<table>
<thead>
<tr>
<th>Program Name:</th>
<th>When and How to Start or Intensify Insulin Therapy in Your Patients with Type 2 Diabetes</th>
</tr>
</thead>
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Learning Objectives

Upon successful completion of each of the continuing education modules, clinicians will be better able to:

1. Determine the optimal time to initiate insulin therapy
2. Initiate a patient with type 2 diabetes on basal insulin therapy
3. Counsel a patient on the role of the addition of bolus insulin to a patient using basal insulin therapy
4. Explore the role of basal-bolus therapy (BBT) in patients with type 2 diabetes
5. Discuss the tools that can maximize the efficacy of insulin therapy while minimizing the risk

Pre/Post Course Survey

1. What is your current comfort level in initiating and titrating insulin therapy in your patients with type 2 diabetes? (1 - not at all comfortable, 5 – very comfortable)
2. What therapy do you most commonly add to in a patient that is not reaching glycemic targets with metformin monotherapy?
   a) Alpha-glucosidase inhibitor (Acarbose)
   b) DPP-4 inhibitor (Alogliptin, Linagliptin, Saxagliptin, Sitagliptin)
   c) Insulin secretagogues (Gliclazide, Glimepiride, Glyburide, Repaglinide)
   d) GLP-1R agonist (Exenatide, Liraglutide)
   e) Insulin
   f) Thiazolidinedione (Pioglitazone)
   g) SGLT2 Inhibitor (Canagliflozin, Dapagliflozin)
   h) Other: ____________________
3. How comfortable are you in discussing the pros and cons of different treatment options for type 2 diabetes? (1 - not at all comfortable, 5 – very comfortable)
4. How comfortable are you in using SMBG readings to adjust a patient’s insulin dosing? (1 - not at all comfortable, 5 – very comfortable)

Post Test

Jonathan H. (58 yo) is in to see you for a follow-up visit to discuss his diabetes management. His glycemic control has not been at target for the last 8-9 months.

You review his lab results:

- A1C = 7.9%
- LDL-C = 1.84 mmol/L
- eGFR = 62 mL/min
- ACR = 2.9 mg/mmol

His home blood pressure monitoring has averaged approximately 130/79 mmHg. His blood pressure in the office today is 134/83 mmHg.

His current medications include:

- Metformin 1000 mg BID
- Sitagliptin 100 mg daily
- Gliclazide MR 90 mg daily
Candesartan 8 mg daily
Atorvastatin 20 mg daily

You decide this is an excellent opportunity to discuss his glycemic control.

1. You start reviewing glycemic control. Which of the following would be the MOST acceptable A1C target for a patient with type 2 diabetes on three antihyperglycemic agents?
   a. ≤ 6.5%
   b. ≤ 7.0%
   c. ≤ 7.5%
   d. ≤ 8.5%

2. Jonathan is complaining about weight gain since starting his current regimen. Which of his medications is most commonly associated with weight gain?
   a. Metformin
   b. Sitagliptin
   c. Gliclazide MR
   d. Atorvastatin

3. You start discussing different options with Jonathan. You discuss the addition of basal insulin. Which of the following insulins would be appropriate for a basal insulin regimen?
   a. Glulisine
   b. Glargine
   c. Aspart
   d. Regular

4. Jonathan agrees with the addition of basal insulin. Which of the following is a common barrier to insulin use in patients with type 2 diabetes?
   a. Weight gain
   b. Belief that insulin use is a personal failure
   c. Fear that insulin causes complications
   d. All of the above

5. It is agreed to start him on basal insulin. Which of the following initiation and titration schedules is the MOST commonly used?
   a. Start 20 units at bedtime and increase at 2 units every 3-4 days while 2 hour post-breakfast reading is > 10 mmol/L
   b. Start 10 units at bedtime and increase by 1 unit daily until the fasting breakfast reading is between 4.0-7.0 mmol/L
   c. Start 1 unit at bedtime and increase by 1 unit daily until the patient is taking 30 units daily
   d. Start 8 units at breakfast and dinner increase by 1 unit at each meal daily while pre-breakfast reading is > 4.5 mmol/L

6. Jonathan has some questions regarding insulin therapy and you start counselling him on some of the key points on insulin therapy. Which of the following statements is TRUE?
   a. The maximum daily dose of basal insulin therapy is 50 units per day
   b. Most antihyperglycemics should be tapered and discontinued when starting basal insulin therapy
   c. Nocturnal hypoglycemia is more common with insulin glargine than NPH insulin
   d. The average weight gain with insulin therapy has been shown to be 6.5 kg at 10 years

7. Jonathan returns several months later and he is no longer reaching glycemic targets with his basal insulin regimen. He is currently taking 45 units of basal insulin and his A1C is 7.8% but his fasting
plasma glucose is between 4.0-7.0 mmol/L. You start discussing insulin intensification by adding a bolus insulin. Which of the following statements is TRUE?

a. He should test his blood glucose level with SMBG at least four times daily
b. Physician led titration is more effective than self-titration at reaching glycemic targets
c. There are several blood glucose meters that can help with insulin titration
d. Basal plus regimens are rarely used and most patients transition from basal insulin to a basal-bolus regimen with 4 injections of insulin per day

8. Jonathan is concerned about hypoglycemia risk with the addition of bolus insulin. Which of the following is an appropriate statement to use regarding hypoglycemia on insulin therapy?

a. It is normally treated with 250 mL of a diet soft-drink
b. After administering a carbohydrate source he should check his blood glucose again in 2 hours to ensure he is not dropping again
c. Glucagon is needed for most patients with severe hypoglycemia reactions
d. After initial treatment, a starch and a protein should be taken if the meal is more than 1 hour after a hypoglycemic event

9. When starting Jonathan on a bolus insulin, which of his medications would normally be discontinued?

a. Metformin
b. Sitagliptin
c. Gliclazide MR
d. All of the above

10. Jonathan has returned 2 years later and is no longer reaching his glycemic targets. Which of the following statements regarding basal-bolus and Continuous Subcutaneous Insulin Infusion is TRUE?

a. Basal-bolus offers flexibility due to insulin adjustments to food and exercise levels
b. Basal-bolus always requires carbohydrate counting
c. With continuous subcutaneous insulin infusion there is a lower risk of ketoacidosis compared to basal-bolus insulin
d. Basal-bolus insulin therapy tends to be more expensive than continuous subcutaneous insulin infusion therapy

Introduction

This program is designed to help healthcare professionals determine which patients with type 2 diabetes are candidates for insulin therapy. It will review the management of different issues that can develop in patients initiated on insulin therapy. The role of different insulin regimens in the management of type 2 diabetes will be discussed. The program will list some suggested tools that can help both the clinician and the patient maximize both the efficacy and safety of insulin therapy in type 2 diabetes.

Discussion Forum

1. What do you feel are the largest PATIENT barriers to starting insulin therapy in patients with type 2 diabetes and how do you overcome them in your practice?
2. What do you feel are the largest CLINICIAN barriers to starting insulin therapy in patients with type 2 diabetes?
3. In your practice, do you allow patients to self-titrate their insulin? (Please explain your reasoning for your choice)
4. Do you feel that most primary care clinicians should be able to initiate, monitor and adjust patients with type 2 diabetes on insulin therapy?
Visit 1 – Initiating Insulin in Patients with Type 2 Diabetes

Learning Objectives
Upon successful completion of this continuing education module, the clinician will be better able to:

1. Discuss the individualization of A1C target for patients with diabetes
2. Tailor the choice of pharmacologic options for patients with type 2 diabetes
3. Initiate a patient with type 2 diabetes on basal insulin regimen
4. Review the Canadian Diabetes Association (CDA) Guidelines recommended self-monitoring of blood glucose (SMBG) testing frequency

Patient Introduction - Meet Allison
Allison (50 yo) is in to see you for her regular 6 month follow-up for her diabetes management. You notice a major change in her interest in her diabetes, compared to other appointments over the last few years. In the past, she never seemed too worried about her glycemic control as she “knew many people who were doing much worse.”

She mentions that her older brother with type 2 diabetes was told about 3 months ago that his kidneys were not working well and he was referred to a nephrologist as he may have to start on dialysis. Her brother is devastated and she is worried that this could happen to her.

None of her family members with diabetes have had any major problems with their diabetes in the past. She took the last 3 months to do what she could to improve her diabetes control.

Patient Profile
Through your discussion and review of her chart, you discover the following:

- Type 2 diabetes for approximately 9 years
- She has completely changed her lifestyle. She has been watching her diet and started walking every day for at least 30 minutes
- She has lost 20 lbs over the last couple of months and is currently around 90 kg (200 lbs)
- Her blood pressure has improved, and her home readings average 127/78 mmHg
- You pull up her latest lab report and see the following figures:
  - A1C – 8.3%
  - Fasting blood glucose – 8.9 mmol/L
  - Serum creatinine – 77 umol/L
  - eGFR – 73 mL/min
  - LDL cholesterol – 1.82 mmol/L
  - Potassium – 4.2 mmol/L
  - Albumin to creatinine ratio (ACR) – 1.8 mg/mmol
- Her current medications are:
  - Metformin 1 gm BID
  - Sitagliptin 100 mg daily
  - Gliclazide MR 120 mg once daily
  - Atorvastatin 20 mg daily
  - Ramipril 10 mg daily

She is disappointed with the lab results and was hoping her blood sugar would have really improved with the changes she has made.
You congratulate her on the positive changes to her lifestyle. You feel that she is motivated to further improve the control of her diabetes. You decide it is an excellent opportunity to discuss each of the options to help her reach her glycemic targets.

**Optimizing Glycemic Control**

Optimal glycemic control is fundamental to the management of patients with diabetes. All patients should be encouraged to reach their glycemic targets and clinicians should work collaboratively with them to determine the optimal method to attain these goals. The importance of glycemic control in patients with type 2 diabetes was demonstrated in the *United Kingdom Prospective Diabetes Study* (UKPDS) where each 1.0% reduction in A1C level was associated with a:

- 37% decline in the relative risk of microvascular complications
- 14% lower rate of myocardial infarction
- 21% reduction in the deaths from diabetes

At the diagnosis of type 2 diabetes, there is a decrease in beta cell mass and beta cell function that continues to decrease over time. The management of type 2 diabetes must be dynamic, as the regimen will normally intensify over the duration of the disease.

Each clinician must work collaboratively with the patient to determine the optimal method to reach glycemic targets and reduce the risk of diabetic complications.

**Determining the Glycemic Target**

In the *2013 Canadian Diabetes Association (CDA) clinical practice guidelines* the role of individualized glycemic targets was reviewed. The guidelines provide tools to help clinicians determine the most appropriate A1C target for a specific patient with diabetes.

