The University of Auckland, The University of Waikato & NZSSD

PRESENTS

PACIFIC DIABETES MANAGEMENT COURSE

THE UNIVERSITY OF AUCKLAND
Te Whare Wānanga o Tāmaki Makaurau
NEW ZEALAND

THE UNIVERSITY OF WAIKATO
Te Whare Wānanga o Waikato

New Zealand Society for the Study of Diabetes
NZSSD

Your session will start shortly

with support & facilitation from AOTEAROA DIABETES COLLECTIVE Aotearoa Diabetes Collective

Your session will start shortly

Welcome to the 2025

Pacific Diabetes Management Course

Housekeeping

- Please stay on **mute** during the webinar
- You can ask questions anytime during the webinar using the **Q+A function**
  - Any question is fine and will be answered at the end of the session
  - You can **upvote** questions that you want answered first
  - You can also ask questions verbally at the end of the session – please use the hand function if able
- **Confidentiality is a must** – These sessions will be recorded and available in a public format
- **Respect** one another
  - This is a collaborative, non-judgemental learning environment for everyone

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PACIFIC DIABETES MANAGEMENT COURSE

with support & facilitation from Aotearoa Diabetes Collective

Webinar 3.

New diabetes medication, technology + management algorithm

Glucose lowering therapies in Aotearoa New Zealand

Oral

- **Metformin**
- SGLT2 inhibitors e.g. *Empagliflozin (Jardiance)*
- **Vildagliptin (Galvus)**
- Pioglitazone (Vexazone)
- Acarbose (Accarb)
- ***Sulfonylureas (Glipizide/Gliclazide)***

Injectable

- *GLP1Ra*
  - *Dulaglutide (Trulicity) - weekly*
  - *Liraglutide (Victoza) – daily*
  - *Semaglutide (Wegovy) - weekly*
- ***Insulin***
  - *Basal insulin*
  - *Prandial insulin*
    - *Bolus insulin*
    - *Premixed or co-formulated insulin*
  - *Correction insulin*

Glucose lowering therapies in Aotearoa New Zealand

Oral

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SGLT2i + GLP1Ra

- **Relative game changers in the management of T2D**
  - Potent agents in secondary prevention of CV + renal disease independently of glucose reduction
    - Lead to weight loss + reductions in BP & do not cause hypoglycaemia alone
    - Benefits are additional to metformin, statins, ACEi/ARB, aspirin + reductions on HbA1c
    - NNT are < 20 to prevent CV event, renal failure or admission for heart failure

- Reductions in glucose levels **dependent on baseline glycaemia** but **likely > for GLP1RA**
  - - 6 mmol/mol if baseline HbA1c 56 mmol/mol vs - 25 mmol/mol if baseline HbA1c > 69 mmol/mol
  - Mean weight loss 2-3 kg at 2 years + mean reduction in BP of 2-3 mmHg
    - New GLP1Ra lead to ~ 15% body loss + beware of sarcopenia
  - Glucose lowering effects of SGLT2i decrease with declining renal function but CVD benefits maintained

When should we use SGLT2i and/or GLP1Ra?

- 2nd line management in all with T2D + renal OR CV disease OR 5 year CV risk ≥ 10% **regardless of HbA1c**
  - **SGLT2i likely preferable if renal disease and/or heart failure predominate**

- 2nd line management if weight loss desirable with **HbA1c above target** on metformin
  - **Reductions in glucose levels and weight likely greater for dulaglutide + liraglutide than empagliflozin**

- 3rd line management if normal weight with **HbA1c above target** on metformin + vildagliptin

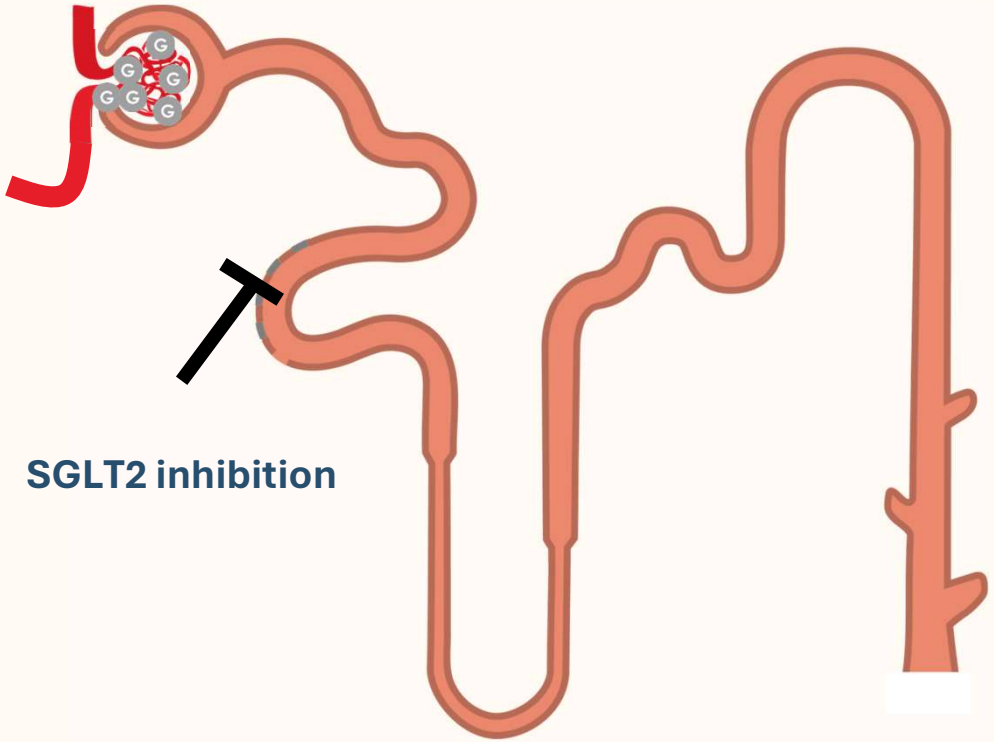
- No safety data in pregnancy, breastfeeding, children < 10 years of age and end stage renal disease
  - SGLT2i safe when started when eGFR > 20 mL/min + GLP1Ra safe if eGFR > 15 mL/min

