Intensifying insulin

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

Dr Adri Kok
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Click here to watch the video

You need to watch the videos in order to complete the CPD Questionnaire

Module 4: Intensifying insulin

Objectives of this module

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

Why is intensification of insulin therapy important?

Following initiation with insulin, the intensification of insulin therapy is key to maintaining long-term glycaemic control and ensuring that complications do not develop. Best practice demands that the clinician continues to focus on patient support and patient education throughout their management of this chronic condition. 'Clinical inertia' should be avoided and mutually agreed HbA_{1c} targets should drive a diligent approach to treatment.

There is considerable evidence of the detrimental effects of delaying insulin intensification; a UK study showed that only 31% of patients requiring insulin intensification actually received additional therapy, despite their HbA_{1c} being above target (≤7%).[1]

In Brazil, with its comparable economic situation to South Africa, 60% of patients with an HbA_{1c} >8% and on insulin therapy did not benefit from further intensification during the first two years following initiation of insulin therapy and titration to first appropriate level.[2]

Pressures on doctors may prevent diabetes care processes from happening, but appropriate use of available time, the involvement of support nurses and educational resources can all be harnessed to deliver better care without putting undue pressure on the responsible clinician.

This module will concentrate on providing practical clinical cues to further required action for the achievement of better glycaemic control in individual patients.

How to intensify insulin therapy?

Four clinical scenarios develop, depending on which type of insulin was selected at initiation of therapy.

Other modules

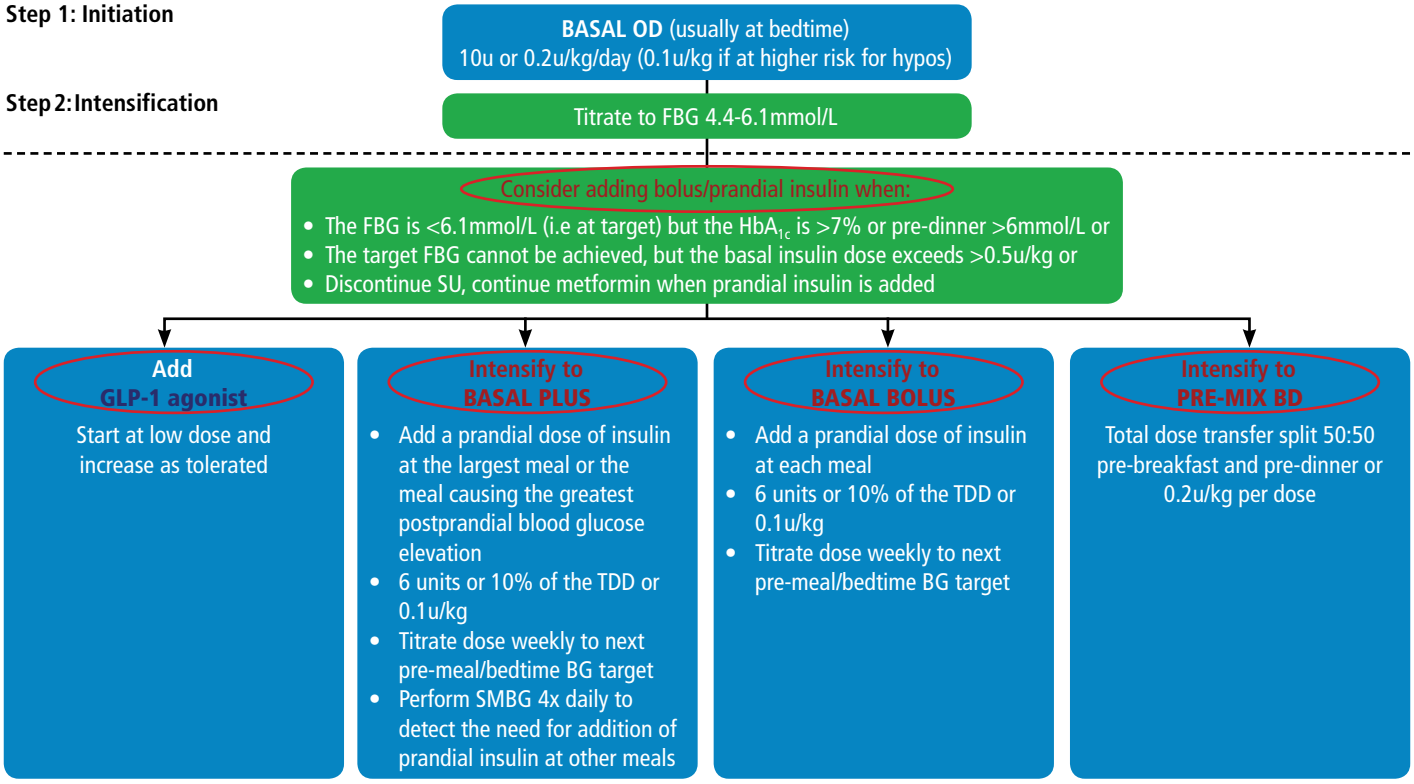
Module 1
To explain when insulin use is appropriate and essential