An A1C target of ≤ 7.0% applies for most patients with type 1 and type 2 diabetes. In some patients with type 2 diabetes, an A1C target of ≤ 6.5% can be considered to reduce the risk of nephropathy and retinopathy. This lower target is most appropriate in patients with:

- A shorter duration of diabetes
- No evidence of significant cardiovascular disease
- Longer life expectancy
- The lower target does not result in a significant increase in hypoglycemia

In the 2013 guidelines, an A1C target of 7.1-8.5% was recommended for some patients with specific circumstances that would not warrant tight glycemic control. The circumstances in which one would consider an A1C target of 7.1-8.5% are listed in table 1. Figure 1 reviews the CDA guidelines recommended targets for glycemic control.

**Clinical Practice Tip:**

It is important for clinicians to remember that for the vast majority of patients with diabetes, the A1C target is ≤ 7.0%. The glycemic target of 7.1-8.5% should only be selected for patients with specific situations and should not be used as justification for the lack of control in all patients with diabetes.

The CDA guidelines offer the *[Individualizing your Patient’s A1C Target]* interactive tool to help clinicians determine the optimal glycemic target.
An accredited version is available online at www.rxBriefCase.com until July 31, 2016.

**Table 1 – Circumstances to Consider an A1C target of 7.1-8.5%**

- Limited life expectancy
- High level of functional dependency
- Extensive coronary artery disease at high risk of ischemic events
- Multiple comorbidities
- History of recurrent severe hypoglycemia
- Hypoglycemia unawareness
- Longstanding diabetes for whom it is difficult to achieve an A1C ≤7.0% despite effective doses of multiple antihyperglycemic agents, including intensified basal-bolus insulin therapy

**Figure 1 – CDA Guidelines Recommended Glycemic Targets**

*A target A1C ≤6.5% may be considered in some patients with type 2 diabetes to further lower the risk of nephropathy and retinopathy which must be balanced against the risk of hypoglycemia.*

**Figure 2 – CDA Guidelines Recommended Management of Hyperglycemia in Type 2 Diabetes**

Consider 7.1-8.5% if:
- Limited life expectancy
- High level of functional dependency
- Extensive coronary artery disease at high risk of ischemic events
- Multiple co-morbidities
- History of recurrent severe hypoglycemia
- Hypoglycemia unawareness
- Longstanding diabetes for whom it is difficult to achieve an A1C ≤7%, despite effective doses of multiple antihyperglycemic agents, including intensified basal-bolus insulin therapy

**Pharmacotherapy in Type 2 Diabetes**

Glycemic control in patients with type 2 diabetes is an important goal to reduce the patient’s risk of serious morbidity and mortality. Patients with type 2 diabetes may be able to reach their glycemic targets with only lifestyle interventions, but the majority will require starting and intensification of pharmacotherapy over the course of their disease.

There is an increasing number of antihyperglycemic agents for clinicians to use to help patients reach their glycemic targets. This allows for clinicians to tailor the diabetes treatment regimen for a specific patient and circumstance. In general, most antihyperglycemic agents will decrease A1C level by approximately 0.5-1.5% depending on the agent used and the baseline A1C level. The higher the initial A1C level, the greater the reduction for each agent. The CDA guidelines recommended management of hyperglycemia in type 2 diabetes is reviewed in figure 2.

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Figure 2 – CDA Guidelines Recommended Management of Hyperglycemia in Type 2 Diabetes

At diagnosis of type 2 diabetes
Start lifestyle intervention (nutrition therapy and physical activity) +/- Metformin

A1C < 8.5%
If not at target (2-3 mos)
Start metformin immediately Consider initial combination with another antihyperglycemic agent
Start/Increase metformin
If not at glycemic target

A1C ≥ 8.5%
Symptomatic hyperglycemia with metabolic decompensation
Initiate insulin +/- metformin

Add an agent best suited to the individual:

Patient Characteristics
- Degree of hyperglycemia
- Risk of hypoglycemia
- Overweight or obese
- Comorbidities (renal, cardiac, hepatic)
- Preferences and access to treatment
- Other

Agent Characteristics
- BG lowering efficacy and durability
- Risk of inducing hypoglycemia
- Effect on weight
- Contraindications and side effects
- Cost and coverage
- Other

Add an agent best suited to the individual (agents listed in alphabetical order):

<table>
<thead>
<tr>
<th>Class</th>
<th>Relative A1C lowering</th>
<th>Hypoglycemia</th>
<th>Weight</th>
<th>Other therapeutic considerations</th>
<th>Cost</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alpha-glucosidase inhibitor (acarbose)</td>
<td>1</td>
<td>Rare</td>
<td>neutral to 1</td>
<td>Improved postprandial control, GI side effects</td>
<td>$5</td>
</tr>
<tr>
<td>Incretin agents:</td>
<td>2</td>
<td>Rare</td>
<td>neutral to 2</td>
<td>GI side effects</td>
<td>$555</td>
</tr>
<tr>
<td>DPP-4 Inhibitors</td>
<td>3</td>
<td>Rare</td>
<td>neutral to 3</td>
<td>Gluconide efficacy and durability</td>
<td>$5555</td>
</tr>
<tr>
<td>GLP-1 receptor agonists</td>
<td>4</td>
<td>Rare</td>
<td>neutral to 4</td>
<td>Gluconide efficacy and durability</td>
<td>$5555</td>
</tr>
<tr>
<td>Insulin</td>
<td>5</td>
<td>Yes</td>
<td>5</td>
<td>No dose ceiling, flexible regimens</td>
<td>$5555</td>
</tr>
<tr>
<td>Insulin secretagogue:</td>
<td>6</td>
<td>Yes</td>
<td>6</td>
<td>Less hypoglycemia in context of missed meals but usually requires TID to QID dosing Gluconide and glimepiride associated with less hypoglycemia than glubulipride</td>
<td>$5</td>
</tr>
<tr>
<td>Meglitinide</td>
<td>7</td>
<td>Yes</td>
<td>7</td>
<td>Gluconide efficacy and durability</td>
<td>$5</td>
</tr>
<tr>
<td>Sulfonylurea</td>
<td>8</td>
<td>Yes</td>
<td>8</td>
<td>CHF, edema, fractures, rare bladder cancer (pioglitazone), cardiovascular controversy (rosiglitazone), 6-12 weeks required for maximal effect</td>
<td>$5</td>
</tr>
<tr>
<td>TZD</td>
<td>9</td>
<td>Rare</td>
<td>9</td>
<td>CHF, edema, fractures, rare bladder cancer (pioglitazone), cardiovascular controversy (rosiglitazone), 6-12 weeks required for maximal effect</td>
<td>$5</td>
</tr>
<tr>
<td>Weight loss agent (orlistat)</td>
<td>10</td>
<td>None</td>
<td>10</td>
<td>GI side effects</td>
<td>$555</td>
</tr>
</tbody>
</table>

If not at glycemic target
- Add another agent from a different class
- Add/Intensify insulin regimen

Make timely adjustments to attain target A1C within 3 to 6 months

† - Note – The CDA Recommended Pharmacotherapy will be updated in August 2015
Starting with Metformin

In patients with an initial A1C < 8.5%, clinicians can consider a course of lifestyle recommendations alone for 2 to 3 months or the initiation of metformin at diagnosis. For patients with an initial A1C ≥ 8.5%, metformin should be started at diagnosis with consideration for dual pharmacologic therapy immediately.

Clinical Practice Tip:
Some clinicians are unsure of which patients with an A1C <8.5% should start with lifestyle only and which patients should be started on the combination of metformin and lifestyle.

It is important to discuss both options with the patient. Some patients will be motivated to make major lifestyle changes and would be excellent candidates for lifestyle only as the primary treatment. Other patients will not be willing to make dramatic lifestyle adjustments and are unlikely to meet their glycemic targets in 2-3 months. If through the discussion with the patient you both feel the latter is the case, then metformin should be initiated at diagnosis.

Metformin is the initial antihyperglycemic medication for most patients with type 2 diabetes. The guidelines recommended metformin as initial pharmacotherapy based on its:

- Efficacy in lowering blood glucose
- Relatively mild side effect profile
- Long-term safety track record
- Negligible risk of hypoglycemia
- Lack of causing weight gain

Adding an Agent to Metformin Monotherapy

Diabetes is a progressive condition in which glycemic control is likely to deteriorate over time. Most patients that are able to meet glycemic targets with metformin monotherapy, will eventually need the addition of other antihyperglycemic agents.

Clinical Practice Tip:
Although the maximum dose for metformin is 2550 mg/day (850 mg TID) the maximum EFFECTIVE dose is between 850-1000 mg BID.

The selection of add-on agents should be based on their relative efficacy, adverse effects (e.g. hypoglycemia risk, weight) and specific patient characteristics. Table 2 reviews specific agent and patient characteristics that can be used to help to tailor antihyperglycemic options for an individual patient. Table 3 reviews some of the key points regarding each class of agents from the guidelines including their efficacy at lowering A1C when added to metformin therapy.

Clinical Practice Tip:
When a patient fails to reach glycemic targets with two antihyperglycemic agents, clinicians should reassess the regimen before the addition of the next agent. In some cases, there may be some benefit of eliminating a currently used agent and replacing it with a more effective medication to reach glycemic targets. (e.g. an example of this could be replacing a DPP-4 inhibitor with a GLP-1 receptor agonist)
Clinical Practice Tip:

Remember the availability of fixed dose combination antihyperglycemic agents that can lessen the pill burden for patients and allow for changes in the regimen.

<table>
<thead>
<tr>
<th>Table 2 – Patient and Agent Characteristics to Consider when Selecting Add-on Therapy</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Patient Characteristics</strong></td>
</tr>
<tr>
<td>• Degree of hyperglycemia</td>
</tr>
<tr>
<td>• Risk of hypoglycemia</td>
</tr>
<tr>
<td>• Overweight or obese</td>
</tr>
<tr>
<td>• Comorbidities (renal, cardiac, hepatic)</td>
</tr>
<tr>
<td>• Preferences and access to treatment</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Table 3 – Key Agent Properties for Antihyperglycemic Agents in Type 2 Diabetes</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Medications</strong></td>
</tr>
<tr>
<td>Alpha–glucosidase inhibitors</td>
</tr>
<tr>
<td>(Acarbose)</td>
</tr>
<tr>
<td>DPP-4 Inhibitors</td>
</tr>
<tr>
<td>(Alogliptin, Linagliptin, Saxagliptin, Sitagliptin)</td>
</tr>
<tr>
<td>GLP-1 Receptor Agonists</td>
</tr>
<tr>
<td>(Exenatide, Liraglutide)</td>
</tr>
<tr>
<td>Insulin</td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td>Sulfonylureas</td>
</tr>
<tr>
<td>(Gliclazide, Glimepiride, Glyburide)</td>
</tr>
<tr>
<td>Meglitinides</td>
</tr>
<tr>
<td>Nateglinide Repaglinide</td>
</tr>
<tr>
<td>Thiazolidinedione (TZD)</td>
</tr>
<tr>
<td>Pioglitazone Rosiglitazone</td>
</tr>
<tr>
<td>Weight Loss Agents</td>
</tr>
<tr>
<td>Orlistat</td>
</tr>
</tbody>
</table>

† - This table will be updated by the CDA guideline committee in August 2015
‡ - Absolute A1C reduction when added to metformin monotherapy
The Introduction of SGLT2 Inhibitors

The SGLT2 inhibitors (have been recently introduced into the Canadian marketplace (dapagliflozin, canagliflozin) and others are likely soon to be launched (empagliflozin). These agents inhibit glucose uptake from the proximal tubule by blocking SGLT2 uptake. This results in increased glucosuria.

