012. https://www.clinicaltrials.gov/ct2/show/NCT01730534

[37] Pfeffer M et al. Lixisenatide in Patients with Type 2 Diabetes and Acute Coronary Syndrome. NEJM 2015; 373 (23): 2247–2257. http://www.nejm.org/doi/pdf/10.1056/NEJMoa1509225

[38] Marso SP et al. Semaglutide and Cardiovascular Outcomes in Patients with Type 2 Diabetes. NEJM 2016; 375 (19): 1834–1844. http://www.nejm.org/doi/pdf/10.1056/NEJMoa1607141

[39] Ionnidis I. Diabetes treatment in patients with renal disease: Is the landscape clear enough? World J Diabetes 2014; 5(5): 651–658. https://f6publishing.blob.core.windows.net/c441084e-1909-4fa4-869c-2fc4844ec861/WJD-5-651.pdf

[40] Addendum to Policies, Guidelines and Consensus Statements: Pharmacologic Management of Type 2 Diabetes: 2015 Interim Update. Can J Diabetes 2015; 39 (5): 440. http://www.canadianjournalofdiabetes.com/article/S1499-2671(15)00569-9/pdf

[41] Michels W et al. Performance of the Cockcroft-Gault, MDRD, and New CKD-EPI Formulas in Relation to GFR, Age, and Body Size. Clin J Am Soc Nephrol 2010; 5(6): 1003–1009. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2879308/

[42] National Institute of Health (NIH). Estimating Glomerular Filtration Rate (GFR). https://www.niddk.nih.gov/health-information/health-communication-programs/nkdep/lab-evaluation/gfr/estimating/Pages/estimating.aspx

[43] Wharton S et al. Diabetes Canada 2018 Clinical Practice Guidelines for the Prevention and Management of Diabetes in Canada: Weight Management in Diabetes. Can J Diabetes 2018; 42 (Suppl 1): S124-129. http://guidelines.diabetes.ca/docs/cpg/Ch17-Weight-Management-in-Diabetes.pdf

[44] Pinto et al. Efficacy of SGLT2 inhibitors in glycemic control, weight loss and blood pressure reduction: a systematic review and meta-analysis. Diabetology & Metabolic Syndrome 2015; 7 (suppl 1): A58: 1–2. https://dmsjournal.biomedcentral.com/track/pdf/10.1186/1758-5996-7-S1-A58?site=dmsjournal.biomedcentral.com

[45] Health Canada Guidance Document on Product Monographs 2014/06/01: 11. http://www.hc-sc.gc.ca/dhp-mps/prodpharma/applic-demande/guide-ld/monograph/pm_mp_2013-eng.php and download PDF.

[46] Gerich J. Pathogenesis and management of postprandial hyperglycemia: role of incretin-based therapies. International Journal of General Medicine 2013; 6: 877–895. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3884108/pdf/ijgm-6-877.pdf

[47] Choudhary P et al. Do high fasting glucose levels suggest nocturnal hypoglycaemia? The Somogyi effect-more fiction than fact? Diabetic Medicine 2013; 30 (8): 914–917. http://onlinelibrary.wiley.com/doi/10.1111/dme.12175/pdf

[48] Hoi-Hansen T et al. The Somogyi phenomenon revisited using continuous glucose monitoring in daily life. Diabetologia 2005; 48 (11): 2437–2438. https://link.springer.com/content/pdf/10.1007%2Fs00125-005-1946-5.pdf

[49] Monnier L et al. Magnitude of the Dawn Phenomenon and Its Impact on the Overall Glucose Exposure in Type 2 Diabetes. Diabetes Care 2013; 36 (12): 4057–4062. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3836163/pdf/4057.pdf

[50] Lipsombe L et al. Diabetes Canada 2018 Clinical Practice Guidelines for the Prevention and Management of Diabetes in Canada: Pharmacologic Glycemic Management of Type 2 Diabetes in Adults. Can J Diabetes 2018; 42(Suppl 1): S88-S103. http://guidelines.diabetes.ca/docs/cpg/Ch13-Pharmacologic-Glycemic-Management-of-Type-2-Diabetes-in-Adults.pdf

