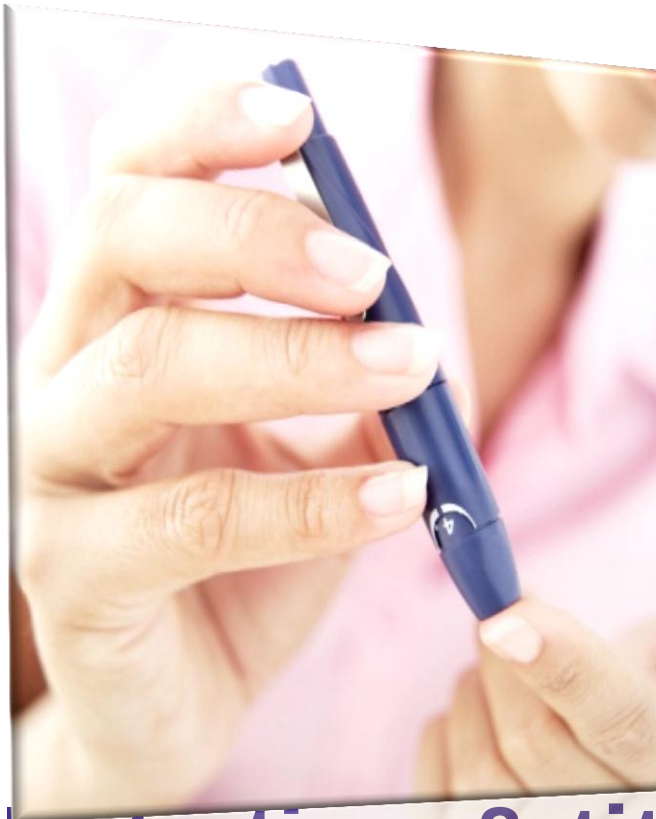




Insulin Leadership Summit

THE FUTURE OF TYPE 2 DIABETES IN PRIMARY CARE FROM SANOFI-AVENTIS



Initiating & titrating insulin & switching in General Practice

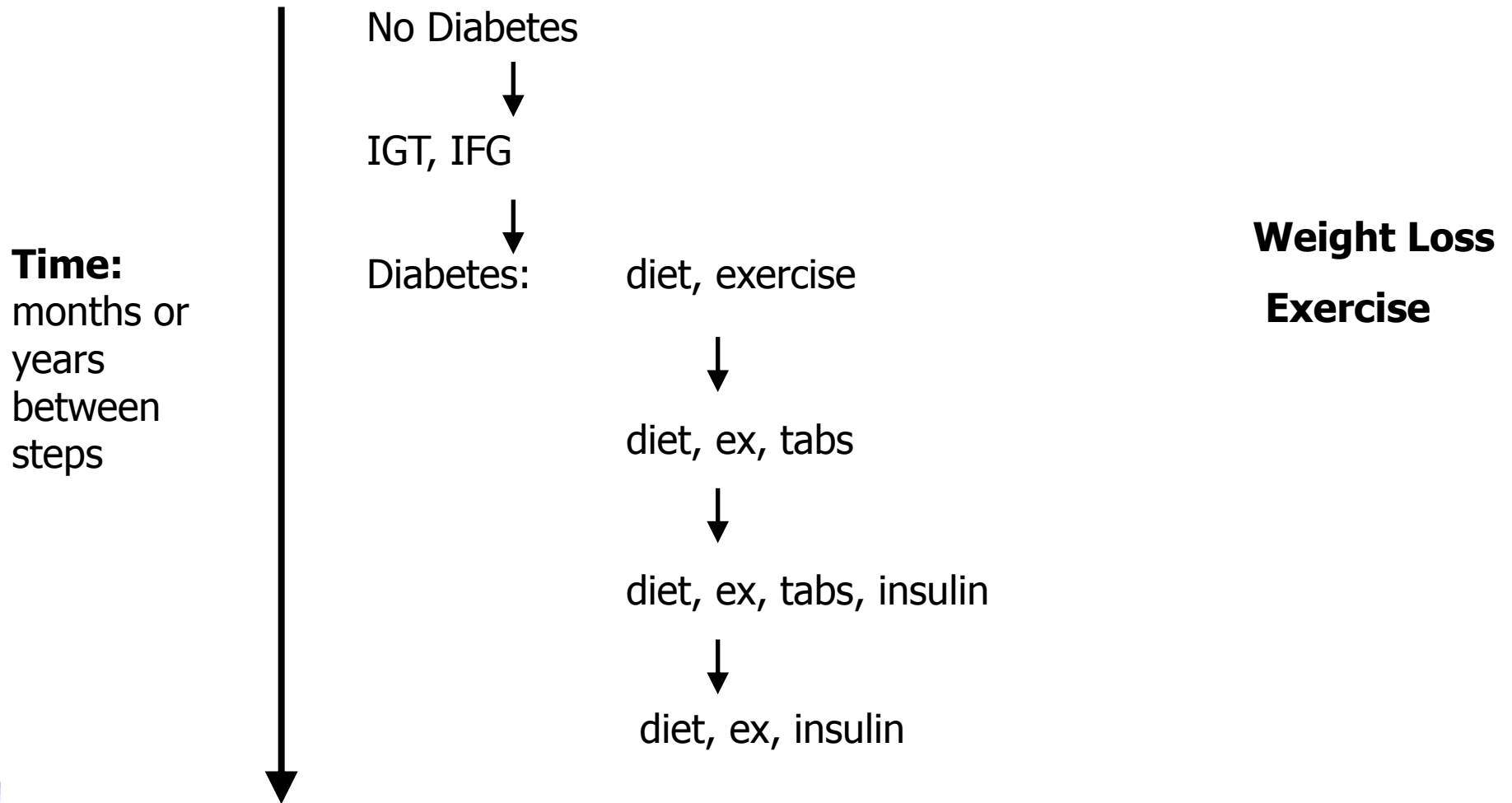
Workshop 1

Workshop goal

To make participants
comfortable in the timely
initiation
and
titration of insulin



