Diabetes education material

How do I assess plasma glucose control?

There are four different ways to assess plasma glucose control:

1. Fasting plasma glucose (FPG) (No caloric intake for at least 8 hours)

2. Oral glucose tolerance test (OGTT) in which the plasma glucose concentration is measured two hours after taking a glucose solution (75 g anhydrous glucose dissolved in water)

3. Glycosylated hemoglobin (HbA1c)

4. Random plasma glucose (any time of the day without regard to the interval since the last meal) (1)

According to the result of HbA1c, FPG or OGTT tests, individuals can be classified as outlined in Table 1.

Table 1 Glucose test result classification (1)

Test result	FPG (mmol/l)	OGTT (mmol/l)	HbA1c (%)
Normal	$FPG \leq 6$	$OGTT < 7.8$	$HbA1c < 6$
Impaired	$6.1 \leq FPG < 7$	$7.8 \leq OGTT < 11.1$	$6 \leq HbA1c \leq 6.4$
Diabetes	$FPG \geq 7$	$OGTT \geq 11.1$	$HbA1c \geq 6.5$

If one of these measurements was indicating diabetes without any hyperglycemia symptoms, the test should be repeated on another day to confirm the diagnosis (1).

If the random plasma glucose testing result was indicating diabetes (≥ 11.1 mmol/l) but the individual was not experiencing any hyperglycemia symptoms, an alternate test (FPG, OGTT or HbA1c) is required to confirm the diabetes diagnosis (1).

Individuals who have impaired glucose tolerance, impaired fasting glucose or HbA1c between 6% and 6.4 % are considered to be in the 'pre-diabetes' stage (1). Those patients as well as patients with diabetes are at high risk (1.5 times and 2-4 times (respectively)) of developing cardiovascular disease (CVD) when compared to individuals with normal glucose metabolism (2).

Abnormalities in glucose metabolism are often associated with metabolic syndrome which is defined as having any three of the following disorders:

1. Elevated waist circumference, depending on the patient's ethnicity:

   - Canada, United states: ≥ 88 cm for females and ≥ 102 cm in males

   - Europe, Middle East, Sub Sahara Africa and Mediterranean ≥ 80 cm for females and ≥ 94 cm in males

   - Asia and South and Central America ≥ 80 cm for females and ≥ 90 cm in males

2. Blood pressure ≥ 130 mm Hg systolic and/or ≥ 85 mm Hg diastolic

3. Fasting plasma glucose ≥ 5.6 mmol/l

4. Serum triglycerides ≥ 1.7 mmol/l

5. HDL < 1.3 mmol/l in females and < 1 mmol/l in males (1).

Individuals who are 40 years and older or at high risk using a risk calculator (e.g.

CANRISK which is available from http://www.diabetes.ca/documents/for-

professionals/NBI-CANRISK.pdf) should be screened for diabetes using FPG and/or

HbA1C. Individuals with additional risk factors for diabetes (e.g. metabolic syndrome,

history of prediabetes and a first degree relative with diabetes) and those at very high risk

using a risk calculator should be screened more frequently and/or earlier (1).