This increased glucose excretion is primarily responsible for both the positive and negative effects of these medications (Table 4).

<table>
<thead>
<tr>
<th>Positive Effects</th>
<th>Negative Effects</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Reduction in A1C level</td>
<td>• Increased renal excretion of glucose also increases the risk of urinary tract infections and genital mycotic infections</td>
</tr>
<tr>
<td>• Insulin independent mechanism of action</td>
<td>• Increased diuresis can lead to volume depletion. Most commonly a concern in the elderly and those on loop diuretics</td>
</tr>
<tr>
<td>• Reduction in weight</td>
<td>• Caution in patients with reduced renal function (not to be started in patients with eGFR of &lt; 60mL/min)</td>
</tr>
<tr>
<td>• Reduction in blood pressure</td>
<td></td>
</tr>
<tr>
<td>• Both agents can be used in combination with metformin, sulfonylurea or insulin therapy</td>
<td></td>
</tr>
<tr>
<td>o Canagliflozin is also indicated in combination metformin and either a sulfonylurea or pioglitazone</td>
<td></td>
</tr>
</tbody>
</table>

When compared to the other agents in figure 2, SGLT2 inhibitors are associated with approximately:

- A 0.7-1.0% A1C reduction when added to metformin
- A 1-4 kg reduction in weight
- A 2-7 mmHg reduction in systolic blood pressure

SGLT2 inhibitors offer clinicians another option for patients with type 2 diabetes and have some key advantages and disadvantages compared with other antihyperglycemics. Clinicians can consider this option in patients who are interested in A1C, blood pressure and weight reduction and are not concerned with their unique adverse effect profile.

Revisit our Patient – Allison

Allison is currently being managed with the maximum effective doses of metformin, gliclazide and sitagliptin.

You discuss the different options with Allison to improve her glycemic control. These include the addition of another agent (e.g. acarbose, insulin, orlistat, SGLT2 inhibitor, TZD) and/or the substitution of sitagliptin with exenatide or liraglutide.

Allison’s current A1C reading is 8.3%. The change of sitagliptin to a GLP-1 receptor agonist (e.g. exenatide or liraglutide) is not likely to allow her to reach her target of ≤ 7.0%. The addition of acarbose, orlistat, a SGLT2 inhibitor or a TZD is unlikely to reach the recommended glycemic target. Insulin initiation is likely one of the only agents that will help her reach her glycemic target. The other option that may help her reach her A1C target would be to change her DPP-4 inhibitor to GLP-1 agonist and adding an SGLT2 inhibitor (this combination is currently off-label in Canada).

You decide to review the different options with Allison.
The Importance of Involving the Patient in the Management of Diabetes

Each person with diabetes is unique. They each have different levels of commitment to achieving the necessary diabetes goals and risk reduction. Patients with diabetes tend to make the vast majority of decisions outside of the healthcare setting. For this reason, it is important that their goals and wishes be taken into consideration when selecting any antihyperglycemic agent.

For some patients, they are willing to make the effort to achieve optimal control and others will feel the negatives will outweigh any positives of reaching a specific diabetes goal. Clinicians should explain the risks and benefits of each treatment option and its role in the management of diabetes. This is especially important for patients initiating injection therapy as this delivery system will require more training and commitment from the patient.

Without partnering with the patient and setting mutually agreed upon goals for treatment, there is an increased risk of nonadherence and poor patient satisfaction to the prescribed diabetes treatment.

**Clinical Practice Tip:**

It is important for clinicians to ask the patients their thoughts without making assumptions. Some clinicians will assume a specific patient will not want to start a specific therapy (e.g. insulin). These assumptions are many times wrong. Without asking patients, clinicians may act as a major barrier to a patient reaching their glycemic targets.

**Discussing Antihyperglycemic Therapies with a Patient**

There are many considerations when selecting an antihyperglycemic agent for a patient with type 2 diabetes. Clinicians can eliminate specific choices due to contraindications or issues such as reduced renal function. Many times there will be multiple options that are suitable for a specific patient. At this point, clinicians should present these options to the individual.

Although some clinicians may feel discussing each option with a patient to be too burdensome and confusing for a patient, it can be done very efficiently. When discussing each option, it is important to focus on the points that are relative to the patient. These can be summarized by discussing the benefits of the agents and balancing with the risks (Table 5).

**Table 5 – Points to Cover with Patients when Discussing Different Pharmacotherapy Options**

<table>
<thead>
<tr>
<th>Benefits of Adding an Agent</th>
<th>• The level of A1C lowering of a specific agent with respect to their glycemic target</th>
</tr>
</thead>
<tbody>
<tr>
<td>Risks of Adding an Agent</td>
<td>• Hypoglycemia</td>
</tr>
<tr>
<td></td>
<td>• Weight gain</td>
</tr>
<tr>
<td></td>
<td>• Other common adverse effects (e.g. GI upset)</td>
</tr>
</tbody>
</table>

**Clinical Practice Tip:**

When presenting the different treatment options, it is recommended that you start with your recommended course agent. For example saying something such as:

• “There are three different options we can use to improve your blood sugar level. I would recommend ________, as I think it is the best fit for you at this point in time. Would you like to hear about the pros and cons of each option?”
Revisit our Patient – Allison
You discuss the different options with Allison. She is very concerned about her blood glucose levels and wants to do everything she can to lower her risk of diabetic complications. She is nervous about starting insulin therapy but based on your discussion she would like to hear more information.

You decide to review basal insulin initiation and review some of the most common concerns with insulin initiation and the recommended strategy of basal insulin initiation.

Insulin Therapy in Type 2 Diabetes
For many patients and clinicians, insulin therapy is delayed and used as the last resort for patients with type 2 diabetes. The CDA guidelines clearly state that insulin is a treatment option for consideration for patients with diabetes. The guidelines recommend insulin in type 2 diabetes as:

- The initial treatment choice in patients with symptomatic hyperglycemia with metabolic decompensation
- As add-on therapy in patients who are not reaching glycemic targets

It is important to stress that insulin therapy is just another treatment option for diabetes. It has benefits and adverse effects, just like every other antihyperglycemic option. It is many times the ideal choice in patients who are not reaching glycemic targets on multiple antihyperglycemic agents.

Table 6 provides clinicians with some strategies to start the discussion of insulin therapy with patients.
Table 6 – Strategies to Consider when Discussing Insulin Initiation with Patients

**Presenting insulin as an option in patients currently taking other antihyperglycemic therapy:**
- “Based on your current blood sugar levels, I would recommend insulin as a possible treatment option. It can be added to your other medications and is very effective at helping you reach your diabetes goals.”

**Asking about specific concerns:**
- “Some people have concerns with starting insulin therapy. Do you have any concerns or questions about using insulin?”

**Address any concerns:**
- “I can understand your concerns. Let’s discuss each of these together and see if insulin is the best option for you.”

**Stress the key points of insulin (benefits followed by the negatives)**
- Highly effective at helping you reach your A1C target
- Once daily injection, that you take before going to bed
- Injections are done with very small needles and are practically painless
- By lowering your blood sugar, we can lower your risk of complications
- Most patients find it relatively easy to add insulin to their lifestyle
- Insulin is associated with weight gain
- Insulin can increase the risk of hypoglycemia

**Tell them you and other educators will support them:**
- “I will help you through this process and provide you with tools that will make it easier to manage your diabetes with insulin.”

---

**Clinical Practice Tip:**
Many clinicians have threatened patients with the use of insulin if they do not properly manage their diabetes. This practice is strongly discouraged. Many patients with type 2 diabetes will eventually require insulin therapy and they could view insulin initiation as a personal failure versus just another treatment option for diabetes management.

**Barriers to Insulin Therapy**
There are both patient and clinician barriers to initiating insulin. Many times this leads to a delay in glycemic control. Knowing and addressing these barriers can help to improve a patient’s acceptance of insulin therapy.

The initiation of insulin in a patient with type 2 diabetes is ultimately a patient’s decision. Some patients will make the decision fairly easily, where most will accept the idea and others could resist this option. It is important that clinicians address potential patient issues and concerns. Some of the most common patient concerns regarding insulin therapy are reviewed in Table 7.

Clinicians can many times be a major barrier to insulin therapy. They may make assumptions that a patient will be upset or will refuse the therapy, without even offering it as an option. Many times these assumptions are incorrect and can prevent the patient from reaching their diabetes management goals. It is important to frame insulin therapy as not a “unique” management option, but just another option to help a specific patient reach their glycemic goals.
Table 7 – Accessing and Addressing Patient Concerns regarding Insulin Therapy

<table>
<thead>
<tr>
<th>Concern</th>
<th>Potential Strategies</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fear of needles or pain of injections</td>
<td>• Describe and show the very fine insulin needles&lt;br&gt;o Needles are finer than SMBG lancets that the patient is likely already using&lt;br&gt;• Demonstrate by having the patient insert the needle without injecting&lt;br&gt;• Offer insulin pens with a very fine and short needle</td>
</tr>
<tr>
<td>Fear of hypoglycemia</td>
<td>• Discuss insulin onset of action and how to minimize the risk&lt;br&gt;• Use tools that ensure proper dosing&lt;br&gt;• Discuss treatment and management&lt;br&gt;• Provide <a href="#">written information on recognizing and treating</a> &lt;br&gt;• Consider rapid and long-acting analogues to reduce the overall risk</td>
</tr>
<tr>
<td>Weight gain</td>
<td>• Educate about strategies to minimize weight gain (e.g. lifestyle and maintaining on other antihyperglycemics)</td>
</tr>
<tr>
<td>Impact on lifestyle, loss of personal freedom</td>
<td>• Basal insulin start is only once daily. Once started, administration becomes very fast and convenient for most patients&lt;br&gt;• Allows for greater flexibility in diabetes management&lt;br&gt;• Proper glycemic control leads to reduction of complications that could have a major impact on the patient’s life&lt;br&gt;• Insulin pens can simplify administration</td>
</tr>
<tr>
<td>Belief that insulin means diabetes is worse or “end of the line”</td>
<td>• Review all of the treatment options&lt;br&gt;• Explain that insulin is a normal addition for many patients when the beta-cells can no longer produce sufficient insulin</td>
</tr>
<tr>
<td>Insulin use is a personal failure</td>
<td>• Tell patients early in the course of their disease that beta-cell function decreases with time&lt;br&gt;• Avoid statements such as “You’ve failed oral agents”. Consider statements such as “These oral agents are no longer doing what they should be doing.”&lt;br&gt;• Avoid using insulin as a threat to patients</td>
</tr>
<tr>
<td>Insulin causes complications</td>
<td>• This concern occurs as insulin is started late in the course of the patient’s disease when complications have many times already occurred&lt;br&gt;• Proper glycemic control is a recommended strategy to reduce complication risk&lt;br&gt;• “The sugar is the enemy, not the treatment.”</td>
</tr>
</tbody>
</table>

Initiating Basal Insulin

The CDA guidelines provide a recommended strategy for basal insulin initiation ([Appendix 3](#)). The recommended basal insulin titration regimen is reviewed in table 8.

