

# START

the transition to **insulin**

## Insulin initiation in type 2 diabetes

Created by South African experts, this unique interactive learning programme will help you to successfully initiate insulin therapy in your patients with diabetes and to confidently manage their continuing care.

### What you will gain...

Participation in this fully accredited CPD programme gives you the opportunity to learn how:

- ✦ Appropriate selection of patients for insulin therapy can significantly improve prognosis;
- ✦ Insulin can be easily and safely initiated by understanding and applying some simple steps; and
- ✦ To select the right insulin for the right patient at the right time

### How you will learn...

**START offers you the opportunity to freely obtain CPD points**

- ✦ **e-based learning** in five modules – each module earns 3 CPD points
- ✦ **Watch** accompanying advice and tips from South African experts
- ✦ **Download** practical materials supporting you and your patients when you initiate insulin

### Expert panel



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## Module editor



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## Module 3: Insulin initiation in type 2 diabetes

### Objectives of this module

- To support clinicians and build confidence in initiating insulin and intensifying therapy

### Introduction

Over the last few years, many new anti-hyperglycaemic drugs have been introduced into the clinicians' armamentarium for the treatment of type 2 diabetes (T2DM). This may give the impression that insulin therapy, which is still vital for a large number of people, has moved down 'the rankings' of antidiabetic medications.

While some of these non-insulin therapies may offer benefits beyond just managing a patient's glucose levels, insulin therapy remains essential to many people with diabetes because long-term glucose control is necessary to prevent long-term complications.<sup>1</sup>

### When is insulin therapy indicated?

In essence, insulin is indicated for use in two circumstances. The first - at ANY TIME, including at the time of diagnosis, when the patient presents with some form of metabolic decompensation (Figure 1). After initiating insulin in these circumstances, the patient might need to be on insulin therapy only for the short-term; as glycaemic control returns, the patient may well be able to transition back onto oral therapy.

The second situation is to include insulin in a third-line therapy, following failure to achieve target using a regimen of two oral agents. This is especially important when a third oral agent or a glucagon-like peptide-1 (GLP-1) receptor agonist (RA) is unlikely to achieve the desired results.<sup>2</sup> When a T2DM patient is already on combination therapy using oral agents and an injection GLP-1 RA, and is not at the desired target (Table 1), the clinical approach would need to consider the initiation of insulin therapy.

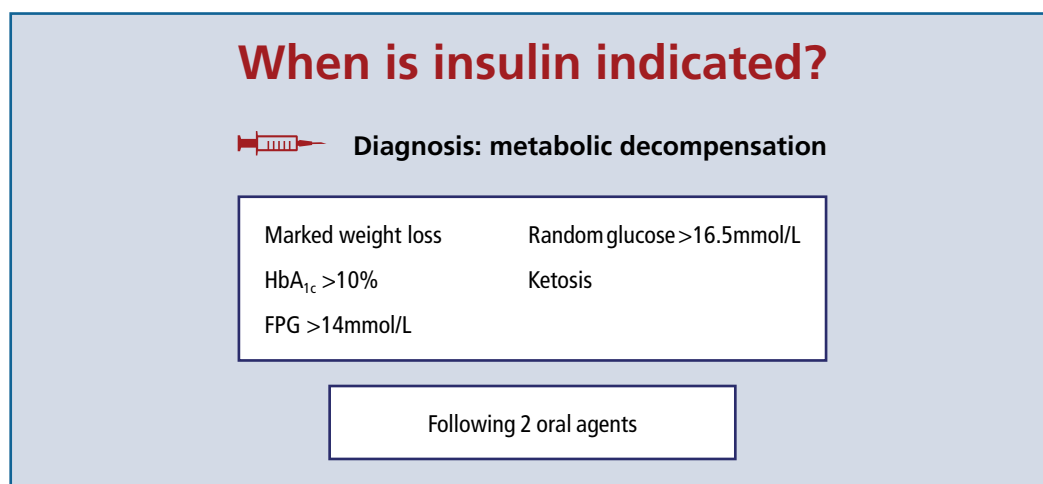


Figure 1. When is insulin indicated?<sup>2</sup>

### Other modules

#### Module 1

To explain when insulin use is appropriate and essential

#### Module 2

To provide clinical guidance on insulin choice in South Africa

#### Module 4

To provide tools and guidance in the effective use of patient-centred insulin regimens

