Workshop goal

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

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

Linda

T2D

6 years

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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

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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)

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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/m^2
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/ l <30

Medications

Metformin	1000 mg bd
Gliclazide	160mg bd
Aspirin	100 mg daily
Atorvastatin	40 mg daily
Cilazapril	10mg daily

Reviewing A1C target

You previously set an A1c target of ≤53mmol/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

- 1% fall in A1C reduces microvascular complications by 37%,[1] but risk of:[2]
  - Hypoglycaemia ⇧
  - Weight gain (approx 2kg) ⇧

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1. Stratton IM et al. *BMJ* 2000; 321: 405–12; 2. Phillips PJ. *Medicine Today* 2007; 8(4): 43-52.

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

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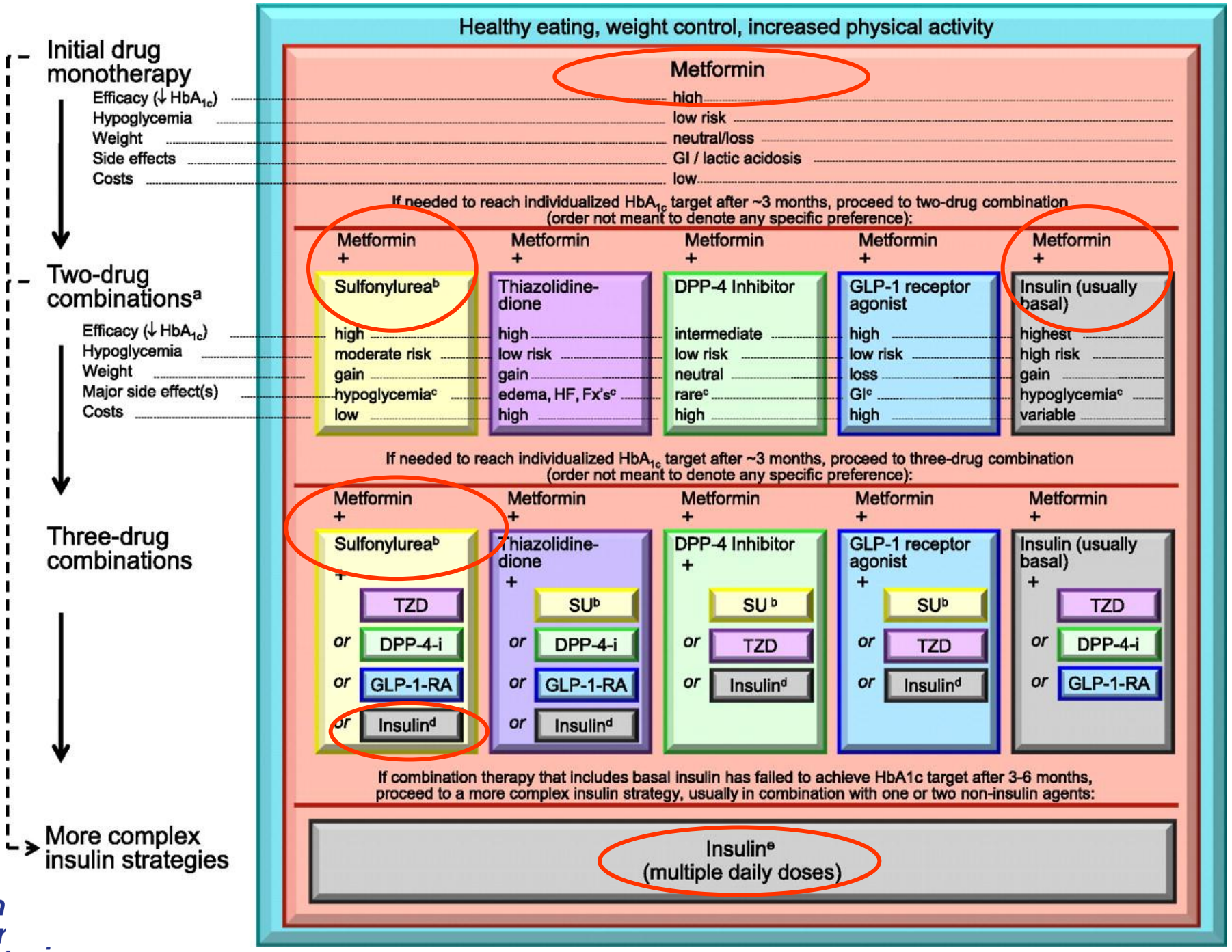
Position Statement ADA/EASD 2012