The CDA guidelines provide an [Insulin Prescription Tool](#) to help clinicians initiate insulin therapy in patients with type 2 diabetes.
Table 8 – CDA Guidelines Recommended Titration of Basal Insulin Added to Oral Antihyperglycemics

- Insulin should be titrated to achieve target fasting BG levels of 4.0 to 7.0 mmol/L.
- Individuals can be taught self-titration, or titration may be done in conjunction with a healthcare provider.
- Suggested starting dose is 10 units once daily at bedtime.
- Suggested titration is 1 unit per day until target is reached.
- A lower starting dose, slower titration and higher targets may be considered for elderly or normal weight subjects.
- In order to safely titrate insulin, patients must perform SMBG at least once a day fasting.
- Insulin dose should not be increased if the individual experiences 2 episodes of hypoglycemia (BG <4.0 mmol/L) in 1 week or any episode of nocturnal hypoglycemia.
- For fasting BG levels consistently <5.5 mmol/L, a reduction of 1 to 2 units of insulin may be considered to avoid nocturnal hypoglycemia.
- Oral antihyperglycemic agents (especially secretagogues) may need to be reduced if daytime hypoglycemia occurs.

Clinical Practice Tip:

Some clinicians are not comfortable with patients self-titrating insulin therapy. The goal with diabetes education is self-management. Providing the patient with dosing adjustment schedules can help empower them to take control of their diabetes.

Checklist for Insulin Initiation

When initiating a patient on any injection therapy, there is some administration education that must be provided. With the collaboration of healthcare professionals, it is common for several clinicians to provide the different components of this education.

The CDA guidelines has an extensive tool regarding insulin pen initiation. The insulin pen start checklist for healthcare providers can be downloaded from the CDA guideline website.

Table 9 provides a basic checklist for insulin preparation.

Table 9 – Basic Checklist for Insulin Initiation

- Discuss the progressive nature of diabetes
- Verbalize that insulin is an appropriate treatment at this time
- Explain the insulin administration device (pen, syringe)
- Select the needle length
- Demonstrate injection technique and have the patient self-inject to assess technique
- Demonstrate skin preparation
- Demonstrate injection sites and site rotation
- Discuss the storage of insulin
- Review appropriate disposal of syringes/pen needles
- Review the recognition, prevention and treatment of hypoglycemia
- Discuss the SMBG requirements and titration algorithm
Clinical Practice Tip:
A great tool clinicians can use for educating patients on appropriate insulin injection technique is the FIT Technique Plus* - Technique for all.

Revisit our Patient – Allison
You feel Allison is motivated to start insulin therapy. You provide her with the education and titration schedule for basal insulin therapy. You schedule another appointment for a couple of weeks to determine how she is managing her insulin therapy. You encourage her to call your office if she has any concerns.

Key Learning Points – Visit 1
1. Optimal glycemic control is a fundamental component of managing a patient with diabetes
2. Most patients with diabetes have an A1C target of ≤ 7.0%
3. Tailor the treatment options for type 2 diabetes based on patient and agent characteristics
4. Involving the patient in treatment choices is important to ensure patient buy-in and improve adherence and treatment satisfaction
5. Many patients with type 2 diabetes will eventually require insulin therapy to reach glycemic targets
6. Insulin therapy should be presented just like every other treatment option
7. Proper education can overcome most barriers with insulin initiation in patients with type 2 diabetes
Visit 2 – Managing Issues with Insulin Therapy

Learning Objectives

Upon successful completion of this continuing education module, the clinician will be better able to:

1. Answer some of the most frequently asked questions regarding insulin therapy
2. Discuss the role of self-monitoring of blood glucose in insulin titration
3. Provide a patient with the current Canadian Diabetes Association (CDA) guidelines recommended SMBG testing frequency
4. Review the symptoms and management of hypoglycemia

Meet our Patient - Allison

Our patient Allison (50 year) (see visit 1, for detailed case discussion) has returned for her 2 week follow-up visit, after starting basal insulin therapy with insulin glargine therapy. At your last visit, she was prescribed 10 units once daily and instructed to increase it by 1 unit daily until her morning fasting reading was between 4-7 mmol/L.

When you ask her how she is making out with the insulin, she says that it is not agreeing with her. She has had some serious side effects from the insulin therapy.

She mentions she was increasing her dose every night as you explained and was up to 18 units before bedtime. She says it felt like a very high dose and when she went online she saw people taking much less. She felt “strange” last week and was a bit shaky and dizzy. She thought it was a low blood sugar reaction, so quickly grabbed a glass of orange juice, sat down and it went away after a few minutes. After that episode, she decided to decrease her dose to 16 units per day and not to increase it until she saw you. When questioned further, she states that she did not test her blood sugar when she felt strange, but was sure it must have been a low blood sugar reaction.

She is worried that the insulin dose may be too high for her and she wants to know if she should just take her metformin 1000 mg BID, gliclazide MR 120 mg daily and sitagliptin 100 mg daily. She is very worried that she is going to make a mistake with her insulin dosing.

You decide to review hypoglycemia and the role of her insulin therapy.

Insulin Management

There are issues that can develop with insulin therapy. These can include issues with administration, dosing, adherence and hypoglycemia. Many of these can be addressed through appropriate counselling and patient education.

Patients using insulin therapy commonly do not take the prescribed regimens. A Veteran Affairs study in the United States, found that on average patients using insulin used an average of 77% of the prescribed dose. The authors concluded that the level of injection compliance and the prescribed regimen or both, were inadequate to achieve good glycemic control.

A study of 1250 physicians found that glucose control among insulin-treated patients is inadequate in part due to insulin omission, nonadherence and the lack of dose adjustment. Many patients that are prescribed insulin therapy, are not using it properly to reach their recommended targets.
Common Management in Patients on Insulin Therapy

Patients with diabetes can commonly present in practice with issues regarding their therapy. By properly managing these issues, clinicians can play a major role in ensuring proper use and glycemic control with insulin therapy.

The addition of basal insulin is a major change for some patients. They are commonly concerned with the administration and potential adverse effects from the therapy. Clinicians should be prepared for common concerns regarding insulin therapy. Table 10 reviews many of these common issues.

**Table 10 – Commonly Asked Questions Regarding Insulin Therapy**

<table>
<thead>
<tr>
<th>Question</th>
<th>Answer</th>
</tr>
</thead>
<tbody>
<tr>
<td>What is the usual dose that most patients will need to achieve insulin target?</td>
<td>Some clinicians and patients are concerned regarding dosing of insulin. The dose of insulin will vary based on the patient and factors such as obesity, insulin resistance, long-standing diabetes can impact the final dose to help a patient reach glycemic target. At basal insulin initiation, the average dose required to achieve the goal is approximately 47 units and in many patients it is commonly 0.7-0.8 units per kg. The total daily insulin dose for patients with type 2 diabetes is usually 1.0-1.5 units/kg/day and a small number of patients will require higher dosing as high as 2.0 units/kg/day. For our patient Alisson, she may require up to 90-180 units daily and we should educate her that it will take some time to reach this level. The insulin dosing for patients with type 1 diabetes is approximately 0.3-0.8 units/kg/day, except in adolescents where it can range from 1.0-1.5 units/kg/day.</td>
</tr>
<tr>
<td>Is there a maximal dose of insulin a patient can receive?</td>
<td>There is no “absolute” maximal dose for insulin and the amount administered is tailored specifically for the patient’s needs. When the patient is exceeding 3.0 units/kg/day, further evaluation by an endocrinologist is warranted.</td>
</tr>
<tr>
<td>How much insulin can I take in one injection?</td>
<td>If a single injection of basal insulin exceeds the amount the device can deliver of if the injection becomes uncomfortable, the patient may split it into two injections. The larger the dose, the more delayed the action of NPH and short-acting insulin.</td>
</tr>
<tr>
<td>What range should my bedtime blood glucose be?</td>
<td>Some experts recommend a bedtime target of 7 mmol/L for NPH insulin and 6 mmol/L for long acting insulin basal analogues.</td>
</tr>
</tbody>
</table>
| What if I am low, when am I supposed to take my insulin?                | This will depend on the type of insulin and regimen. Rapid-acting analog and short-acting insulin doses can be adjusted based on carbohydrate intake, exercise and blood glucose level. In patients using basal insulin, the use of insulin detemir or glargine have been associated with a lower risk of nocturnal hypoglycemia compared to intermediate acting NPH insulin. The use of glargine U300 has been associated with a lower risk of nocturnal hypoglycemia compared to insulin glargine. Prevention of nocturnal hypoglycemia is a priority and the addition of a
bedtime carbohydrate snack may be necessary if bedtime blood glucose levels warrant it (< 6-8mmol/L), if there has been sustained exercise that day or the patient has consumed alcohol.

- Patients should be encouraged to see the impact of carbohydrate administration on blood glucose levels both at night and in the morning. This could be used as a teaching moment to determine the amount of carbohydrate required based on the bedtime blood glucose level and their current insulin dose.

### What do I do if I miss a bolus or basal injection?

- For the most part, missing an insulin dose will induce hyperglycemia but not cause a significant risk to the patient with type 2 diabetes.
- Course of action will depend on the type of insulin, the regimen and how long since the missed dose.
- Bolus doses can be adjusted with the next meal to accommodate for the current blood glucose level.

### What do I do if I am unsure whether I gave my bolus or basal injection?

- For basal insulin, it would be very difficult to determine if the insulin was given or missed until several hours after the dose (usually while the person is sleeping).
- The risk of nocturnal hypoglycemia is more of a concern than morning hyperglycemia. For this reason, the patient should not administer another dose.
- Increasing blood glucose testing frequency should be encouraged.
- If one suspects that they may have taken the bolus insulin at bedtime they should recheck their blood glucose 1 hour later to see if the glucose is falling rapidly.
- Consider providing an insulin pen or blood glucose meter with memory to track the doses of insulin.