Progression of Type 2 Diabetes



Linda

**T2D
6 years**



Linda

- ☆ 51-year-old pathology laboratory technician (works day shifts)
- ☆ Presents for annual review of her T2D following a reminder letter triggered by the diabetes recall system
- ☆ Has completed the routine tests requested on the pathology slip that was included with the reminder letter in time for this visit
- ☆ Diagnosed with T2D 6 years ago
- ☆ Married with two sons in secondary school



History (1)

- ☆ You have managed Linda's diabetes on and off since diagnosis
 - Her oral hypoglycaemic agents (OHAs) have been slowly increased to get better control

- ☆ Linda checks blood glucose most days — mainly first thing in the morning; occasionally before dinner
 - Comments that her 'morning test' (i.e. fasting blood glucose [FBG]) is usually well over 8 mmol/L)



History (2)

- ☆ Retinal screening 2 months— no problems found
- ☆ Non-smoker who drinks alcohol at weekends
 - A few Friday night drinks with work colleagues; occasional wine on Saturday evenings
- ☆ Led a sedentary life prior to diabetes diagnosis but has become more active with your help:
 - Regular yoga class once a week
 - Organises walks with friends once a week



Examination

Height: 1.60 m

Weight: 84 kg

BMI: 33 kg/m²

Waist: 99 cm

BP: 135/90 mmHg

Feet : Sensation adequate, pulses easily felt

Urinanalysis: No abnormalities noted



Pathology results

HbA _{1c}	(99 mmol/mol)(11.2%)
TC	4.3 mmol/L <5
TG	2.1 mmol/L <2
HDL	1.1 mmol/L >1
LDL	2.7 mmol/L <3.4
eGFR	>60 mL/min
ACR	4g/mmol <3.5
Microalbuminuria	40 mg/ I <30

Medications

Metformin	1000 mg bd
Gliclazide	160 mg bd
Atorvastatin	40 mg daily
Cilazapril	5 mg daily

5 year CVD risk is 5-10%



Reviewing A1C target

You previously set an A1c target of ≤ 53 mmol/mol (7%) with Linda, but her A1c has been slowly creeping up.

Would you revise Linda's A1c target at this point?

1. Yes, I would give her an interim target of 64 mmol/mol
2. No, an A1c of ≤ 53 mmol/mol is still appropriate
3. No, leave for now and review later
4. Not sure

Setting an A1C target

- ☆ 11mmol/mol drop or 1% fall in A1C reduces microvascular complications by 37%,¹ but risk of:²



- Hypoglycaemia
- Weight gain (approx 2kg)



