INSULIN INITIATION IN TYPE 2 DIABETES

A/Prof Mark Savage: Endocrinologist
Dr Jessica Triay: Endocrinologist
Dr Jessica Disler: Endocrinology advanced trainee
Karen Gray: Credentialled diabetes eduactor

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Topics to be covered

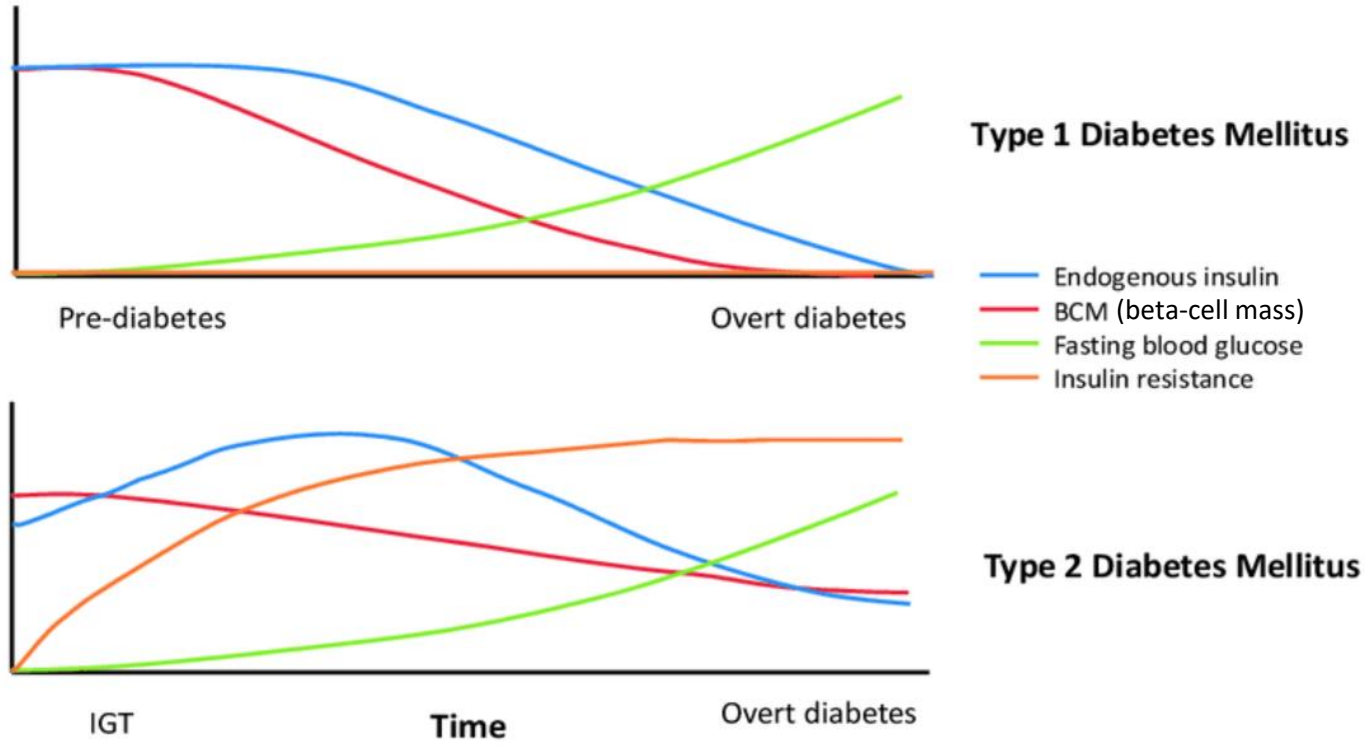
- Identifying the requirement for insulin therapy
- Types of insulin available
- Addressing patient concerns
- Role of diabetes education
- Insulin starting dose and choice
- Titration and glycaemic targets
- Glycaemic variability and hypoglycaemia

Identifying Requirement For Insulin Therapy In Type 2 Diabetes

Dr Jessica Disler
Endocrinology Advanced Trainee

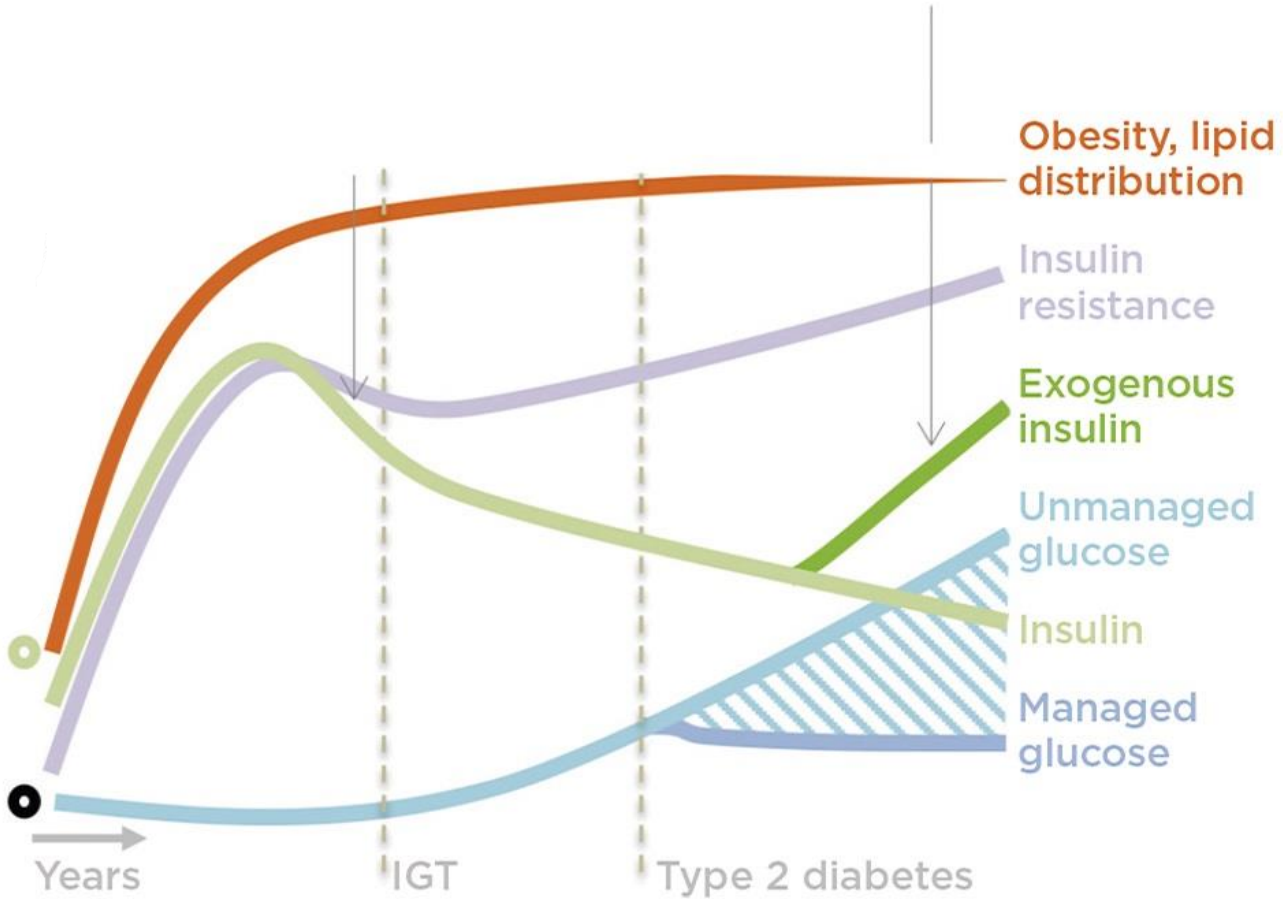
Type 1 vs Type 2 Diabetes

- Common end stage (dysglycaemia and the need for exogenous insulin)
- Insulin deficiency vs insulin resistance
- Residual endogenous insulin production and beta-cell mass



Eriksson (2011)