### What will happen if I have low blood sugar throughout the night? Will I die? Will I wake up?

- Nocturnal hypoglycemia is very concerning as many times it is asymptomatic and can often last for > 4 hours.
- Many patients are unaware of hypoglycemia during sleep as the sympahtoadrenal response to hypoglycemia is reduced.
- Clinicians should question patients for symptoms of nocturnal hypoglycemia:
  - Tingling of the lips and tongue
  - Headache
  - Difficulty getting up in the morning
  - Nightmares
  - Night sweats
- The switch of the intermediate insulin NPH to a long-acting insulin analogue (detemir, glargine, glargine U300) can reduce the risk of nocturnal hypoglycemia.
- For fasting BG levels consistently <5.5 mmol/L, a reduction of 1 to 2 units of basal insulin may be considered to avoid nocturnal hypoglycemia.

### How much weight will I gain on insulin?

- Weight gain is associated with insulin therapy and is partly due to a decreased glycosuria and basal metabolic rate that may occur as a result of improved glycemic control.
- The average weight gain in the UKPDS trial was 6.5 kg at 10-year follow-
Strategies to help to reduce weight gain from insulin therapy:

- Ensure sufficient insulin doses without overdosing
- Decrease the frequency of hypoglycemia and the need to treat it
- Provide education on the importance of diet and exercise in weight control, as well as examples of healthier choices (i.e. low-fat/low-calorie foods)
- Utilize insulin with noninsulin antihyperglycemic therapies
- Ensure insulin administration matches the carbohydrate counting

Tools to Aid with Insulin Administration

There are a variety of tools that can help with the administration of insulin and to ensure the patient is optimizing its use, while minimizing the risk of problems. Two of the most common tools are insulin pens and blood glucose monitors.

Insulin Pens

Insulin pen technology simplifies administration for patients using insulin therapy. Many of these pens are preloaded with insulin and only require the patient to add a pen needle tip, check for insulin flow and dial the number of units for their dose. In most patients with diabetes, the use of insulin pens should be encouraged as they can increase adherence and accuracy of insulin administration. The CDA guidelines has an extensive tool regarding insulin pen initiation. The insulin pen start checklist for healthcare providers can be downloaded from the CDA guideline website.

Blood Glucose Meters

Self-monitoring of blood glucose (SMBG) is crucial for all patients using insulin therapy. It allows for self-titration and ensures the patient is dosing correctly to reduce the risk of hypoglycemia and to optimize control. The CDA guidelines have provided clinicians with some recommendations regarding testing frequency in patients with diabetes. Table 11 reviews the SMBG testing frequency for different diabetes management regimens. Table 12 discusses situations where increasing or decreasing SMBG testing frequency may be required.

Clinical Practice Tool

The CDA guidelines has developed an SMBG frequency and pattern tool to help guide clinicians on the recommended SMBG testing for their patients with diabetes.

Clinical Practice Tip:

The recommended minimum SMBG testing frequency for patients using insulin therapy is at least as often as insulin administration. For example, a patient administering two doses of insulin per day should test a MINIMUM of twice daily.
### Table 11 – CDA Guidelines Recommended SMBG Testing Frequency

<table>
<thead>
<tr>
<th>Situation</th>
<th>SMBG Recommendation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Use multiple daily injections of insulin (≥ 4 times per day)</td>
<td>SMBG ≥ 4 times per day</td>
</tr>
<tr>
<td>Using insulin &lt; 4 times per day</td>
<td>SMBG at least as often as insulin is given</td>
</tr>
<tr>
<td>Pregnant (or planning pregnancy) Hospitalized or acutely ill</td>
<td>SMBG individualized and may involve SMBG ≥ 4 times per day</td>
</tr>
<tr>
<td>Starting a medication associated with hyperglycemia (e.g. prednisone)</td>
<td>SMBG individualized and may involve SMBG ≥ 2 times per day</td>
</tr>
<tr>
<td>Experiencing an illness known to cause hyperglycemia</td>
<td></td>
</tr>
</tbody>
</table>

### Table 12 – CDA Guidelines Recommendations for SMBG Frequency Adjustments

<table>
<thead>
<tr>
<th>Situation</th>
<th>SMBG Recommendation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Using an antihyperglycemic agent known to cause hypoglycemia</td>
<td>SMBG at times when symptoms of hypoglycemia occur or at times when hypoglycemia has previously occurred</td>
</tr>
<tr>
<td>Has an occupation that requires strict avoidance of hypoglycemia</td>
<td>SMBG as often as is required by employer</td>
</tr>
<tr>
<td>Not meeting glycemic targets</td>
<td>SMBG ≥ 2 times per day, to assist in lifestyle and/or medication changes until such time as glycemic targets are met</td>
</tr>
<tr>
<td>Newly diagnosed with diabetes (&lt;6 months)</td>
<td>SMBG ≥ 1 time per day (at different times of day) to learn the effects of various meals, exercise and/or medications on blood glucose</td>
</tr>
<tr>
<td>Treated with lifestyle and oral agents and is meeting glycemic targets</td>
<td>Some people with diabetes might benefit from very infrequent checking (SMBG once or twice per week) to ensure that glycemic targets are being met between A1C tests</td>
</tr>
</tbody>
</table>

### SMBG Meter Selection

There are a large number of SMBG meters for patients with diabetes. Overall, these meters are effective at testing a patient’s blood glucose and provide a reading that can allow for adjustments in lifestyle or antihyperglycemic agents. The choice of meter is based on meter availability, added tools/functions of the meter and clinician/patient preference.

#### Basal Insulin Titration Meter

One meter in Canada is specifically designed for patients with basal insulin therapy. It promotes self-adjustments of insulin therapy based on parameters set by the clinician. With this meter, the clinician:

- Sets the starting dose of basal insulin
- Sets the fasting blood glucose target range (e.g. 4.0-7.0 mmol/L)
- Sets the titration schedule (e.g. increase by 1 unit every day if above 7 mmol/L, decrease if fasting below 4mmol/L)

Once the meter is setup, it supports the patient through the titration process and can help to improve the safety of insulin therapy and help to optimize the dose of the patient. The steps the patient follows each day with this meter are discussed in table 13.
Table 13 – Patient Steps for Using the Meter that Aids in Insulin Titration

- If the patient tests between 4AM and 11AM, the meter will ask the patient if the reading is a fasting reading
- Based on the parameters set by the clinician, the meter will advise the patient to increase their evening dose if the patient is above the test range or decrease the dose if below the test range
- It will display to the patient if the dose needs to be increased or decreased
- When the patient goes to administer their insulin dose in the evening, they click on the insulin dose button on their meter. If the dose has been changed, it will show them their new dose and they can log it
- The meter remembers the new dose for the next day allowing for adjustments up or down based on their fasting blood glucose reading

Clinical Practice Point:

Initiating patients on insulin can be difficult for many clinicians as they are worried about the risk of hypoglycemia or poor management. This meter option is designed to be a tool that allows the patient to carry your recommendations and titration schedule with them at all times. The meter will help to dynamically adjust the basal insulin dose to minimize hypoglycemia and maximize glycemic control.

Revisit Our Patient – Allison

You discuss the reaction with Allison. You explain that it is difficult to determine if what she experienced was hypoglycemia. You stress that it is important that she test her blood sugar to see if she is truly hypoglycemic.

You explain that there are some patients that experience “relative hypoglycemia” where a person does not truly have low blood sugar but the body experiences the same symptoms as it is not accustomed to the lower blood sugar levels of better control.19

You decide to review the management of hypoglycemia in patients with diabetes

Hypoglycemia

The risk and fear of hypoglycemia is one of the largest barriers to appropriate glycemic control. It is estimated that 70-80% of patients with type 2 diabetes using insulin to achieve good metabolic control, experience hypoglycemia.19 All patients taking insulin and insulin secretagogues are at increased risk of hypoglycemia. It is important for clinicians to review symptoms of hypoglycemia, prevention strategies and its management regularly and especially when there is intensification in therapy.

Symptoms of Hypoglycemia

The signs and symptoms of hypoglycemia can be divided into two categories:20

- Autonomic
- Neuroglycopenic

Autonomic symptoms are the result of the activation of the autonomic nervous system and the release of epinephrine into the circulation.21 Neuroglycopenic symptoms are the result of glucose deprivation in the brain.22 The autonomic symptoms occur before neuroglycopenic symptoms.21 The most common symptoms of hypoglycemia are listed in table 14.
Table 14 – Symptoms of hypoglycemia

<table>
<thead>
<tr>
<th>Autonomic (neurogenic)</th>
<th>Neuroglycopenic</th>
</tr>
</thead>
<tbody>
<tr>
<td>Trembling</td>
<td>Difficulty concentrating</td>
</tr>
<tr>
<td>Palpitations</td>
<td>Confusion</td>
</tr>
<tr>
<td>Sweating</td>
<td>Weakness</td>
</tr>
<tr>
<td>Anxiety</td>
<td>Drowsiness</td>
</tr>
<tr>
<td>Hunger</td>
<td>Vision changes</td>
</tr>
<tr>
<td>Nausea</td>
<td>Difficulty speaking</td>
</tr>
<tr>
<td>Tingling</td>
<td>Headache</td>
</tr>
<tr>
<td></td>
<td>Dizziness</td>
</tr>
</tbody>
</table>

Classification of Hypoglycemia Severity

Table 15 lists the CDA Guidelines classification for the severity of a hypoglycemic reaction.

<table>
<thead>
<tr>
<th>Mild</th>
<th>Moderate</th>
<th>Severe</th>
</tr>
</thead>
<tbody>
<tr>
<td>Autonomic symptoms are present. The individual is able to self-treat</td>
<td>Autonomic and neuroglycopenic symptoms are present. The individual is able to self-treat</td>
<td>Individual requires assistance of another person. Unconsciousness may occur. Plasma glucose level is typically &lt; 2.8 mmol/L</td>
</tr>
</tbody>
</table>

Risk Factors for Hypoglycemia

There are several risk factors for hypoglycemia. These risk factors are reviewed in table 16.