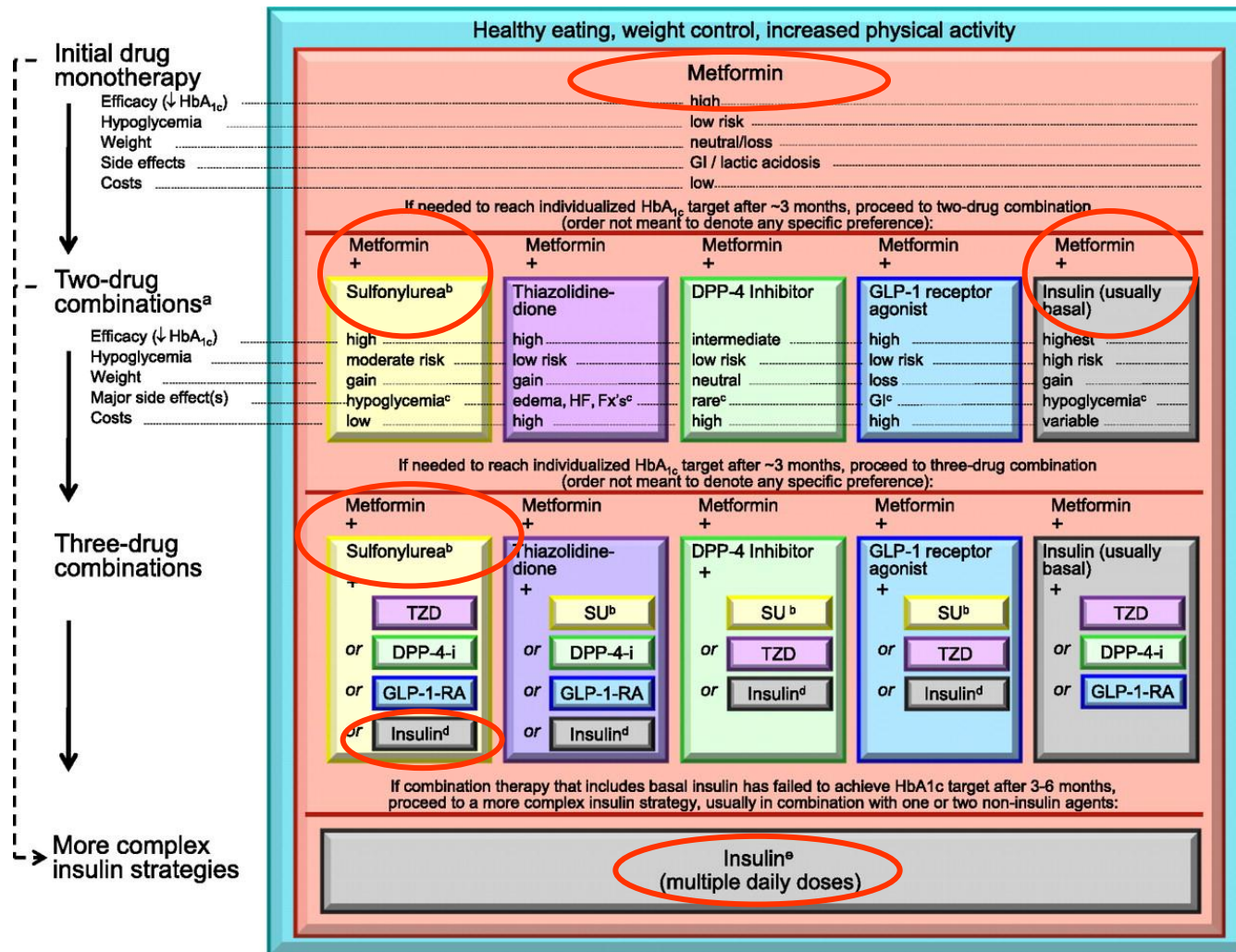
Improving glycaemic control

You decide that an A1C target of ≤ 53 mmol/mol is still appropriate for Linda and discuss with her the best option for improving her glycaemic control.

What treatment change would you recommend to Linda at this point?

1. Add acarbose to existing regimen
2. Add glitazone to existing regimen
3. (Add exenatide or sitagliptin to existing regimen)*
Not Funded in NZ
4. Start insulin

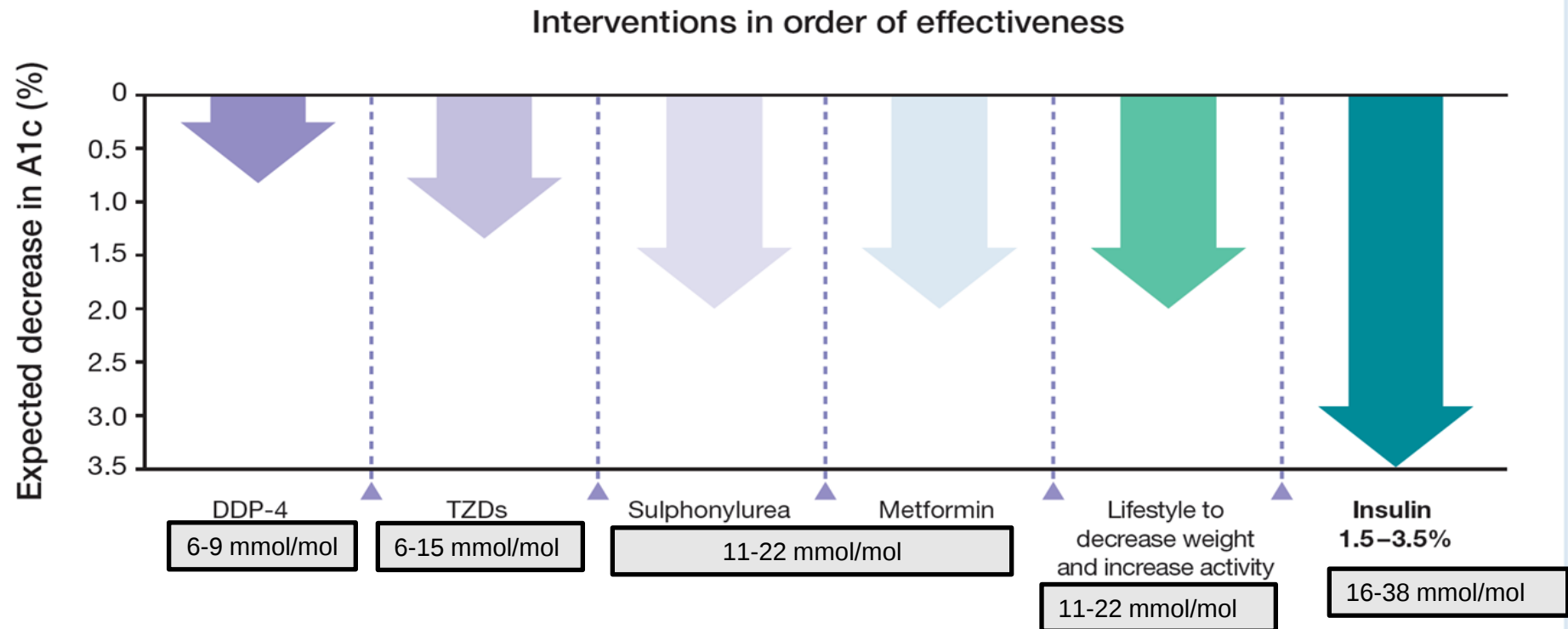
Position Statement ADA/EASD 2012



Inzucchi S E et al. Dia Care 2012;35:1364-1379

HbA1c decrease by agent

A1c lowering potential of individual therapeutic options²



Adapted from Nathan *et al.*, 2009. DDP-4 = Dipeptidyl peptidase-4 inhibitor. TZDs = Thiazolidinedione.

