# Type 2 diabetes management

## What's new?

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*A major paradigm shift has occurred in how we manage patients with type 2 diabetes. Weight loss with intensive diet and lifestyle interventions can result in remission of type 2 diabetes. Medications are now chosen based on patient characteristics and comorbidities (e.g. presence of chronic kidney disease and heart failure, weight and cardiovascular risk), as well as PBS indications.*

Type 2 diabetes is a chronic metabolic disorder characterised by insulin resistance and relative insulin deficiency. The prevalence of type 2 diabetes is rising globally, posing significant challenges to healthcare systems worldwide. Between the years 2000 and 2020, there was almost a three-fold increase in people living with diabetes in Australia, from 460,000 to 1.3 million.[1] About 50,000 Australians were diagnosed with type 2 diabetes in 2021.[1]

GPs play a crucial role in the diagnosis and management of type 2 diabetes because of their frequent patient encounters and comprehensive approach to healthcare delivery. This article provides GPs with the latest insights and practical recommendations in type 2 diabetes management, including lifestyle interventions, medical management, new indications for current therapies and PBS updates.

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### Can remission of type 2 diabetes be achieved?

The Diabetes Remission Clinical Trial (DiRECT) showed that sufficient weight loss can induce remission of type 2 diabetes (Figure 1).[2] This trial compared a weight management program (intervention) with best-practice care (control) in primary care (49 practices) in the UK and recruited 306 individuals aged 20 to 65 years who had been diagnosed with type 2 diabetes within the past six years,

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had a body mass index (BMI) of 27 to 45 kg/m$^2$ and were not receiving insulin. The intervention included withdrawal of antidiabetic and antihypertensive medications, total diet replacement (3452 to 3569 kJ/day formula diet for three to five months), stepped food reintroduction (two to eight weeks) and structured support for long-term weight loss maintenance. The co-primary outcomes were weight loss of 15 kg or more and remission of diabetes defined as a glycated haemoglobin ($HbA_{1c}$) level of less than 6.5% after at least two months off all antidiabetic medications, from baseline to 12 months. The results showed remission rates of 7% (0 to 5 kg weight loss), 34% (5 to 10 kg weight loss), 57% (10 to 15 kg weight loss) and 86% (>15 kg weight loss). This trial was recently replicated in an Australian primary care setting (DiRECT-Aus).[3] The five-year follow up of DiRECT was recently published. After two years of follow up, intervention participants were offered continued low-intensity support (once every three months) for a subsequent three years (extension group = 68% of the intervention group) versus no regular follow up (no extension). At five years, the results showed an average weight loss of 6.1 kg with 13% remaining in remission in the intervention group (Figures 2 and 3).[4] Patients with longer-term type 2 diabetes are likely to have lower rates of remission, and realistic goals are crucial to avoid a sense of failure. Furthermore, those in remission should continue with complication screening and cardiovascular risk modifications. Although bariatric surgery is not widely available on a population level, metabolic surgery is also effective for attaining diabetes remission.

To summarise, an intensive weight management program run in primary care can induce type 2 diabetes remission. Weight loss of 10 to 15 kg and more than 15 kg results in remission of type 2 diabetes in 57% and 86% of patients, respectively, at 12 months. Long-term remission can be achieved if weight regain is minimised.

**Key points**

- **Sodium-glucose cotransporter-2 (SGLT-2) inhibitors now have indications beyond diabetes. They are also now indicated for heart failure with both reduced and preserved ejection fraction and chronic kidney disease independent of type 2 diabetes.**
- **A new PBS change from 1 June 2024 means a patient must 'fail' an SGLT-2 inhibitor before glucagon-like peptide 1 receptor agonists (GLP-1 RAs) can be prescribed.**
- **GLP-1 RAs are not only effective glucose-lowering agents and induce meaningful weight loss, but they also reduce the rates of major adverse cardiovascular events. Similar cardiovascular benefits have been shown in obese patients without diabetes who have established cardiovascular disease.**
- **Recent clinical trials have also shown that semaglutide slows the progression of chronic kidney disease in patients with type 2 diabetes, which are the first clear data showing the renal protection effects of GLP-1 RAs.**
- **An intensive weight management program (diet and lifestyle intervention) can result in type 2 diabetes remission, which is proportional to the amount of weight loss. Weight loss of 10 to 15 kg and more than 15 kg results in a 57% and 86% chance of diabetes remission, respectively. It appears that with weight regain, diabetes will return.**



