




# TOUR D'IABETES

Carolyn Droste

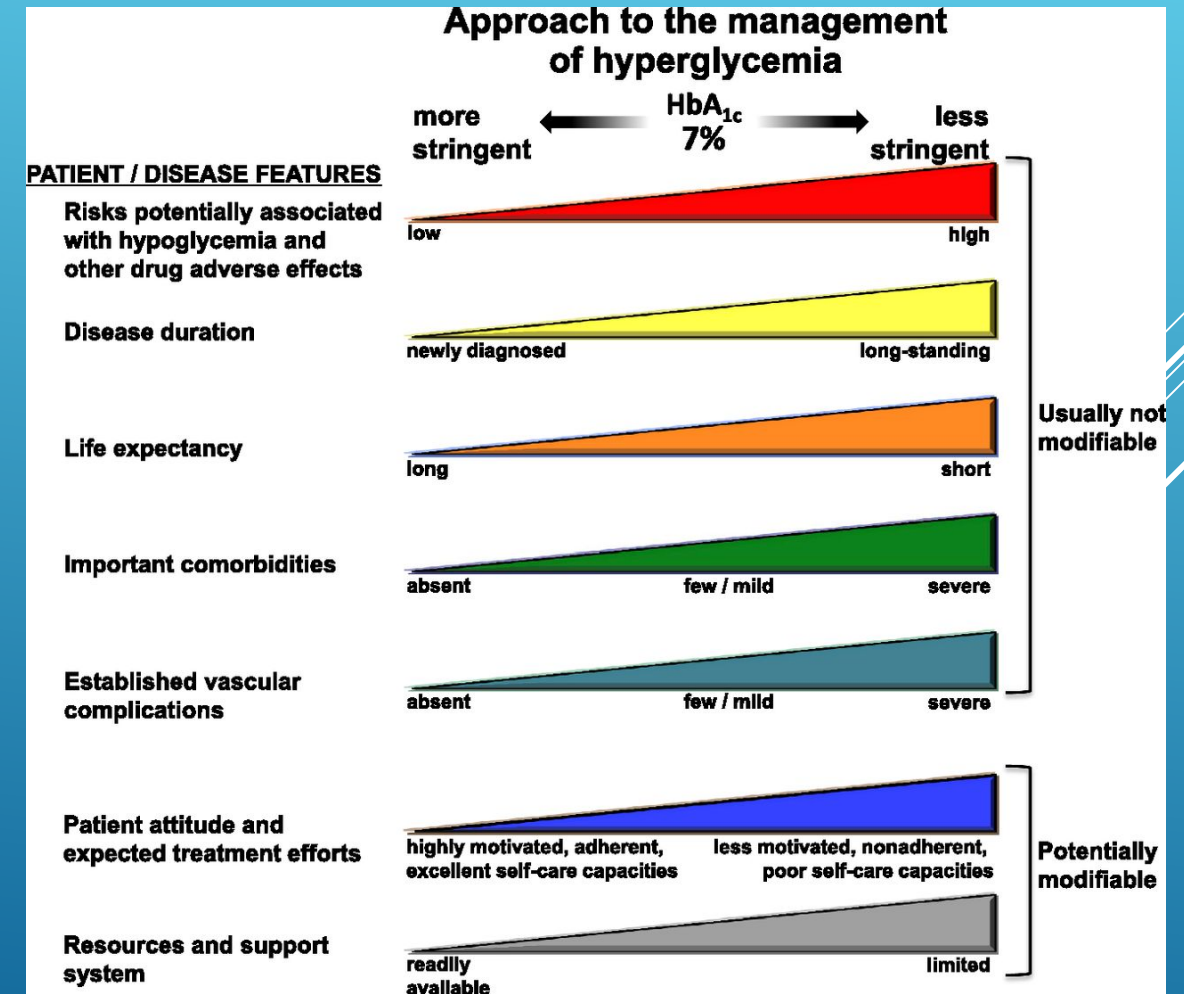


# TYPE 1 DIABETES

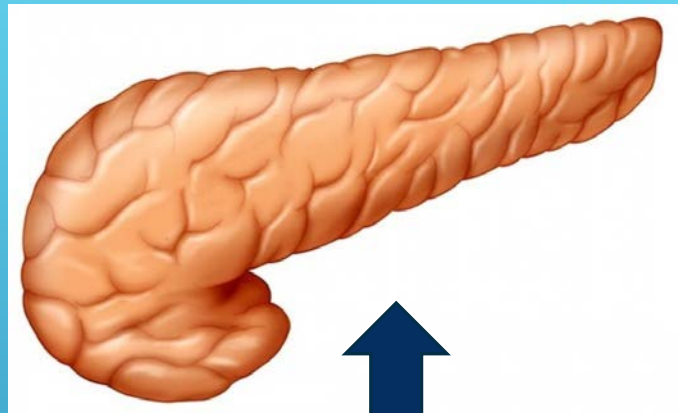
- ▶ Autoimmune disease
  - ▶ Pancreatic  $\beta$  cell destruction
  - ▶ All need insulin replacement
  - ▶ Gold standard is Basal bolus insulin
  - ▶ CSII
- 
- A series of white lines of varying lengths and orientations are positioned in the bottom right corner of the slide, creating a modern, abstract graphic element.