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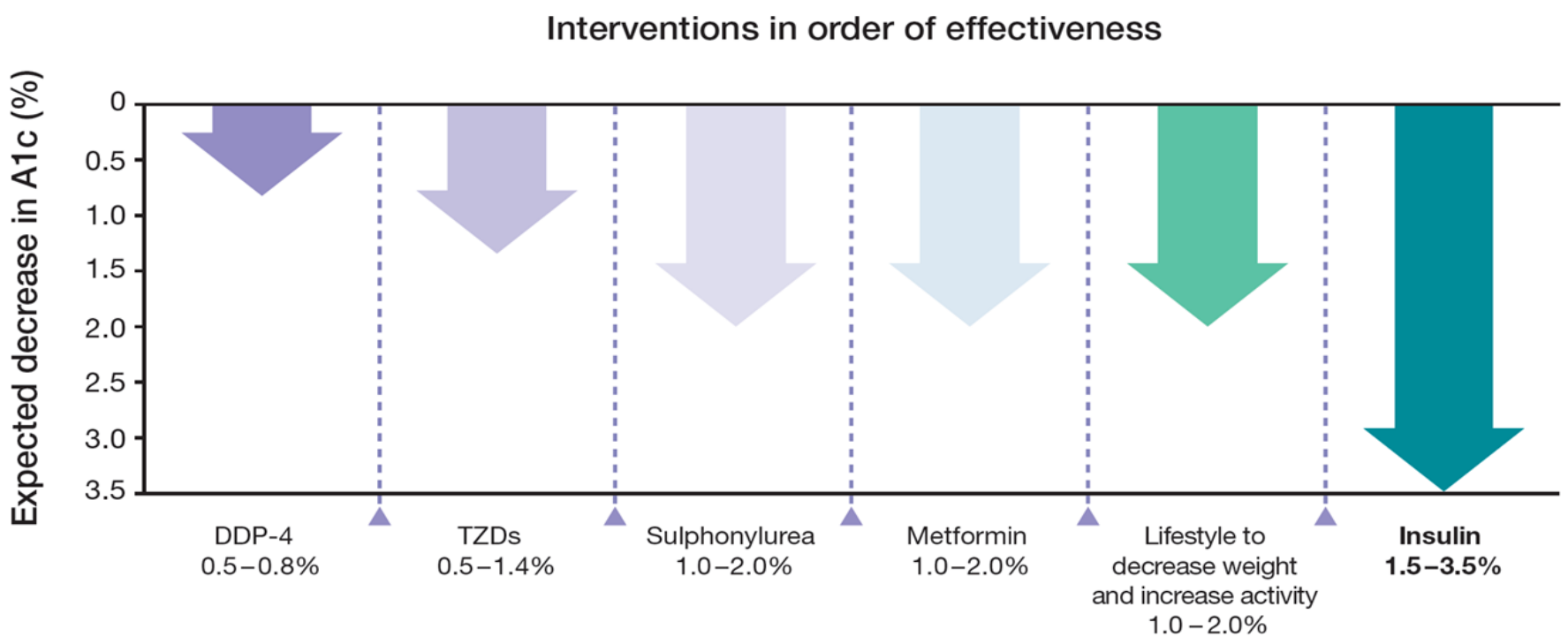
Inzucchi S E et al. Dia Care 2012;35:1364-1379

HbA1c decrease by agent

A1c lowering potential of individual therapeutic options[2]



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

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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. Is she compliant with lifestyle measures and medications? Check for large carb portions with morning/ afternoon tea.
2. Is she monitoring BG readings?
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. hyperthyroidisim, urinary or dental infections, occult malignancy)

↓

A1C still above target – Initiate insulin

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Philips P. *Medicine Today* 2007; 8: 23-34.