Module 2
To provide clinical guidance on insulin choice in South Africa

Module 3
To support clinicians and build confidence in initiating insulin and intensifying therapy

Module 5
To provide key clinical messages and tips from expert clinicians that are practical and easy to introduce in daily practice

Intensifying from a basal only regimen



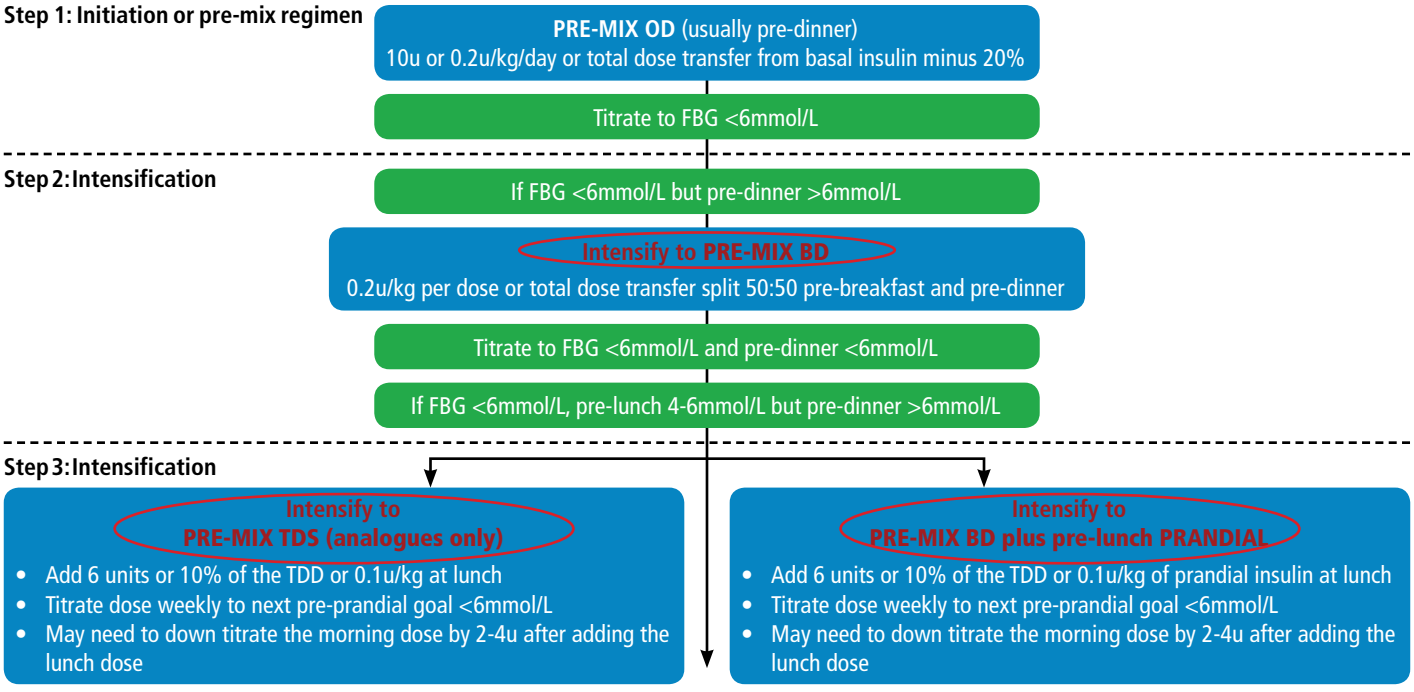
Source: Malaysian Endocrine & Metabolic Society, 2011