Figure 1 below illustrates the screening and diagnosis algorithm for type 2 diabetes as
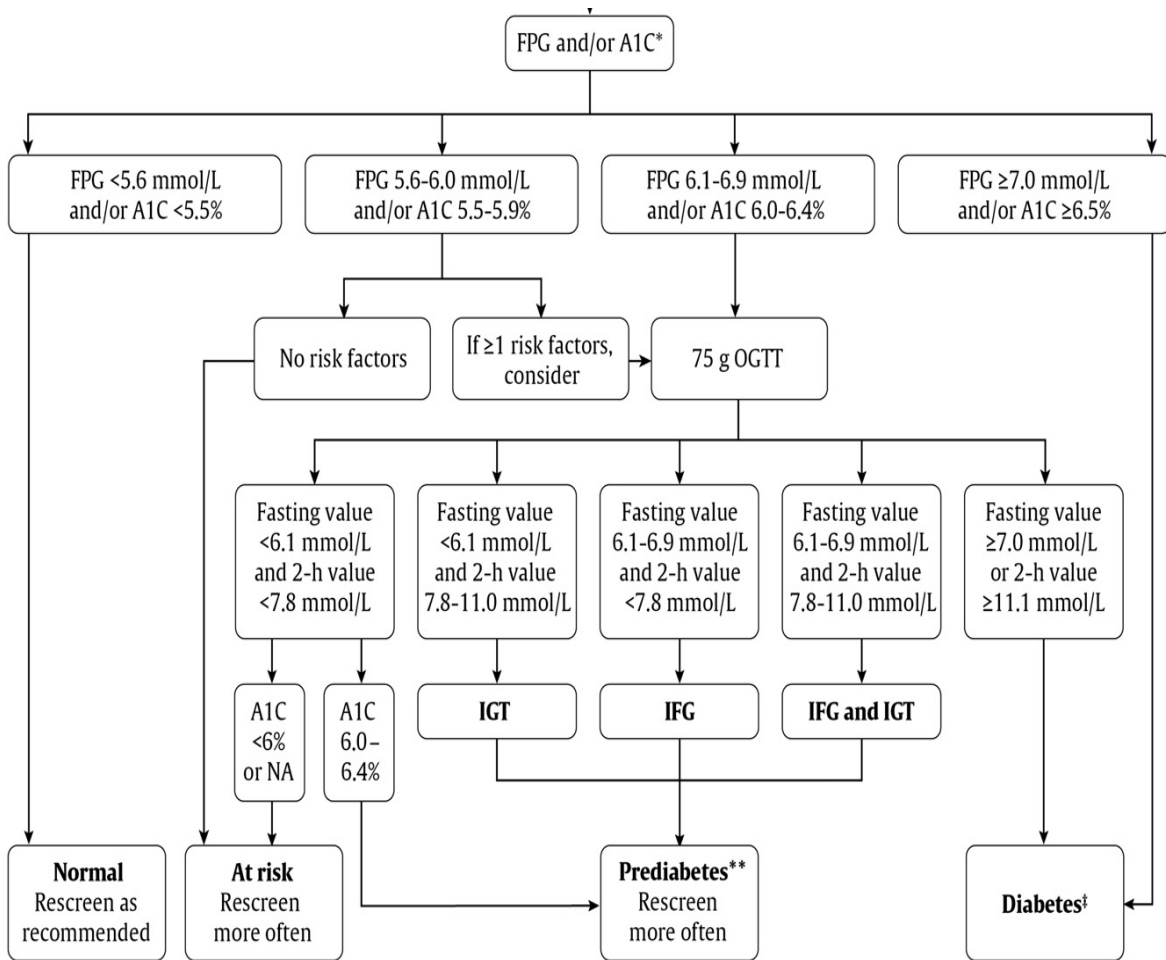
recommended by the CDA (2013) guidelines.

Figure 1 Steps which should be taken according to fasting glucose results (1)

How do I treat type 2 diabetes?

Optimal glycemic control is very important in diabetes treatment.

Diabetes can be treated by:

1. Lifestyle adjustments

2. Oral Antihyperglycemic medications

3. Insulin

Diabetes treatment should be individualized based on the following:

1. Patient characteristics (degree of hyperglycemia, other co-morbidities and patient preference)

2. The properties of the antihyperglycemic medications, e.g. efficacy, contraindications, side effects and risk of hypoglycemia (1).

Type 2 diabetes treatment should start with lifestyle adjustment; if lifestyle adjustment fails to achieve the target blood glucose after 2-3 months, antihyperglycemic medication should be started (1).

Table 2 illustrates all the available antihyperglycemic medications classes and agents.

Table 2 The available antihyperglycemic medication classes and agents (1)

Class & agents	Mechanism of action	Notes
Alphaglucosidase inhibitor Acarbose	Inhibits glycoside hydrolases enzymes which are needed to digest the carbohydrates. (slows the absorption of ingested carbohydrates and helps control rising blood glucose levels after meals)	- Not recommended as initial therapy in patients with HbA1c $\geq$ 8.5% - Should be taken with the first mouthful of food
DPP-4 inhibitor Sitagliptin Saxagliptin Linagliptin	Inhibits the enzyme dipeptidyl peptidase 4. This enzyme breaks down the incretins GLP-1 and GIP gastrointestinal hormones that are released in response to a meal. By preventing GLP-1 and GIP inactivation, GLP-1 and GIP are able to potentiate the secretion of insulin and suppress the release of glucagon by the pancreas.	- New agent with unknown long-term safety data - Should be taken at the same time everyday (usually in the morning, not necessarily with food) - Use with caution in patients with history of pancreatitis