Initiating insulin therapy

You think you need to start Linda on insulin because of her very elevated A1c, however you decide to check a few other things first.

What else do you need to check before starting insulin therapy?

1. That the patient is compliant with all lifestyle measures and medication and whether any modifications could improve glycaemia
2. Is she into Morning tea and afternoon snacks, large carb portions? V drinks ??? Fizzy drinks ??
3. Any possible secondary causes of hyperglycaemia
4. All of above
5. Nothing else

When to introduce insulin therapy

A1C persistently above target



Lifestyle

Patient compliant with agreed modifications?
Any further modifications that can be considered?

Oral hypoglycaemic medication

Is patient taking as prescribed?
Can these be maximised further?

Secondary causes for hyperglycaemia?

Medications (e.g. contraceptive pill, thiazides, beta-blockers, oral corticosteroids) Medical conditions (e.g. hyperthyroidism, urinary or dental infections, occult malignancy)



A1C still above target – Initiate insulin

Diabetes/insulin education

Education on injecting insulin, BGL monitoring, hypos, activity/diet and life with insulin is essential to prepare patients for insulin therapy. Do you do it all yourself or engage other healthcare professionals to assist you? You discuss your plan with Linda and organise this through a Team Care Arrangement.

In your current practice, how would you educate Linda?

1. Do it all yourself
2. Refer to a Specialist/DNS
3. Engage your practice nurse
4. Engage your practice nurse and a DNS
5. Other

Selecting an insulin

You decide to start Linda on insulin and discuss the different insulin profiles with her.

Which insulin would you recommend for Linda and why?

1. Rapid-acting insulin to the meal with the highest preprandial BGL
2. Intermediate-acting insulin in the morning or night
3. Insulin premixed for ease of use
4. Basal insulin to reduce both postprandial and fasting BGLs

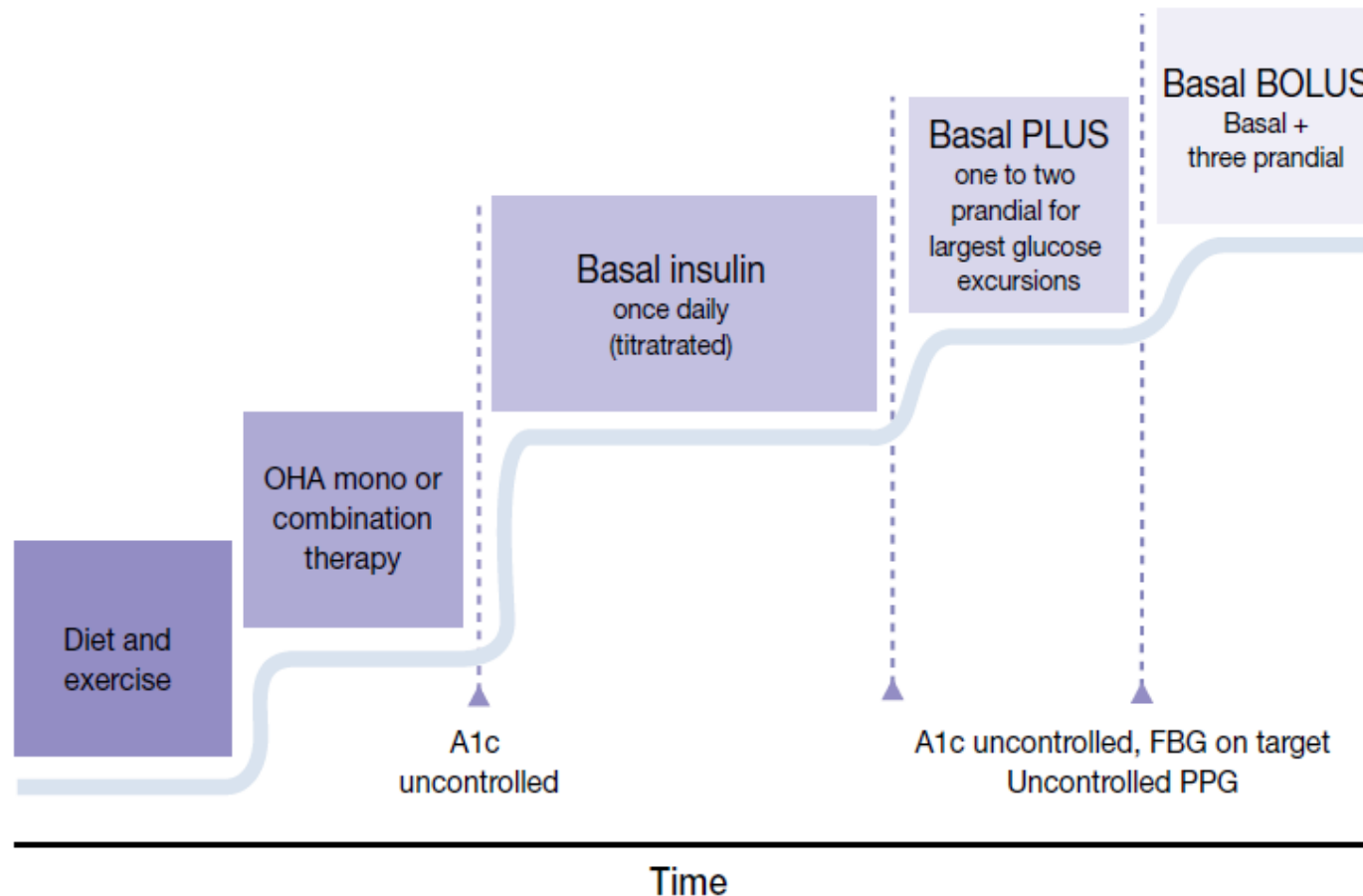
Selecting an insulin

RACGP & ADA/EASD guidelines state...