<table>
<thead>
<tr>
<th>General Risk Factors</th>
<th>Risk Factors for Severe Hypoglycemia</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients with type 1 diabetes</td>
<td>Prior episode of severe hypoglycemia</td>
</tr>
<tr>
<td>Insulin therapy</td>
<td>Current low A1C (&lt;6.0%)</td>
</tr>
<tr>
<td>Insulin secretagogues</td>
<td>Hypoglycemia unawareness</td>
</tr>
<tr>
<td>Inadequate intake of glucose sources (e.g. skipping a meal)</td>
<td>Long duration of insulin therapy</td>
</tr>
<tr>
<td>Increased utilization of blood glucose (e.g. physical activity)</td>
<td>Autonomic neuropathy</td>
</tr>
<tr>
<td>Decreased gluconeogenesis (e.g. occurs with alcohol ingestion)</td>
<td>Low economic status</td>
</tr>
<tr>
<td>Insulin sensitivity increase (e.g. weight loss, physical activity)</td>
<td>Food insecurity</td>
</tr>
<tr>
<td>Insulin clearance decrease (e.g. renal dysfunction)</td>
<td>Low health literacy</td>
</tr>
<tr>
<td></td>
<td>Cognitive impairment</td>
</tr>
<tr>
<td></td>
<td>Adolescence</td>
</tr>
<tr>
<td></td>
<td>Preschool-age children unable to detect and/or treat mild hypoglycemia on their own</td>
</tr>
</tbody>
</table>

Treatment of Hypoglycemia

The CDA clinical practice guidelines have set goals for the treatment of hypoglycemia. These include:

- Detect and treat a low blood glucose level promptly
- Use an intervention that provides the fastest rise in blood glucose to a safe level
• Eliminate the risk of injury and relieve symptoms quickly

The treatment of mild to moderate hypoglycemia involves the ingestion of a carbohydrate source. The recommended CDA treatment protocol is listed in Table 17. Table 18 lists common sources of 15 g of carbohydrates.

<table>
<thead>
<tr>
<th>Table 17 - Treatment Recommendations for Hypoglycemia</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Hypoglycemia Severity</strong></td>
</tr>
</tbody>
</table>
| Mild to Moderate | • A 15 g dose of carbohydrate, preferably glucose or sucrose tablets/solutions, should raise the blood glucose level by approximately 2.1 mmol/L in 20 minutes.  
• For children, the dose should be calculated by weight (0.3 g/kg).  
• Individuals on alpha-glucosidase inhibitors (e.g. acarbose) must use glucose tablets to treat hypoglycemia; milk or honey may also be used.  
• Encourage individuals to wait 15 minutes, retest blood glucose and retreat with another 15 g glucose/sucrose if blood glucose remains <4.0 mmol/L.  
• Regular soft drinks (not diet) and other forms of oral glucose (e.g. honey, fruit juice) can also be taken to relieve hypoglycemia. Although, glucose or sucrose tablets or solutions are preferred.  
• After initial treatment of glucose, 15 g of carbohydrate (starch) and a protein source should be taken if the meal is more than 1 hour after a hypoglycemic event. |
| Severe | • If the individual is conscious and able to take oral treatment:  
  o Treat with 20 g of glucose in tablet form, wait 15 minutes (if possible), retest blood glucose level and retreat with another 15 g glucose if blood glucose level remains <4.0 mmol/L (20 g of glucose will increase blood glucose levels by 3.6 mmol/L in 45 minutes).  
• If the individual is unconscious:  
  o Another person may administer 1.0 mg glucagon subcutaneously or intramuscularly.  
  o This should provide a significant rise in blood glucose from 3.0 to 12 mmol/L within 60 minutes.  
  o For children weighing less than 20 kg, give 0.5 mg (0.5 unit) or a dose equivalent to 20 to 30 µg/kg.  
  o Once the individual is conscious and able to take food orally, hospitalization is probably not necessary, unless there has been a clear overdose of insulin  
  o The individual should be advised to eat some carbohydrate as follow-up treatment to reduce the risk of recurrence  
  o If glucagon is given, caregivers or support persons should call for emergency services and the episode should be discussed with the diabetes healthcare team as soon as possible  
• Glucose gel is not the preferred therapy, since absorption through the buccal mucosa is minimal. The gel must be swallowed to have any significant effect. It is slow to react (<1 mmol/L rise in 20 minutes). |

<table>
<thead>
<tr>
<th>Table 18 – Sources of 15 grams of carbohydrate for the treatment of mild to moderate hypoglycemia</th>
</tr>
</thead>
</table>
| • 15 g of glucose in the form of glucose tablets (depending on the product this could be 3-4 tablets)  
• 15 mL (3 teaspoons) or 3 packets of table sugar dissolved in water |
• 175 mL (3/4 cup) of juice or regular soft drink
• 6 Life Savers (1=2.5 g of carbohydrate)
• 15 mL (1 tablespoon) of honey

Revisit Our Patient

You review the importance of optimizing her insulin to improve her glycemic control and to reduce her risk of complications. Through your discussion, you decide to continue her titration with a prefilled insulin pen with insulin glargine and start her on a meter that will help with the titration. You explain that her new meter will help her adjust the evening dose of insulin.

You review the symptoms, prevention and management of hypoglycemia. You stress that when she feels any of these symptoms she should consider testing her blood glucose and start treatment if her blood glucose level is below 4.0 mmol/L.

You finish by mentioning that she can follow-up with you if she experiences any episodes of hypoglycemia but you stress the importance of following the insulin dose provided by the meter as it will help to get her into the target blood glucose range.

Key Learning Points – Visit 2

1. Many of the most common insulin related management concerns can be easily addressed in primary care
2. Insulin pens can dramatically simplify insulin administration
3. Although any SMBG meter can provide accurate readings, there is one meter that can provide basal insulin titration support. This may help to improve control and safety for patients on basal insulin regimens
4. All patients using insulin should test at least as often as insulin is given
5. Hypoglycemia education is important to provide to any patient starting on insulin therapy
Visit 3 – Intensification of Insulin Therapy – Basal-Plus Strategy

Learning Objectives
Upon successful completion of this continuing education module, the clinician will be better able to:

1. Discuss strategies to use to intensify basal insulin administration
2. Implement the START study protocol of bolus insulin administration
3. Review the pros and cons of intensifying with premix insulin therapy
4. The role of SMBG on the Basal-Plus insulin regimen

Meet our Patient - Allison
It has been 12 months and 4 to 5 appointments (since visit 2). She titrated her basal insulin as prescribed and had reached an A1C of 6.8% approximately 5 months after starting basal insulin therapy.

She has been happy with how well she has been doing and has continued to lose some weight.

Her current antihyperglycemic regimen is as follows:

- Insulin glargine 54 units at bedtime
- Metformin 1000 mg BID
- Sitagliptin 100 mg daily
- Gliclazide MR 120 mg daily

Her A1C reading 3 months ago was 8.1%. You told her to intensify her lifestyle management and wanted to see her in 3 months. Her current labs show her A1C is 7.9%.

When you pull out her log-book you see the following results for the last 2 weeks:

<table>
<thead>
<tr>
<th>Breakfast</th>
<th>Lunch</th>
<th>Supper</th>
<th>Bed</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Before</td>
<td>2 hrs after</td>
<td>Before</td>
<td>2 hrs after</td>
<td>Before</td>
</tr>
<tr>
<td>Monday</td>
<td>5.0</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tuesday</td>
<td>6.2</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Wednesday</td>
<td>7.4</td>
<td></td>
<td>10.9</td>
<td></td>
</tr>
<tr>
<td>Thursday</td>
<td>7.2</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Friday</td>
<td>6.8</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Saturday</td>
<td>5.1</td>
<td></td>
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<tr>
<td>Sunday</td>
<td>6.1</td>
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<tr>
<td>Monday</td>
<td>4.8</td>
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<tr>
<td>Tuesday</td>
<td>5.2</td>
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<td>5.8</td>
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<tr>
<td>Friday</td>
<td>7.9</td>
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<td>Saturday</td>
<td>7.8</td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Sunday</td>
<td>7.0</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Allison is concerned about her A1C. She tells you she is doing everything she can in terms of her lifestyle and is disappointed that her A1C test is not reaching her target. She is wondering what she can do at this point.
You tell Allison that you feel that she is a good candidate for insulin intensification and you discuss the role of adding bolus insulin to her regimen.

**Intensifying the Patient’s Basal Insulin**

Due to the progressive nature of type 2 diabetes and beta-cell decline, treatment with once-daily basal insulin will eventually fail to maintain glycemic control in a substantial number of patients. One systematic review of the literature reviewed 48 trials with 30,588 patients concluded that only 41.4% of patients taking basal insulin regimens are able to reach an A1C level of < 7%. The 4T trial evaluating the addition of different insulin regimens to patients who were not at an A1C target of < 7.0% found that after a year of addition of basal insulin only 27.8% of patients were reaching an A1C target of ≤ 7.0%. The addition of prandial insulin was found to be more effective than basal insulin alone.

This patient is currently taking three oral antihyperglycemic agents plus a dose of basal insulin to control her blood glucose level. With the introduction of basal insulin she was able to reach her A1C target. Over the last 6 months, her glycemic control has started to deteriorate.

This patient’s fasting readings have been mostly in the target range and some of the readings have been on the lower end of the 4.0-7.0 mmol/L target. Intensification of her basal insulin therapy may help to improve glycemic control, but could place her at a higher risk of morning hypoglycemia.

The most common option at this point is to add bolus insulin to her regimen.

**Clinical Practice Tip:**

In a patient that is taking both bolus and basal insulins and is poorly controlled, clinicians should focus on the fasting readings (basal insulin) first and then the post-prandial readings (bolus insulin).

**Addition of Bolus Insulin (Basal-Plus)**

Bolus insulin is normally added prior to either the main meal of the day or to the breakfast meal. It was traditionally added prior to the supper meal in the evening to address the increase in blood glucose levels with the largest meal. One way to select is the dose is to calculate 10% of the basal insulin dose (e.g. for Allison taking 54 units of basal insulin she would start with a bolus dose of ~5 units). The dose is increased by 1 unit daily until the 2-hour post-supper blood glucose readings are between 5.0-8.0 mmol/L. This adjustment commonly involved the need for the clinician to support the patient regularly until they reached this target.

The START trial (Self-Titration with Apidra to Reach Target) study evaluated the addition of bolus insulin prior to the breakfast meal. In this trial, patients on a stable dose of basal insulin were started on self-managed or physician-managed bolus insulin titration with the rapid-acting insulin glulisine. In the self-managed group, patients started with 2 units administered prior to the breakfast meal and titrated until the 2-hour post-breakfast blood glucose reading was between 5.0-8.0 mmol/L. In the physician managed group, the suggested starting dose was 2 units of glulisine but the starting dose, titration and SMBG testing frequency was determined by the physician.

After a mean follow-up of 159.4 days, 28.4% of participants in the self-titration arm vs. 21.2% in the physician arm achieved an A1C level of ≤ 7.0%. This self-management strategy was found to be as effective as the physician-managed algorithm.
Clinical Practice Tip:
A large number of patients that are not reaching A1C targets with basal insulin therapy, have blood glucose levels that start normal in the morning and rise throughout the day. With the addition of the bolus insulin at breakfast, the patient’s glucose level is corrected at lunch, and may lead to better control throughout the day.

Intensification with Premixed Insulin
In some cases, another way to intensify beyond basal insulin monotherapy is changing to premixed insulin which combines either a rapid or short-acting insulin with an intermediate-acting insulin (Humulin® 30/70, Novolin® 30/70, Humalog® Mix 25 or Humalog® Mix 50, NovoMix® 30). The premixed insulin is normally dosed twice daily prior to the breakfast and supper meal.