GLP-1 receptor agonist Exenatide Liraglutide	Activates incretin pathway by utilizing DPP-4 resistant analogue to GLP-1	- New agent with unknown long-term safety data - Contraindicated with personal/family history of medullary thyroid cancer or multiple endocrine neoplasia syndrome type 2 - Use with caution in patients with history of pancreatitis
Sulfonyureas Gliclazide Glimpiride Glyburide	Stimulate the insulin secretion from Beta cells	- Do not use in patients at high risk of hypoglycemia, e.g. elderly, patients who have renal or hepatic failure - Should be taken before meals (no longer than 30 minutes).
Meglitinides Nateglinide Repaglinide	Stimulate the insulin secretion from Beta cells	- Should be taken as close as possible to the meal (0-15 minutes before the meal)
Biguanide Metformin	Suppresses hepatic glucose production (hepatic gluconeogenesis)	- Use as initial treatment in both overweight and non-overweight patients (unless contraindicated) - Should be taken at meal time
Thiazolidinedione Pioglitazone Rosiglitazone	Act by binding to PPARs (peroxisome proliferator-activated receptors), a group of receptor molecules inside the cell nucleus, specifically PPARγ (gamma). When activated, the receptor migrates to the DNA, activating transcription of a number of specific genes. By activating PPARγ Insulin resistance is decreased	- May induce edema or heart failure - Require 6-12 weeks to achieve glycemic effect - Contraindicated in patients with heart failure or left ventricular dysfuntion - Should be taken at the same time everyday (usually in the morning, not necessarily with food).

Insulin **Rapid acting analogues** Aspart Glulisine Lispro **Short acting** Regular **Intermediate acting** NPH (Neutral Protamine Hagedorn) **Long acting basal analogues** Detemir Glargine **Premixed** Premixed Regular-NPH Biphasic insulin aspart Insulin lispro/ lispro protamine		- Highest HbA1c reduction and no maximal dose - Numerous formulations and delivery systems allowing for regimen flexibility - Consider adding a long acting or intermediate acting insulin at bedtime to the oral agents when initiating insulin

Figures 2-5 illustrates the CDA (2013) recommendations for type 2 diabetes management

and dose adjustment based on estimated Glomerular Filtration Rate (eGFR)

Figure 2 Type 2 diabetes management

The flowchart contains the following elements:

- Diagnosis of type 2 Diabetes
- Start lifestyle intervention +/- Metformin

Branching into three:
- HbA1c<8.5%
- HbA1c ≥8.5%
- Symptomatic hyperglycemia with metabolic decomposition

From HbA1c<8.5%:
- If not at target after 2-3 months
- Start/increase Metformin Dose

From HbA1c ≥8.5%:
- Satrt Metformin immediatley Consider initial combination with another agent

From Symptomatic hyperglycemia:
- Initiate insulin +/- Metformin

- Not at target
- Add an agentbest suited to the patient

Branching into three:
- CKD Patients (See eGFR flow chart)
- CVD patients (See CVD patients)
- Elderly/vulnerable (See Elderly/vulnerable flow chart)

Make timely adjustments to attain target HbA1c within 3-6 months

CVD patients

Metformin

Not at target

Add either of the following agents
DPP-4 inhibitors ($\downarrow\downarrow$)
Insulin($\downarrow\downarrow\downarrow$)
Meglitinides($\downarrow\downarrow$)
Sulfonyurea($\downarrow\downarrow$)
GLP-1 receptor agonists($\downarrow\downarrow$ to $\downarrow\downarrow\downarrow$)