- ☆ Start with single daily dose (10 units) of bedtime intermediate-acting insulin or morning or bedtime long-acting insulin^{1,2}
- ☆ Rapid-acting insulin is not necessarily needed at initiation¹
- ☆ Premixed insulin is not recommended during dosage adjustment period²
- ☆ Insulin regimens should be designed taking lifestyle and meal schedule into account²

Stepwise approach for T2D

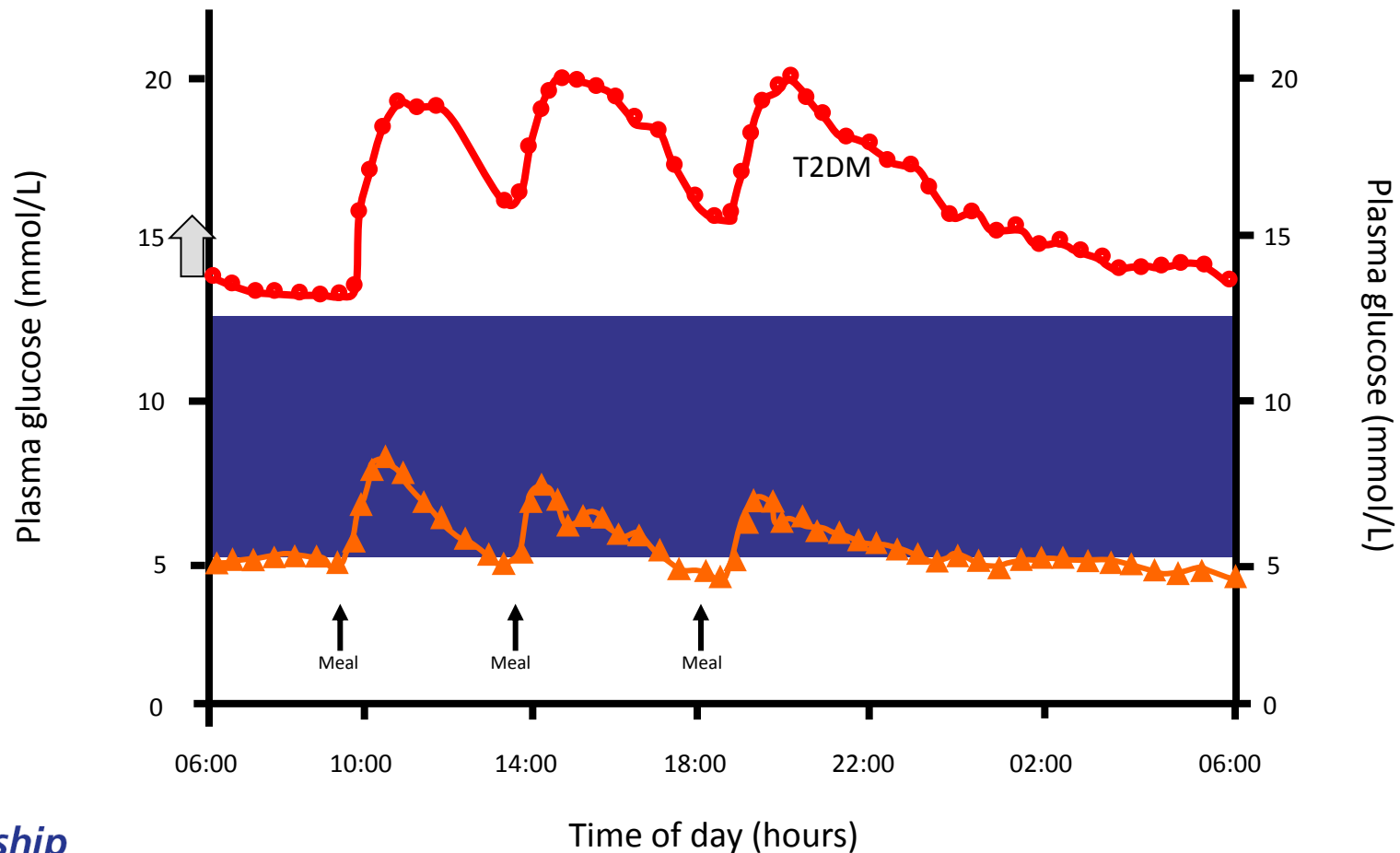
with progressive deterioration of beta cell function



Adapted from Raccach 2008¹. OHA = Oral hypoglycaemic agent, FBG = Fasting blood glucose, PPG = Post-prandial blood glucose.

Why start with basal insulin?