Empagliflozin

- Works by inhibiting SGLT2 in the proximal tubule of the kidney → > 50% filtered glucose excreted
  - Also results in increased urinary Na^+ + H_2O excretion → **improvements in CVD + heart failure**
- Start 10 mg daily either alone or in combination with metformin
  - Dose can be increased to 25 mg daily if HbA1c remains above target
- Education + prevention of adverse effects important
- SGLT2i now pillar of treatment in non-diabetic renal disease + heart failure

How does empagliflozin work?

Ambient Glucose
(8-10mM)



Over 50% of filtered glucose load is now excreted

Adverse effects of SGLT2i

- Polyuria → **typically transient, mild + strongly positively correlated to blood glucose levels**

- Increased genitourinary infections
  - **Typically mycotic infections (e.g. vaginal thrush or balantitis)** rather than UTIs
  - Necrotising fasciitis of the perineum (Fourniers gangrene) is rare

- Transient decrease in eGFR → **up to 25-30% decrease is normal**

- Diabetic ketoacidosis (DKA) → rare affecting ~ 1 in a 1000 + glucose levels often normal
  - **Risk increases with low carbohydrate diet (< 130 g per day) + sick day management critical**

Tips to avoid adverse effects of SGLT2i

- **Appropriate selection of patients**
  - Do not use without specialist advice in T1D, pancreatogenic diabetes or previous DKA
  - Be cautious in those with T2D + insulin deficiency who may have difficulty with sick day management
  - Be cautious in those with frequent mycotic genital infections/UTIs and/or elderly (> 75 years of age)
  - Avoid if significant alcohol intake or in low carbohydrate diet (< 130 g per day) → **refer to dietitian if unsure**

- Consider reduction in insulin and/or sulfonylureas if tight glycaemic control
  e.g. HbA1c < 64 mmol/mol
  - ~ 15-20% reductions in all insulin doses + 50% reductions in sulfonylureas useful starting point

Tips to avoid adverse effects of SGLT2i

- **Consider reduction in diuretics** if no signs of fluid overload (e.g. frusemide 80 mg to 40 mg daily)
  - May also require reduction of antihypertensives if tight BP control (always aim to maximise ACEi/ARBs)

- Discuss the importance of genital hygiene
  - Women should wash ≥ 2 times per day + uncircumcised men ≥ once per day
  - Consider fluconazole 150 mg weekly for 1-2 weeks if high risk

- **Educate patients about sick day management**

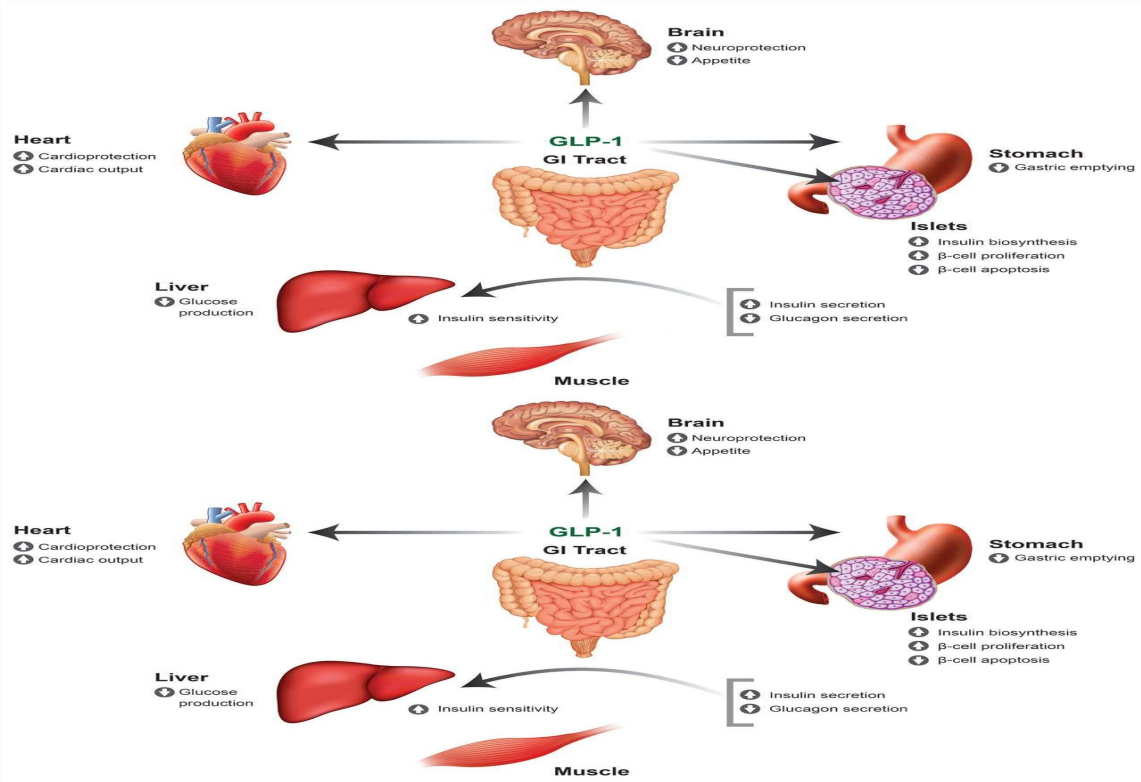
GLP1Ra

- Older GLP1Ra include liraglutide + dulaglutide & newer GLP1Ra include semaglutide + tirzepatide