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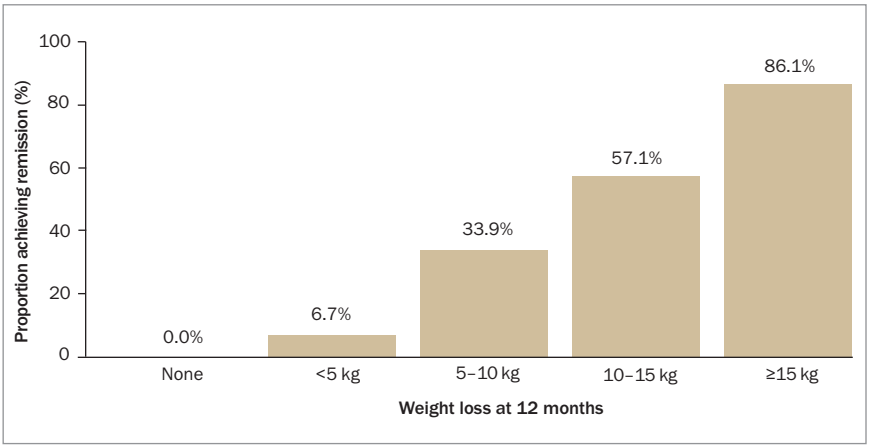


**Figure 1. Proportion of people achieving remission of diabetes in relation to weight loss achieved at 12 months in the Diabetes Remission Clinical Trial (DiRECT).[2]**

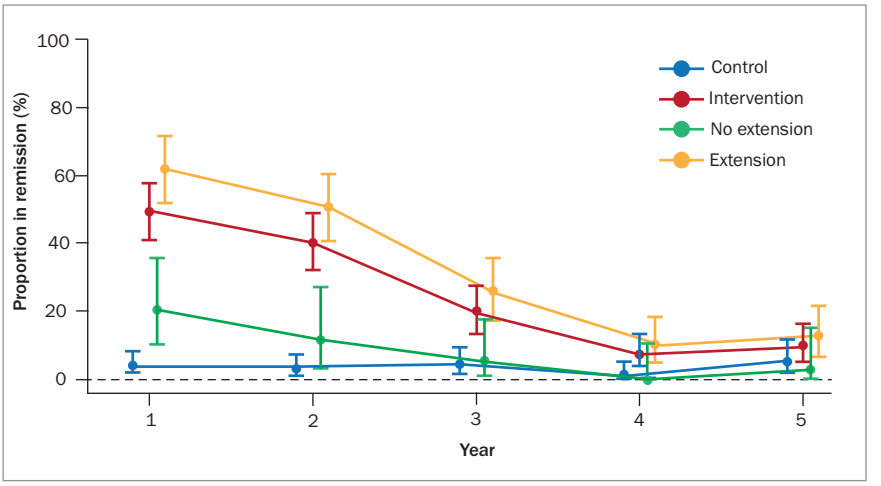


**Figure 2. Proportion of people in remission of diabetes each year in the Diabetes Remission Clinical Trial (DiRECT).[4]**