FBG: fasting blood glucose; SU: sulphonylurea; GLP-1: glucagon-like peptide-1; TDD: total daily dose; BG: blood glucose; SMBG: self-monitoring blood glucose

Consider: If HbA_{1c} >48-53mmol/mol (6.5-7.0%) after 3 months despite titrating prandial doses, or prandial doses >30u/meal, consider:

- Resuming optimisation of basal insulin up to 0.7u/kg
- Perform 7-point SMBG profile
- Relook at barriers to glycaemic control

Intensification of pre-mixed regimens

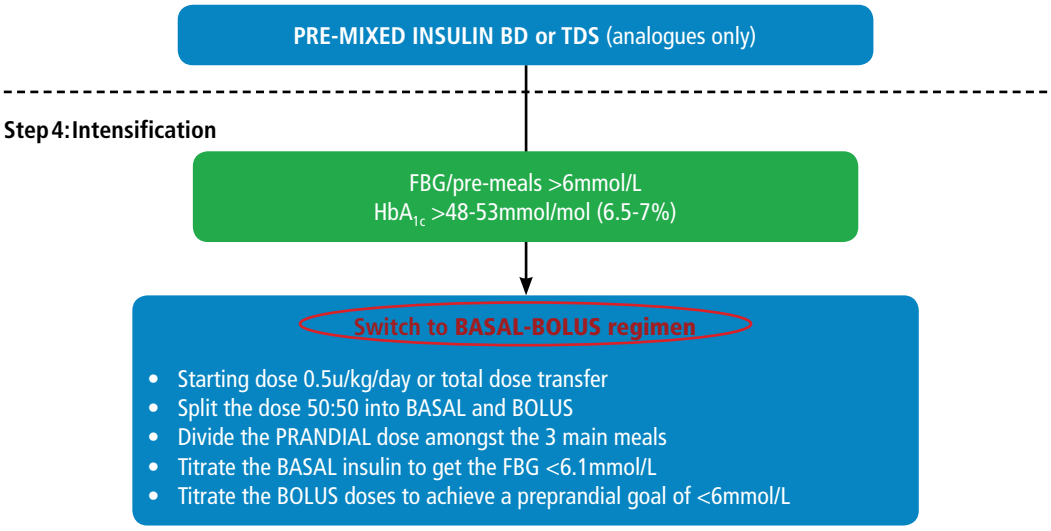


Source: Malaysian Endocrine & Metabolic Society, 2011

FBG: fasting blood glucose; TDD: total daily dose

Consider: Adding a prandial short-/rapid-acting insulin at lunch if additional flexibility is needed. Remember that pre-mix regimens are suitable for people with fixed meal schedules and repetitive carbohydrate intake.

Switch from pre-mixed regimen to basal-bolus

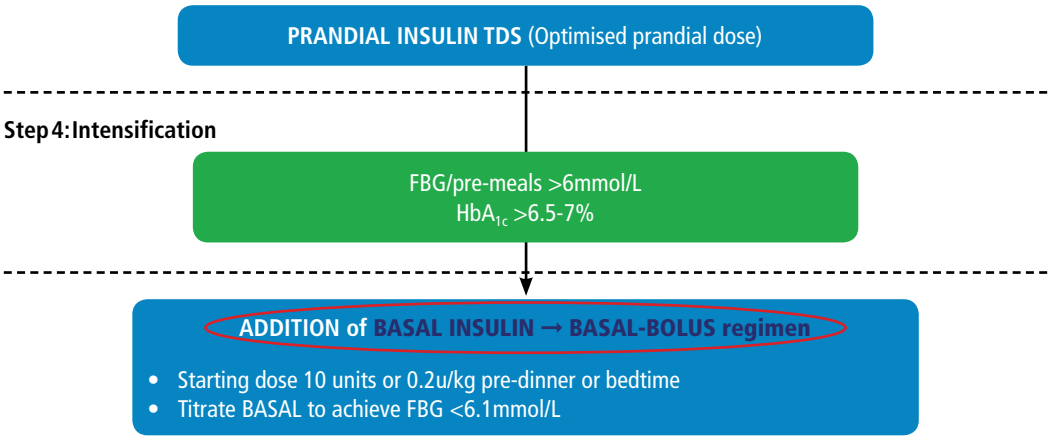


Source: Malaysian Endocrine & Metabolic Society, 2011

FBG: fasting blood glucose

Consider: Some individuals, especially those with starting HbA_{1c} >9% (suggestive of low β-cell reserve), may be initiated on a pre-mix BD regimen. This may be more suitable than a basal-bolus regimen if they have a fixed meal plan and would like to reduce the number of injections per day. If the pre-mix regimen is not working or they would prefer more flexibility, then a basal-bolus regimen is ideal.