The benefits of this regimen include:4

- Simple regimen that requires only two injections to provide basal and bolus insulin coverage throughout the day

The limitations of this regimen include:4

- Lack of mealtime flexibility: will need three meals per day at approximately the same time each day ± snacks
- Increased risk of nocturnal hypoglycemia
- Inability to fine-tune doses unless the person is willing to give a separate injection with rapid/short-acting insulin
- Daytime control may be more difficult (use intermediate-acting insulin as a meal/basal insulin)
- More weight gain may occur
- Given the benefits and limitations of a premixed insulin regimen, this regimen should be considered in a patient who meets the following criteria:
  - Regimented lifestyle in terms of timing and quantity of food and activity
  - Concerns about the patient’s ability to manage 2 types of insulin (basal and bolus)
- The CDA guidelines recommend steps for initiating a premix insulin regimen are reviewed in table 19.

<table>
<thead>
<tr>
<th>Table 19 – CDA Guidelines Recommended Steps for Insulin Initiation9</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Suggested starting dose is 5 to 10 units once or twice daily (prebreakfast and/or presupper).</td>
</tr>
<tr>
<td>• Suggested titration is 1 to 2 units added to prebreakfast dose and/or presupper dose daily until target BG values are reached based on prebreakfast and presupper BG readings.</td>
</tr>
<tr>
<td>• Prebreakfast premixed insulin achieves presupper target BG value (4.0 to 7.0 mmol/L).</td>
</tr>
<tr>
<td>• Presupper premixed insulin achieves target fasting BG value (4.0 to 7.0 mmol/L).</td>
</tr>
<tr>
<td>• 30/70 premixed insulin should be given 30 to 45 minutes before meals.</td>
</tr>
<tr>
<td>• Humalog® Mix 25 or NovoMix® 30 premixed insulin should be given immediately before eating.</td>
</tr>
<tr>
<td>• Stop increasing insulin when both target BG levels are reached.</td>
</tr>
<tr>
<td>• If both BG targets are not reached, continue to increase the relevant dose until both targets achieved.</td>
</tr>
<tr>
<td>• The individual needs to self-monitor BG at least twice daily to safely titrate insulin.</td>
</tr>
<tr>
<td>• Insulin dose should not be increased if the individual experiences 2 or more episodes of hypoglycemia (BG &lt;4.0 mmol/L) in 1 week or any episode of nocturnal hypoglycemia.</td>
</tr>
<tr>
<td>• Oral antihyperglycemic agents (especially secretagogues) may need to be reduced or stopped at the start of this regimen or when daytime hypoglycemia occurs.</td>
</tr>
</tbody>
</table>
Clinical Practice Tip:
The premixed insulin regimen can be an effective method of improving glycemic control in the appropriate patient. For an active and younger patient it does not allow for the flexibility that is often required to maintain control and prevent hypoglycemia due to variance in diet and activity levels.

Other Considerations when Initiating Bolus Insulin
Our patient Allison is currently taking metformin, gliclazide and sitagliptin therapy. When most patients with type 2 diabetes are initiated on bolus insulin therapy, their insulin secretagogues therapy is reduced or discontinued. When bolus insulin is started for Allison, the gliclazide would be stopped or reduced.

Another option that could be considered for Allison instead of bolus insulin addition, is to continue with her current regimen and replace her current DPP-4 inhibitor with a GLP-1 receptor agonist. The GLP-1 receptor agonists are more effective at A1C lowering compared to the DPP-4 inhibitors. The addition of a SGLT2 inhibitor could also be considered. This might be sufficient to allow Allison to reach her A1C target of ≤ 7.0%. The problem is this is only a temporary solution and as her diabetes continues to progress she will likely to need the addition of bolus insulin to maintain glycemic control.

Clinical Practice Tip:
Like most patients with diabetes, there are multiple methods of reaching a patient’s target. It is important to involve them in the process and work together to determine the best possible option for the patient at a specific point in time.

SMBG for Patients on Basal Plus (basal + one bolus)
In the START trial, the patient was told to self-titrate their morning dose of bolus insulin. This can be done effectively with her current meter or any other blood glucose meter.

Once the patient is stabilized, one option is to consider using a meter that will help to adjust her bolus insulin dose based on her fasting reading prior to her breakfast meal. This meter will provide insulin dose suggestions based on the patient’s current dose and current blood glucose reading. The use of this meter and other tools in bolus insulin adjustment will be discussed further in Module 4.

Revisit our Patient – Allison
You present each of the different options to Allison. She feels pretty comfortable with insulin now but is worried that she is going to have to do calculations prior to her meals. You explain that you feel the addition of the bolus insulin prior to her breakfast meal is the best option for her at this point.

You explain that there is a blood glucose meter that can help with the calculations and simplify the regimen. You decide to start her on a bolus insulin and demonstrate the titration regimen from the START trial.

You discuss the titration schedule, reinforce the hypoglycemia education and set a follow-up appointment in a week to see how she is making out with the new regimen.
Key Learning Points – Module 3

1. The addition of bolus insulin can improve glycemic control for patients not reaching targets on basal insulin therapy
2. The START trial demonstrated that self-titration of morning bolus insulin was non-inferior to physician titrated bolus insulin addition
3. Premixed insulin regimens can be used to intensify a basal insulin regimen in the appropriate patient
4. Oral secretagogue therapies should be reduced or discontinued when bolus insulin is added
5. SMBG is utilized to adjust the bolus insulin dose to the optimal level
Visit 4 – Initiation of Basal-Bolus Therapy in a Patient with Type 2 Diabetes

Meet our Patient - Allison

It has been 15 months since visit 3. Allison has been on the basal-plus regimen and has been dosing 58 units of basal insulin at bedtime and 15 units of bolus analogue prior to her breakfast meal.

She has been feeling well and making adjustments to her bolus and basal insulin based on her SMBG readings. She has continued to maintain positive lifestyle changes and has continued to lose weight.

Over the last 6 months, you notice that her A1C values have been close to 8%. She mentions that her brother’s renal condition has deteriorated and he is currently on dialysis. This has caused her some concerns about her complication risk, as she developed peripheral neuropathy over the last year. She would really like to be below her A1C target of 7.0%

She is making out well with her insulin therapy but has taken a new position with her company and will be travelling more frequently. Her meal times and types of foods have not been consistent and she was wondering if she would be a candidate for basal-bolus therapy, similar to her brother.

You decide to review the different options she could use to intensify her therapy.

Learning Objectives

Upon successful completion of this continuing education module, the clinician will be better able to:

1. Discuss the role of basal-bolus therapy in patients with type 2 diabetes
2. Calculate a patient’s correction factor and insulin:carbohydrate ratio
3. Educate a patient to adjust their bolus insulin dose based on their pre-prandial glucose level and carbohydrate intake
4. Review the role of tools to help with carbohydrate counting and a meter that can perform basic dose calculations

Intensifying the Basal-Plus Regimen

There is a proportion of patients with type 2 diabetes that will require bolus insulin throughout the day to control their blood glucose level. Basal-bolus therapy is a highly effective and flexible treatment regimen for patients with diabetes requiring insulin therapy. It requires a commitment from the patient to learn how to dose effectively and to maximize the safety from the regimen.

Another option for this patient would be the initiation of a continuous subcutaneous insulin infusion (CSII) or “insulin pump” therapy.

Basal-Bolus Therapy

The most commonly used regimen with basal bolus therapy involves the administration of 4 doses of insulin per day. This includes a basal insulin dose given at bedtime with either a long-acting insulin analogue (e.g. detemir, glargine, U300 glargine) or NPH insulin. The bolus insulin is administered prior to each meal with a rapid acting insulin (e.g. aspart, glulisine, lispro) or regular insulin.

Table 20 lists the typical insulin injections of a patient using basal bolus therapy and Table 21 lists some of the key advantages and disadvantages of basal bolus therapy.
Table 20: Intensive insulin therapy utilizing four or more injections of insulin

<table>
<thead>
<tr>
<th></th>
<th>Breakfast</th>
<th>Lunch</th>
<th>Supper</th>
<th>Bedtime</th>
</tr>
</thead>
<tbody>
<tr>
<td>Regular/Rapid</td>
<td>Flexible</td>
<td>Flexible</td>
<td>Flexible</td>
<td>Normally fixed dose</td>
</tr>
<tr>
<td>Long acting Analogue*</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

* - An alternative is to give NPH or a long-acting analogue with the breakfast meal and at bedtime but this would increase the number of injections to 5 per day and this may not be acceptable in a particular patient.

Table 21 - Advantages and Disadvantages of Basal Bolus Therapy

<table>
<thead>
<tr>
<th>Advantages</th>
<th>Disadvantages</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Increase in flexibility as the patient can adjust the dose of insulin based on differing food intake and exercise levels</td>
<td>• Need for frequent testing of blood glucose levels (SMBG)</td>
</tr>
<tr>
<td>• Easier to adjust for hyperglycemia</td>
<td>• Carbohydrate counting (for some) and consistent carbohydrate intake for others</td>
</tr>
<tr>
<td>• Reduces the risk of hypoglycemia</td>
<td>• Requires an increased level of dedication by the patient to achieve optimal blood glucose</td>
</tr>
<tr>
<td></td>
<td>• More expensive (due to increased blood glucose testing)</td>
</tr>
<tr>
<td></td>
<td>• Requires more support from clinicians to aid the patient in fine-tuning his regimen</td>
</tr>
</tbody>
</table>

Continuous Subcutaneous Insulin Infusion (Pump Therapy)

With this technology, an insulin pump delivers rapid-acting bolus insulin through an infusion set that is inserted into the subcutaneous tissue of the patient. These pumps not only provide a basal rate but also can be programmed to provide a bolus dose of insulin prior to a meal. Many of these pumps will aid in the calculation of the patient’s bolus insulin dose by incorporating blood glucose measurement into the device, aiding with the mathematics of carbohydrate counting and incorporating the correction factor into the calculations.

Table 22 reviews some candidates that are not good candidates for pump therapy. Table 23 provides some advantages and disadvantages of CSII therapy.