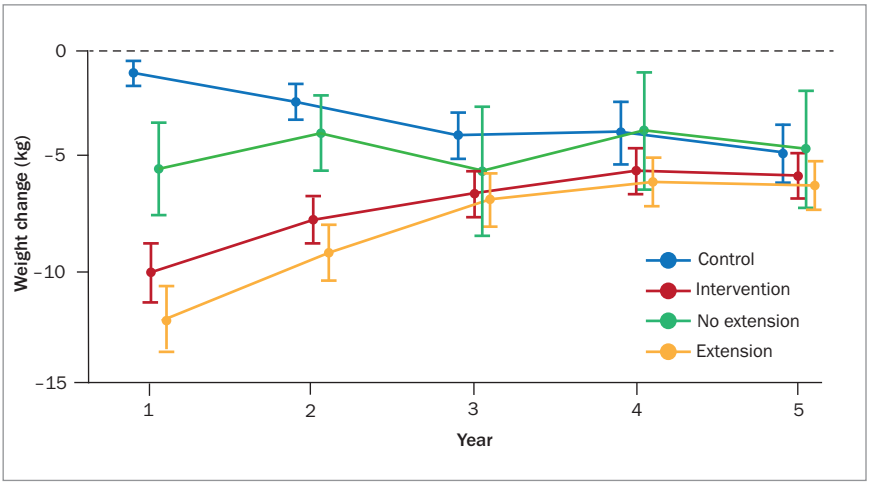


**Figure 3. Weight change since baseline by year in the Diabetes Remission Clinical Trial (DiRECT).[4]**

## Paradigm shift in type 2 diabetes management

### Sodium-glucose cotransporter-2 (SGLT-2) inhibitors

The type 2 diabetes world changed with the presentation of the Empagliflozin, Cardiovascular Outcomes, and Mortality in Type 2 Diabetes (EMPA-REG OUTCOME) trial at the European Association of the Study of Diabetes meeting in Stockholm in 2015.[5] Previous cardiovascular outcome trials had shown that the dipeptidyl peptidase-4 (DPP-4) inhibitors (gliptins) showed no impact on major adverse cardiovascular events (MACE).[6,7] These phase 4 trials were mandated by the FDA, after the apparent increase in MACE with the use of rosiglitazone after a review published in 2007.[8] The EMPA-REG OUTCOME trial demonstrated that patients with type 2 diabetes at high risk for cardiovascular events who received empagliflozin had a significant 14% reduction in MACE. It also demonstrated a significant reduction in secondary endpoints of cardiovascular death, hospitalisations for heart failure and death from any cause.[5] Moreover, there was a suggestion of renal protection (which led the way for the subsequent heart failure and renal-specific trials). This trial changed the way we use pharmacological agents to manage type 2 diabetes. We now use medications not only for glycaemic control, but also to promote an individualised approach by choosing medications for additional benefits based on patient characteristics and comorbidities. The use of SGLT-2 inhibitors has become widespread across general practice, endocrinology, cardiology and nephrology. The relevant safety concerns are addressed in patient resources, which highlight sick day rules and the requirement to withhold before surgery (see: www.health.qld.gov.au/__data/assets/pdf_file/0022/1154380/SGLT2-inhibitor-Patient-Information.pdf).

Since the EMPA-REG OUTCOME trial, SGLT-2 inhibitors have shown benefits in patients with heart failure with reduced ejection fraction (HFrEF) or preserved ejection fraction (HFpEF) and chronic kidney disease (CKD), as well as a reduction in MACE.[9-14] In fact, the SGLT-2 inhibitors (empagliflozin and dapagliflozin) now have PBS listings



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**1. PBS indications for dapagliflozin and empagliflozin for type 2 diabetes, CKD and heart failure***

**CKD**

**Clinical criteria**

- The patient must have a diagnosis of CKD present for at least 3 months AND
- eGFR 25 to 75 mL/min/1.73 $m^2$ † AND
- uACR 22.6 to 565 mg/mmol AND
- The patient must not be receiving treatment with another SGLT-2 inhibitor AND
- The patient must be stabilised on a RAAS inhibitor for at least four weeks, unless medically contraindicated, before starting combination therapy with this drug

Abbreviations: CKD = chronic kidney disease; eGFR = estimated glomerular filtration rate; GLP-1 = glucagon-like peptide-1; $HbA_{1c}$ = glycated haemoglobin; LVEF = left ventricular ejection fraction; RAAS = renin–angiotensin–aldosterone system; SGLT-2 = sodium-glucose cotransporter-2; uACR = urine albumin-to-creatinine ratio.

*Refer to the PBS website for full details.

† eGFR cutoffs according to TGA indications for CKD are 20 mL/min/1.73 $m^2$ for empagliflozin and 25 mL/min/1.73 $m^2$ for dapagliflozin.