Pathogenesis of Type 2 Diabetes

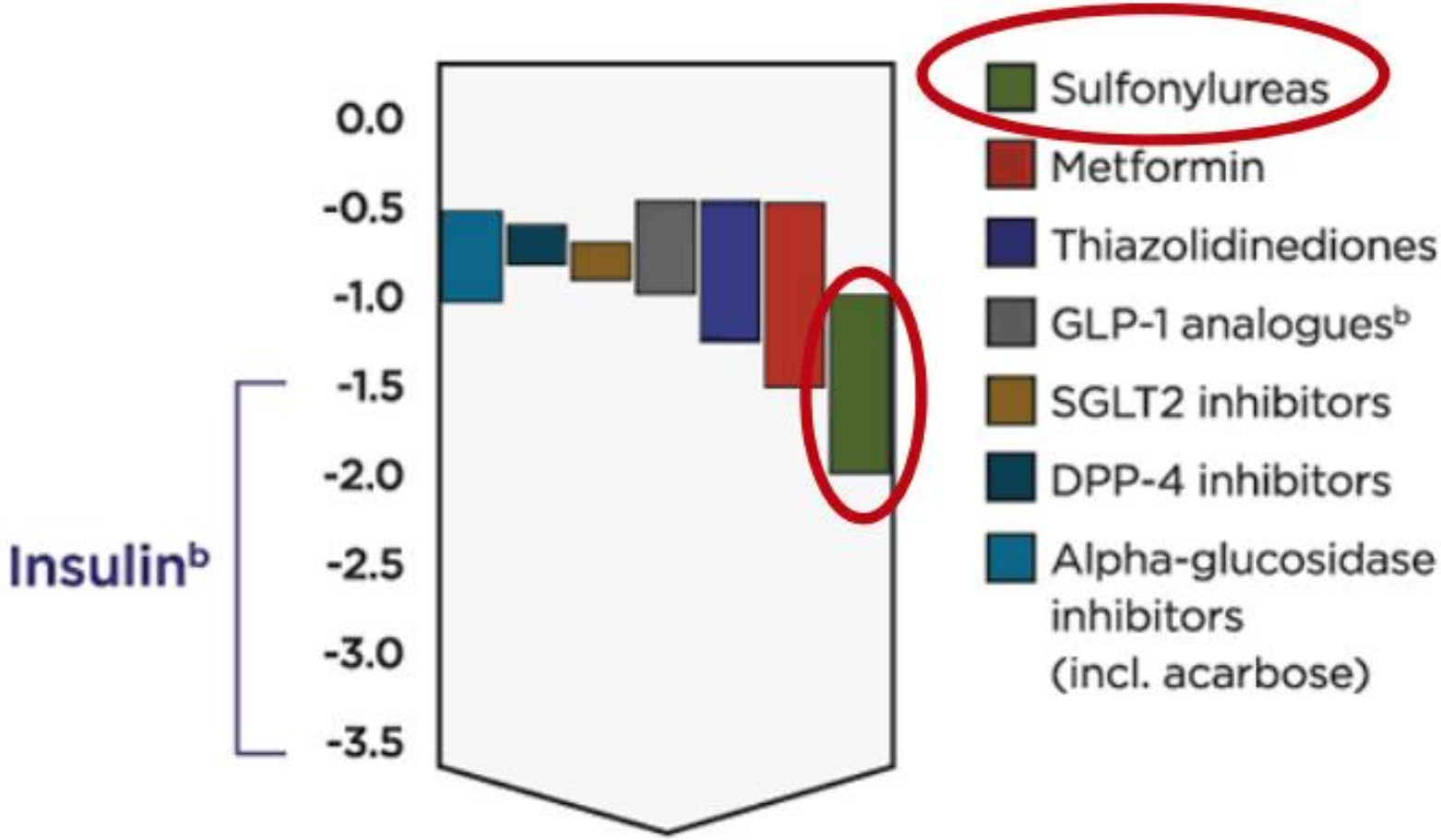


Indications for Insulin in Type 2 Diabetes

- **Insulin deficiency**
  - Severe hyperglycaemia (extremely high HbA1c)
  - Catabolism
  - Ketonaemia or ketonuria
- Refractory to multiple agents and lifestyle interventions
  - Consider continuing some agents
- Individualise choice of therapy and target HbA1c
  - Age
  - Comorbidities

- [Latent autoimmune diabetes in adults (LADA)]
  - Consider endocrinology referral or discussion

Expected HbA1c Reduction



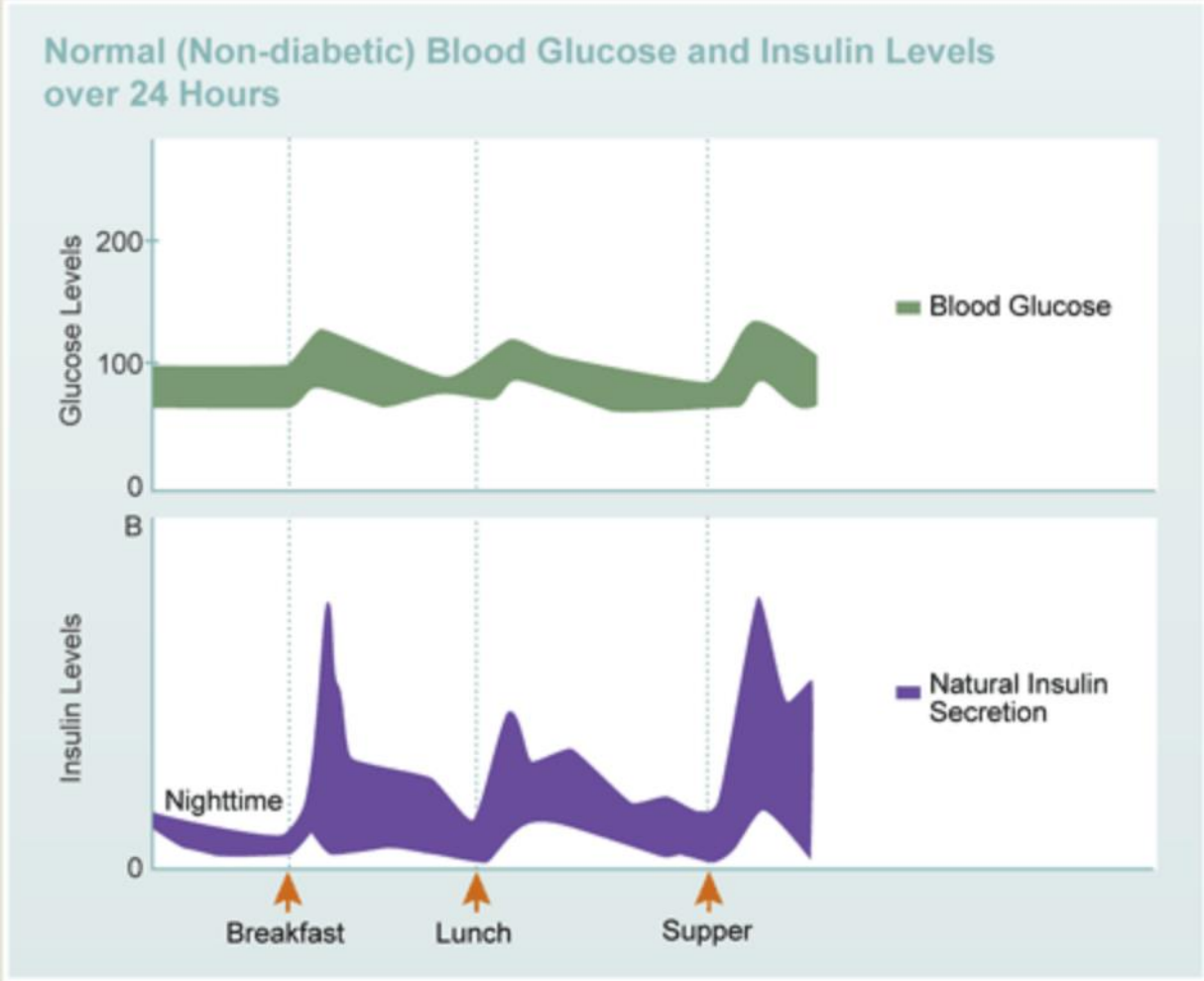
Side Effects of Insulin Therapy

- Weight gain
- Hypoglycaemia
  - Adrenergic
  - Neuroglycopaenia
  - Falls
- Injection site reactions
- Lipohypertrophy
  - Important to assess particularly in poor control