#### Module 5

To provide key clinical messages and tips from expert clinicians that are practical and easy to introduce in daily practice

Table 1. What should we be aiming for in terms of glycaemic control?<sup>2</sup>

Patient type	Target HbA <sub>1c</sub>	Target FPG	Target PPG
Young Low-risk Newly diagnosed No cardiovascular disease	<6.5%	4.0-7.0mmol/L	4.4-7.8mmol/L
Majority of patients	<7%	4.0-7.0mmol/L	5.0-10.0mmol/L
Elderly High-risk Hypoglycaemic unaware Poor short-term prognosis	<7.5%	4.0-7.0mmol/L	<12.0mmol/L

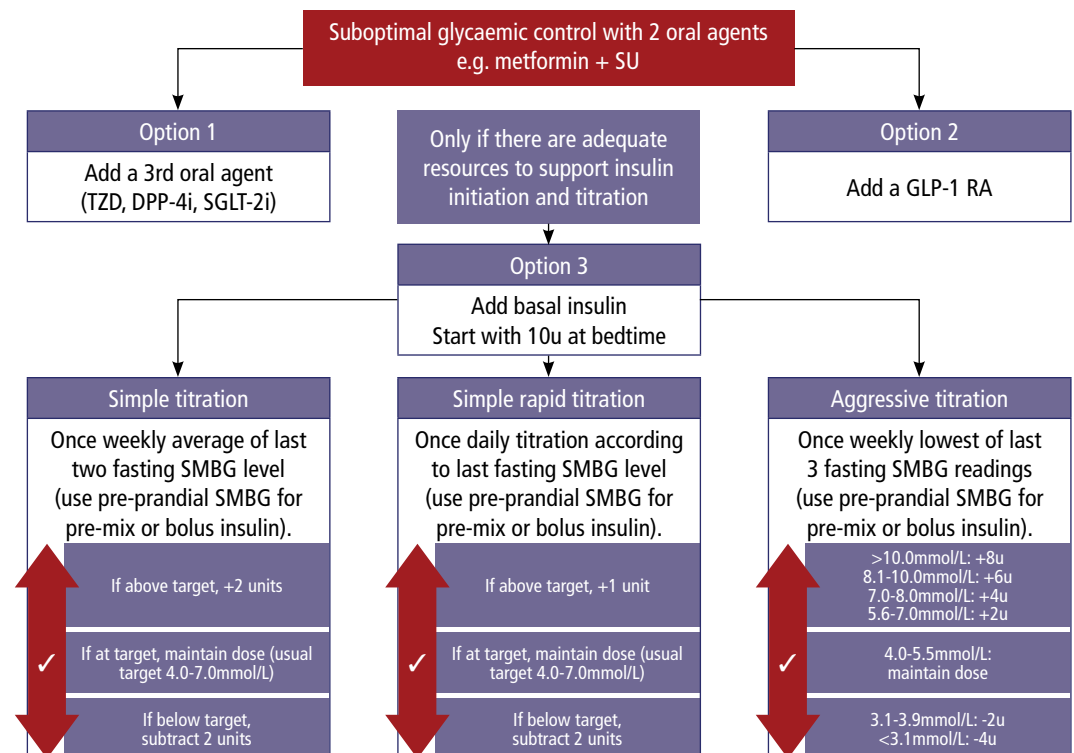
FPG: fasting plasma glucose; PPG: postprandial glucose

## Insulin initiation – choices and dosage

The easiest way to initiate insulin is by adding basal insulin to the patient's current therapy. This approach is also recommended in the insulin therapy options of the latest SEMDSA guidelines. These guidelines make the important point that when newly introducing insulin to a patient, adequate support must be available to guide the patient through the 'journey of insulin'. This includes injection techniques, self-monitoring skills and overcoming fears of weight gain, hypoglycaemia and other real concerns

or imagined myths (Figure 2).<sup>3</sup> Investment of the extra time it takes the clinician to educate the patient at insulin initiation is time saving over the long term, and achieves better glycaemic control with fewer adverse outcomes.