**Type 2 diabetes**

**Clinical criteria**

- The treatment must be used in combination with at least one of metformin, a sulfonylurea and insulin AND
- The condition must be inadequately responsive to at least one of the aforementioned agents AND
- The patient must not be undergoing concomitant PBS-subsidised treatment with a GLP-1 receptor agonist or another SGLT-2 inhibitor
- If using as initial treatment:
  - the treatment must be used in combination with metformin and a dipeptidyl peptidase-4 inhibitor AND
  - $HbA_{1c}$ >7% despite metformin and gliptin treatment OR
  - blood glucose levels >10 mmol/L in more than 20% of tests within 2 weeks before starting treatment

**Chronic heart failure**

**Clinical criteria**

- The patient must have symptomatic heart failure (New York Heart Association classes II, III or IV), independent of LVEF
- If LVEF is 40% or less, add-on to optimal heart failure treatment (must include beta blocker and ACE, angiotensin II antagonist or angiotensin receptor with neprilysin inhibitor unless contraindicated or cannot be tolerated)
- If LVEF is >40%, there must be structural changes on echocardiography that would be expected to cause diastolic dysfunction (e.g. left ventricular hypertrophy), and at least one of i) diastolic dysfunction with high filling pressures; ii) hospitalisation for heart failure in the past 12 months; iii) requirement for IV diuretic therapy in the past 12 months; iv) elevated N-terminal pro brain natriuretic peptide levels
- The patient must not be receiving treatment with another SGLT-2 inhibitor

(streamlined authority required) for HFrEF, HFpEF and CKD independent of diabetes status (i.e. these benefits are seen independent of the glucose-lowering effect) (Box 1). This is the first class of medication in 20 years to slow the progression of CKD. Similarly, SGLT-2 inhibitors are the first class of medication with level 1 evidence to be indicated for HFpEF. There are estimated glomerular filtration rate (eGFR) cutoffs for initiating patients on SGLT-2 inhibitors, which are as follows:

- dapagliflozin: do not initiate if eGFR is less than 25 mL/min/1.73 $m^2$, but continue if the patient is already on with approval from a nephrologist
- empagliflozin: do not initiate if eGFR is less than 20 mL/min/1.73 $m^2$, but continue if the patient is already on with approval from a nephrologist.

These eGFR cutoffs are not because of additional adverse events, but because of a current lack of data (more trials are coming soon). Reassuringly, in patients without type 2 diabetes, there appears to be minimal risk for genital fungal infections, urinary tract infections and other adverse effects, including euglycaemic diabetic ketoacidosis (or SGLT-2 inhibitor-induced diabetic ketoacidosis which can also occur with higher blood glucose levels); however, patient awareness of sick day management remains important (see: www.health.qld.gov.au/__data/assets/pdf_file/0022/1154380/SGLT2-inhibitor-Patient-Information.pdf).

## GLP-1 and GLP-1/GIP receptor agonists

Glucagon-like peptide-1 receptor agonists (GLP-1 RAs) and GLP-1 and glucose-dependent insulinotropic polypeptide (GIP) receptor coagonist are among the newest medications for people with type 2 diabetes. These incretin-based medications have been shown to have impressive $HbA_{1c}$ and weight reduction benefits (Table), but potentially, and more importantly, they also reduce MACE. Liraglutide is a once-daily GLP-1 RA and is also TGA approved for weight loss (but not PBS listed; cost on private prescription is $380 per month). Liraglutide was the first GLP-1 RA to demonstrate a significant reduction in MACE in patients with type 2 diabetes.[15] Dulaglutide was the first weekly GLP-1 RA to show a MACE benefit in the dulaglutide and cardiovascular outcomes in type 2 diabetes (REWIND) trial.[16] Of note, most patients in the REWIND trial had risk factors but not established cardiovascular disease. Subsequently, semaglutide (0.5 mg or 1.0 mg weekly) also showed a MACE benefit in the Trial to Evaluate Cardiovascular and Other Long-term Outcomes with Semaglutide in Subjects with Type 2 Diabetes (SUSTAIN 6).[17] The recently published Semaglutide Effects on Cardiovascular Outcomes in People with Overweight or Obesity (SELECT) trial has generated an enormous amount of interest, reporting a 20% reduction in MACE following introduction of high-dose semaglutide (2.4 mg weekly) in obese patients without diabetes who have established cardiovascular disease (i.e. these benefits are independent of glucose-lowering effects).[18]