Comparison of 24-hour glucose levels in untreated vs treated patients with diabetes



Which basal insulin?

You decide to start Linda on a basal insulin to address her fasting BGL. Which basal insulin would you recommend for Linda?

Which basal insulin would you recommend for Linda and why?

1. Intermediate-acting, human isophane/NPH insulin
2. Long-acting insulin analogue, insulin glargine
3. Long-acting insulin analogue, insulin detemir* Not funded
4. Not sure

Which basal insulin?

	Onset	Peak	Duration	Funded
Intermediate-acting				
Isophane (OD/BD)	1 – 2 h	4 – 12 h	16 – 24 h	Yes
Long-acting				
Glargine (OD)	2 – 4 h	None	24 h	Yes
Detemir (OD/BD)	1 – 2 h	6 – 12 h	20 – 24 h	No

Starting insulin dose

You decide to start Linda on a basal insulin.

What starting dose would you select?

1. 1 U/kg
2. 10 U/day
3. 20 U/day
4. Not sure

[illegible]

Initiating insulin therapy

You decide to start Linda on 10 U of basal insulin.

Would it be best to start Linda on a morning or evening basal dose?

1. Morning
2. Evening
3. Not sure

Timing of single insulin dose

Morning or evening is acceptable

Timing depends on blood glucose profile:

- If fasting BGL is high → give at bedtime
- If fasting BGL on target but evening BGL high → give in morning
- If both are high → give bd NPH or once daily glargine



* Usually the fasting BG target is ≤ 6.0 mmol/L; however, targets may vary from one person to the next.

Insulin management – next steps

You start Linda on 10 U at bedtime of basal insulin and discuss that her dose will need to increase over the next few months to achieve a target FBG of approx 6.0 mmol/L.

This will be done with the help of your Practice Nurse

You explain that it could take a very long time to reach a high enough insulin dose if the dose is increased slowly.

Linda is a little concerned about potential weight gain and wants to increase the dose slowly initially and is willing to try a faster dose increase down the track.

Linda's summary to this point

- ☆ Elevated A1C on optimal doses of two (2) Max dose OHAs
- ☆ Lifestyle measures reviewed, no secondary causes of hyperglycaemia
- ☆ Insulin therapy appropriate
- ☆ Basal insulin most appropriate at this time
- ☆ Bedtime injection of 10 U basal insulin to reduce Linda's fasting BGL
- ☆ Up-titration to be self-managed in consultation with Practice Nurse
- ☆ Linda to return for review in 3 months with pathology tests completed prior to visit



Titrating insulin therapy

Linda was started on 10 U of basal insulin at bedtime. You instructed her to self-manage the dose up-titration in consultation with your Practice Nurse.

Which schedule would you choose to advise Linda regarding up-titrating her dose in consultation with your Practice Nurse?

1. Slow schedule: increase 2 U every 3 days
2. Fast schedule: increase by 2-8 units of insulin depending on fasting BGL over previous 3 days
3. Not sure

Dose adjustment – first fix fasting

Two dose adjustment schedules possible:

1. SLOW SCHEDULE (CAN BE PATIENT-LED)

Increase by **2 units of insulin every 3 days**

continue until fasting BGL is ≤ 6.0 mmol/L

Increase dose only if FBG >4 mmol/L and accordingly decrease dose if FBG is <4 mmol/L.
Titration reviewed by HCPs at each contact.

Adapted from RACGP 2009/10 and Davies et al 2005.

Dose adjustment – first fix fasting

2. FAST SCHEDULE (PHYSICIAN-MANAGED)

Increase by 2–8 units of insulin depending on fasting BGL over previous 2–3 days

Mean fasting blood glucose (mmol/L)	Increase in insulin dose
<4	* See below
4–5.9	No change
6–6.9	2 units
7–7.9	4 units
8–10	6 units
>10	8 units

Starting dose 10 units, adjust dose twice weekly to reach the target FBG of <6mmol/L

Insulin dose may be decreased (small decreases of 2 to 4 units) if there is severe hypoglycaemia (requiring assistance) or if BGL <3.0 mmol/L in preceding week.

Do not increase insulin dose if fasting BGL <4 mmol/L at any time in preceding week.

Adapted from Phillips PJ. *Medicine Today* 2007; 8(3): 23–34.

Reviewing OHA use

Linda is doing well on basal insulin and had no problems with the slow up-titration process. Linda is now stable at 45 units of basal insulin daily. Linda asks if she still needs her OHAs.

Would you rationalise Linda's OHAs at this point?

1. Stop all her OHAs straight away
2. Consider stopping one after A1C is under control
3. Definitely not stop any OHAs
4. Not sure

Linda's OHAs

- ☆ Don't stop OHAs immediately
 - Stopping OHAs may require more insulin
 - Get A1c under control and consider stopping OHAs later
- ☆ Understand what each drug does
 - Metformin [& glitazones] = insulin sensitisers
 - ☆ Should be continued
 - Sulphonylureas = insulin secretagogues
 - *** Review dose
- ☆ Discontinue if side effects are an issue
 - Metformin:
 - SU:
- ☆ Glitazone: fluid retention, weight gain, cardiovascular risks, bone Fractures in menopausal women.