Alternatively, the clinician and patient may prefer a pre-mix insulin for people with fixed meal schedules and a regular carbohydrate intake. More complex regimens may be needed at the outset (Figure 3).<sup>3</sup>

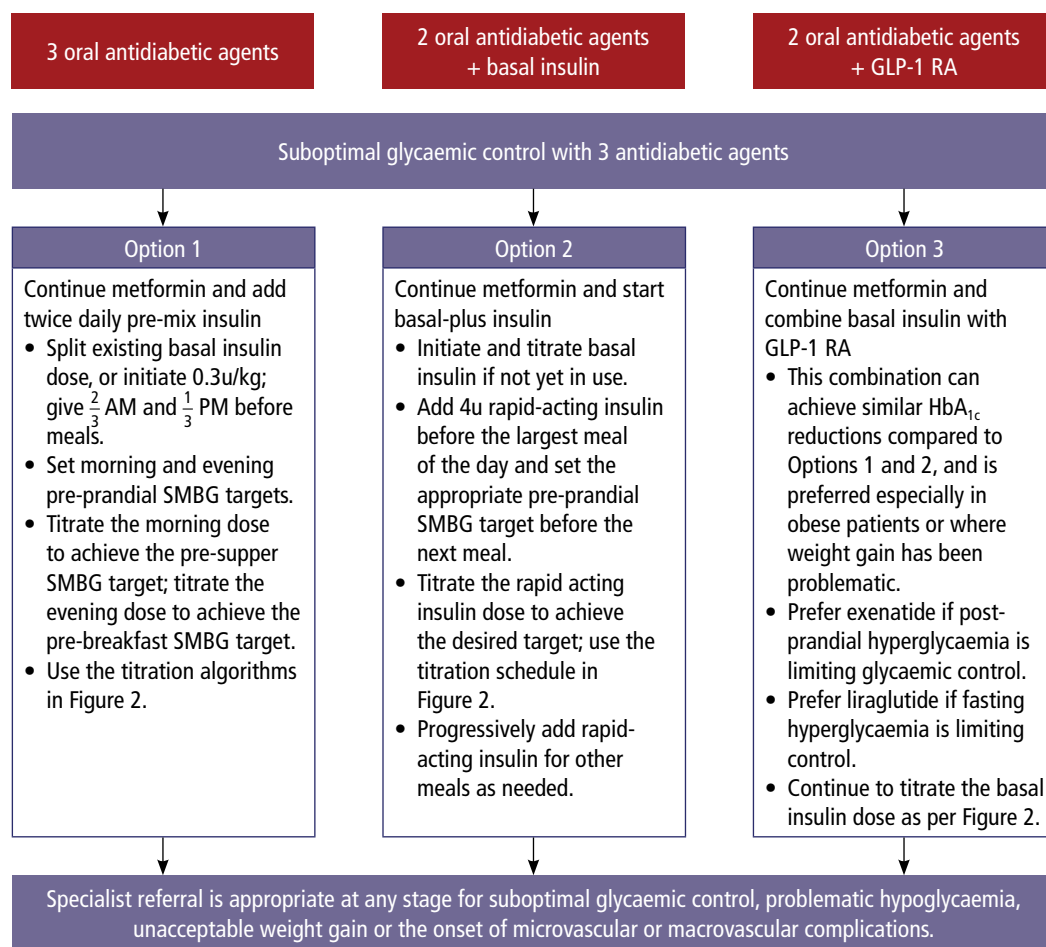


SU: sulphonylurea; TZD: thiazolidinedione; DPP-4i: DPP-4 inhibitor; SGLT-2i: SGLT-2 inhibitor; GLP-1 RA: GLP-1 receptor agonist; SMBG: self-monitoring of blood glucose

\*Do not combine a GLP-1 RA inhibitor or SGLT-2 inhibitor

Figure 2. Initiating and titrating basal insulin therapy<sup>3</sup>

*Investment of the extra time it takes the clinician to educate the patient at insulin initiation is time saving over the long term, and achieves better glycaemic control with fewer adverse outcomes*



GLP-1 RA: GLP-1 receptor agonist; SMBG: self-monitoring of blood glucose

Figure 3. Complex (combination injection) therapies<sup>3</sup>

## What support/advice is needed for the patient at insulin initiation?

It is important that the clinician starts talking about the future possibility of insulin therapy not only when the patient necessarily requires it, but soon after the time of diagnosis.

Patients regularly make a very negative association with starting insulin therapy, often because they have had family members who have suffered a significant complication, such as amputation, shortly after initiating insulin. The complication arising from long-term poor glycaemic control is then blamed on the insulin therapy, which does not have anything to do with it. Therefore, it is essential to actually plant that little seed when starting discussions about diabetes management with the patient.