Recently, the Evaluate Renal Function with Semaglutide Once Weekly (FLOW) trial was published.[19] The trial was stopped early due to interim analysis showing statistical benefit in renal endpoints. In this study, 3533 patients with type 2 diabetes and CKD (eGFR of 50 to 75 mL/min/1.73 $m^2$ and urine albumin-to-creatinine ratio 33.9 to 565 mg/mmol or an eGFR of 25 to 50 mL/min/1.73 $m^2$ and urine albumin-to-creatinine ratio of 11.3 to 565 mg/mmol) were randomised to receive



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**Table. Comparison of the injectable incretin-based therapies available for type 2 diabetes**

| | Liraglutide 1.8 mg | Dulaglutide 1.5 mg | Semaglutide 1 mg | Tirzepatide (5 to 15 mg) |
|---|---|---|---|---|
| Administration | Subcutaneous daily | Subcutaneous weekly | Subcutaneous weekly | Subcutaneous weekly |
| Recommended eGFR | >15 mL/min/1.73 m$^2$ | >15 mL/min/1.73 m$^2$ | >30 mL/min/1.73 m$^2$ | Can be used in patients with renal impairment (including end-stage renal disease) |
| Cardiovascular protection | Yes | Yes | Yes | Trial not reported |
| Renal protection | No data | No data | Yes | No data |
| $HbA_{1c}$ reduction | ~1.2% | ~1.4% | ~1.8% | 2 to 2.3% |
| Weight loss | ~3 kg | ~3 kg | ~6.2 kg | 7.8 to 12.4 kg |
| TGA indications | Type 2 diabetes and weight loss | Type 2 diabetes | Type 2 diabetes and weight loss | Type 2 diabetes |
| Listed on the PBS | No | Yes | Yes, for type 2 diabetes | No |
| Monthly cost | ~$380 | $31.60 on PBS | $31.60 on PBS and ~$140 on private script | ~$320 to $645 |

Abbreviations: eGFR = estimated glomerular filtration rate; $HbA_{1c}$ = glycated haemoglobin.

semaglutide 1 mg or placebo. There was a statistically significant 24% reduction in progression of CKD and death from kidney-related or cardiovascular causes, including a 21% reduction in kidney-specific endpoints (dialysis or transplantation, at least a 50% reduction in eGFR from baseline or eGFR <15 mL/min/1.73 m$^2$). Semaglutide slowed the annual decline in eGFR by 1.16 mL/min/1.73 m$^2$ ($p<0.001$). These are the first clear data showing the renal protection effects of GLP-1 RAs.