Intensification from prandial regimen to basal-bolus regimen



Source: Malaysian Endocrine & Metabolic Society, 2011

FBG: fasting blood glucose

Consider: Prior to insulin initiation and after collection and analysis of the SMBG pattern, some patients may have normal FBG but isolated postprandial glucose elevations and an elevated HbA_{1c} - a prandial only insulin may be appropriate as a starting regimen in these individuals.

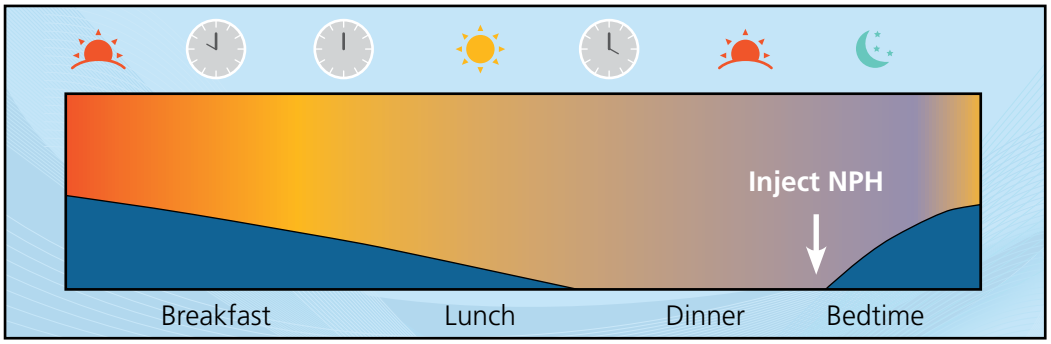
Optimising the insulin dose

There are five key elements to optimising the insulin dose:

1. Set a target HbA_{1c} and other glucose levels
2. Collect appropriate data
3. Analyse the data measuring all the interventions
4. Adjust the dose and support patient with concerns
5. Remeasure HbA_{1c} and other targeted glucose levels.

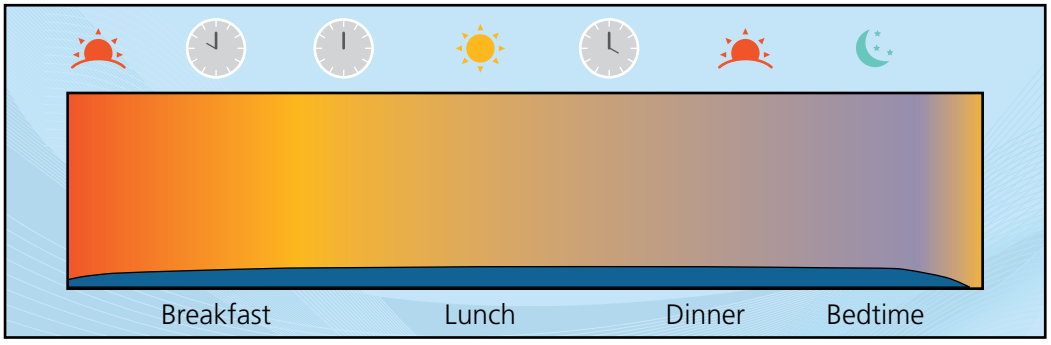
Visualisation of the prescribed regimens can be a helpful prompt to the points of titration, monitoring and intensification.