When a patient reaches the point where insulin therapy is required, the most important aspect is probably that the patient feels comfortable with the injection technique. They need to be able to inject confidently when they walk out after the first consultation, knowing that their fear about insulin is not warranted. Secondly, it is vital to understand there is no point in the patient being on insulin therapy if they are not testing their blood glucose levels appropriately; the patient must understand what the clinician would like them to do in terms of testing, and understand the information they need to guide them in making dose adjustments in their therapy.

## Injection techniques

There are numerous videos with descriptive illustrations to assist the patient with starting and following good injection techniques and, most importantly, minimising the complication of lipohypertrophy using injection rotation.

For the primary care professional guiding patients on best injection practices, a global programme presents useful key recommendations (Table 2).<sup>3</sup>



Click here to  
watch the video

*The aim of using  
basal insulin  
is to achieve  
normalisation of  
the pre-breakfast  
or fasting blood  
glucose*

A useful video is available to view and download of Dr Zane Stevens describing insulin injection technique using a syringe and vial.

**Table 2. Key recommendations on insulin delivery<sup>3</sup>**

- Use the shortest needles (4mm pen and 6mm syringe needles)
- Avoid intramuscular (IM) injections, especially with long-acting insulins, as severe hypoglycaemia may result
- Lipohypertrophy is a frequent complication of therapy and correct site rotation is essential
- Psychological hurdles to insulin injections must be addressed early in diabetes care
- Inappropriate disposal of used sharps poses a risk of infection with blood-borne pathogens – training on effective disposal strategies is very important
- Safe use of the insulin device must be addressed in the training for insulin use.

In addition, BD Education Centre provides five golden rules for injection techniques.

### Golden rules for injection techniques

1. Insulin and GLP-1 RAs must be deposited into healthy subcutaneous fat tissue, avoiding the intradermal and IM spaces as well as scars and lipohypertrophy
2. 4mm pen needles inserted at 90 degrees are recommended for all adults regardless of age, gender or body mass index (BMI). If patients need to use needle lengths >4mm or a syringe, or where the presumed skin surface to muscle distance is less than the needle length, they must use a correctly lifted skinfold to avoid IM injections
3. Recommended sites for injection are abdomen, thigh, buttocks, upper arms:
  - Abdomen within the following boundaries: ~1cm above symphysis pubis, ~1cm below lowest rib, ~1cm away from umbilicus and laterally at the flanks
  - Upper 3<sup>rd</sup> anterior lateral aspect both thighs
  - Posterior lateral aspect of both upper buttocks and flanks
  - Mid 3<sup>rd</sup> posterior aspect of upper arm
4. Detect and avoid injection into areas of lipodystrophy
5. Rotation of injection sites is critically important and can be correctly performed by:
  - Spacing injections within site, approximately one finger's breadth apart
  - Using a single injection site no more frequently than every 4 weeks.



*"I know that in a busy GP practice people do not have the time to be phoning their patients on a daily basis and titrating the insulin, so patients need to have the ability to do so. When titrating insulin, it's really important that patients understand what the targets of their blood sugar are, and this is determined by what the clinician decides the target HbA<sub>1c</sub> should be"*

Dr Zane Stevens

## Self-monitoring – patient input and doctor follow-up

It is vital to explain to patients that self-monitoring is placing the responsibility of glucose control in the patient's hands, because they are the ones who are going to make the day-to-day adjustments of their treatment. The responsibility of the clinician is to explain clearly what they expect the patient to do. For example, if the patient is starting on a basal insulin injection once per day at night before going to bed, the clinician expects them to test their glucose in the morning (Figure 4).

"As a little caveat to that, I often teach my patients who are on basal insulin therapy that at least twice per week they should also monitor what their blood glucose is before they are going to bed because, if you think about it, there are two reasons why a blood sugar might be high in the

mornings; either the dose of the basal insulin was inadequate and the patient's blood glucose continues to rise, or it is as a result of what they are eating at supper time, their sugar is just too high before they are going to bed and therefore they wake up high the following morning."