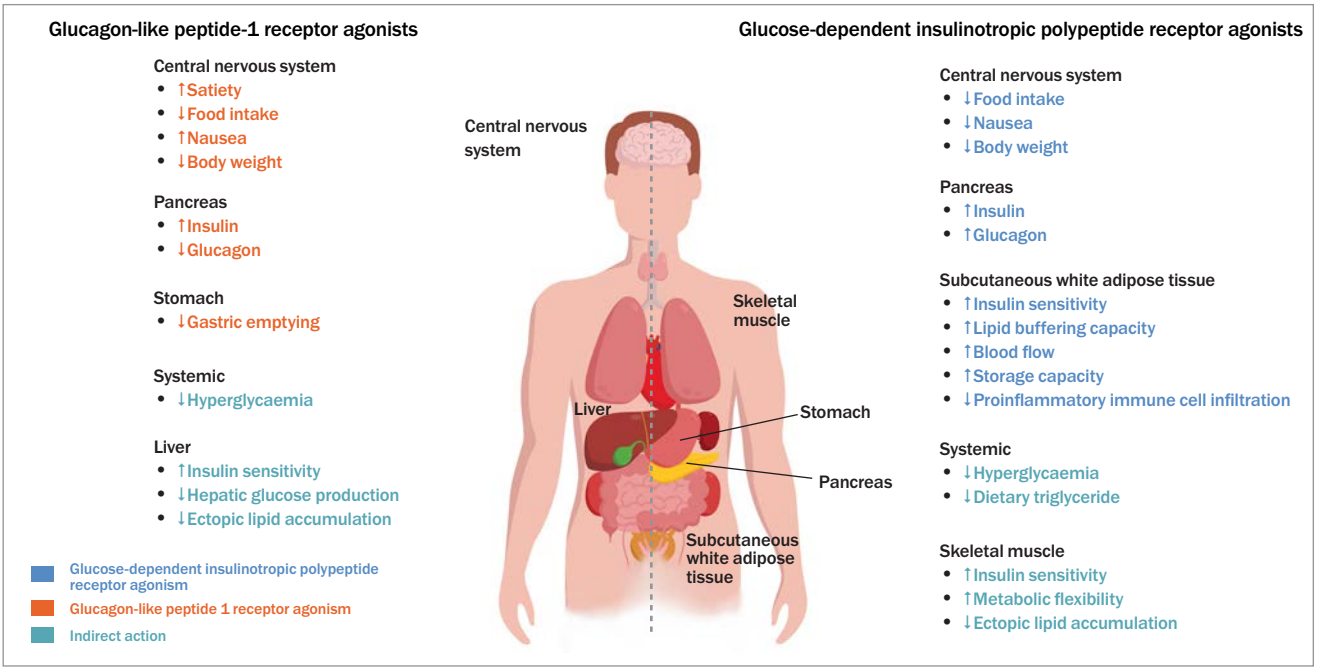


**Figure 4. Benefits of glucagon-like peptide-1 (GLP-1) receptor agonists and glucose-dependent insulinotropic polypeptide (GIP) in type 2 diabetes. Note complementary and differential effects. At the level of the central nervous system, GIP reduces nausea, whereas GLP-1 receptor agonists increase nausea. There is a differential effect on glucagon secretion: GLP-1 receptor agonists reduce glucagon secretion, whereas GIP promotes glucagon secretion. There appear to be some specific adipose tissue and skeletal muscle effects with GIP.[25]**

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**2. PBS criteria for finerenone in patients with type 2 diabetes and CKD**

- Patient must have a diagnosis of CKD present for at least three months and not have known significant nondiabetic renal disease
- Patient must have an eGFR >25 mL/min/1.73 m$^2$
- Patient must have an uACR >22.6 mg/mmol
- Patient must be stabilised on either an ACE inhibitor or an ARB unless medically contraindicated
- The treatment must be used in combination with an SGLT-2 inhibitor unless contraindicated or intolerant
- Patient must not be receiving treatment with another selective nonsteroid MRA, a renin inhibitor or potassium-sparing diuretic
- Patient must not have established heart failure with reduced ejection fraction with an indication for treatment with an MRA
- Patient must discontinue treatment with this drug prior to initiating renal replacement therapy, defined as dialysis or kidney transplant

Abbreviations: CKD = chronic kidney disease; eGFR = estimated glomerular filtration rate; SGLT-2 = sodium-glucose cotransporter-2; MRA = mineralocorticoid receptor antagonist; uACR = urine albumin-to-creatinine ratio.

**3. Finerenone dosing**

| | |
|---|---|
| eGFR >60 mL/min/1.73 m$^2$ | Start at 20 mg once daily |
| eGFR 25 to 59 mL/min/1.73 m$^2$ | Start at 10 mg once daily |
| eGFR <25 mL/min/1.73 m$^2$ | Not recommended |

Measure serum potassium level and eGFR four weeks after starting or increasing dose
- If potassium level is >5.5 mmol/L, withhold finerenone
- If potassium level is 4.9 to 5.5 mmol/L, maintain dose
- If potassium level is <4.8 mmol/L, increase dose to 20 mg

Abbreviation: eGFR = estimated glomerular filtration rate.