- Work predominantly by activating GLP1 receptors in pancreatic beta-cells, stomach + brain
  - Increases glucose-dependent insulin secretion → **does not cause hypoglycaemia alone**
  - Decreases gastric emptying + appetite → **typically results in weight loss**

- Unlike endogenous GLP1, GLP1RA are resistant to breakdown by dipeptidyl peptidase IV
  - **When starting GLP1RA need to stop vildagliptin as redundant + may still cause adverse effects**

GLP1Ra



Hinnen et al. Diabetes Spectrum 2017; 30(3):202

Dulaglutide (Trulicity)

- **Available only as 1.5 mg s/c weekly injection** (0.75 mg, 3 mg + 4.5 mg doses not in NZ)
  - Can be injected any time on any day of the week → missed doses may be given up to 3 days late
  - **May add a 2nd injection per week if tolerating well + HbA1c remains above target**

Adverse effects of GLP1Ra

- Nausea → common but typically transient, mild + vomiting, constipation or diarrhoea rare
- Injection site reactions → typically transient + mild only e.g. redness, nodules
- Hypoglycaemia if on insulin and/or sulfonylureas
  - If HbA1c < 64 mmol/mol reduce insulin by ~ 15-20% + sulfonylureas by 50%
  - May need cessation of low dose sulfonylureas + prandial insulin if high risk
- Pancreatitis + medullary thyroid hyperplasia/carcinoma (controversial)
  - Equal rates of pancreatitis in GLP1RA + placebo groups & medullary thyroid cancer only in rodents
  - Do not monitor lipase or amylase

Tips to avoid adverse effects of GLP1Ra

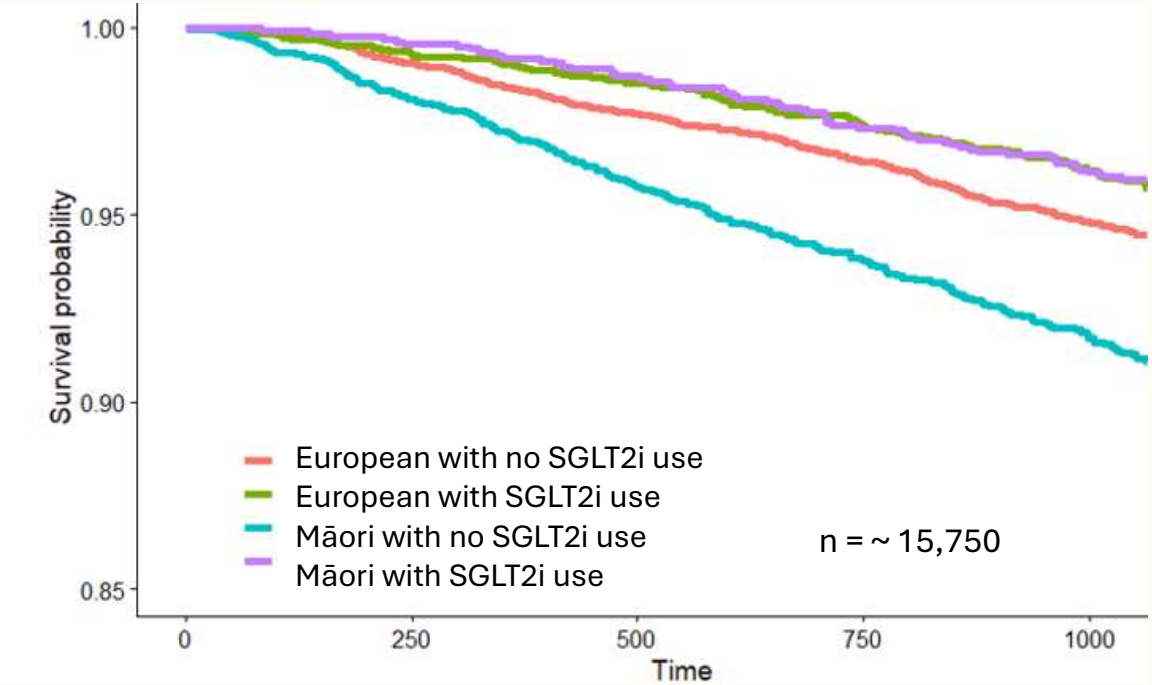
- **Appropriate selection of patients**
  - Do not use without specialist advice in T1D or pancreatogenic diabetes
  - Avoid in those with GI disease (e.g. gastroparesis, uncontrolled GORD, IBD)
  - Avoid in severe pancreatitis or medullary thyroid cancer/MEN2 syndrome
  - Be cautious using in the elderly (> 75 years of age)

- Ensure adequate hydration

- **Provide advice on how to reduce adverse GI effects:**
  - Eat to appetite + eat smaller meals more slowly
  - Avoid fried/fatty foods, alcohol, + eating within 2 hours of bed
  - Knowledge that GI effects usually transient very reassuring + pharmacy education useful

Why these medications are important

Survival Curves for Europeans and Māori with T2D ± empagliflozin use



- 70% with T2D + CVRD on best meds
  - 2.5 – 10 fold better than rest of world
- Curves are similar for Pacific peoples
- Abolished disparities in prescribing + mortality within 3 years

Pioglitazone

- Thiazolidinedione that activates perioxisome proliferator-activated receptors (PPAR) gamma + alpha
  - **Reduces insulin resistance** by ↓ lipolysis & ↑ glucose uptake by skeletal muscle + adipose tissue
  - Decreases hepatic glucose output
  - **Does not cause hypoglycaemia unless on sulfonylureas and/or insulin**