Avoid
Thiazolidinediones

If not at target

Add another agent from a different class

Add/Intensify insulin regimen

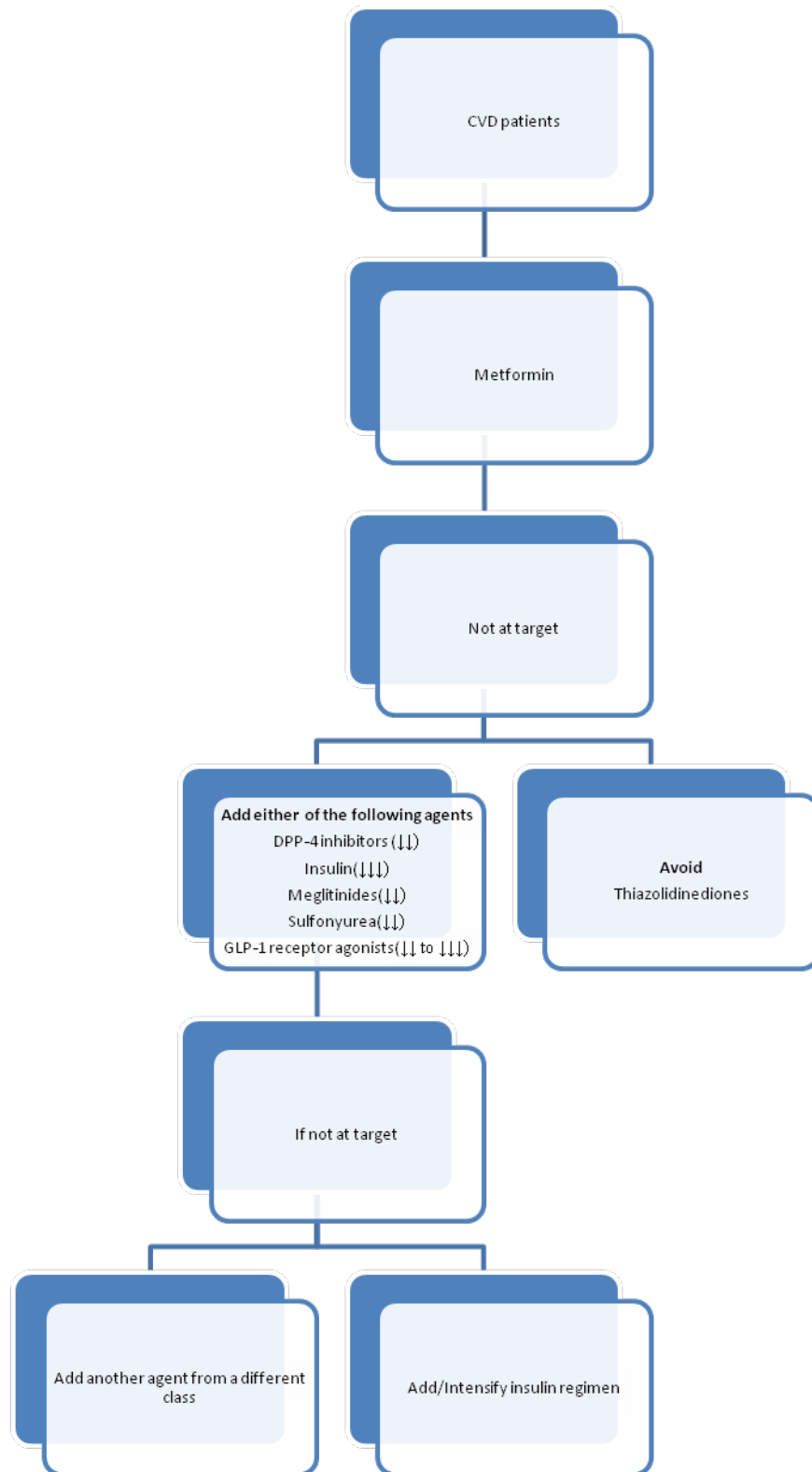