Diabetes/insulin education

Education on injecting insulin, BGL monitoring, hypos, activity/diet and lifestyle 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 <u>not</u> necessarily needed at initiation[1]

- ☆ **Premixed insulin** is <u>not</u> recommended during dosage adjustment period[2]

- ☆ Insulin regimens should be designed taking **lifestyle** and **meal schedule** into account[2]

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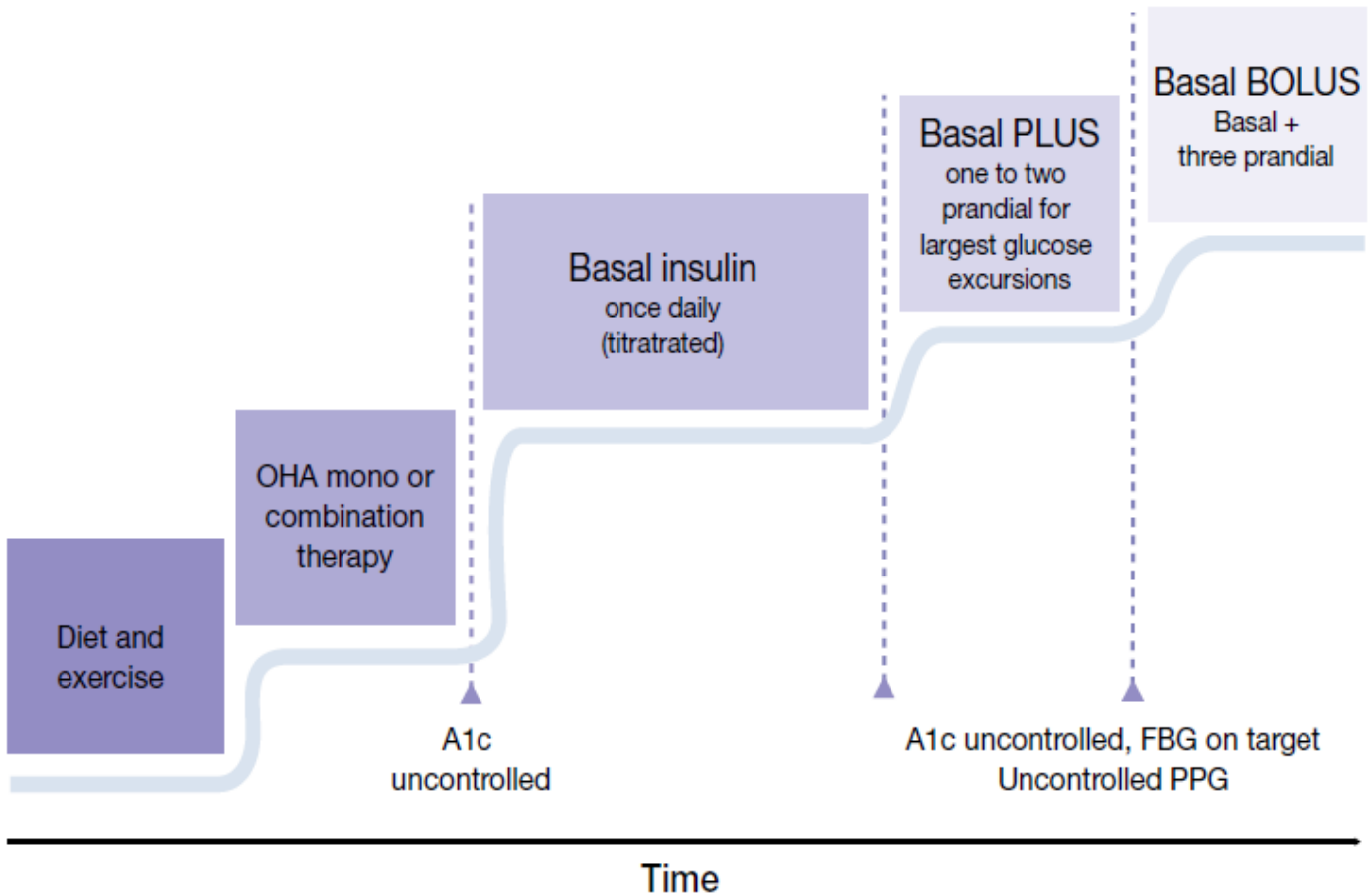
1. DA/RACGP Diabetes management in general practice 2009/10. 2. Nathan D *et al*. *Diabetes Care* 2009; 32: 193–203.