- **Reduces CVD** independently of effect on glucose levels (no independent benefits on renal disease)
  - Also improves fatty liver disease independently of effects on glucose levels

- Maximal mean reduction in HbA1c ~ 15 mmol/mol + more effective in women
  - **Full effects of pioglitazone are not seen for > 8 weeks**
  - **Useful 3rd or 4th line agent particularly as alternative or adjunct to metformin if insulin resistant**

Pioglitazone

- Adverse effects + precautions/contraindications often limit use
  - Fluid retention → **do not use if macular oedema, heart, liver or renal failure** (~ mean 2-3 kg weight gain)
  - ↓ bone mineral density + fractures → **do not use if known/high risk for osteoporosis**
  - ↑ bladder cancer in rodent studies → **do not use if previous bladder cancer**
  - No safety data so **do not use in pregnancy, breastfeeding, < 18 years of age or T1D**

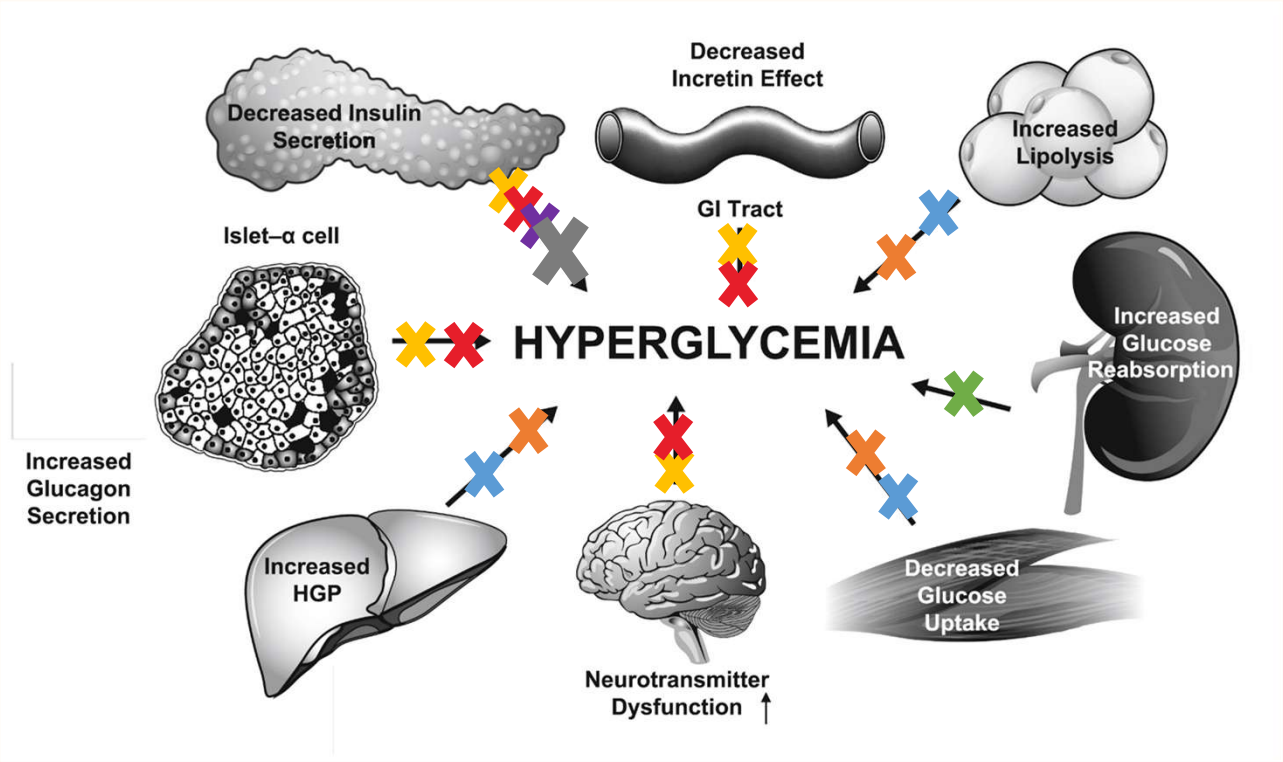
- Start at 15 mg daily + can increase by 15 mg per day per month until maximum 45 mg daily as required
  - May need to reduce doses of insulin and/or sulfonylureas if risk of hypoglycaemia (e.g. HbA1c < 64 mmol/mol)
  - **Due to delay in effects often easier to base any dose increase on 3 monthly HbA1c**
  - Consider periodic DEXA scans in long-term use

Acarbose

- Inhibits intestinal alpha glucosidase **reducing absorption of carbohydrates**
- May lead to mild weight loss but **no known independent benefits** on reducing CVD or renal disease
- Start at 50 mg tds + increase to 100 mg tds as required (often required in low carb diet)
  - May need to reduce doses of insulin and/or sulfonylureas if risk of hypoglycaemia (e.g. HbA1c < 64 mmol/mol)
  - No safety data in pregnancy, breast feeding or children < 18 years of age
- Seldom used due to significant GI adverse effects

The ‘ominous octet’

- Metformin
- Pioglitazone
- Vildagliptin
- GLP1RA
- Empagliflozin
- Sulfonylureas
- Insulin