(DPP-IV inhibitors/incretin mimetics)

Practice points

- ☆ Don't delay insulin initiation
- ☆ Keep it simple for you and patient - 10 units basal insulin
- ☆ Ensure patient has expectation that basal dose will increase and what the dose may end up at
- ☆ Titrate! Fix the fasting first! Then look for hidden hypers

Starting a patient with type 2 diabetes on basal insulin – a check list

Before starting basal insulin

- A1c persistently above target (i.e. A1c >7%)[†]
- Address other possible causes of hyperglycaemia:[†]
 - Lack of compliance
 - Suboptimal use of oral hypoglycaemic medications (OHAs)
 - Secondary causes (e.g. lifestyle, exercise, diet, co-morbidities) or other medications
- Discuss barriers to/concerns about starting insulin with patient[†]
- Arrange GP Management Plan/Team Care Arrangement if necessary – explain role of other healthcare professionals in patient education and monitoring

Starting basal insulin

Step 1: Select basal insulin and basal insulin device[†]

Step 2: Commence basal insulin 10 units morning or night – add it to the oral hypoglycaemic agents (OHAs)[†]

- If fasting blood glucose level (FBG) is high → give basal insulin at **bedtime**[†]
- If FBG is on target but predinner blood glucose level (BGL) is high → give basal insulin in the **morning**[†]

Step 3: Fix the fasting blood glucose (FBG) – adjust basal insulin dose (according to the schedule below)² to reach FBG target of 4–6 mmol/L³ (adjust target to the individual)

Patient-led self titration option^{2,3}



Alternatively, a faster physician-managed titration option can be followed: adjust basal insulin dose every 2–4 days based on mean FBG over preceding 2 days.[†]

After starting basal insulin

- Once FBG is on target, check the other (evening) preprandial BGL and bring within target. If evening preprandial BGL is high, consider adding a second basal insulin[†] dose if the other preprandial BGL remains high[†]
- Review A1c at 3 months
 - Consider stopping sulfonylurea and decreasing dose of metformin and/or glitazone[†]
- Find hidden hyperglycaemia (if A1c ≥ 7%)
 - If preprandial BGLs are on target but A1c and postprandial BGLs are not, review need for a dose of rapid-acting insulin (basal plus prandial insulin) to manage postprandial hyperglycaemia[†]

[†] Unlike isophane insulin and insulin detemir, insulin glargine is not approved for twice daily dosing

References

1. Phillips PJ. *Medicine Today* 2007; 8 (3): 23–34.
2. Davies M et al. *Diabetes Care* 2005; 28: 1282–8.
3. Diabetes Australia/RACGP. Diabetes management in general practice. 14th edn. 2008/9.
4. Riddle M et al. *Diabetes Care* 2003; 26: 3080–86.

Simple switching

☆ Refer to guide



Type of Insulin

Daily dose

Long acting insulin dose

NPH

NPH once daily

Use 100% of daily dose once daily

NPH twice daily

Initially 80% of total daily dose once daily (bedtime)

A Guide to switching T2DM patients from twice daily NPH insulin to once daily Lantus.^{2,3*}

NPH = Protaphane®/Humulin NPH®	Lantus starting dose
If patient on once daily NPH	Use 100% of the daily basal component e.g. 75u of NPH = 75u of Lantus
If patient on twice daily NPH	Use 80% of the total basal dose once daily - see chart below

Conversion chart: If total twice daily NPH dose is... Starting dose of once daily Lantus should be:

Total NPH	Lantus	Total NPH	Lantus	Total NPH	Lantus	Total NPH	Lantus	Total NPH	Lantus
20u	16u	47u	38u	75u	60u	101u	81u	129u	103u
21u	17u	48u	39u	76u	61u	102u	82u	130u	104u
22u	18u	49u	40u	77u	62u	103u	83u	131u	105u
23u	19u	50u	41u	78u	63u	104u	84u	132u	106u
24u	19u	51u	41u	79u	63u	105u	85u	133u	106u
25u	20u	52u	42u	80u	64u	106u	86u	134u	107u
26u	21u	53u	42u	81u	64u	107u	86u	135u	108u
27u	22u	54u	43u	82u	65u	108u	87u	136u	109u
28u	22u	55u	44u	83u	66u	109u	88u	137u	110u
29u	23u	56u	45u	84u	67u	110u	89u	138u	110u
30u	24u	57u	45u	85u	67u	111u	90u	139u	111u
31u	25u	58u	46u	86u	68u	112u	90u	140u	112u
32u	26u	59u	47u	87u	69u	113u	91u	141u	113u
33u	26u	60u	48u	88u	70u	114u	91u	142u	114u
34u	27u	61u	49u	89u	70u	115u	92u	143u	115u
35u	28u	62u	50u	90u	71u	116u	93u	144u	116u
36u	29u	63u	50u	91u	72u	117u	94u	145u	117u
37u	30u	64u	51u	92u	73u	118u	94u	146u	118u
38u	30u	65u	52u	93u	74u	119u	95u	147u	119u
39u	31u	66u	52u	94u	75u	120u	96u	148u	120u
40u	32u	67u	53u	95u	75u	121u	97u	149u	120u
41u	33u	68u	54u	96u	76u	122u	98u	150u	121u
42u	34u	69u	55u	97u	77u	123u	99u	151u	122u
43u	34u	70u	55u	98u	78u	124u	99u		
44u	35u	71u	57u	99u	79u	125u	100u		
45u	36u	72u	58u	100u	79u	126u	100u		
46u	37u	73u	58u	100u	80u	127u	100u		

*Recommendations provided here should be used as a guide only. Total Lantus dose should be determined individually and adjusted based on the patient's individual response, depending on the patient's HbA1c. Consider the adjustment of oral antidiabetic drugs. Close metabolic monitoring under medical supervision is recommended during the transition period.