Stepwise approach for T2D
with progressive deterioration of beta cell function



Adapted from Raccah 2008'. OHA = Oral hypoglycaemic agent, FBG = Fasting blood glucose, PPG = Post-prandial blood glucose.

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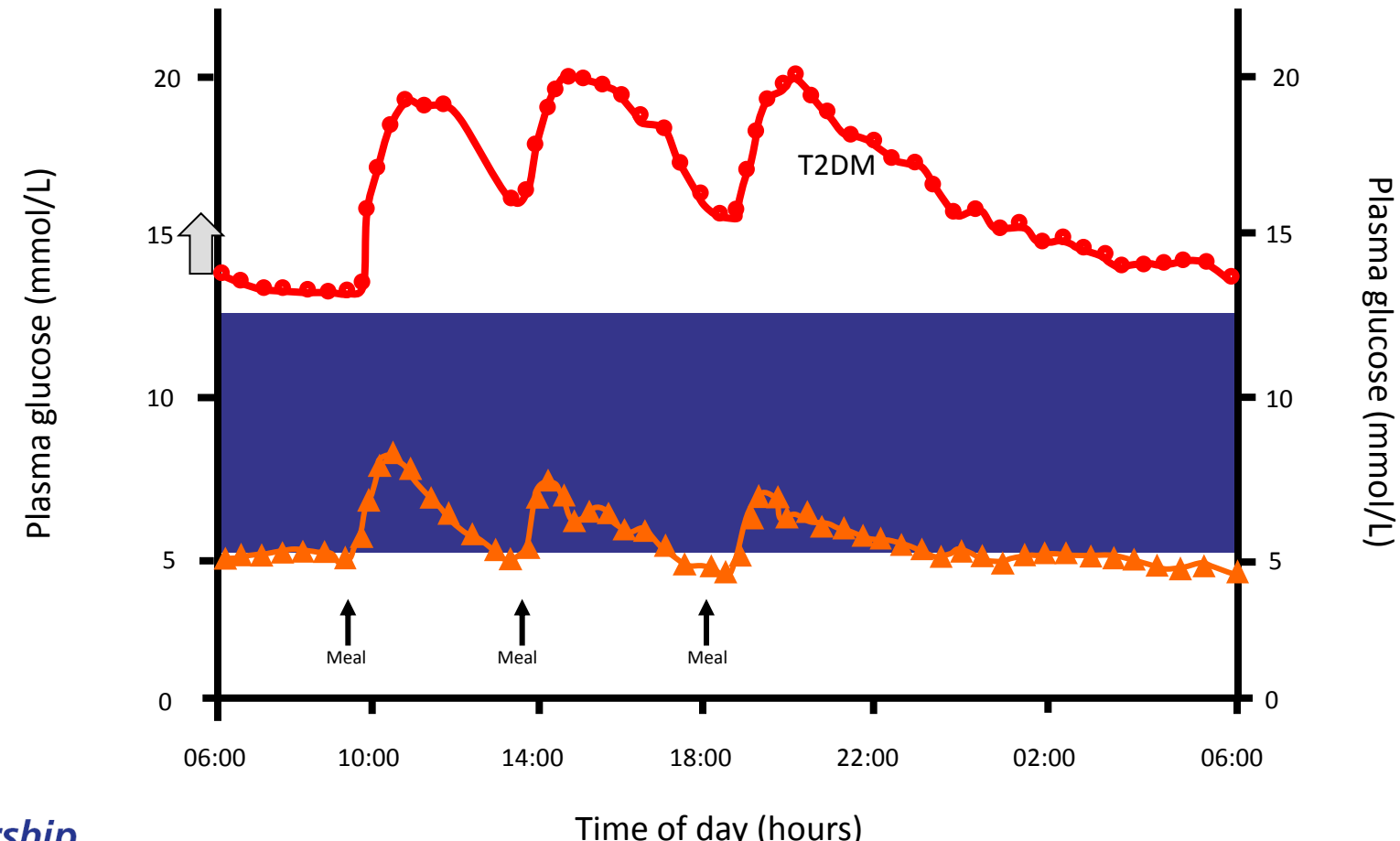
Why start with basal insulin?