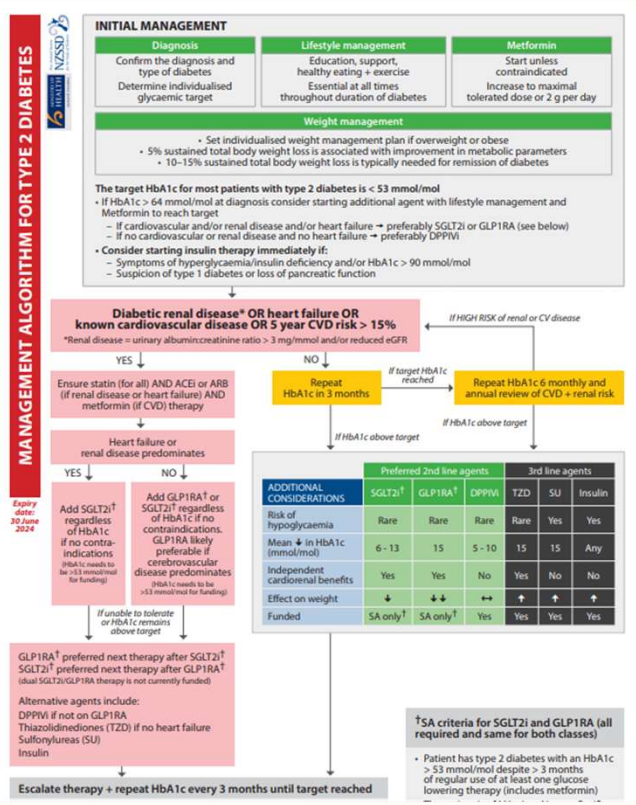


Summary of glucose lowering therapies

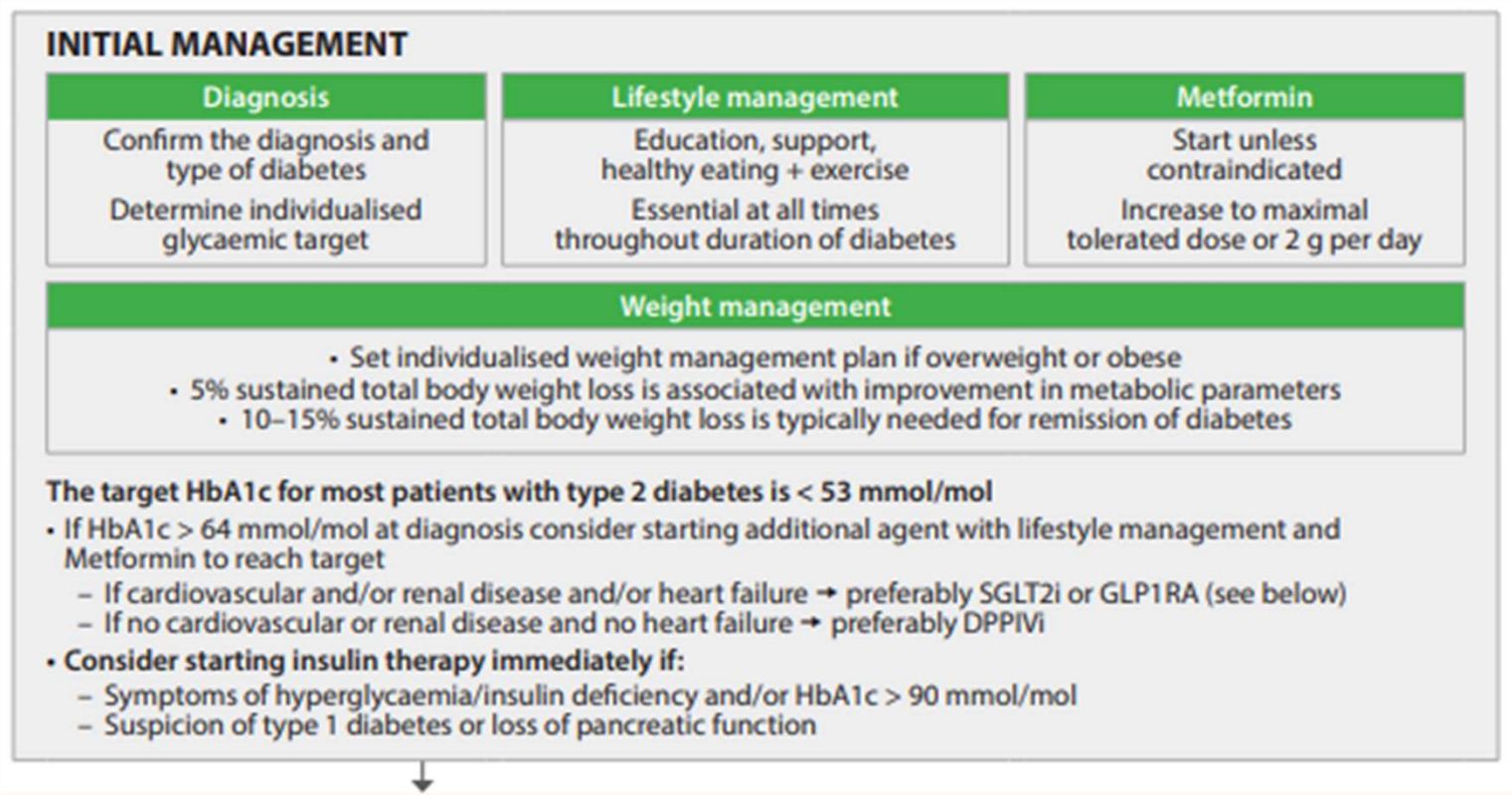
	Metformin	Vildagliptin	Pioglitazone	Acarbose	Empagliflozin	GLP1Ra	Sulfonylureas	Insulin
Risk of hypoglycaemia	Rare	Rare	Rare	Rare	Rare	Rare	Yes	Yes
Mean maximal HbA1c ↓	15	5-10	15	5-10	15	15-20	15	Any
Independent cardiorenal benefits	**Yes**	No	**CV only**	No	**Yes**	**Yes**	No	No
Effect on weight	↓	↔	↑	↔	↓	↓↓	↑	↑↑
Funded	Yes	Yes	Yes	Yes	SA only	SA only*	Yes	Yes