# TYPE 2 DIABETES

- ▶ Target HbA1c, individualise treatment
- ▶ Treat to target early
- ▶ Cardiovascular risk factor management



GLP1  
Incretin  
Aglucosidase

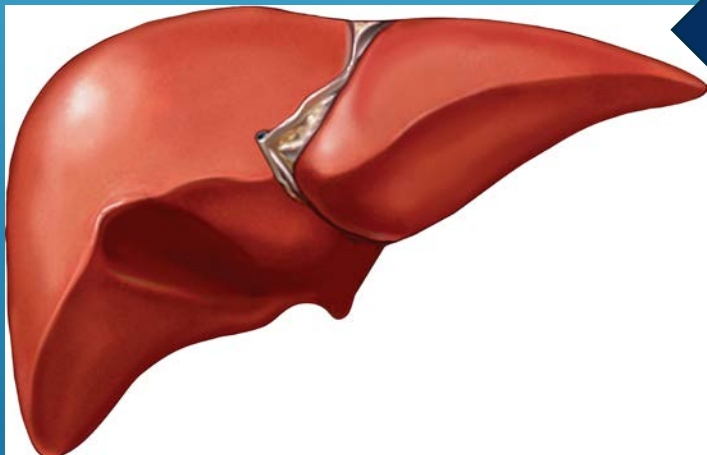


SU  
Incretin



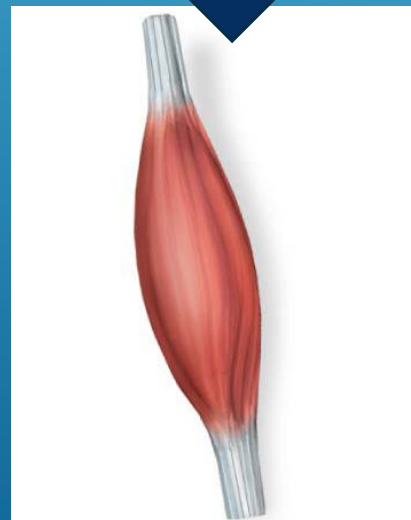
GLP1  
Incretin

HYPERGLYCAEMIA

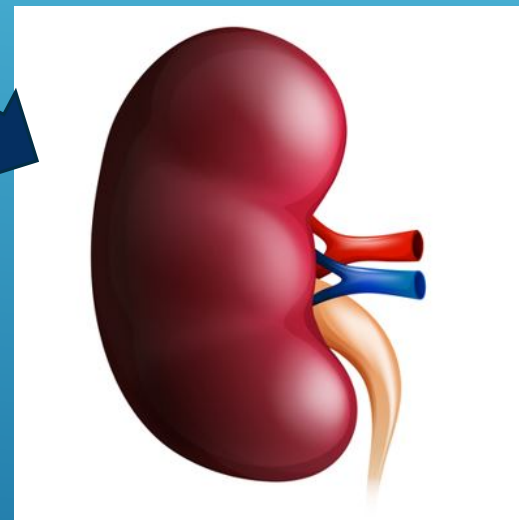


Metformin  
TZD

TZD



Metformin  
TZD



SGLT2



## Mono-therapy

Efficacy\*  
Hypo risk  
Weight  
Side effects  
Costs\*

## Dual therapy†

Efficacy\*  
Hypo risk  
Weight  
Side effects  
Costs\*

## Triple therapy

## Combination injectable therapy‡

Healthy eating, weight control, increased physical activity, and diabetes education

### Metformin

high  
low risk  
neutral / loss  
GI / lactic acidosis  
low

*If HbA<sub>1c</sub> target not achieved after ~3 months of monotherapy, proceed to 2-drug combination (order not meant to denote any specific preference—choice dependent on a variety of patient- and disease-specific factors):*