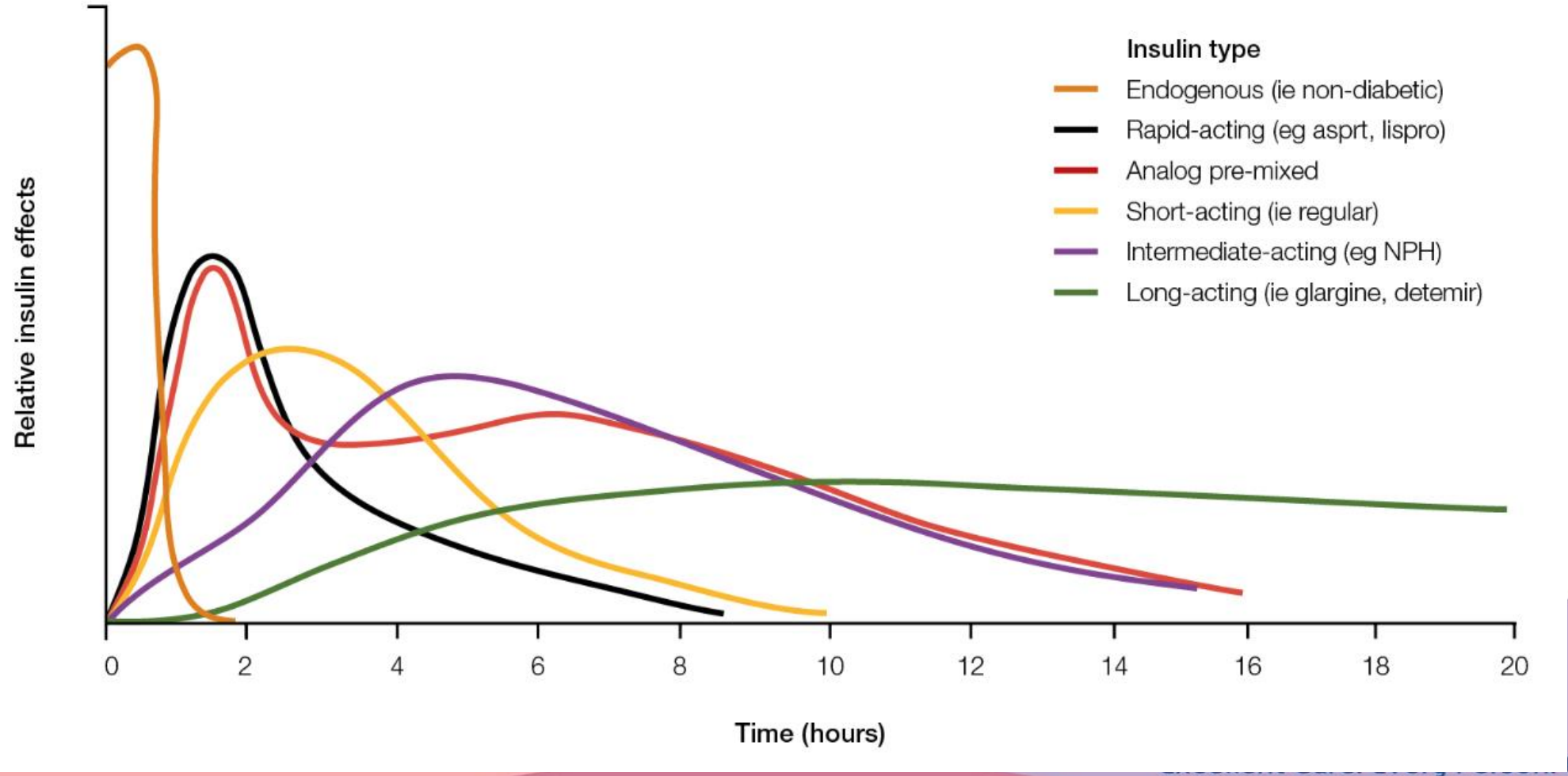
Types of Insulin

Dr Jessica Disler
Endocrinology Advanced Trainee

Endogenous Insulin



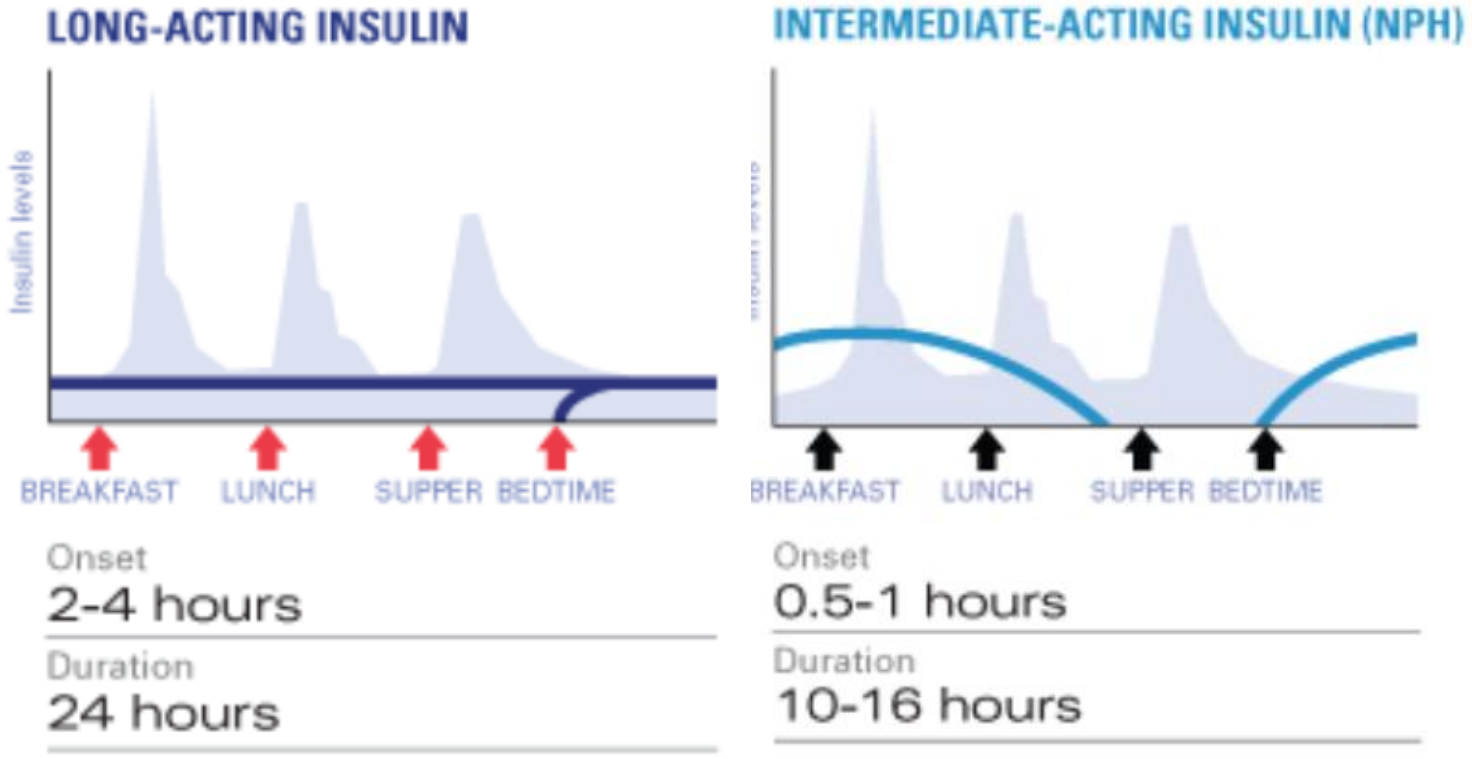
Insulin Profiles



Types of Exogenous Insulin

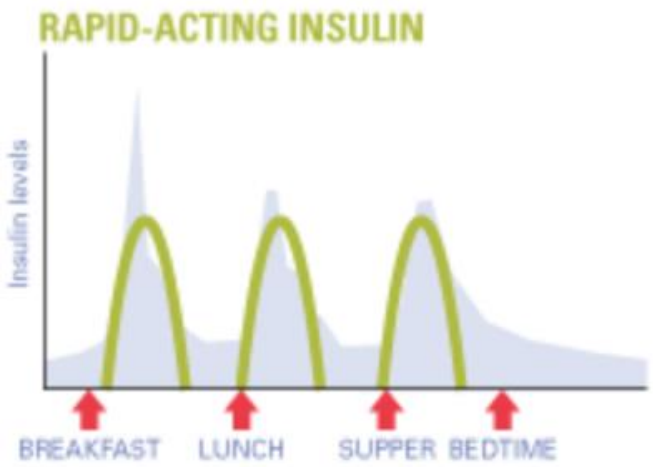
- Basal
- Prandial
- Mixed

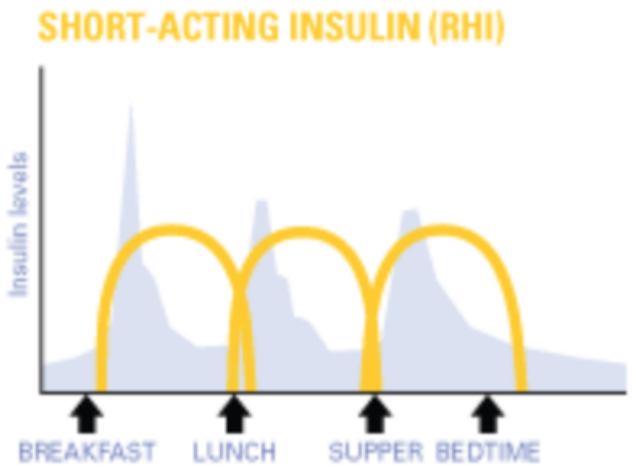
Basal Insulin



Prandial Insulin

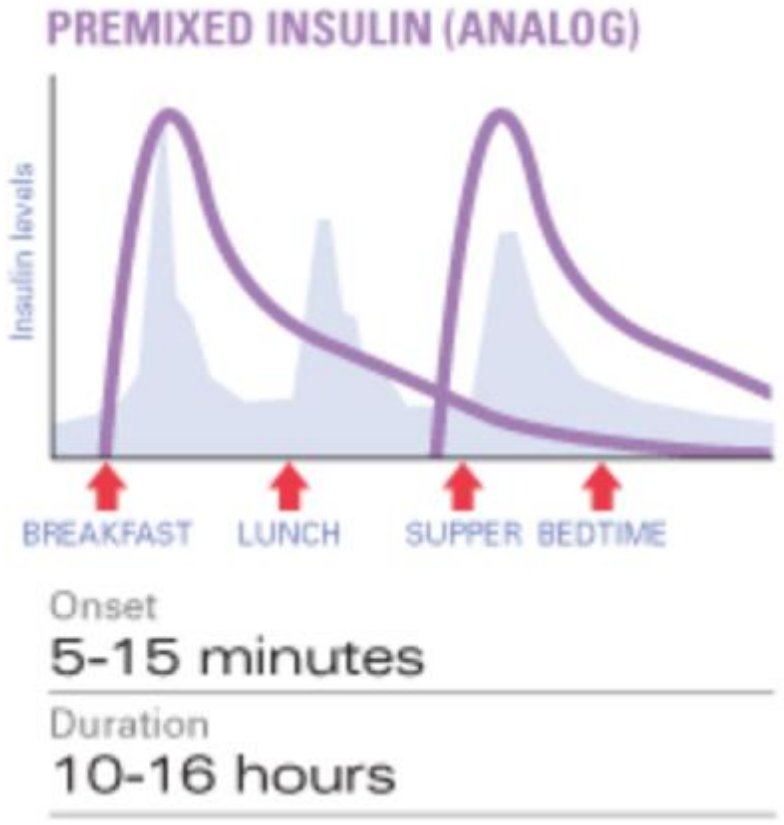
- Rapid-acting
- Short-acting





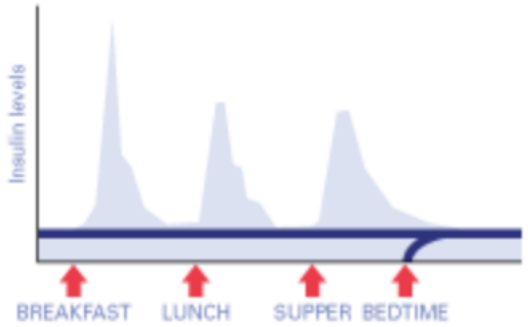
Mixed Insulin

- Intermediate + rapid acting
- Ultra-long acting + rapid acting



BASAL (Lantus®)

LONG-ACTING INSULIN

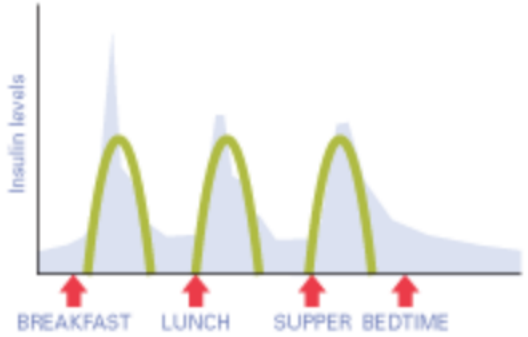


Onset
2-4 hours

Duration
24 hours

PRANDIAL

RAPID-ACTING INSULIN

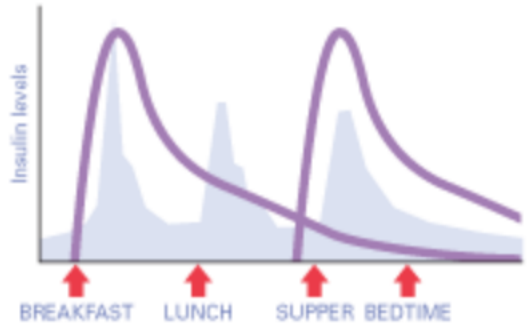


Onset
~5 minutes

Duration
4-5 hours

PREMIX

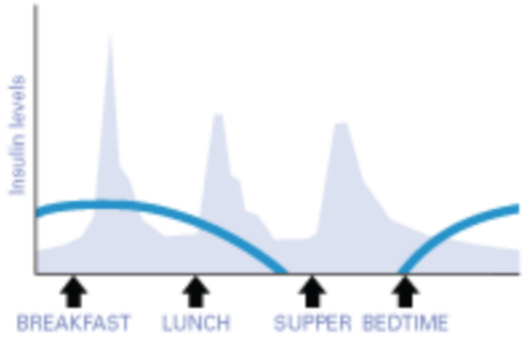
PREMIXED INSULIN (ANALOG)



Onset