Management algorithm for T2D in Aotearoa

- www.t2dm.nzssd.org.nz
- See Moodle resources



First-line management for T2D in Aotearoa



INITIAL MANAGEMENT

Diagnosis	Lifestyle management	Metformin
Confirm the diagnosis and type of diabetes Determine individualised glycaemic target	Education, support, healthy eating + exercise Essential at all times throughout duration of diabetes	Start unless contraindicated Increase to maximal tolerated dose or 2 g per day

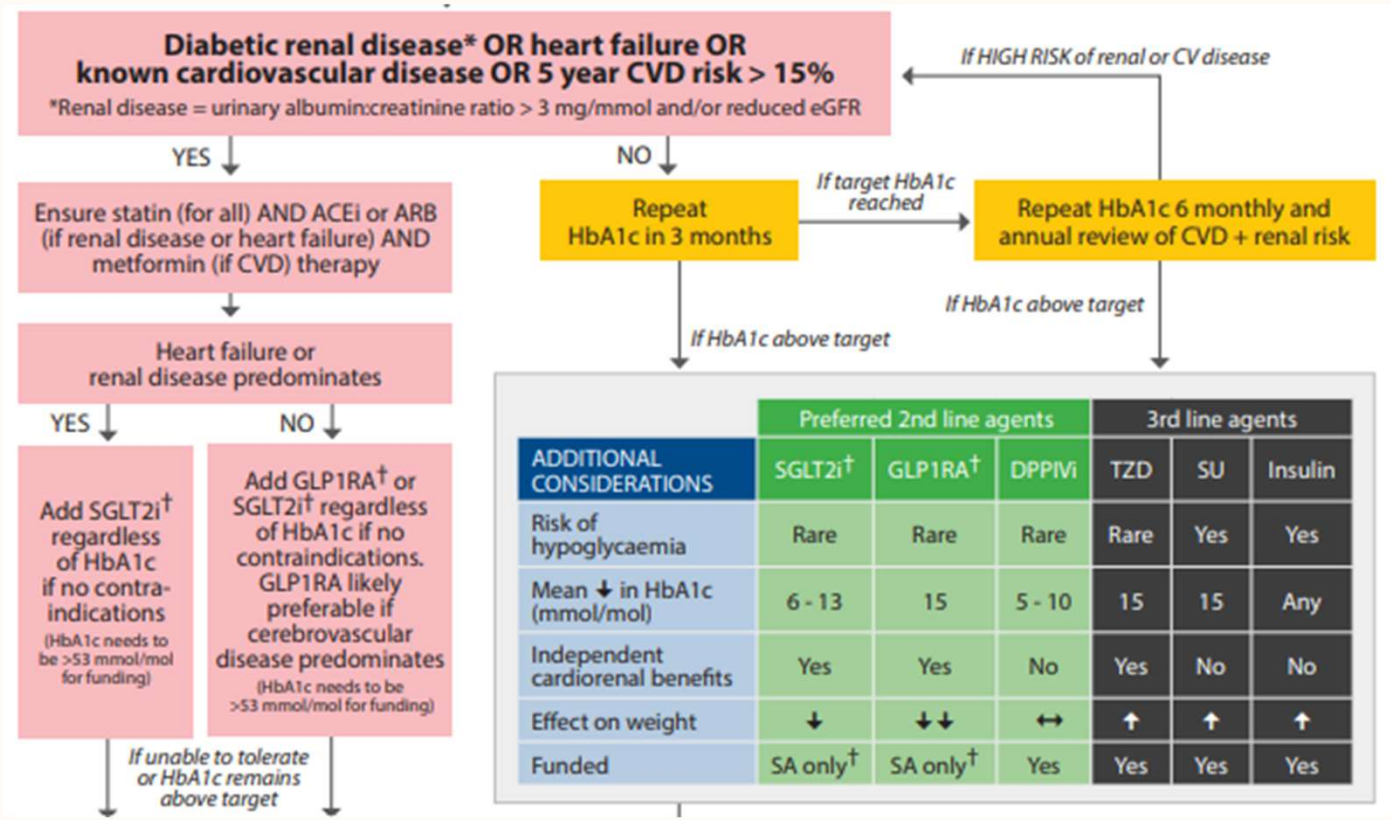
Weight management

- Set individualised weight management plan if overweight or obese
- 5% sustained total body weight loss is associated with improvement in metabolic parameters
- 10–15% sustained total body weight loss is typically needed for remission of diabetes

The target HbA1c for most patients with type 2 diabetes is < 53 mmol/mol

- If HbA1c > 64 mmol/mol at diagnosis consider starting additional agent with lifestyle management and Metformin to reach target
  - If cardiovascular and/or renal disease and/or heart failure → preferably SGLT2i or GLP1RA (see below)
  - If no cardiovascular or renal disease and no heart failure → preferably DPPIVi
- **Consider starting insulin therapy immediately if:**
  - Symptoms of hyperglycaemia/insulin deficiency and/or HbA1c > 90 mmol/mol
  - Suspicion of type 1 diabetes or loss of pancreatic function