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



Adapted from Hirsch I *et al. Clin Diabetes* 2005; 23: 78–86.

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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

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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

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Adapted from Clinical Practice Guidelines: Type 1 Diabetes in Children and Adolescents by Australian Paediatric Endocrine Group. p58
Accessed at www.pharmac.govt.nz Feb10, 2012

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

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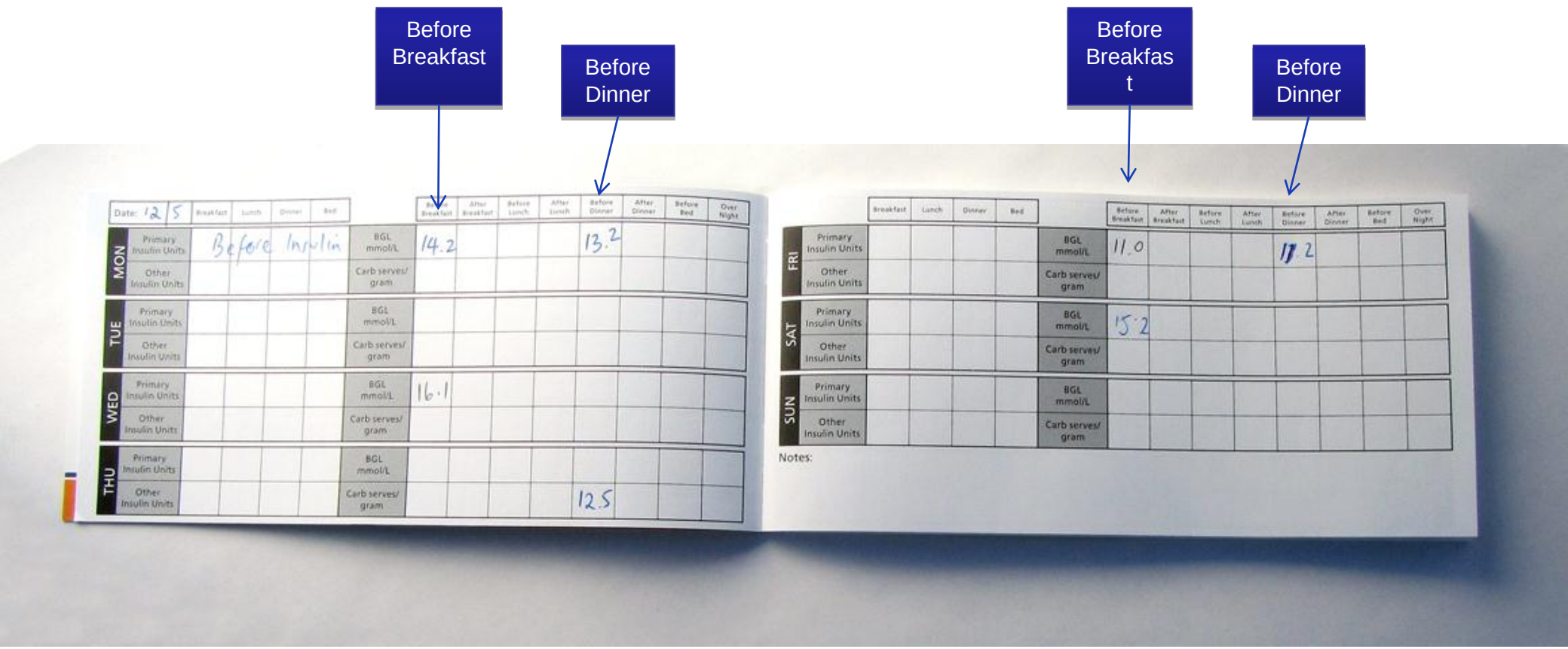
Linda's BGLs during past week (before starting insulin)