Metformin +	Metformin +	Metformin +	Metformin +	Metformin +	Metformin +
Sulfonylurea	Thiazolidine-dione	DPP-4 inhibitor	SGLT2 inhibitor	GLP-1 receptor agonist	Insulin (basal)
high efficacy moderate risk gain weight hypoglycemia low costs	high efficacy low risk gain weight edema, HF, fxs low costs	intermediate efficacy low risk neutral weight rare side effects high costs	intermediate efficacy low risk loss weight GU, dehydration high costs	high efficacy low risk loss weight GI side effects high costs	highest efficacy high risk gain weight hypoglycemia variable costs

*If HbA<sub>1c</sub> target not achieved after ~3 months of dual therapy, proceed to 3-drug combination (order not meant to denote any specific preference—choice dependent on a variety of patient- and disease-specific factors):*

Metformin +	Metformin +	Metformin +	Metformin +	Metformin +	Metformin +
Sulfonylurea + TZD or DPP-4-i or SGLT2-i or GLP-1-RA or Insulin <sup>s</sup>	Thiazolidine-dione + SU or DPP-4-i or SGLT2-i or GLP-1-RA or Insulin <sup>s</sup>	DPP-4 inhibitor + SU or TZD or SGLT2-i or Insulin <sup>s</sup>	SGLT2 inhibitor + SU or TZD or DPP-4-i or Insulin <sup>s</sup>	GLP-1 receptor agonist + SU or TZD or Insulin <sup>s</sup>	Insulin (basal) + TZD or DPP-4-i or SGLT2-i or GLP-1-RA

*If HbA<sub>1c</sub> target not achieved after ~3 months of triple therapy and patient (1) on oral combination, move to injectables; (2) on GLP-1-RA, add basal insulin; or (3) on optimally titrated basal insulin, add GLP-1-RA or mealtime insulin. In refractory patients consider adding TZD or SGLT2-i:*

Metformin +

Basal insulin + Mealtime insulin or GLP-1-RA

# DPP IV INHIBITORS

- ▶ “gliptins”
- ▶ Sita, saxa, lina, alo, vilda
- ▶ Most are renally excreted – need to change doses
- ▶ Lina is not
- ▶ Lina and sita on PBS for triple therapy, insulin