Management is then based on renal disease, CVD or equivalent risk

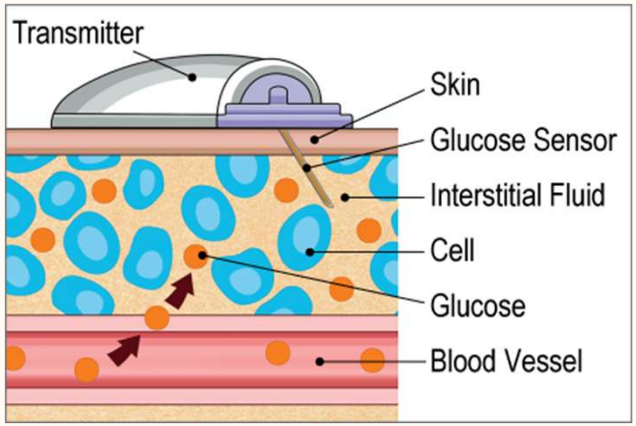


	Preferred 2nd line agents			3rd line agents		
ADDITIONAL CONSIDERATIONS	SGLT2i†	GLP1RA†	DPPIVi	TZD	SU	Insulin
Risk of hypoglycaemia	Rare	Rare	Rare	Rare	Yes	Yes
Mean ↓ in HbA1c (mmol/mol)	6 - 13	15	5 - 10	15	15	Any
Independent cardiorenal benefits	Yes	Yes	No	Yes	No	No
Effect on weight	↓	↓↓	↔	↑	↑	↑
Funded	SA only†	SA only†	Yes	Yes	Yes	Yes

Diabetes technology

What is continuous glucose monitoring (CGM)?

- Continuous glucose monitors consist of:
  - Sensor – measures glucose levels in interstitial fluid
  - Transmitter – transmits data to a receiver
  - Receiver – **displays glucose levels + rate of change of glucose levels in real-time**
    - most people use their smart phone as the receiver
    - customisable alarms for high and low glucose levels



- Basic standard of care in T1D + increasingly other types of diabetes worldwide
  - Enables automated insulin delivery when combined with an insulin pump

- CGM is now funded in Aotearoa NZ for type 1, pancreatogenic + rare forms of monogenic diabetes under SA

What does CGM look like?

dexcom one+

Linx

FreeStyle Libre 2 PLUS

Overview of CGM results

AGP Report

31 August 2022 - 13 September 2022 (14 Days)

LibreView

GLUCOSE STATISTICS AND TARGETS

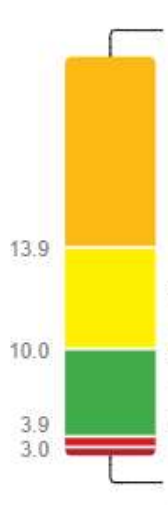
31 August 2022 - 13 September 2022	**14 Days**
% Time Sensor is Active	**65%**

Ranges And Targets For	Type 1 or Type 2 Diabetes
Glucose Ranges	**Targets** % of Readings (Time/Day)
Target Range 3.9-10.0 mmol/L	Greater than 70% (16h 48min)
Below 3.9 mmol/L	Less than 4% (58min)
Below 3.0 mmol/L	Less than 1% (14min)
Above 10.0 mmol/L	Less than 25% (6h)
Above 13.9 mmol/L	Less than 5% (1h 12min)
Each 5% increase in time in range (3.9-10.0 mmol/L) is clinically beneficial.	

Average Glucose	**14.1** mmol/L
Glucose Management Indicator (GMI)	**9.4% or 79 mmol/mol**
Glucose Variability	**35.4%**

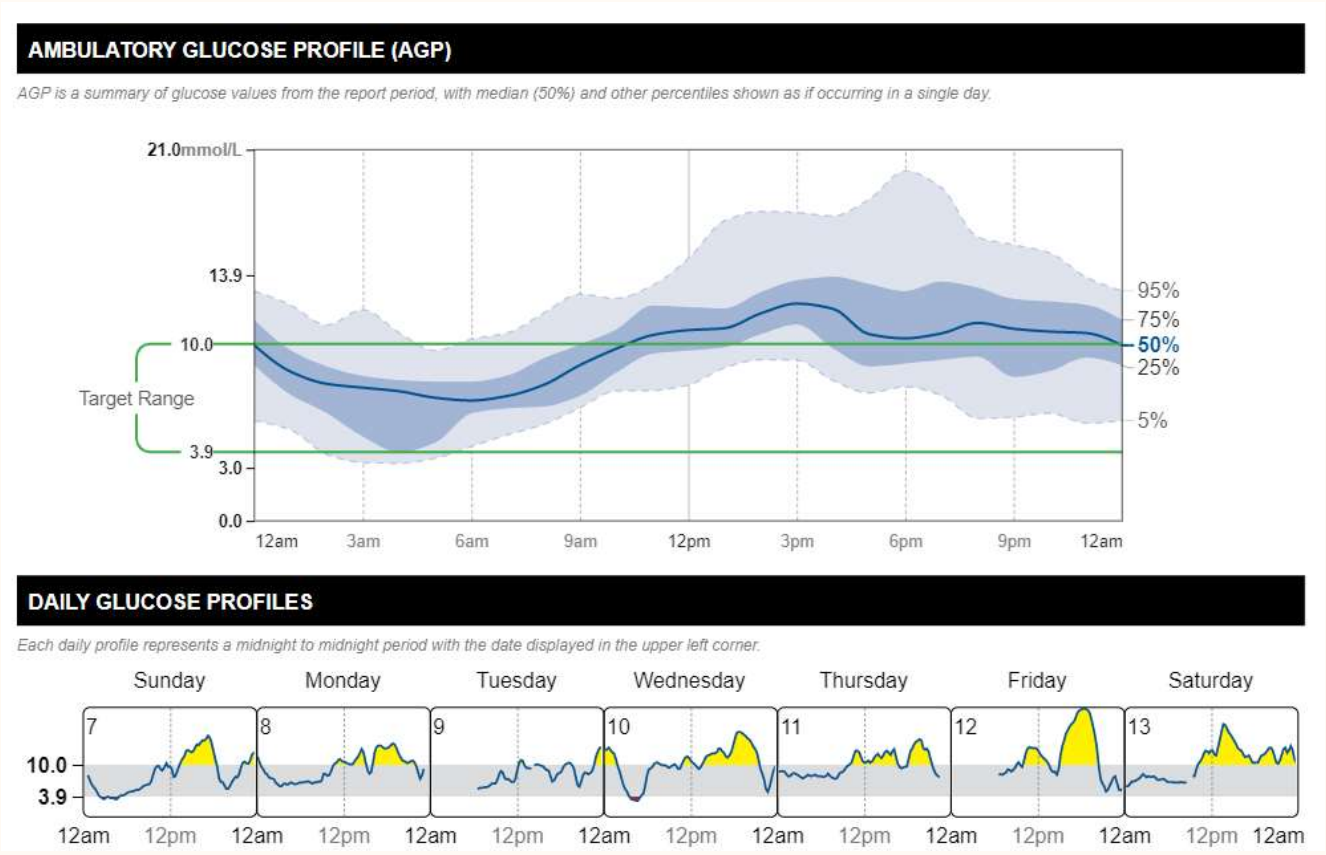
Defined as percent coefficient of variation (%CV)