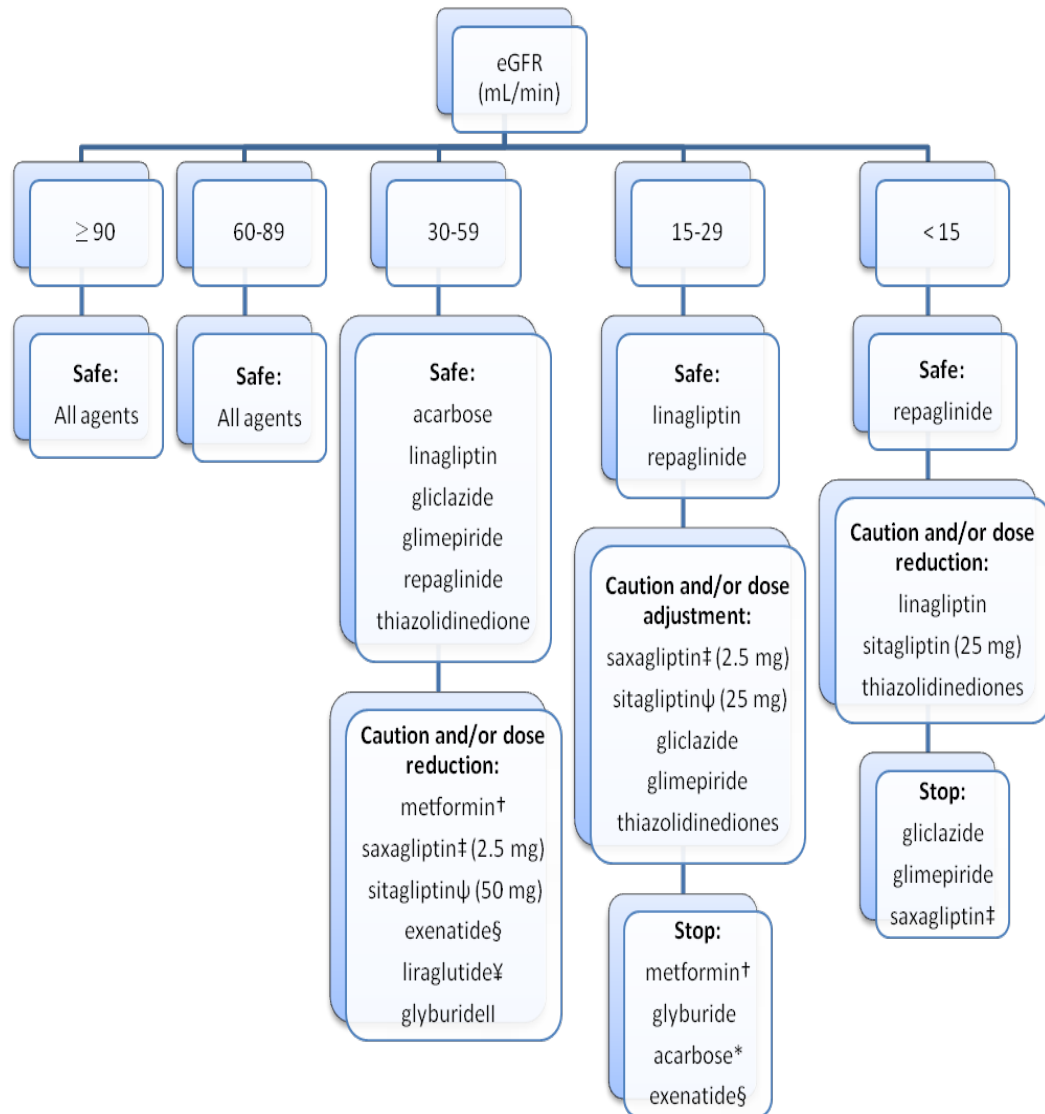- $\downarrow$ represents relative HbA1c lowering when an agent is combined with Metformin