Basal only: human intermediate



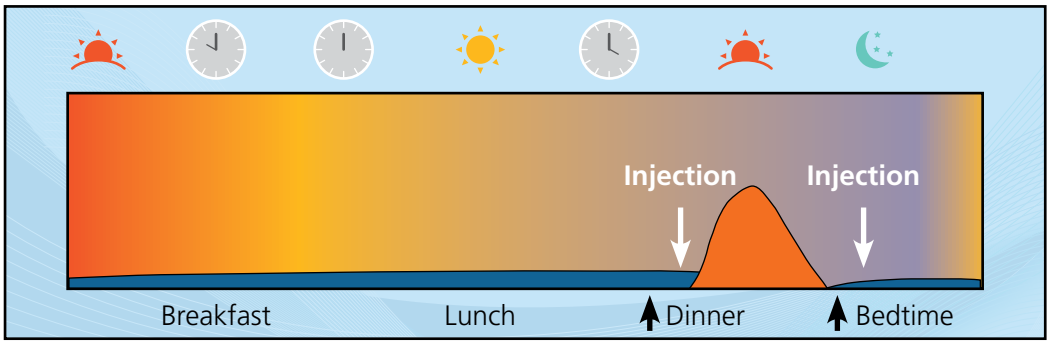
- Requires re-mixing
- Pronounced peak 4-6 hours after injection
- May require a snack to avoid hypoglycaemia
- Titrate to target FBG avoiding evening hypoglycaemia
- Full testing profile
- Consider intensification or added daytime support

Basal analogues



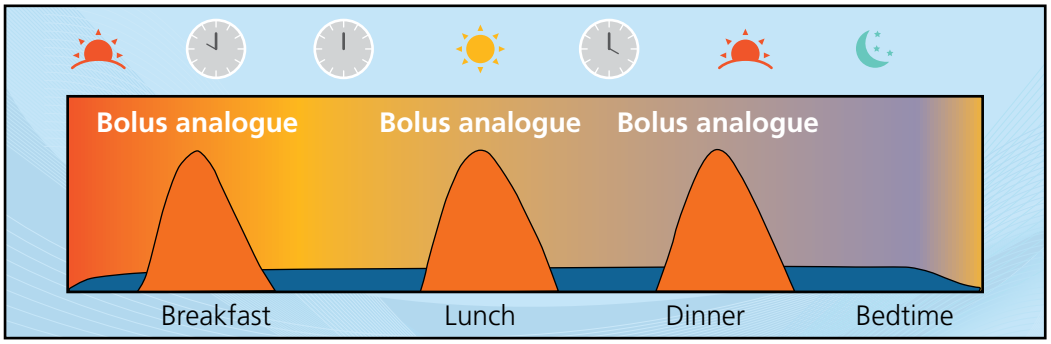
- Reduced risk of hypoglycaemia
- Structured monitoring throughout the day
- Basal only can be titrated to either nocturnal hypoglycaemia or 1u/kg/day, most doctors would titrate to 50u max (not 1u/kg/day) and consider a **regimen change** by adding a prandial bolus insulin
- Options from here are either to go to pre-mix once daily or basal plus
- Oral medications are typically only discontinued after basal plus or pre-mix BD
- **Titration** is to FBG
- Regimen change is required if FBG cannot be brought to target

Basal plus: glargine plus analogue



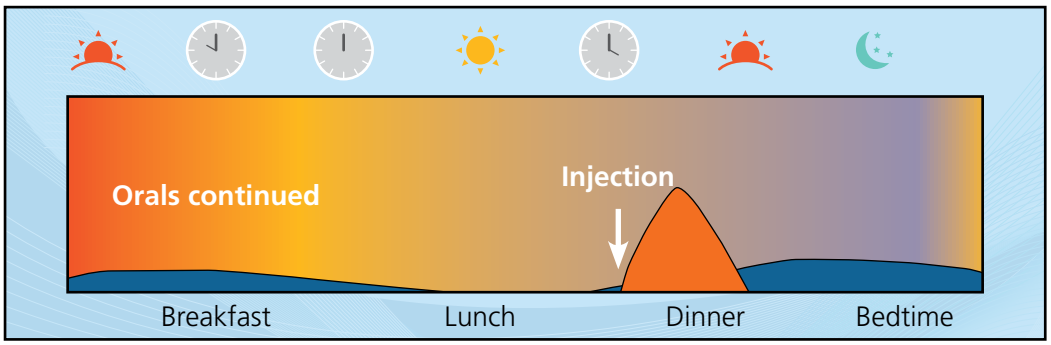
- The basal **regimen is changed** by adding a bolus (rapid-acting insulin) at the largest meal of the day, often dinner or if postprandial readings are being collected then at the meal with the biggest rise
- **Titration** is to FBG
- Failure would entail a **regimen change** to include bolus insulin at another meal
- Postprandial FBG not achieved or not within range at end of day