5-15 minutes

Duration
10-16 hours

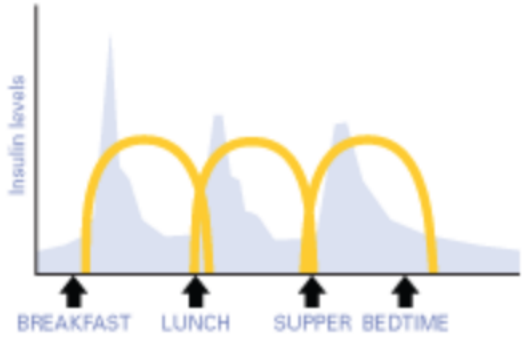
INTERMEDIATE-ACTING INSULIN (NPH)



Onset
0.5-1 hours

Duration
10-16 hours

SHORT-ACTING INSULIN (RHI)



Onset
30 minutes

Duration
Up to 6 hours

Key Points

- Insulin is indicated in insulin deficiency
  - Based on clinical parameters
- Individualise insulin choice to patient's glycaemic profile and targets

Time to Start Insulin?
Role of the Diabetes Educator

Karen Gray

Team Leader, Diabetes Service

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Addressing Patient Concerns

- Fear of needles
- Fear of addiction
- Fear of ‘hypo’s’
- “I might lose my licence..”
- Gaining weight
- Feeling like a failure
- Too much information to remember
- Will I have to be on it forever
- What if I do it wrong?
- My next door neighbour started insulin then went blind…

How can a diabetes educator help?