If the blood glucose before bedtime is in fact already high, and this is translated to a high blood sugar in the morning, then the problem is no longer an ineffective basal insulin dosage but rather the PPG levels which need to be addressed. Another strategy is motivating the patient to eat less carbohydrates with their meal and to adjust the basal insulin therapy accordingly. The aim of using basal insulin is to achieve normalisation of the pre-breakfast or fasting blood glucose.

### Long-acting insulin

	Before breakfast	2hrs	Before lunch	2hrs	Before supper	2hrs at bedtime	Low sugars
Monday	X						
Tuesday							
Wednesday	X					X	
Thursday							
Friday	X					X	
Saturday							
Sunday							

### Mix insulins

	Before breakfast	2hrs	Before lunch	2hrs	Before supper	2hrs at bedtime	Low sugars
Monday	X					X	
Tuesday							
Wednesday	X					X	
Thursday							
Friday	X					X	
Saturday							
Sunday							

### More complex regimens: Long- and short-acting

	Before breakfast	2hrs	Before lunch	2hrs	Before supper	2hrs at bedtime	Low sugars
Monday	X		X		X	X	
Tuesday							
Wednesday	X		X		X	X	
Thursday							
Friday	X		X		X	X	
Saturday							
Sunday							

Figure 4. Outpatient glucose monitoring

## Alternative self-monitoring strategies

If the patient has been started on a pre-mix, rather than a basal, insulin once per day at supper time, monitoring of only the morning blood sugar is necessary.

If the patient has started with a pre-mix insulin twice per day, the practical mantra is to 'test, inject and eat'. Each time that they have breakfast and dinner, they are giving their two injections, testing their sugar, injecting and then eating. The blood glucose values from before supper and before breakfast are used to adjust their treatment (Figure 2).

It is vital that the clinician empower their patient to adjust therapy by themselves. "I know that in a busy GP practice people do not have the time to be phoning their patients on a daily basis and titrating the insulin, so patients need to have the ability to do so. When titrating insulin, it's really important that patients understand what the targets of their blood sugar are, and this is determined by what the clinician decides the target HbA<sub>1c</sub> should be," Dr Stevens stresses. For the majority of patients, the target should be an HbA<sub>1c</sub> of around 7%. In practical terms this means the patient should wake up with a fasting blood sugar that is 4.0-7.0mmol/L, and

that if they are testing two hours after a meal, their glucose levels should still be in single digits.

Patients started on basal insulin are typically told to increase the dosage of their basal insulin by two units every third day, until an optimal morning blood sugar is reached. "So often, a patient is started with ten units of basal insulin at night time and over the next three days, if their blood glucose on average is still higher than seven, this would be increased to twelve units; and the process continued until a normalised fasting blood sugar is obtained."

With pre-mixed insulins, the patient would try to achieve the same fasting blood glucose of 4.0-7.0mmol/L before breakfast and if that remains high, it means that the evening dose needs to be increased. If the blood glucose before dinnertime remains higher than the target (>10mmol/L), the morning dose needs to be increased appropriately until both of the levels are at target. These actions are all determined by the agreed target HbA<sub>1c</sub> and the patient needs to know and understand what they are testing day-to-day.

*For the majority of patients, the target should be an HbA<sub>1c</sub> of around 7%. In practical terms this means the patient should wake up with a fasting blood sugar that is 4.0-7.0mmol/L, and that if they are testing two hours after a meal, their glucose levels should still be in single digits*

## Indications for referral

Primary care practitioners are key to successfully managing T2DM patients.

Red flags that should prompt referral to either an endocrinologist or a specialist clinic are:

- Glycaemic targets are unmet with basal insulin doses >0.8u/kg to >60u daily
- If glycaemic targets are unmet after 6 months of treatment
- If the patient is not able to adjust to intensification to a basal-bolus regimen, specialist intervention may help to overcome this hurdle
- Glycaemic targets are unmet with pre-mix insulin doses >60u twice daily.

# Case study

The CPD questions are based on applying the principles of insulin initiation.