Basal bolus with glargine once daily + analogue



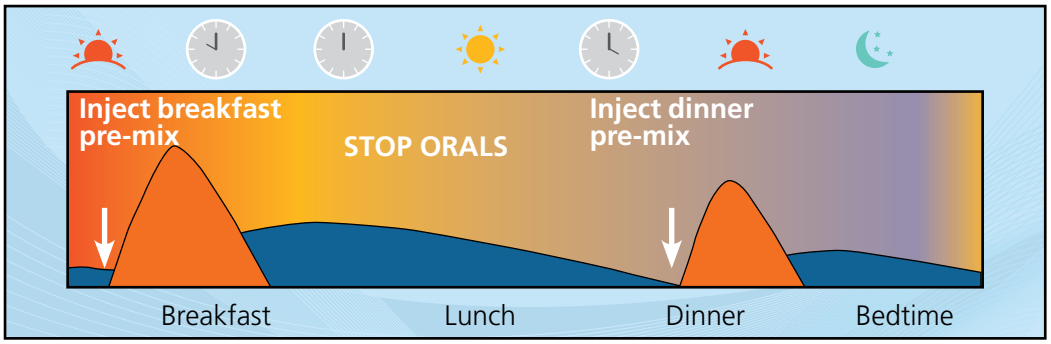
- Control at and between meals
- Switch to pre-mix if injection load too great. Alternatively further dose intensification
- **Titration** is to pre-lunch, pre-dinner and pre-breakfast readings
- Failure would entail a **regimen change** to include a bolus at the remaining meal of the day

Analogue pre-mix once daily



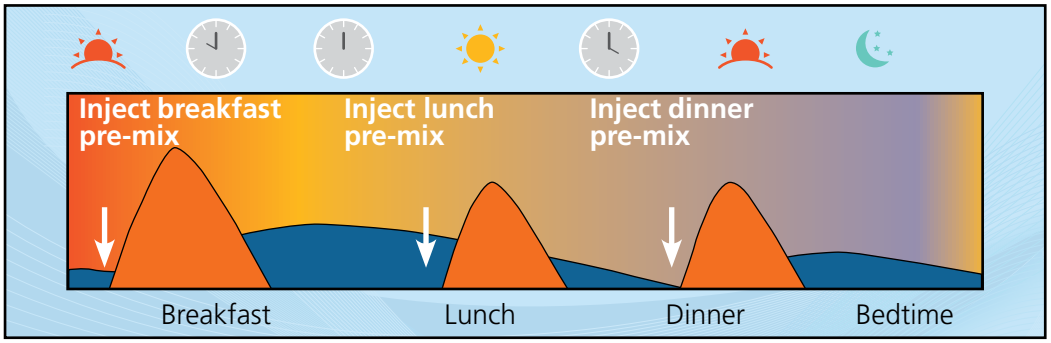
- **Titration** is to FBG
- This choice of pre-mix versus basal plus is provider and country dependent
- Pre-dinner readings above target is an indication to **change regimen** by adding a pre-mix dose at breakfast
- Initiate at dinner time
- Achieve FBG minus hypoglycaemia

Analogue pre-mix twice daily



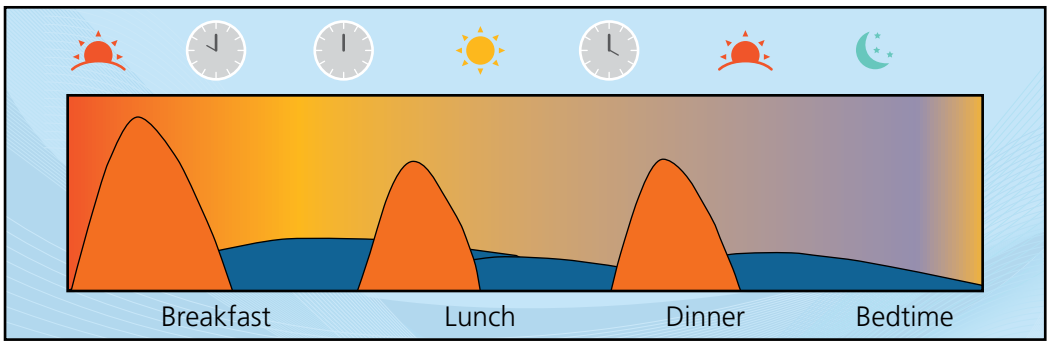
- **Titration** is to pre-breakfast and pre-dinner readings
- **Regimen** may need to be changed to add a lunch bolus dose to get dinner to target
- This could be first choice for insulin initiation if the HbA_{1c} is >9%
- Added daytime insulin required