12 May



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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

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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 ≤6.0mmol/L; however, targets may vary from one person to the next.

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1. Phillips PJ *Medicine Today*, 2007; 8 (3): 23-34; 2. Davies M *et al*. *Diabetes Care* 2005; 28: 1282-88; 3. Rosenstock J *et al*. *Diabetologia* 2008; 51(3): 408-16. 4. Diabetes Australia/RACGP. Diabetes management in general practice. Guidelines for type 2 diabetes 15th ed, 2009/10.

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

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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 rapid 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

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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 = insulin sensitisers
    - ☆ should be continued
  - Sulphonylureas = insulin secretagogues
    - ☆ Continuing metformin/Sulphonylurea/both with basal insulin is associated with significantly lower insulin requirement
- ☆ Discontinue if side effects are an issue
  - Metformin:
  - SU:
- ☆ Glitazone: fluid retention, weight gain, cardiovascular risks (DPP-IV inhibitors/incretin mimetics)

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1. Phillips PJ. Medicine Today 2007; 8(3): 23-34; 2. Phillips PJ. Aust Fam Physician, 2006; 35: 975-78; 3. Phillips PJ. Medicine Today 2007; 8(6): 43-52; 4. Nathan D et al. Diabetologia 2008; 52: 8-11; 5. Nathan D et al. Diabetologia 2006: 49: 1711-21. 5. SIGN guidelines on Management of Diabetes; 2010.

Type of Insulin	Daily dose	Long acting basal 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)**

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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%)[1]
- Address other possible causes of hyperglycaemia:[1]
  - 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[1]
- 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**[1]

Step 2: **Commence basal insulin 10 units morning or night – add it to the oral hypoglycaemic agents (OHAs)**[1]

- If fasting blood glucose level (FBG) is high ➔ give basal insulin at **bedtime**[1]
- If FBG is on target but predinner blood glucose level (BGL) is high ➔ give basal insulin in the **morning**[1]

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/L[3] (adjust target to the individual)**

Patient-led self titration option[2,3]

Increase dose only if FBG > 4 mmol/L and accordingly decrease dose if FBG is < 4 mmol/L. If mean FBG is ≥ 5.5 mmol/L and < 6.7 mmol/L, increase by 0–2 U. Titration reviewed by healthcare professionals at each contact.
Adapted from RACGP 2009/10 and Davies *et al.* 2005.

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.[1]

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[1]
- **Review A1c at 3 months**
  - Consider stopping sulfonylurea and decreasing dose of metformin and/or glitazone[1]
- **Find hidden hyperglycaemia (if A1c ≥ 7%)**
  - If prepandial 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[1]

† Unlike isophane insulin and insulin determir, 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.

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Thank you

☆ **Comments and questions…**

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