**Patient:** Preesha, 50-year-old Indian female

## Reason for visit

- A T2DM patient for 9 years
- Is currently expressing concern about her glucose control
- Her elder brother was referred to a nephrologist 3 months earlier with kidney problems and he is devastated; she is worried that the same thing could happen to her
- She has completely changed her life-style over the past 10 weeks, watching her diet and walking 30 minutes daily
- Preesha currently weighs 90kg, having lost 9kgs

## Current therapy

- Metformin 1g bid
- Vildagliptin 50mg bid
- Gliclazide MR 120mg once daily
- Atorvastatin 20mg daily
- Ramipril 10mg daily

## Investigations

- HbA<sub>1c</sub> 8.3%
- FBG 9.8mmol/L
- Serum creatinine 77µmol/L
- eGFR 73ml/min/1.73m<sup>2</sup>
- LDL-cholesterol 1.82mmol/L
- Potassium 4.2mmol/L
- Albumin-to-creatinine ratio (ACR) 1.8mg/mmol

## Home readings for blood pressure

- 127/78mmHg
- Her blood tests were done a week prior

## Case study questions

1. What is the HbA<sub>1c</sub> target for this patient?

- A. 7%                      B. >7%                      C. <7%

### Expert comment

The new Clinical Guidelines Committee of the American College of Physicians recommends that patients with T2DM should be treated to achieve an A<sub>1c</sub> between 7% and 8%.

2. What alternative therapies can be used to reach the desired target?

- A. Any oral agents: SGLT-2 inhibitor or pioglitazone                      C. Insulin
- B. Substitute DPP-4 inhibitor with a GLP-1 RA                      D. None of the above

### Expert comment

While clinical considerations are always subject to patient preference, this patient is motivated to avoid target organ disease and she will benefit to a greater extent with insulin than any of the other antidiabetic agents, none of which would achieve the desired HbA<sub>1c</sub> lowering of >1.5%.



3. The decision is to initiate insulin. Which insulin is preferable?

A. Twice-daily pre-mix insulin

B. An analogue basal insulin

### Expert comment

The value of a basal insulin in this situation relates to less weight gain and less hypoglycaemia. In the '4-T' trial, weight gain was lower than with biphasic insulin twice-daily and prandial insulin.

4. What would be the starting dose of basal insulin at bedtime?

A. 10u

B. 15u

C. 8u

### Expert comment

The SEMDSA guidelines advise a starting dose of 10u at bedtime, ensuring that patient support from the clinician or allied healthcare staff is available.

5. On self-monitoring of her blood glucose following basal insulin (analogue), Preesha's fasting blood glucose levels are shown below. Based on the SMBG what would you advise?

	Pre-breakfast	2hrs	Pre-lunch	2hrs	Pre-dinner	2 hours
Mon	10					
Tues	12					
Wed	9					
Thurs						
Fri						
Sat						
Sun						

A. Monitor for a further week

D. A and B

B. Increase the basal insulin dosage by 2 units

E. A and C

C. Decrease the basal insulin dosage by 2 units

After this intervention, Preesha is asked to monitor pre-breakfast and 2-hours after dinner levels for the next few days. Her chart now shows:

	Pre-breakfast	2hrs	Pre-lunch	2hrs	Pre-dinner	2 hours
Mon	10					
Tues	12					
Wed	9					
Thurs	8					12
Fri	7					11
Sat	8					
Sun						

## 6. What in your view is the next best step?

- A. Increase the basal insulin by 2 units  
 B. Decrease the basal insulin by 2 units  
 C. Add a mealtime insulin with dinner  
 D. A and C  
 E. B and C

## Expert comment

This profile demonstrates how the glucose levels fall overnight, suggesting that the problem is not a deficiency of basal insulin but rather a post-dinner rise in blood glucose. A step-up approach of adding a prandial short-acting insulin would work well.

## 7. The following week her pre-breakfast levels are in single digits: Mon 5.6, Tues 7.1, Wed 6.5, Thurs 5.8. When do you want to see Preesha again?

- A. 1 month  
 B. 3 months  
 C. 6 months

Preesha comes for a consultation 3 months later. Her pre-breakfast levels are <8mmol/L on 54u basal insulin, but her HbA<sub>1c</sub> is still above target at 7.9%.

8. Why is the HbA<sub>1c</sub> not yet at target?

- A. Her PPG levels are low  
 B. She has gained weight  
 C. Her PPG levels are high

## Expert comment

The most likely reason is that her PPG levels are high.

Preesha then refers to her diary and points out that she has been testing her blood glucose after lunch (her main meal everyday over the past week.) Her blood glucose after lunch is 10.3-13.2mmol/L. She has been doing this because she is not losing weight anymore and is in fact 1kg heavier and is concerned about this. Insulin intensification strategies are now needed.

## References

Click on reference to access the scientific article

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