Analogue pre-mix twice daily plus meal analogue

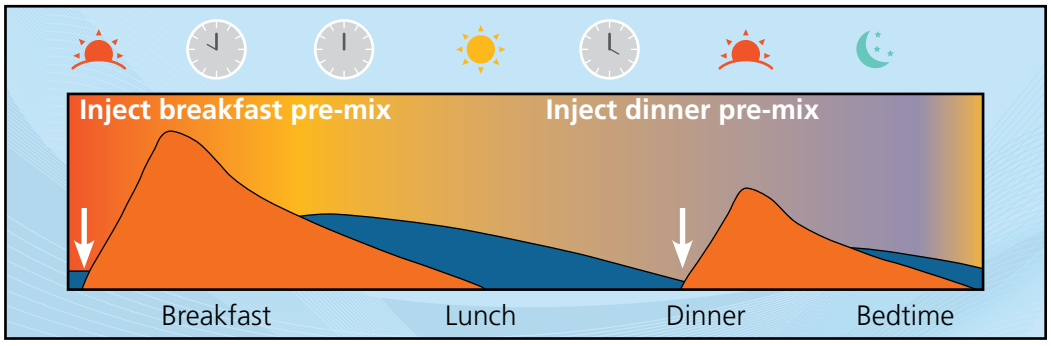


- Add another pre-mix injection at lunch
- Monitor breakfast, lunch, dinner and bed time

Analogue pre-mix three times daily



Pre-mix human insulin twice daily



- Peaks at about 3 hours = increased risk of delayed hypoglycaemia
- Inject 30 mins prior to each meal
- Fixed injection schedules
- Monitoring breakfast, lunch and dinner

Glycaemic targets – including the blood glucose levels that match the HbA_{1c}

Glycaemic targets in terms of glycated haemoglobin, as measured by the HbA_{1c} assay, is widely accepted. The relationship between HbA_{1c} and average glycaemia was established many years ago but was hampered by the then limited measurement of glucose value. More recent estimates have been based on at least 2 days of continuous glucose monitoring, with 7-point daily SMBG performed at least three days per week.[3] This widely accepted relationship is shown in Table 1.[4]

Table 1. Average fasting and postprandial glucose levels in relation to HbA_{1c}

Target HbA_{1c}	Target FBG	Target PPG
<6.5%	4-7mmol/L	<8mmol/L
<7%	4-7mmol/L	<10mmol/L
<8%	4-7mmol/L	<12mmol/L
FBG: fasting blood glucose; PPG: postprandial glucose		

A further refinement has been to use these A_{1c}-derived average glucose (ADAG) study results to determine the average blood glucose at pre-meal, post-meal and bedtime to a variety of HbA_{1c} targets. These results can help both patients and clinicians set realistic day-to-day SMBG schedules to achieve individualised HbA_{1c} goals (Table 2).[4]

Table 2. Average glucose levels for specified HbA_{1c} levels[4]

	HbA_{1c} <7.0% (IFCC 53mmol/L)	HbA_{1c} <7.5% (IFCC 58mmol/L)
Mean fasting blood glucose (range) mmol/L	8.0 (7.4-8.6)	8.6 (7.9-9.3)
Mean pre-meal blood glucose (range) mmol/L	7.8 (7.4-8.2)	8.7 (8.3-9.1)
Mean post-meal blood glucose (range) mmol/L	8.9 (8.6-9.3)	9.7 (9.3-10.2)
Mean bedtime blood glucose (range) mmol/L	8.6 (8.0-9.1)	10.0 (9.1-10.8)
IFCC: International Federation of Clinical Chemistry		

Importantly, the Diabetes Control and Complications Trial (DCCT) related the relative risk of progression of diabetic complications by mean HbA_{1c}, giving the clinician and patient confidence in the validity of the chosen parameters and targets.

Testing and glucose control

Everyday T2DM patients are coping with inter-day insulin variability, insulin resistance and the complex pathophysiology of diabetes (Figure 1).