Lantus is now fully funded for all T2DM patients requiring insulin.¹



Next steps for newly started patients on Lantus²

Adapted from HACCP 2017/2 and Davies et al., 2005.
* If for three days in a row rising > 6 mmol/L, increase the dose by 2 u; if then is severe hypoglycaemia (requiring assistance or the use of > 40 mmol/L in the preceding week, do not increase the insulin dose. If the fasting BG is > 4.0 mmol/L at any time in the preceding week.

Adapted from Phillips 2008 and Davies et al., 2005.
* If the insulin dose may be decreased once decrease of 2-4 units if there is severe hypoglycaemia (requiring assistance or the use of > 40 mmol/L in the preceding week, do not increase the insulin dose. If the fasting BG is > 4.0 mmol/L at any time in the preceding week.

Step 1: Fix the fasting blood glucose - adjust the Lantus² dose using one of the schedules below^{2,3*} to achieve RACGP target FBG of 4-6 mmol/L.⁴

Schedule 1 - Patient self titration^{2,3*}



Schedule 2 - Physician managed titration^{2,3*}

Mean FBG (mmol/L)	Change in Lantus ² Dose
<4	Reduce by 2 to 4 units ²
4-6	No change
6-8	+ 2 units
8-10	+ 4 units
>10	+ 6 units

Adjust the Lantus² dose once weekly to achieve a FBG of 4-6 mmol/L. The mean FBG is calculated based on the FBG results for the last 3 days.^{2,3*}

After starting Lantus²

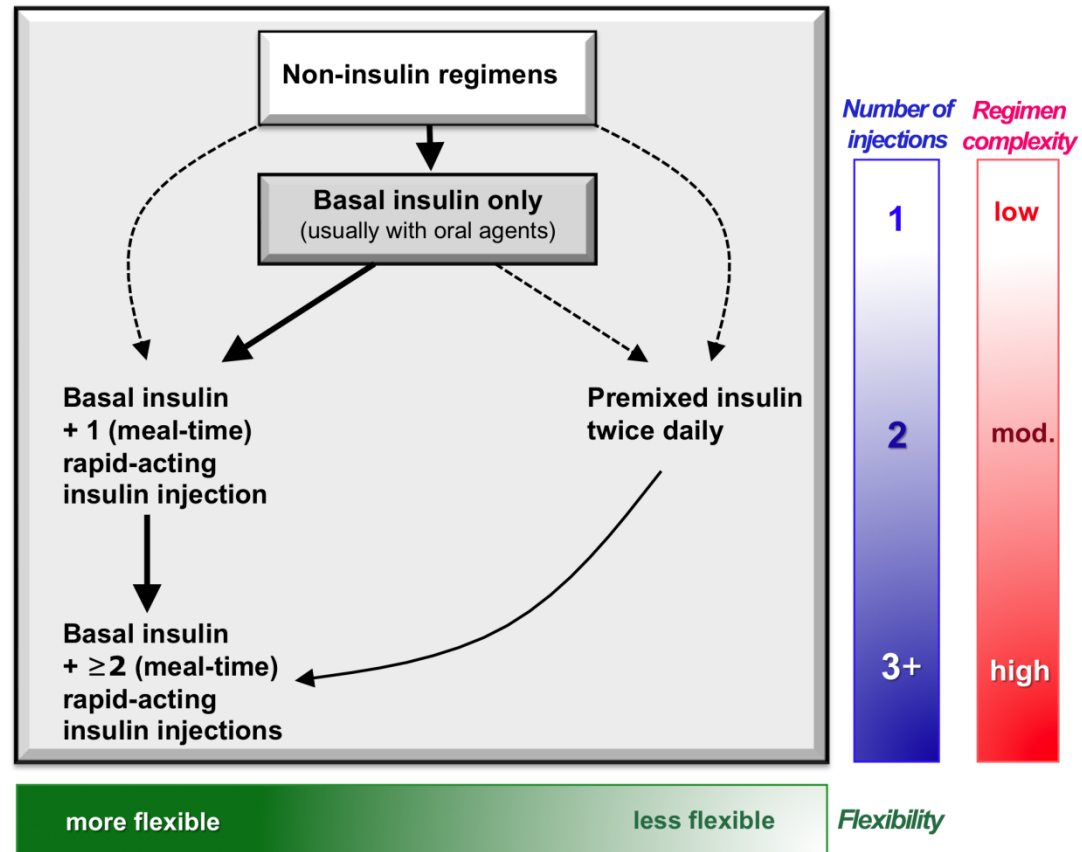
Step 2: Once FBG is on target, confirm the evening (or other) preprandial BGL is on target.
Step 3: Review A1c at 3 months²

Consider reviewing and adjusting the dose of OADs required²

Step 4: Find hidden hyperglycaemia if A1c ≥ 7% or ≥ 55 mmol/mol^{2,3*}

If preprandial BGLs are on target but A1c and postprandial BGLs are not, review need for a dose of rapid-acting insulin to manage postprandial hyperglycaemia²

Sequential Insulin Strategies in T2DM



Thank you

☆ Comments and questions...