Figure 3 Type 2 diabetes management in CVD patients

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                    │  Eldery/Vulnerable      │
                    │  patients               │
                    └─────────────────────────┘
                                │
                    ┌─────────────────────────┐
                    │       Metformin         │
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                    │      Not at target      │
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             ┌──────────────────┴──────────────────┐
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 │ Add either of the following  │      │         Avoid            │
 │ agents                       │      │      Sulfonyurea         │
 │ DPP-4 inhibitors (↓↓)*       │      │      Meglitinides        │
 │ Insulin (↓↓↓)                │      └──────────────────────────┘
 │ Thiazolidinediones (↓↓)      │
 │ GLP-1 receptor agonists      │
 │ (↓↓ to ↓↓↓)                  │
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 │       If not at target       │
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 │ Add another agent│  │ Add/Intensify insulin│
 │ from a different │  │ regimen              │
 │ class            │  └──────────────────────┘
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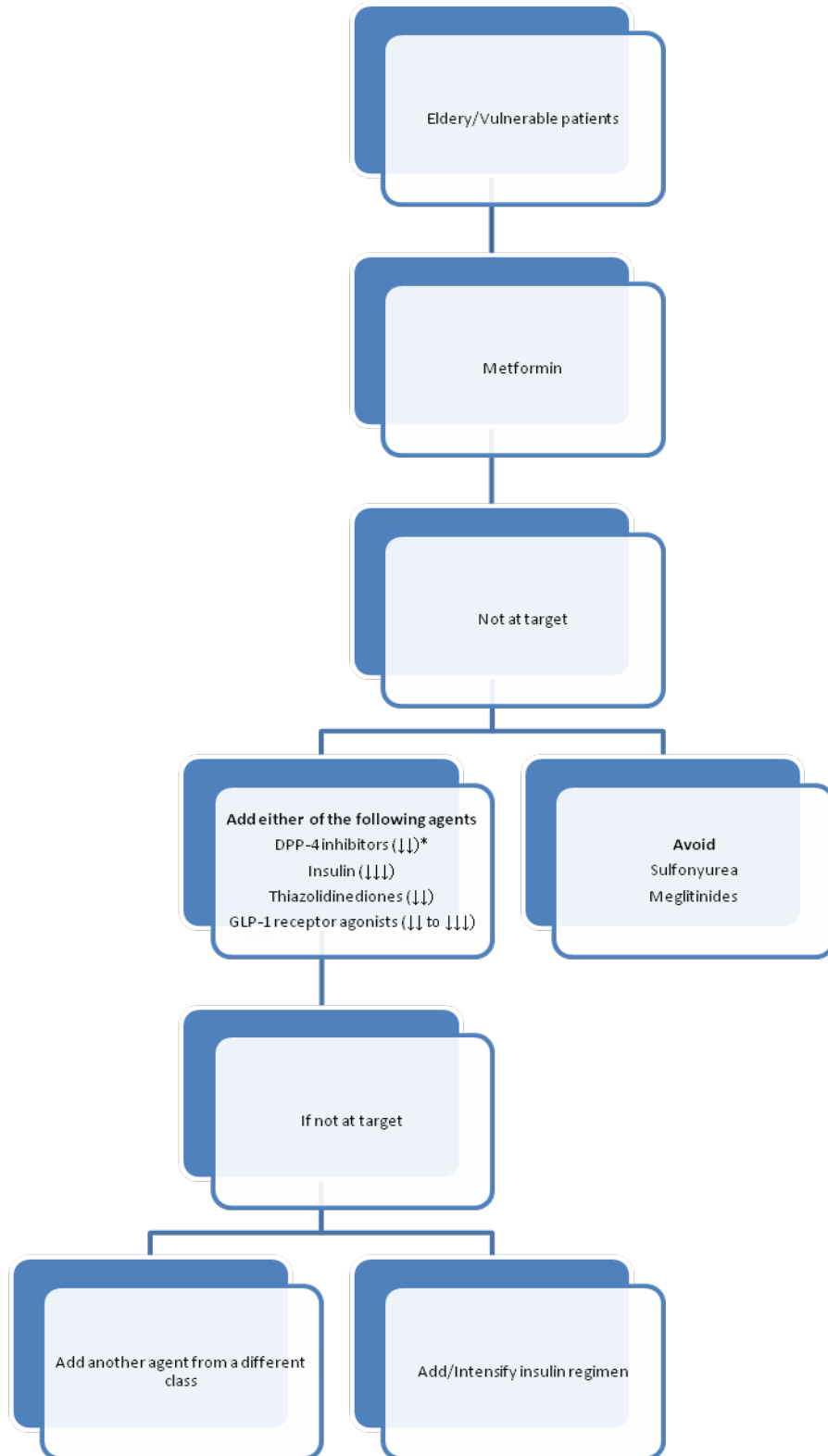
- ↓ represents relative HbA1c lowering when an agent is combined with Metformin

Figure 4 Type 2 diabetes management in elderly/vulnerable patients

eGFR (mL/min)

≥90 — Safe: All agents

60-89 — Safe: All agents

30-59 — Safe: acarbose, linagliptin, gliclazide, glimepiride, repaglinide, thiazolidinedione
Caution and/or dose reduction: metformin†, saxagliptin‡ (2.5 mg), sitagliptinψ (50 mg), exenatide§, liraglutide¥, glyburide||

15-29 — Safe: linagliptin, repaglinide
Caution and/or dose adjustment: saxagliptin‡ (2.5 mg), sitagliptinψ (25 mg), gliclazide, glimepiride, thiazolidinediones
Stop: metformin†, glyburide, acarbose*, exenatide§

< 15 — Safe: repaglinide
Caution and/or dose reduction: linagliptin, sitagliptin (25 mg), thiazolidinediones
Stop: gliclazide, glimepiride, saxagliptin‡

† Metformin may be used in certain circumstances if eGFR is 20-29 mL/min, but requires very diligent monitoring for acidosis.
‡Saxagliptin should be dose adjusted to 2.5 mg daily when eGFR is 30-50 mL/min
ψ Sitagliptin should be dose adjusted to 50 mg daily eGFR is 30-50 mL/min, and to 25 mg daily when eGFR is <30 ml/min
§ Exenatide should be dose adjusted to 5 mcg bid when eGFR is 30-50 mL/min
¥Liraglutide should be stopped when eGFR ≤ 50 mL/min
* Acarbose should be stopped when eGFR ≤ 25 mL/min
|| Glyburide should be monitored closely when eGFR <50 mL/min

Figure 5 Type 2 diabetes management based on eGFR

What are the glycemic control targets?