- Specialist in diabetes – credentialed with Australian Diabetes Educators Association

Your trusted partner in diabetes care

- Usually able to take more time with the patient
- Address patient fears and concerns
- Assess and teach appropriate delivery device
- Explain insulin action and why to give it at the appropriate times
- Talk about how to prevent the risks associated with insulin
- Feed back to referring GP

Where to find a diabetes educator..

- Public – Bendigo Region
  - **Bendigo Community Health Service Eaglehawk**
    - Clinics at Epsom, Queen St, Eaglehawk and Kangaroo Flat Centres
    - Small fee for service
  - **Bendigo Health Diabetes Educators**
    - Refer via Bendigo Health Referral Centre
    - Triage with BCHS
    - Fee for community health patients at BH
      - $14.90
      - $9.80 HCC

Referral to Credentialled Diabetes Educator

- Private Educators in Bendigo
  - GP Practice own educator
  - Local Private CDE's
    - Fusion Allied Health – Deb Ludeman RN CDE
    - Happy Diabetes Health – Paul Skipper RN CDE
    - Simply Diabetes – Karen Gray RN CDE
  - GP Management Plan and EPC minimum 2 visits required, depending on who is following up??
    - May be a GAP payment for patient education

What to put in the referral

- Diabetes type, date of diagnosis
- Comorbidities
- Context of insulin commencement
  - Insulin type, dose
  - Expectations for BG target
- Patient engagement
  - Are they ready for this change
- Plan for follow-up
  - Who and when
  - expectation for CDE engagement

- Consider dietitian referral

Insulin Prescription..

Commencement dose of insulin with choice of device

- Prescription given to patient – ready for first appointment
- Order appropriate device ie insulin pen or penfill cartridge if the patient is to have a **non-disposable**

pen device

- Consider dexterity and/or vision concerns

Initiation of Insulin Therapy and Stabilisation in an Ambulatory Setting

To be completed by the referring medical officer.

Referral to : Credentialled Diabetes Educator Bendigo Health	**Date of Referral:**
Patient Details UR: Full Name: DOB: Address: Contact Details:	**Referring Doctor:** Name: Address: Business Ph: After hours contact:

Type of Diabetes: ☐Type 1 ☐ Type 2 ☐ Gestational ☐ LADA
Date of Diagnosis:

Laboratory results: HbA1c: BGL: Urine/ Blood Ketones:
Please attach other relevant test results.

Current Diabetes Medications:

Insulin Therapy Titration:
Please tick appropriate section otherwise referral is invalid

☐ The referring doctor wishes the diabetes educator to manage ongoing insulin dose adjustment.
☐ The referring doctor will manage ongoing insulin adjustment.

Insulin Therapy Order:
Type of Insulin:

Starting dosage:

Time and Regimen:

Target blood glucose range: Fasting ( ) Post Prandial ( )
Size of Incremental adjustments:

In Type 2 diabetes, is current oral therapy to be continued as "combination therapy"?
☐ Yes *If yes, please state type of oral agent and dosage*
☐ No

Expectations for progress reports: ☐ Weekly ☐ Fortnightly
Method: ☐ Fax ..... or ☐ Letter

Other Comments:

Referring doctor name:
Referring doctor signature:

Non-Disposable Pens

- For penfill cartridges
- Advantages
  - Less space taken up for storage
  - Less 'disposable plastic'
  - Can be smoother delivery
- Each insulin company has a version of non-disposable pen
- Can be supplied at no cost by diabetes educators

Non-Disposable Pens – Half Unit

- Delivers half unit increments
- Not usually needed with type 2 patients

(great for children)

Education

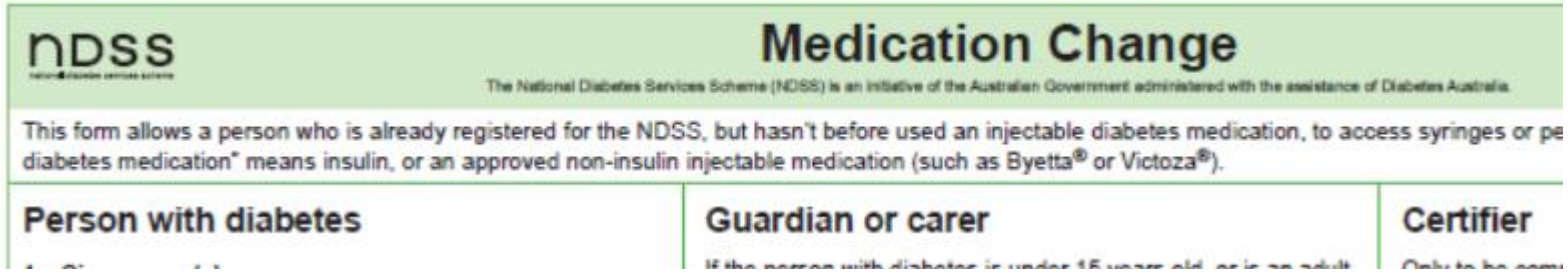
- Take time
  - Patient's own pace
  - Barriers addressed
  - Careful explanation
- Let them try – first injection or 'dry run' in clinic
- Devices – pens, syringes
  - Pre-loaded and disposable
  - Non-disposable
- Pen needle length
  - 4mm, 6mm
  - Single use
  - Injection angle 90°

First Visit

- Explain benefits of insulin
- Check NDSS
- Show injection technique
- First injection supervised
- Discuss hypoglycaemia – recognition and how to manage it
- Discuss potential weight gain and how to minimise
- Daily management – injections, needle changes, SMBG, targets, titration, when and who to call
- Sharps disposal
- Provide instruction sheet to follow for injection at home
- Plan follow up visit
- Who to contact for concerns

NDSS Requirement

- NDSS upgrade to insulin – medication change form
  - Free pen-needles or syringes
  - Patient eligible for ongoing glucose strips
  - GP or CDE sign off



NDSS

Medication Change

The National Diabetes Services Scheme (NDSS) is an initiative of the Australian Government administered with the assistance of Diabetes Australia

This form allows a person who is already registered for the NDSS, but hasn't before used an injectable diabetes medication, to access syringes or pe
diabetes medication" means insulin, or an approved non-insulin injectable medication (such as Byetta® or Victoza®).

Person with diabetes	Guardian or carer	Certifier

Follow up visit..

- Listen to concerns/issues
- Review the glucose record book
- Review injection technique
- Begin/continue titration to target BG

Injection sites – rotate!

- Rotation of injection sites important
- Check for lipohypertrophy each visit
    - Occurs if using same site continually

Because he knew the importance of daily injection site rotation, George went to extremes to avoid problems.