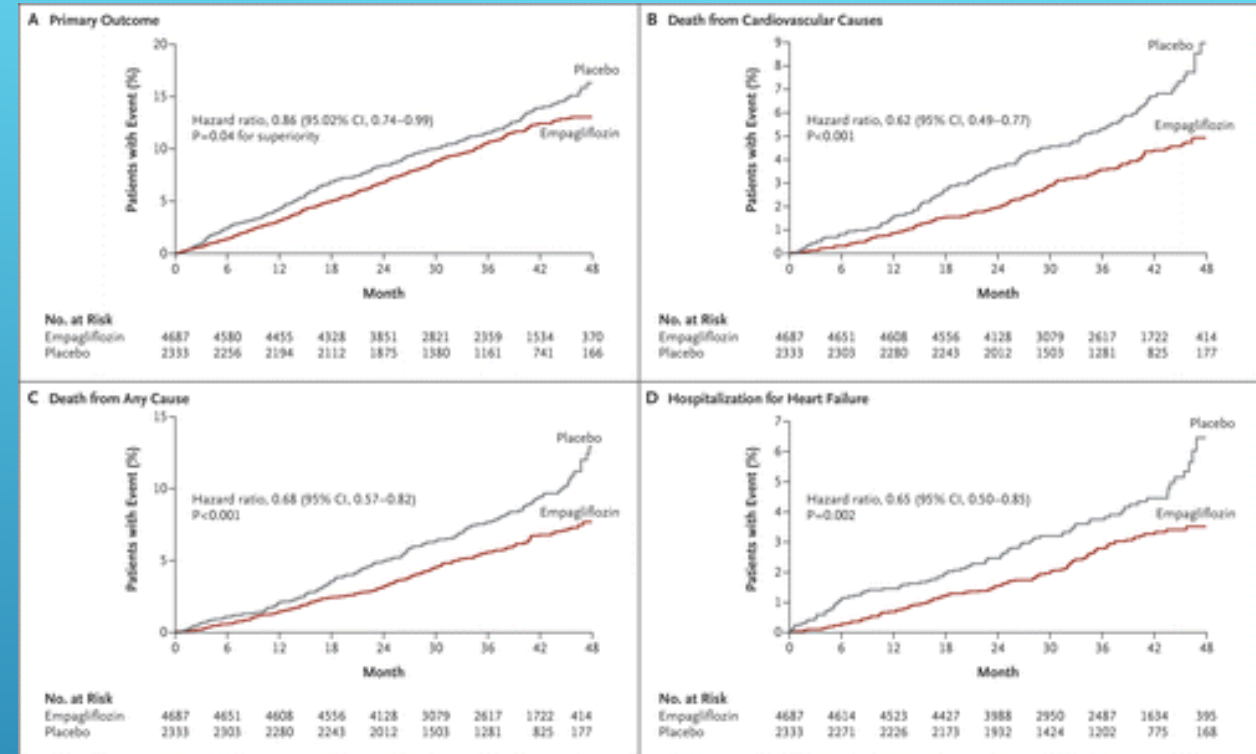
# GLP1 AGONISTS

- ▶ Exenatide (Byetta, Bydureon)
- ▶ (Liraglutide)
- ▶ With insulin



# SGLT2 INHIBITORS

- ▶ “Gliflozins”
- ▶ Empa, Dapa (Cana)
- ▶ Triple therapy, with insulin
- ▶ EMPA-REG





# Summary of non-insulin treatments

	Metformin	SU	SGLT2 inhibitor	DPP-4 inhibitor	TZDs	GLP-1 agonist
Key adverse events/ side effects	Lactic acidosis, gastro-intestinal <sup>1,2</sup>	Hypoglycaemia, weight gain <sup>1</sup>	Genital infections, UTI, postural hypotension <sup>4,17</sup>	Potential risk of pancreatitis <sup>1,17</sup>	Oedema, CHF, fracture <sup>1,3</sup>	Nausea vomiting and potential risk of pancreatitis <sup>1</sup>
Risk of hypoglycaemia	Low in monotherapy Increased risk when combined with insulin/SU <sup>1,9</sup>	Yes (common) <sup>1,17</sup>	Low in monotherapy Increased risk when combined with insulin/ SUs <sup>4,17</sup>	Low in monotherapy Increased risk when combined with insulin/ SUs <sup>1,6</sup>	Low in monotherapy Increased risk when combined with insulin/ SU <sup>1,3</sup>	Low in monotherapy Increased risk when combined with SU <sup>1,9</sup>
Effect on weight	Neutral or slight loss <sup>9,15</sup>	Gain <sup>1,9</sup>	Loss <sup>4,17</sup>	Neutral <sup>9,17</sup>	Gain <sup>1,9</sup>	Loss <sup>1,9</sup>
Renal impairment (CrCl – mL/min)	Stop when <60 <sup>2</sup> (as per PI)	Stop when <30 <sup>15</sup>	Stop when <45 for Empagliflozin <sup>14,16</sup> & Canagliflozin <sup>7,16</sup>  Stop when <60 for Dapagliflozin <sup>5,16</sup>	Dose adjustments (except linagliptin) <sup>15</sup>	No dose adjustment <sup>15</sup>	Stop when <30 <sup>10,15</sup>
Cardiovascular outcomes	Likely to reduce CV events in the overweight <sup>17</sup>	Unclear – possible increase CV risk <sup>1,18</sup>	No evidence of increased risk <sup>12,13</sup> (Trials ongoing)	No evidence of increased risk (CHF signal investigation) <sup>1</sup>	Increased CHF <sup>9</sup> / Decrease MI <sup>11</sup>	No evidence of increased risk <sup>1</sup> (trials ongoing)
<div> <div>Few adverse events or possible benefit</div> <div>Use with caution</div> <div>Likelihood of adverse events</div> </div>						

1. Inzucchi SE *et al. Diabetes Care* 2015;38:140–9. 2. Diaformin PI. Approved 02 Feb 2011. 3. Pioglitazone PI. Amended 03 Jul 2014. 4. Thynne *et al. Australian Prescriber* 2014;37. 5. Dapagliflozin PI. Amended 28 Apr 2014. 6. NPS RADAR February 2013 – Sitagliptin, vildagliptin, saxagliptin. 7. Canagliflozin PI. Amended 11 Aug 2014. 8. RACGP General Practice management of type 2 diabetes 2014-15. 9. Garber AJ *et al. Endocr Pract* 2013;19:536–57. 10. Exenatide PI. Amended 19 May 2014. 11. Dormandy JA *et al. Lancet* 2005;366:1279–89. 12. Neumiller JJ. *Drugs Context* 2014;3:212262. 13. Davis T *et al. Australian Prescriber* 2013; 26th Nov Ed. 14. Empagliflozin PI. Approved 30 Apr 2014. 15. Gunton JE *et al. Med J Aust* 2014;201:650-3. 16. Peene B, Benhalima K. *Ther Adv Endocrin Metab* 2014;5:124–36. 17. NPS July 2014 – Resources and Activities on Type 2 Diabetes. Box 2. 18. Monami M *et al. Diabetes Obes Metab* 2013;15:938–53.