Glycemic control targets should be individualized based on the following:

- Age

- Diabetes duration

- Life expectancy

- Risk of severe hypoglycemia

- Presence or absence of cardiovascular disease (1)

In their (2013) guideline CDA recommend a target of HbA1c ≤ 7% in most patients with diabetes (1).

In patients with diabetes and at least one of the following: limited life expectancy, high level of functional dependency, extensive coronary artery disease, hypoglycemia unawareness, history of recurrent severe hypoglycemia, multiple co-morbidities and longstanding difficulty in achieving a target of HbA1c ≤ 7% despite the intensive treatment a less strict target is recommended (7.1 ≤ HbA1c ≤ 8.5) (1).

A target of HbA1c ≤ 6.5% is recommended in certain patients to further reduce the risk of microvascular complications but this target has to be balanced against hypoglycemia risk (1).

A fasting or pre-prandial plasma glucose target of 4-7 mmol/l and a two hour post-prandial plasma glucose target of 5-10 mmol/l are required to achieve an HbA1c target of ≤ 7%. If the HbA1c target was not achieved by the aforementioned post-prandial plasma glucose target, it should be lowered to 5-8 mmol/l (1).

How do I monitor and follow up patients with diabetes?

When diabetes treatment is initiated or adjusted, plasma glucose should be monitored on daily basis in order to know how to adjust the lifestyle, oral diabetes medication and the insulin dose. HbA1c should also be monitored as it is important to understand how high or low was the plasma glucose on average over the last three months (3).

The CDA (2013) guidelines recommend testing HbA1c every three months to make sure that the targets are achieved and maintained. When targets have been achieved HbA1c should be tested at least every six months (1).

Self monitoring should be done at least three times per day (pre and post prandial) if the patient is taking insulin more than once a day. If the patient is taking once daily insulin and other oral hypoglycemic agent(s), testing at least once daily at different times of the day is recommended. If targets have been achieved in patients who are not receiving insulin or oral agents associated with hypoglycemia, testing can be done on PRN basis (1).

What should I tell the patient?

Hypo and Hyper glycemia

Individuals with diabetes should watch for episodes of HYPOGLYCEMIA (plasma glucose concentration dropping below a certain level [4 mmol/L before the meals, 5 mmol/L after the meals]) or HYPERGLYCEMIA (plasma glucose concentration becoming higher than a certain level [more than 7 mmol/L before the meals, more than 10 mmol/L after the meals]) (1, 4).

Depending on the severity of the episode, HYPOGLYCEMIA can be associated with neurogenic (autonomic) symptoms (i.e. trembling, palpitations, sweating, anxiety, hunger, nausea and tingling) as well as neuroglycopenic symptoms (i.e. difficulty concentrating, confusion, weakness, drowsiness, vision changes, difficulty speaking, headache and dizziness).

- Mild episodes are associated with autonomic symptoms where the patient is able to self-treat

- Moderate episodes are associated with both autonomic and neuroglycopenic symptoms where the is able to self-treat

- Severe episodes require assistance from another individual. The patient might be unconscious (1)

HYPOGLYCEMIA can also occur while sleeping, when this happens the symptoms can be:

- Waking up with HYPOGLYCEMIA

- Continue to sleep but experiencing nightmares, sweating or morning headaches

- Unusual high blood sugar reading on the next morning (4)

Causes of HYPOGLYCEMIA

HYPOGLYCEMIA can be caused by:

- Not consuming the usual amount of food

- Exercising for longer than the usual time

- Certain Diabetes medication (most common cause) which induce Insulin secretion in the body (glimeperide, glyburide, gliclazide, repaglinide, nateglinide) or insulin (1, 4)

Treating HYPOGLYCEMIA

The goals of HYPOGLYCEMIA treatment are to avoid the harm, relieve the symptoms and to provide a quick rise of the plasma glucose to a safe level (1).

- Treating Mild to Moderate cases:

- ➤ A fast acting carbohydrate (15 g of glucose) (3 or 4 glucose tablets, 1 tablespoon of honey, 3 teaspoons or 3 packets of table sugar dissolved in water, 175 ml of juice or regular soft drink, 6 lifesavers (hard candy)) (each has 2.5 g of carbohydrates) should be given to a conscious patient with mild to moderate HYPOGLYCEMIA, patients are encouraged to wait for 15 minutes and then check their plasma glucose, if still low (less than 4mmol/L) they should repeat the same steps. This will increase the plasma glucose by 2.1 mmol/l in 20 minutes.