Hypoglycaemia

- Rule of 15
  - Low BGL treat with 15 gm High GI carb
  - Check BG again in 15 mins
  - If still < 4.0 repeat 15 gm high GI carb
  - When > 4.0 give low GI carb

  - Advise to carry glucose
  - Care with driving
- Glucagen Hypokit – not required for type 2
  - Expensive
  - Goes out of date
  - May not be very effective in type 2 DM

Extra Information for Patients

- Sharps containers – available free from council on a replacement system
- VicRoads requirements when on insulin

  Over “5” to drive campaign.
- Hypo management
  https://www.baker.edu.au/-/media/documents/fact-sheets/baker-institute-factsheet-treating-hypoglycaemia.pdf
- Advice on how to manage if special situations such as surgery, fasting or steroids

  Ongoing reviews and support

Resources

- https://www.nps.org.au/australian-prescriber/articles/starting-insulin-treatment-in-type-2-diabetes
- https://www.adea.com.au/wp-content/uploads/2013/08/uploadfile-1363317690514293bac20dc-Draft%20Guiding%20principles%20for%20managing%20insulin%20Version%201%202%20%20%20Jan%202013.pdf
- https://www.adea.com.au/wp-content/uploads/2009/10/Injection-Technique-Checklist.pdf
- CHSA website starting insulin: https://www.chsa-diabetes.org.au/consumer/Insulin%20T2D_FINAL_Nov%2018.pdf
- Simple Steps https://www.simple-steps.com.au/new-to-insulin to help understand insulin

Choosing insulin starting dose, What to prescribe, & Early titration

Primary Care Insulin Initiation

Dr Jessica Triay

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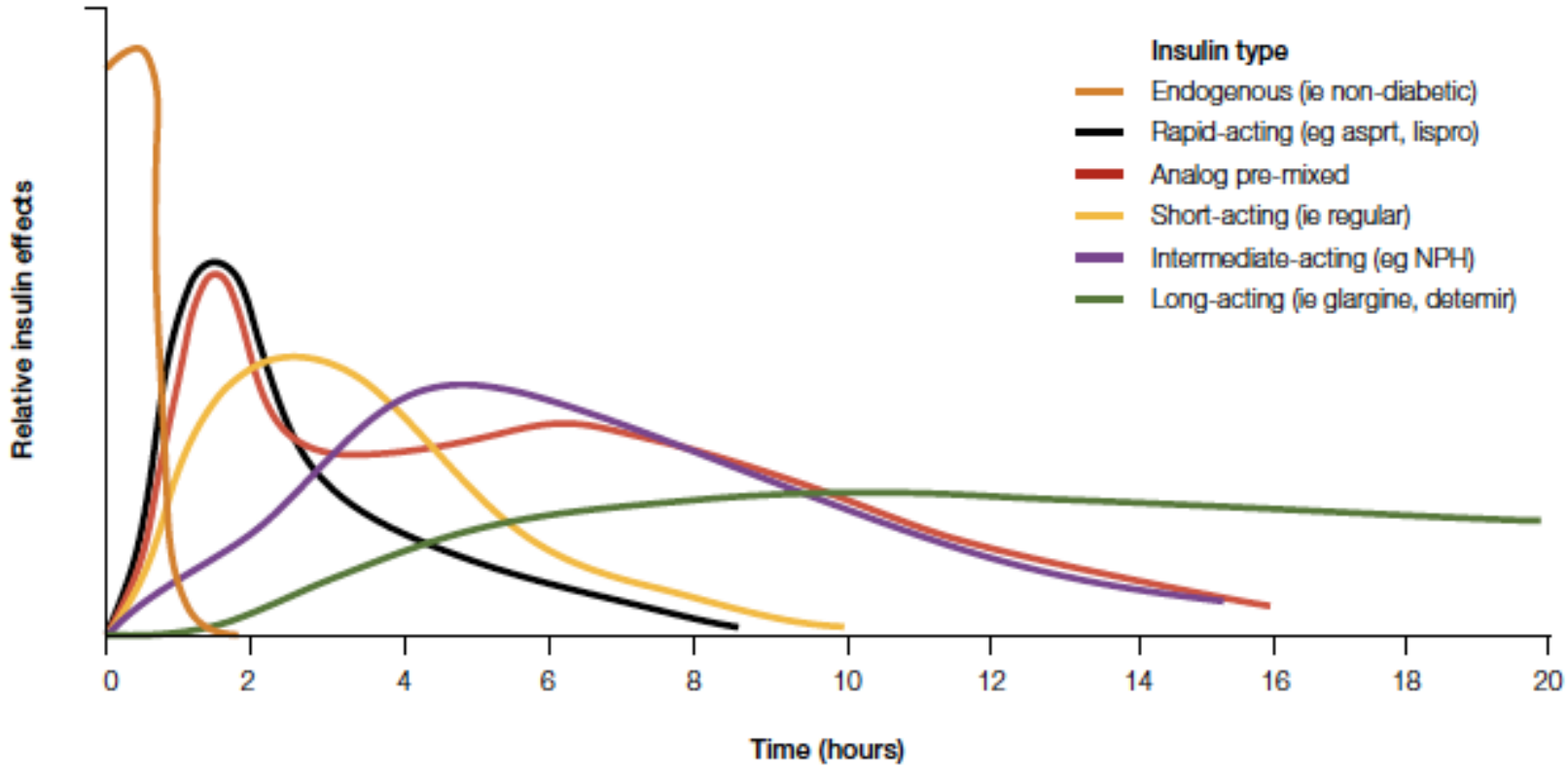
Look at the blood sugar pattern. Which insulin best fits with the profile?

- Prior to choosing insulin regimen, if possible, 3 days of intensive glucose monitoring for daily profile.
- Pre- and 2 hours post- largest meal of the day

- Consider how do these compare with targets:
  - Fasting and pre-prandial 6-8 mmol/L
  - 2 hour post-prandial 6-10 mmol/L
    (post meal rise < 2.5 mmol/L)

Look at the blood sugar pattern.
Which insulin choice matches the profile?



Concurrent OHAs

- Generally continue to reduce insulin requirements, flatten glucose profile, and reduce hypoglycaemia unless:
    - Side effects
    - No response to OHA
    - Significant treatment burden

Fasting hyperglycaemia

Before breakfast	After breakfast	Before lunch	After lunch	Before dinner	After dinner
10.3	11.4	9.8	10.2	8.7	9.9
11.2	12.1	8.9	9.0	9.3	9.7

- Once daily basal insulin
- Before bed is simplest regimen

Post-prandial hyperglycaemia

Before breakfast	After breakfast	Before lunch	After lunch	Before dinner	After dinner
10.3	11.4	9.8	10.2	8.7	14.7
11.2	12.1	8.9	9.0	9.3	15.9

- Often have hyperglycaemia at other times
- Options basal-bolus vs premixed insulin

Basal-Bolus vs. Mixed/Biphasic insulin

	Basal Bolus	Mixed Biphasic
Highly variable carbohydrate intake	✓	✗
Variable daily routine	✓	✗
Strict control needed	✓	✗
Concerns about weight gain	✓	✗
Concerns about compliance/convenience	✗	✓

Starting dose, timing and testing

- **Start low and go slow!**
- Allow time to become confident with insulin administration and safety
  - Basal insulin 8-10 units
  - Mixed insulin 8-10 units once daily with largest meal (dinner)

Weight based starting dose

- Useful if need to gain more rapid control, or likely to require much higher insulin doses. Needs closer observation.
    - Start as 0.2 units/kg then titrate
    - e.g. 100kg patient, commence with 20 units

Titration

- Review at least weekly after initiation
- Titrate to a specific glucose target level (chosen to be appropriate for insulin chosen)

>10	increase by 4 units
8-10	increase by 2 units
7-7.9	Wait or increase 2 units
6-6.9	No change
4-5.9	Reduce by 2 units
<4 **or Hypoglycaemia symptoms**	Reduce by 4 units

Adjust titration according to response observed

- Good response - may wish to reduce sizes of insulin increments
- Limited response - may wish to increase size of insulin increments
- Some patients may be taught how to self-titrate according to algorithm to safe cut offs

Example Case

Before breakfast	After breakfast	Before lunch	After lunch	Before dinner	After dinner
10.3	11.4	11.0	11.3	10.1	10.2
11.2	12.1	12.2	13.7	12.3	13.9

- Robert 67 years old, BMI 41, normal renal function, retired truck driver, HbA1c 10% (86 mmol/mol)
- metformin 1000 mg BD, gliclazide MR 120 mg, empagliflozin 25 mg, linagliptin 5 mg
- Chose insulin type and starting dose

Before breakfast	After breakfast	Before lunch	After lunch	Before dinner	After dinner
10.3	11.4	11.0	11.3	11.1	10.2
11.2	12.1	12.2	13.7	12.3	13.9

- Long acting insulin 10 units nocte commenced 4 days ago
- What now?