Table 22 - Characteristics of Patients that are NOT Good Candidates for CSII Therapy

<p>| |</p>
<table>
<thead>
<tr>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>• Unable or unwilling to perform multiple daily insulin injections (≥3 to 4 daily), frequent blood glucose monitoring (≥4 to 6 daily), and carbohydrate counting</td>
</tr>
<tr>
<td>• Lack motivation to achieve tighter glucose control and/or have a history of non-adherence to insulin injection protocols</td>
</tr>
<tr>
<td>• History of serious psychological or psychiatric condition(s) (e.g. psychosis, severe anxiety, or depression)</td>
</tr>
<tr>
<td>• Reservations about pump usage interfering with lifestyle (e.g. contact sports or sexual activity)</td>
</tr>
<tr>
<td>• Unrealistic expectations of pump therapy (e.g. belief that it eliminates the need to be responsible for diabetes management)</td>
</tr>
</tbody>
</table>
Table 23 - Advantages and Disadvantages of CSII Therapy

<table>
<thead>
<tr>
<th>Advantages</th>
<th>Disadvantage</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Provides more flexibility in meal timing than MDI, as basal insulin is delivered continuously.</td>
<td>• Requires motivation, technical ability and financial resources (more expensive).</td>
</tr>
<tr>
<td>• Less day-to-day variation in insulin absorption</td>
<td>• May develop hyperglycemia and ketones quickly if insulin delivery is stopped for several hours.</td>
</tr>
<tr>
<td>• Eliminates the need for multiple daily injections (change infusion set every 2 to 3 days)</td>
<td>• Risk of infusion-site infections.</td>
</tr>
<tr>
<td>• More flexibility in adjusting basal dose</td>
<td>• Requires access to diabetes professional(s) experienced in CSII therapy.</td>
</tr>
<tr>
<td>• Can bolus between meals to correct for hyperglycemia without taking an injection</td>
<td>• Cost of supplies may not be covered by the patient’s insurance plan</td>
</tr>
</tbody>
</table>

Working with the Patient to Decide the Optimal Regimen

All patients with diabetes must be given the opportunity to be involved in the selection of treatment options for their diabetes.

For patients requiring basal and bolus insulin, the choice of regimen will depend on a variety of factors such as:

• Patient preference
• Efficacy
• Risk of hypoglycemia (especially nocturnal hypoglycemia and patients with hypoglycemia unawareness)
• Cost of the regimen
• Cost of the supplies (e.g. blood testing strips, infusion sets, insulin pump)
• Other patient factors (e.g. cognitive ability, need for portability, performing contact sports)

Ultimately both basal bolus and CSII regimens can be very effective in providing therapy for patients with either type 1 or type 2 diabetes. They can provide optimal control and flexibility to adjust the regimen based on daily lifestyle issues (e.g. diet, exercise). The choice should be based on an open discussion and a collaborative decision with the patient on the optimal therapy for his diabetes.

Revisit our Patient – Allison

You discuss the different options with Allison. She knows from other people with diabetes that her plan does not cover the cost of the insulin pump or the necessary supplies. She is comfortable using her insulin pen and would like to try the basal-bolus therapy format.

You are thinking of adding another dose of bolus insulin prior to her lunch meal. You ask her to increase her SMBG testing frequency before her lunch meal and 2 hours after. You explain that you will follow a similar titration to the addition of bolus insulin to her breakfast and adjust based on her 2-hour post-lunch reading or pre-next meal SMBG testing.

You refer her to a dietitian to discuss impact of diet on insulin adjustments. You feel it is important to see a dietitian as the increase in travel will lead to variability in her insulin requirements due to change in meal times and intake.
You decide to review the basics of carbohydrate counting and the tools to help her with this adjustment.

**Basal-Bolus Therapy Without Carbohydrate Counting**
There are some patients who are candidates for basal-bolus therapy but are not initially candidates for carbohydrate counting. In these individuals, clinicians can still initiate basal-bolus therapy but the patient should have a consistent intake of carbohydrates. These patients are initiated on a low bolus dose prior to meals and titrated based on the pre-meal blood glucose readings.

The primary advantage of this regimen is it does not require carbohydrate counting. The primary disadvantage with this regimen is the patient has to consume a relatively consistent amount of carbohydrates with each meal to reduce the risk of blood glucose excursions.

**Carbohydrate Counting and Insulin Adjustments**
Every patient with diabetes should have access to a dietitian trained in diabetes management. They can provide the patient with dietary recommendations to help improve their overall control. They can also provide direction on the impact of specific foods on blood glucose levels.

With basal bolus insulin regimens, patients will adjust their insulin intake based on their pre-meal SMBG. Although many patients can comfortably do these calculations in their head, this can be a limiting factor for some individuals.

Two important factors for bolus insulin adjustment are the:
- Correction factor
- Insulin to carbohydrate ratio

These factors will adjust the insulin requirements based on the SMBG reading before the meal, and the number of carbohydrates being consumed.

**Correction factor**
The correction factor is used to calculate the additional insulin required to correct hyperglycemia. A correction factor predicts how much one extra unit of insulin will reduce the glucose level. To calculate correction factor use the following formula:

\[
\text{Correction factor} = \frac{100}{\text{Total Daily Dose of insulin}}
\]

**Total daily dose of insulin** = total basal dose + total of all bolus injections given in the day

The correction factor is used by patients to adjust their insulin based on their preprandial glucose reading. This is done with the following formula:

\[
\text{Insulin required} = \frac{(\text{Actual blood glucose} - \text{target blood glucose})}{\text{Correction Factor}}
\]

This formula will calculate the extra number of units of insulin required to manage a patient with a higher than target blood glucose prior to a meal. For example, a patient with a correction factor of 2, with a pre-meal glucose of 8.3 mmol/L and a target of 6.0 mmol/L would require \([(8.3-6.0)/2= 1.15\text{ or } \sim1\] one extra unit of insulin to correct for this higher than target reading.
Insulin to Carbohydrate Ratio

The insulin to carbohydrate ratio is used to determine the number of grams of carbohydrates that are addressed by 1 unit of insulin. It is calculated using the following formula:

\[
\text{Insulin:Carb Ratio} = \frac{\text{Normal amount in grams of carbohydrate consumed}}{\text{Normal dose of insulin required}}
\]

If a patient normally eats 60 grams of carbohydrates and requires 8 units of insulin for that meal, their insulin to carbohydrate ratio is \((60/8 = 7.5 \sim 8\) or 1 unit of insulin will address 8 grams of carbohydrates). This ratio allows the patient to adjust the amount of bolus insulin based on the anticipated number of carbohydrates they are going to ingest.

Using these two factors, patients can adjust their bolus insulin based on their current blood glucose level and what they plan to eat. For basal bolus therapy to work most effectively the patient needs to be able to:

- Calculate the amount of carbohydrates they are going to consume
- Adjust the bolus dose based on intake and carbohydrate content of the meal

Fortunately, there are tools that can help with both of these.

Clinical Practice Tip:

It is common for patients to have slightly different insulin:carbohydrate ratios at each meals. This can affect the calculations slightly at each meal time.

Carbohydrate Calculation

There are a large number of publications that can provide patients with the carbohydrate content of specific foods. The Canadian Diabetes Association’s Beyond the Basics has the number of grams of available carbohydrates for common foods.

The Carbs and Cals App for smart phones is a tool that provides a highly visual approach to determine the carbohydrate content of a specific portion size. The patient selects the portion they are eating from a photo of a number of portions. They are given the carbohydrate content of the portion (Figure 3 provides an example of different portions of lasagna). This tool is useful as it is comprehensive and provides a visual of the different portions versus relying on the use of a scale and tables. It is highly portable and can allow for carbohydrate calculation easily when the patient is not eating a regular meal at home.
SMBG Meter that Helps with Bolus Insulin Calculations

There is one SMBG meter that can provide the above calculations for patients using basal bolus therapy to manage their insulin.

This meter can increase both the efficacy and safety of basal bolus therapy for:

- A patient starting on basal bolus therapy
- The patient having difficulty with calculating the appropriate bolus dose
- The patient that is concerned they are going to make a mistake in their calculations

Patients on Basal Bolus WITHOUT Carbohydrate Counting

The clinician programs the meter with their usual bolus doses for each meal and the correction factor. The patient tests their blood glucose prior to their meal. Based on the SMBG reading and the usual dose of bolus insulin, the meter uses the correction factor to increase or decrease the usual dose of insulin. It will provide patients with a recommended dose of bolus insulin for that meal.

Patients on Basal Bolus WITH Carbohydrate Counting

The clinician programs the meter with the patient’s correction factor and insulin:carbohydrate ratio. The patient tests their blood glucose prior to a meal and enters the number of carbohydrates they are planning to ingest. The meter will then, using the correction factor, increase or decrease to provide the dose of bolus insulin required for the SMBG reading. It will then calculate the number of units of insulin required by the patient to manage the amount of carbohydrates. This provides a patient with their recommended bolus dose for the specific meal. The meter manages the calculations for the patient and thus reduces the risk of calculation errors.
Clinical Practice Tip:
Consider asking all your patients that are actively carbohydrate counting and adjusting insulin if they are having any problems or concerns with insulin adjustments. The Carbs & Cals app and this meter can simplify the calculations tremendously.

Utilization of SMBG Reports
The use of SMBG logbooks is encouraged by diabetes professionals. A Canadian study found that only 53% of patients with type 1 diabetes and 59% of patients with type 2 diabetes were accurate in reporting their SMBG results in their log books. Most meter manufacturers have software that allow for the downloading of SMBG results from the meter. These programs are valuable as they allow for the visualization of blood glucose patterns. This can allow for easier adjustments in the patient’s lifestyle and medication regimen.

The meter that aids in the calculation of bolus doses also logs the insulin doses given and carbohydrates eaten. This can be used by the clinician to adjust the insulin regimen as well as adjust the insulin:carbohydrate ratio and correction factor based on the patients results.

Figures 4 and 5 provide examples of the reports that are available from these SMBG programs.
Figure 4 – Basal Titration Example from the Diabetes Management Software
Clinical Practice Tip:
The reports from these programs can be used as both documentation and tracking insulin doses and control over time. Past and current reports can be used as a teaching tool for your patients with diabetes.

Revisit our Patient – Allison
Through your consultation with Allison you feel that she is comfortable with the addition of other bolus doses of rapid-acting insulin. You refer her to a dietitian to provide more information regarding carbohydrate counting.

You discuss her insulin dose titration and program her meter to help her with her insulin adjustments. She feels motivated to make the changes to control her diabetes and is looking forward to the flexibility her new regimen provides.

You ask her to make another appointment in a week to allow the two of you to adjust her regimen based on the addition. You finish by quickly reviewing how to use her meter to track her carbs, insulin and results and review the management of hypoglycemia.
Key Learning Points – Module 4

1. Patients not reaching targets for basal-plus regimens can be intensified with basal bolus and CSII therapy
2. Basal bolus and CSII therapy are both effective and offer tremendous flexibility in terms of diet and lifestyle
3. The correction factor and insulin:carbohydrate ratio are required for carbohydrate counting
4. There are several tools that can help with carbohydrate counting
5. There is a meter available to help with the bolus insulin calculations for patients on basal bolus and basal-plus regimens
Ask the Expert (video)

1. What do you feel are the most significant patient and clinician barriers to starting insulin in type 2 diabetes?

2. Which patients with type 2 diabetes do you feel are the best candidates for insulin therapy add-on?

3. When do you feel that intensification of insulin regimen is indicated and how do you ensure patient buy-in?

4. Please discuss the START protocol and the results from the study

5. What technologies do you recommend to improve the effectiveness and safety of insulin therapy?
References