[51] The Honorable K. Ogilvie, chair. Prescription Pharmaceuticals Canada: Off-label use. Standing Senate Committee on Social Affairs, Science and Technology. January 2014: 3–5. http://www.parl.gc.ca/Content/SEN/Committee/412/soci/rep/rep05jan14-e.pdf

[52] Gliclazide product monograph. July 13, 2016. http://www.servier.ca/sites/default/files/webform/products/EN%20-%20Diamicron%2080%20%20PM%20%20July%2013%2C%202016.pdf?ts=1489623099

[53] CPS, Ottawa (ON); Canadian Pharmacists Assoc; 2017 cited Dec 10/2017.

[54] Prasad-Reddy L and Isaacs D. A Clinical Review of GLP1 Receptor Agonists: efficacy and safety in diabetes and beyond. Drugs Context 2015; 4: 1-19. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4509428/pdf/dic-4-212283.pdf

[55] Rosenstock J and Ferrannini E. Euglycemia Diabetic Ketoacidosis: A Predictable, Detectable, and Preventable Safety Concern with SGLT2 Inhibitors. Diabetes Care 2015; 38 (9): 1638–1642. http://care.diabetesjournals.org/content/38/9/1638.full-text.pdf

[56] Handelsman Y et al. American Association of Clinical Endocrinologists and American College of Endocrinology Position Statement on the Association of SGLT-2 Inhibitors and Diabetic Ketoacidosis. Endocrine Practice 2016; 22 (6): 1–10. https://aace.com/files/position-statements/SGLT-2-position-statement.pdf

[57] Parkin C and Davidson J. Value of Self-Monitoring Blood Glucose Pattern Analysis in Improving Diabetes Outcomes. Journal of Diabetes Science and Technology 2009; 3 (3): 500–508. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2769875/pdf/dst-03-0500.pdf

[58] Gerich J. Pathogenesis and management of postprandial hyperglycemia: role of incretin-based therapies. Int J Gen Med 2013; 6: 877–895. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3884108/pdf/ijgm-6-877.pdf

[59] Ganiats T. Variability in Insulin Action: Mechanisms, Implications, and Recent Advances. The Internet Journal of Family Practice 2006; 5 (2): 1–9. https://print.ispub.com/api/0/ispub-article/8977

[60] Novolin ge insulin product monograph. March 11, 2016. http://www.novonordisk.ca/content/dam/Canada/AFFILIATE/www-novonordisk-ca/OurProducts/PDF/novolin-product-monograph.pdf

[61] Lantus insulin product monograph. October 19, 2017. http://products.sanofi.ca/en/lantus.pdf

[62] Tambascia M et al. Evidenced based clinical use of insulin premixtures. Diabetology & Metabolic Syndrome 2013; 5 (50): 1–10. https://dmsjournal.biomedcentral.com/track/pdf/10.1186/1758-5996-5-50?site=dmsjournal.biomedcentral.com

[63] Toujeo insulin product monograph. May 28, 2015. http://products.sanofi.ca/en/toujeo-solostar.pdf

[64] Tresiba insulin product monograph. August 25, 2017. http://www.novonordisk.ca/content/dam/Canada/AFFILIATE/www-novonordisk-ca/OurProducts/PDF/tresiba-product-monograph.pdf

[65] Swinnen SG et al. Insulin detemir versus insulin glargine for type 2 diabetes mellitus. Cochrane Library 6 JUL 2011. http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD006383.pub2/full#CD006383-fig-00113 (summary) http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD006383.pub2/epdf (full 62 page document)

[66] Inzucchi SE et al. Management of hyperglycemia in type 2 diabetes: a patient-centered approach. Position statement of the American Diabetes Association (ADA) and the European Association for the Study of Diabetes (EASD). Diabetologia 2012; 55: 1577–1596. https://link.springer.com/content/pdf/10.1007%2Fs00125-012-2534-0.pdf

[67] Tambascia M et al. Evidenced-based clinical use of insulin premixtures. Diabetology & Metabolic Syndrome 2013; 5(50): 1–10. https://dmsjournal.biomedcentral.com/track/pdf/10.1186/1758-5996-5-50?site=dmsjournal.biomedcentral.com