Before breakfast	After breakfast	Before lunch	After lunch	Before dinner	After dinner
10.3	11.4	11.0	11.3	10.0	10.2
11.2	12.1	12.2	13.7	12.3	13.9

- Long acting insulin increased to 14 units 4 days ago. What now?
  - Review technique and administration
  - Change titration regimen to allow for larger increments
  - Direct to increase every 3-4 days by 2 units if fasting glucose $\geq$ 8 mmol/L mmol/L and arrange follow up for review

Before breakfast	After breakfast	Before lunch	After lunch	Before dinner	After dinner
7.9	8.2	6.9	7.4	7.3	8.4
7.7	8.9	7.1	7.2	6.8	8.1

- Long acting insulin is now 32 units at bed time
- Continues on metformin 1000 mg BD, gliclazide MR 120 mg, Empagliflozin 25 mg, sitagliptin 100 mg
- Has seen a dietitian, walking more in the day

Example Case

Before breakfast	After breakfast	Before lunch	After lunch	Before dinner	After dinner
10.3	11.4	9.9	10.2	10.4	14.7
11.2	12.1	8.9	9.0	9.3	15.9
13.2	10.3	8.2	8.3	7.9	12.8
10.4	11.9	12.7	13.2	12.4	14.9

- Sue 54 F, BMI 33, normal renal function
- Secretary part time, looks after grandchildren two days a week
- Metformin 1000 mg BD, dapaglifloxin 10 mg, saxagliptin 5 mg
- What insulin choice? What starting dose?

Before breakfast	After breakfast	Before lunch	After lunch	Before dinner	After dinner
10.3	11.4	9.9	10.2	10.4	11.4
9.7	11.2	10.3	11.6	10.8	11.5
10.9	9.7	8.8	8.6	7.9	9.6
10.1	9.8				

- Sue opted for 25% insulin lispro and 75% insulin lispro protamine sulfate suspension 8 units commenced with evening meal 3 days ago
- What do you recommend now?

Before breakfast	After breakfast	Before lunch	After lunch	Before dinner	After dinner
8.9	9.2	8.2	8.7	8.1	9.2
8.1	7.4	7.8	8.2	7.5	8.2
8.2	9.7	8.8	8.6	7.9	9.6

- 25% insulin lispro and 75% insulin lispro protamine sulfate suspension now up to 12 units with evening meal and 8 units breakfast on work days only
- What do you recommend now?

Before breakfast	After breakfast	Before lunch	After lunch	Before dinner	After dinner
6.9	7.1	6.4	6.9	7.2	8.3
6.8	5.9	6.3	7.1	6.7	7.5
6.2	6.8	7.2	7.9	6.1	7.9

- 25% insulin lispro and 75% insulin lispro protamine sulfate suspension 18 units with evening meal 12 units breakfast on work days only
- Continues on metformin 1000 mg BD, dapaglifloxin 10 mg, linagliptin 5 mg

Example Case

Before breakfast	After breakfast	Before lunch	After lunch	Before dinner	After dinner
10.3	11.4	9.9	10.2	10.4	14.7
11.2	12.1	8.9	9.0	9.3	15.9
13.2	10.3	8.2	8.3	7.9	12.8
10.4	11.9	12.7	13.2	12.4	14.9

- John 77, BMI 29, renal impairment eGFR 25. Retired teacher
- Listed for total hip replacement next month but HbA1c 11.4%. Diabetes control has deteriorated significantly over last 8 months due to reduced mobility
- What insulin choice? What starting dose?

Before breakfast	After breakfast	Before lunch	After lunch	Before dinner	After dinner
9.7	10.9	8.7	10.3	9.1	11.7
10.2	11.5	9.8	10.9	9.3	13.9
12.4	13.8	10.2	10.7	9.8	12.3

- long acting insulin 8 units before bed
- Rapid acting insulin 5 units before evening meal

Before breakfast	After breakfast	Before lunch	After lunch	Before dinner	After dinner
5.7	6.2	5.2	6.2	7.1	7.4
6.2	7.3	6.7	6.4	6.9	8.1

- Long acting insulin titrated up to 28 units before bed
- Rapid acting insulin 8, 6, 12 with meals

Safely escalating doses, recognising when hypoglycaemia is a problem & glucose variability

A/Prof Mark Savage
Endocrinologist

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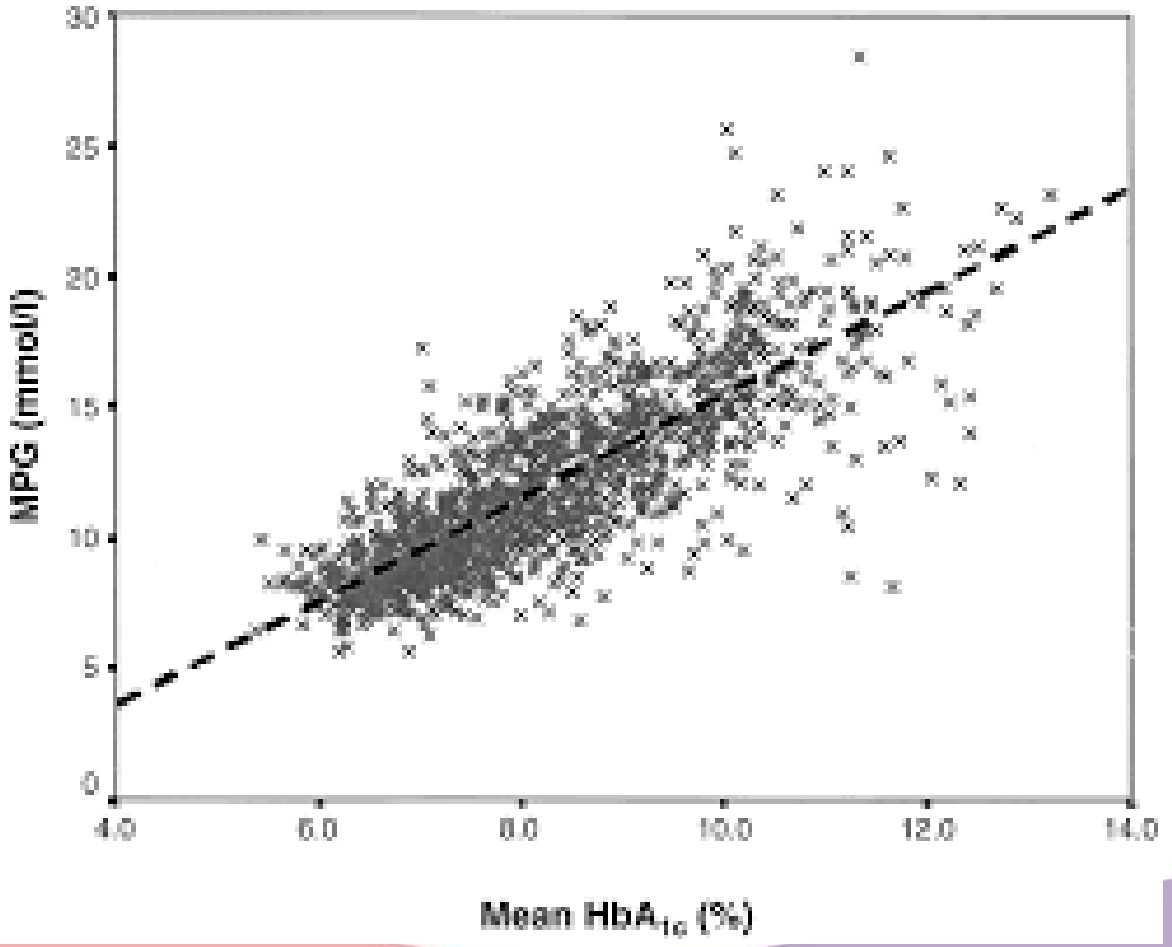
Overview/Introduction

- This talk will focus on T2DM
- CHO counting, pump management and Dose Adjustment For Normal Eating (DAFNE)/Flexit etc. for type 1 management is tricky
  - Should be done by very interested and focussed Primary Care Physicians
  - Or specialists
- Some type 1 folk ***not*** on intensive regimens will follow principles to be discussed – because not numerically literate or lifestyle issues dictate

Take Home #1

- #1 HbA1c is not always related to blood glucose – even in those with normal haemoglobin