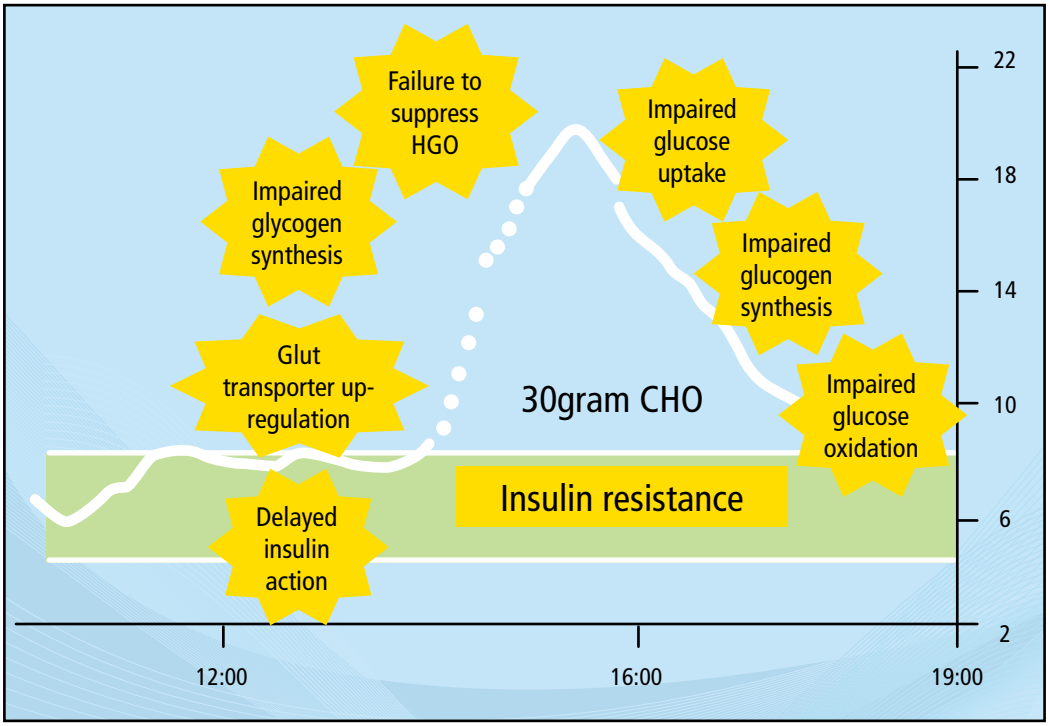


Figure 1. Structured testing or continuous glucose monitoring

Structured testing or continuous glucose monitoring can build confidence and an ability to manage glucose levels to desired targets. Diabetes management requires testing and different insulin regimens require different testing protocols (Table 3).

Table 3. SMBG protocols recommended for different insulin regimens

	Breakfast		Lunch		Dinner		Bedtime	2am
	Pre-	Post-	Pre-	Post-	Pre-	Post-	Pre-	
Basal only	x				O		O	
Basal plus	x				x	x		
Basal-bolus	x	O	x	O	x	O	x	
Pre-mix OD (dinner)	x				x		x	
Pre-mix human BD	x		x		x		x	O
Pre-mix analogues BD	x		x		x		x	
Pre-mix analogues TDS	x	O	x	O	x	O		

Three consecutive days of blood glucose testing (x) is required for pattern recognition and dose adjustment. Occasional PPG readings (o) are beneficial when fine-tuning prandial dosages and when documenting PPG glucose elevations.

There is a disconnect between the information the healthcare professional wants to know from testing and why the patient performs the tests at a particular time (Table 4). This can lead to a biased view as patients may tend to test when they 'feel funny'. Nonetheless, research has shown that physician-led intervention based on self-monitoring does work,[5] and leads to significantly improved glycaemic control and facilitates intensification efforts. This is true regardless of the sophistication of the glucose monitoring system used by the patient, e.g. SMBG measurements, ambulatory glucose profile (AGP) monitoring and/or real-time continuous glucose monitoring. [The ADVANCE programme hosted on the deNovo Medica site adds further insight on using testing optimally in clinical practice – link to Insulin Therapy – Surfing the Curve]

Table 4. Why test?

Healthcare professionals	Patients
• Collect adequate BG data for analysis • Hypothesis testing » Is there dysglycaemia? » Is the FBG at target? » Is there postprandial dysglycaemia? • Requires SMBG at specific times	• What is my blood glucose right now? • I am feeling funny » Am I high or low? • I need to exercise • I need to drive a car • I want to know what this food did to my BG • Testing is often random and inadequate for medication or lifestyle adjustments

References

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