- Treating Severe Cases:

- ➤ 20 g of carbohydrates (preferably as glucose tablets or equivalent) should be given to a conscious patient with severe HYPOGLYCEMIA, patients are encouraged to wait for 15 minutes and then check their plasma glucose if still low

(less than 4mmol/L) they should administer 15 g of glucose in the forms mentioned earlier. 20 g of carbohydrates should increase the plasma glucose by 3.6 mmol/l in 45 minutes.

➢ If the patient with severe HYPOGLYCEMIA is unconscious at home 1mg glucagon should be administered subcutaneously or using the intramuscular route. Emergency services should be called.

If intravenous route is available 10-25 g of glucose (20 to 50 cc of Dextrose 50% in water) should be administered over 1 to 3 minutes.

To prevent repeated HYPOGLYCEMIA after treating it, the patient should have his meal or have a snack (a snack which contains protein and carbohydrates, e.g. half a peanut butter or cheese sandwich or cheese and crackers) if the meal is an hour or more away.

Care givers and support persons should know the symptoms of HYPOGLYCEMIA and how deal with it (1, 4).

Delayed hypoglycemia can occur as result of alcohol consumption with or after the evening meal in patients who are using insulin or insulin secretagogues. Those patients should be advised to monitor their plasma glucose, adjust their insulin dose and consume carbohydrates to prevent hypoglycemic episodes (1).

If kept under control HYPOGLYCEMIA can only be an unpleasant feeling and nothing more (1, 4).

Symptoms of HYPERGLYCEMIA according to the plasma glucose level:

(i)   11 mmol/L: Thirst, flushed face, drowsiness

(ii)   17 mmol/L: Fruity breath odor, loss of appetite, abdominal pain

(iii)   21 mmol/L: Heavy breathing, fast heartbeat

(iv)   23 mmol/L: Loss of consciousness, nausea, vomiting, dehydration (5)

Lifestyle adjustment tips for diabetes patients

Lifestyle adjustment plays a vital role in diabetes treatment; this includes healthy eating, exercise and weight loss (6).

Below are some tips for diabetes patients to help them employ the lifestyle adjustment

Eating three meals per day separated by a maximum of six hours will help the body to regulate the plasma glucose (the patient can also add a healthy snack (which can be composed of low fat cheese and whole grain crackers or one medium apple or a small banana or peanut butter, whole grain crackers and low fat milk)) (6).

When considering healthy eating, the patient should try to:

- Have more fiber rich foods such as whole grain products, fruits and vegetables, lentils and dried beans and peas because fiber rich foods will help the patient to feel fuller for longer and may help reducing his/her cholesterol and blood sugar.

- Reduce the sugar and sweets consumption such as deserts, regular pop, jam and honey as they will increase his/her blood glucose

- Limit his/her consumption of high fat food such as fried foods, chips and pastries since they can cause weight gain which is not recommended in diabetes patients as it increases the difficulty of diabetes control

The plate on the left hand side of the page represents the 'healthy eating' plate. This plate is divided into three sections:

- The largest section which represents ½ of the plate should be composed of vegetables (at least two kinds) as they are high in fibers and nutrients and have low calories. The amount of vegetables can be as much as the patient can hold in both hands.

- The second section which represents ¼ of the plate should be composed of grains and starches, i.e. corn, pasta, potato, rice, noodles, whole grain cereals or whole grain bread. This part of the plate will provide the patient with the energy his/her body needs. The amount of grains and starches can be as the size of the patient's fist.

- The third section which also represents ¼ of the plate should be composed of meat and alternatives, i.e. fish, lean meat, chicken, lentils, low fat cheese, eggs or beans. This will provide the patient with the protein his/her body needs. The amount of

meat and alternatives can be as the size of the patient's palm

and the thickness of his/her small finger.

A glass of milk (250 ml) (1% or skimmed milk) or low fat yogurt plus a whole fruit (its

size should be as the size of the patient's fist) will complete the meal.

If the patient wants to have a fatty component (butter, margarine, gravy) in his/her meal,

he/she should try to limit this to the size of the tip of his/her thumb (6).

Some physical activity should be added to the patient's daily routine as this will help to

control his/her blood sugar (6). The CDA (2013) guidelines recommend that patients with

diabetes should exercise at least 3 days per week (with no more than 2 consecutive days

without exercise) for a minimum of 150 minutes. This exercise should be moderate to

vigorous and should involve resistance as well as aerobic exercise. Patients are

encouraged to set physical activity aims and plan strategies to overcome any anticipated

barriers and keep a physical activity log where they record their exercises (1).

References:

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