HbA1c to Mean Plasma Glucose



What are the BGL Targets in T2DM? Take home message #2

- Depends…….
- There is a relationship in **early and uncomplicated** T2DM between glycaemic control and CVD
- So, early uncomplicated T2DM aim HbA1c < 53 mmol/mol or 7%

What are the BGL Targets in T2DM? Take home message #2

- For the elderly and those with established complications such as CVD; neuropathy and renal disease
  - Treat blood pressure
  - Treat lipids
  - Then treat glucose
- Avoid hypos in this group – ***evidence of probable harm if too aggressive ACCORD study discontinued due to higher death rate***
- HbA1c ***not*** required to be < 53 mmol/mol or 7%, for most of these therefore reasonable to be < 64 mmol/mol (8%)

RACGP T2DM Targets

- So…….
- HbA1c targets to be individualised (RACGP)
- Where safe aim for <53 mmol/mol (< 7%)

Hypoglycaemia

- Hypoglycaemia
  - “Four is the Floor”
  - Classic symptoms are adrenergic
  - If loss of symptoms then neurogenic take over – confusion, behavioural, coma
  - Chronically low BGLs leads to poor or absent warnings
  - Best predictor of serious hypoglycaemic risk is previous severe hypoglycaemia

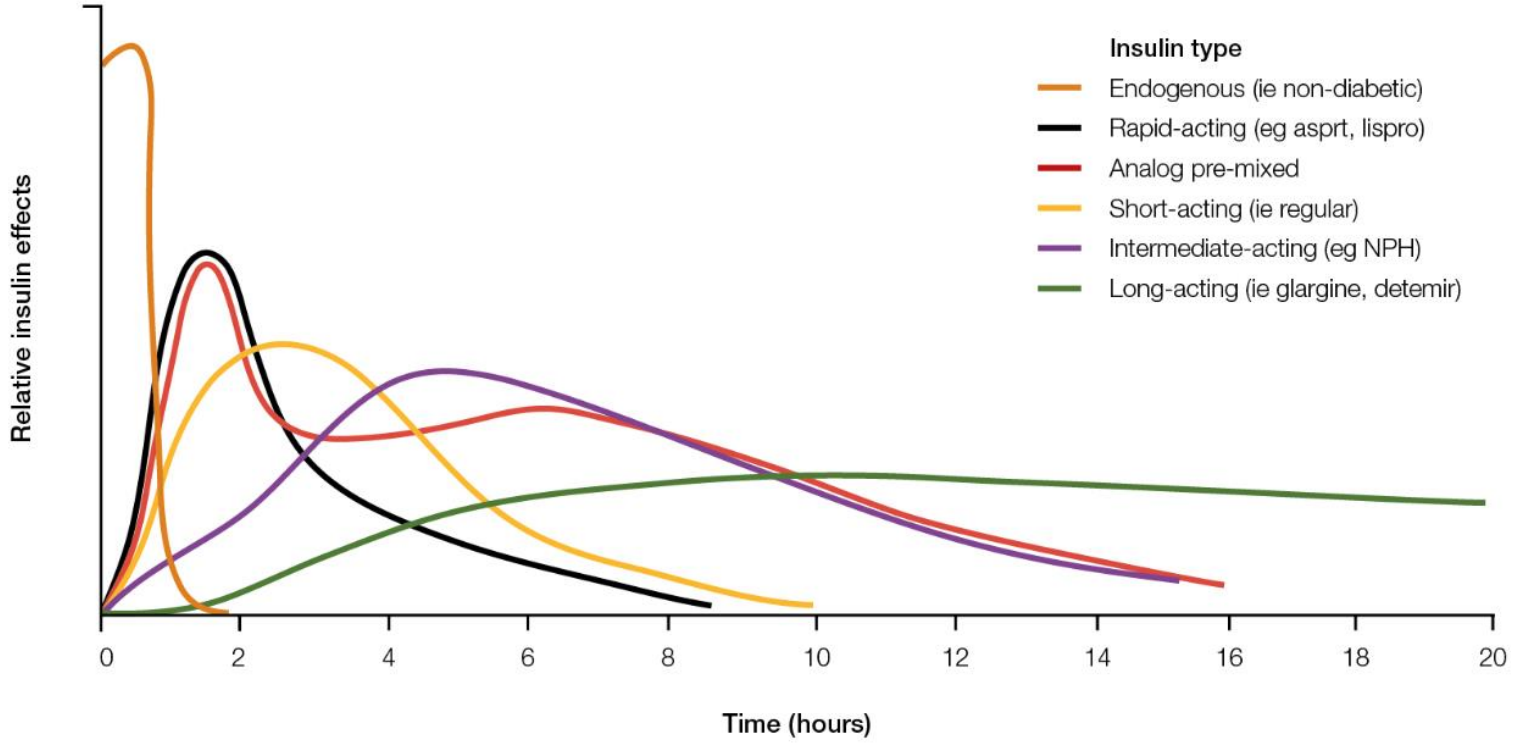
Hypoglycaemia Prevention

- Acknowledge and address the problem in every person treated with insulin or an insulin secretagogue at every consultation
- What frequency does low blood glucose occur- explainable or unexplainable?
- Review SMBG records/examine meter
- At what level does the person detect/develop symptoms of hypoglycemia?

Hypo Prevention 2

- Do others ever detect hypoglycemia before the person with diabetes?
- Risk factors that result in relative or absolute hyperinsulinemia – CHO, exercise etc.
- Timing/type and dose of insulin or insulin secretagogue–MDI increases risk in T2DM vs basal insulin
- Situations in which exogenous or endogenous glucose delivery is decreased – gastroparesis or liver cirrhosis
- Renal failure (increases insulin half life)

Reminder – sub cut insulin is a really bad treatment for diabetes



Escalation of Insulin Doses

- Depends on insulin type
  - Rapid acting analogues can be increased every day or two - dependent on response to post prandial 2 hour levels
  - Fixed Mix better to increase after a few days of blood glucose results to ascertain a pattern
  - Adjust dose before abnormal levels
  - Long acting insulin and insulin analogues increase every few days

Increasing Basal Insulin

- Patients can alter their own insulin
- BB glucose is best indicator in most patients
- Advise to increase intermediate and long acting insulin by 2 units every 3 days
  - Stop increase when BB glucose < 7 mmol/L
  - Stop increase if hypos occur

Increasing Pre Meal Rapid Acting Insulin

- To be taken 15-20 minutes before – ideally
- The 2 hour post prandial blood glucose level best indicator, aim 4-10 mmol/L

Fixed Mix most challenging

- A biphasic suspension of 30% soluble insulin aspart (rapid-acting human insulin analogue) and 70% protamine-crystallised insulin aspart (intermediate-acting human insulin analogue 24 units am and 16 evening

BB	AB	BL	AL	BD	AD	BB	Night
3.5		11.4		7.4		12.2	
4.1		13.7		8.2		10.7	

- Suggestions?
- Dietitian for CHO assessment and drop evening dose (hypos); maybe increase am dose too, but BD OK…..
- Maybe Basal – Bolus needed

Lantus, Toujeo and Ryzodeg

- Evidence for fewer hypos overnight in patients in randomised trials with good HbA1c levels (about 53 mmol/mol or 7%)
- Most real life patients have poorer control so hypos less of an issue
- Much more cost effective to engage Diabetes Educator rather than spending tax-dollars on expensive sexy insulins.
- NICE in UK recommend once or twice daily Protaphane (NPH) as the starting insulin
- Best indicator of insulin trial outcomes is the Trial Sponsor

Glucose variability

- Glycaemic variability (GV), refers to swings in blood glucose levels
- Has a broader meaning because it alludes to blood glucose oscillations, including hypoglycaemic periods and postprandial increases, as well as blood glucose fluctuations that occur at the same time on different days – despite there being little difference in behaviour, CHO intake or exercise.

Variability

- Impossible to measure accurately without CGM/Flash monitoring; but frequent HBGM results can provide an insight.
- Time in target (agreed for now to be 4-10 mmol/L) of 70% suggests less variability.

If too random…..

Summary

- More results from the patient the easier it is to adjust
- Take one's time
- Be methodical
- If you want 3 opinions ask 2 Endocrinologists!