TIME IN RANGES



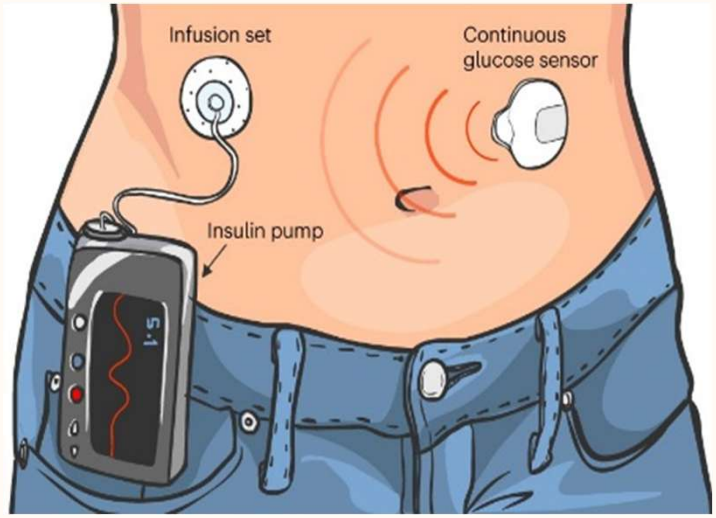
Very High	>13.9 mmol/L	**52%**	(12h 29min)
High	10.1 - 13.9 mmol/L	**26%**	(6h 14min)
Target Range	3.9 - 10.0 mmol/L	**22%**	(5h 17min)
Low	3.0 - 3.8 mmol/L	**0%**	(0min)
Very Low	<3.0 mmol/L	**0%**	(0min)

Ambulatory glucose profile



What is automated insulin delivery (AID)?

- AID is the current gold standard for treating T1D
  - Consists of CGM, pump + algorithm
- AID system will adjust insulin delivery based on predicted glucose levels
- People need to bolus for food + change infusion sites at least ever 3 days
- Only have rapid-acting insulin on board so need plan + back up insulin in case of pump failure



Take home messages

- SGLT2 inhibitors + GLP1Ra are relative game changers in managing type 2 diabetes
- Newer medications reduce CV + renal disease up and above effects of glucose levels
  - Will not cause hypoglycaemia alone & SGLT2i + GLP1Ra typically lead to weight loss
- Management of T2D is now primarily focused on reducing complications of diabetes + weight if appropriate
  - Increasing access to best medications important for the Pacific
- CGM + AID are now gold standards of care for type 1 diabetes

Upcoming webinars

1. **Lifestyle management, Metformin & Vildagliptin**
   Niue - Monday September 8th at 6pm
   Cook Islands - Monday September 8th at 7pm
   Aotearoa, NZ - Tuesday September 9th at 5pm
   Zoom link

2. **Sulfonylureas & Insulin + Management of Hypoglycaemia**
   Niue - Monday September 15th at 6pm
   Cook Islands - Monday September 15th at 7pm
   Aotearoa, NZ - Tuesday September 16th at 5pm
   Zoom link

3. **New Diabetes Medication, Technology & Management algorithm**
   Niue - Monday September 22nd at 6pm
   Cook Islands - Monday September 22nd at 7pm
   Aotearoa, NZ - Tuesday September 23rd at 5pm
   Zoom link

4. **Glycaemic, Blood Pressure & Lipid Targets + Management**
   Niue - Monday September 29th at 6pm
   Cook Islands - Monday September 29th at 7pm
   Aotearoa, NZ - Tuesday September 30th at 5pm
   Zoom link

5. **Diabetes and Sick Day Management, Driving & Pregnancy**
   Niue - Monday October 6th at 6pm
   Cook Islands - Monday October 6th at 7pm
   Aotearoa, NZ - Tuesday October 7th at 5pm
   Zoom link

6. **Management of Complications Related to Diabetes**
   Niue - Monday October 13th at 6pm
   Cook Islands - Monday October 13th at 7pm
   Aotearoa, NZ - Tuesday October 14th at 5pm
   Zoom link

7. **Inpatient Management of Diabetes**
   Niue - Monday October 20th at 6pm
   Cook Islands - Monday October 20th at 7pm
   Aotearoa, NZ - Tuesday October 21st at 5pm
   Zoom link

Case for discussion – Mr K

- 53 year old man with type 2 diabetes (HbA1c 60 mmol/mol), heart failure + chronic kidney disease with Cr 160 umol/L (eGFR 28 mL/min)
  - Current regimen metformin 500 mg twice daily + Mixtard 20 units twice daily

- He has family in New Zealand and is keen to travel to NZ to access best treatment. What medication would you advise?

- Would you try to get him off insulin?

- What would you do if his new medication supply ran out?

Discussion