[68] Mosenzon O & Raz I. Intensification of Insulin Therapy for Type 2 Diabetic Patients in Primary Care: Basal-Bolus Regimen versus Premix Insulin Analogs. Diabetes Care 2013; 36 (Supplement 2): S212–S218. http://care.diabetesjournals.org/content/36/Supplement_2/S212

[69] Swinnen S et al. Insulin Therapy for Type 2 Diabetes. Diabetes Care 2009; 32 (Supplement 2): S253–S259. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2811456/pdf/zdcS253.pdf

[70] Owen D. Clinical Evidence for the Earlier Initiation of Insulin Therapy in Type 2 Diabetes. Diabetes Technology & Therapeutics 2013; 15 (9): 776–785. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3757533/pdf/dia.2013.0081.pdf

[71] Canadian Diabetes Association (CDA) Diabetes Educator Section, *Building Competency in Diabetes Education: Advancing Practice 3rd Edition*. Toronto, ON. 2014.

[72] Mayfield J and White R. Insulin Therapy for Type 2 Diabetes: Rescue, Augmentation, and Replacement of Beta-Cell Function. American Family Physician 2004; 70 (3): E489–E501. http://www.aafp.org/afp/2004/0801/p489.pdf

[73] White JR. Advances in Insulin Therapy: A Review of New Insulin Glargine 300 U/ml in the Management of Diabetes. Clinical Diabetes 2016; 34 (2): 86–91. http://clinical.diabetesjournals.org/content/34/2/86

[74] Yale JF. Instruction sheet for acarbose initiation. http://www.dryale.ca/en-health-worksheets.html

[75] Robinson D et al. Diabetes Canada 2018 Clinical Practice Guidelines for the Prevention and Management of Diabetes in Canada: Diabetes and Mental Health. Can J Diabetes 2018; 42 (Suppl 1): S130-141. http://guidelines.diabetes.ca/docs/cpg/Ch18-Diabetes-and-Mental-Health.pdf

[76] Sigal RJ et al. Canadian Diabetes Association 2013 Clinical Practice Guidelines for the Prevention and Management of Diabetes in Canada: physical activity and diabetes. Can J Diabetes 2013; 37 (suppl 1): S40-S44. http://www.canadianjournalofdiabetes.com/article/S1499-2671(13)00019-1/pdf

[77] Green B, Merendino J & Jibrin J. The Best Life Guide to Managing Diabetes and Pre-diabetes. Book published by Simon and Schuster. 2009. https://goo.gl/qsk2pU

[78] McFarlane P et al. Diabetes Canada 2018 Clinical Practice Guidelines for the Prevention and Management of Diabetes in Canada: Chronic Kidney Disease in Diabetes. Can J Diabetes 2018; 42 (Suppl 1): 201-209. http://guidelines.diabetes.ca/docs/cpg/Ch29-Chronic-Kidney-Disease-in-Diabetes.pdf

[79] Hopewell NJ: Scherer Clinical Communication & Editorial Review Board. Strategies for Managing Special Situations in the Patient with Type 2 Diabetes. 2007. http://www.schererclin.com/documents/scherer_spec_sit_print.pdf

[80] Sudhakaran S and Surani S. Guidelines for Perioperative Management of the Diabetic Patient. Surgery Research and Practice. 2015: 1–8. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4452499/pdf/SRP2015-284063.pdf

[81] Metformin product monograph. August 22, 2017. http://www.sanofi.ca/products/en/glucophage.pdf

[82] Zinman B et al. Empagliflozin, Cardiovascular Outcomes, and Mortality in Type 2 Diabetes. NEJM 2015; 373 (22): 2117–2128. http://www.nejm.org/doi/pdf/10.1056/NEJMoa1504720

[83] Marso SP et al. Liraglutide and Cardiovascular Outcomes in Type 2 Diabetes. NEJM 2016; 375 (4): 311–322. http://www.nejm.org/doi/pdf/10.1056/NEJMoa1603827

[84] Ganiats T. Variability in Insulin Action: Mechanisms, Implications, and Recent Advances. The Internet Journal of Family Practice 2006; 5 (2): 1–9. https://print.ispub.com/api/0/ispub-article/8977