Tirzepatide is the first-in-class dual GLP-1/GIP receptor agonist. In a head-to-head trial (patients with type 2 diabetes), tirzepatide at doses of 5 mg, 10 mg and 15 mg outperformed semaglutide at a dose of 1 mg. The estimated mean change from baseline in $HbA_{1c}$ was 1.86% for semaglutide and 2.01%, 2.24% and 2.3% with 5 mg, 10 mg and 15 mg of tirzepatide, respectively. The changes in body weight were 6.7% with 1 mg semaglutide and 8.5%, 11% and 13.1% with 5 mg, 10 mg, and 15 mg of tirzepatide, respectively.[20] Of note, tirzepatide has not been trialled against high-dose semaglutide (2.4 mg), which is the dose employed in weight loss trials and is now available in Australia for the treatment of overweight and obesity in the FlexTouch pen device at doses and cost per month of 0.25 mg ($260), 0.5 mg ($260), 1.0 mg ($260), 1.7 mg ($380) and 2.4 mg ($460). Despite tirzepatide requiring injections with a vial, needle and syringe (a new multidose device option is available this month) and no PBS listing (cost ranges from $320 to $645 per month), this medication sold out in Australia within three months (available again from mid-February 2024). The weight loss benefits observed with the use of semaglutide and tirzepatide are far better in patients without type 2 diabetes. The SURMOUNT-1 trial evaluated the efficacy and safety of tirzepatide in adults with obesity or overweight who did not have diabetes and reported weight losses of 16%, 21.4% and 22.5% at 72 weeks with 5 mg, 10 mg and 15 mg of tirzepatide, respectively.[21] The Semaglutide Treatment Effect in People with Obesity (STEP-1) trial demonstrated 14.9% body weight loss at 68 weeks with semaglutide 2.4 mg.[22] Recent studies following withdrawal of these therapies do show weight regain in the majority of patients, suggesting that long-term treatment is required.[23,24] A summary of the incretin effects is shown in Figure 4.[25] It is an exciting time for the management of type 2 diabetes, with a number of other injectable and oral therapies in the pipeline. A Study of Tirzepatide Compared With Dulaglutide on Major Cardiovascular Events in Participants With Type 2 Diabetes (SURPASS-CVOT) is due to report in 2025–26.

## Adjunctive therapies in patients with type 2 diabetes to address complications

### Retinopathy

It is worth revisiting the use of fenofibrate to slow the progression of diabetic retinopathy. Data from the Fenofibrate Intervention and Event Lowering in Diabetes (FIELD) study demonstrated benefits in patients with moderate to severe nonproliferative retinopathy, proliferative retinopathy and macular oedema.[26] Fenofibrate needs to be renally adjusted (if eGFR is >60 mL/min/1.73 m$^2$, the dose should be 145 mg; if eGFR is 30 to 60 mL/min/1.73 m$^2$, start with 48 mg daily and increase to 96 mg daily if no adverse effects on renal function are observed). A rapid drop in $HbA_{1c}$ level can worsen pre-existing retinopathy but it is important to note that this is not a medication-specific effect.[17]

### Chronic kidney disease and cardiovascular disease

Finerenone, a selective nonsteroidal mineralocorticoid receptor antagonist (MRA), received its PBS listing (streamline authority required) for use in patients with type 2 diabetes and CKD on 1 July 2023 (Box 2). The Efficacy and Safety of Finerenone in Subjects With Type 2 Diabetes Mellitus and the Clinical Diagnosis of Diabetic Kidney Disease (FIGARO-DKD) trial and Finerenone in Reducing Kidney Failure and Disease Progression in Diabetic Kidney Disease (FIDELIO-DKD) trial were undertaken and looked at a four-point MACE (cardiovascular death, nonfatal myocardial infarction, nonfatal stroke, hospitalisation for heart failure) and renal endpoints (at least 40% reduction in eGFR, need for renal replacement therapy or death from renal causes).[27,28] Patients had an eGFR range of 25 to 90 mL/min/1.73 m$^2$ and varied levels of albuminuria (albumin-to-creatinine ratio of 3.4 to 565 mg/mol) depending on the trial. All patients were stabilised on renin-angiotensin system



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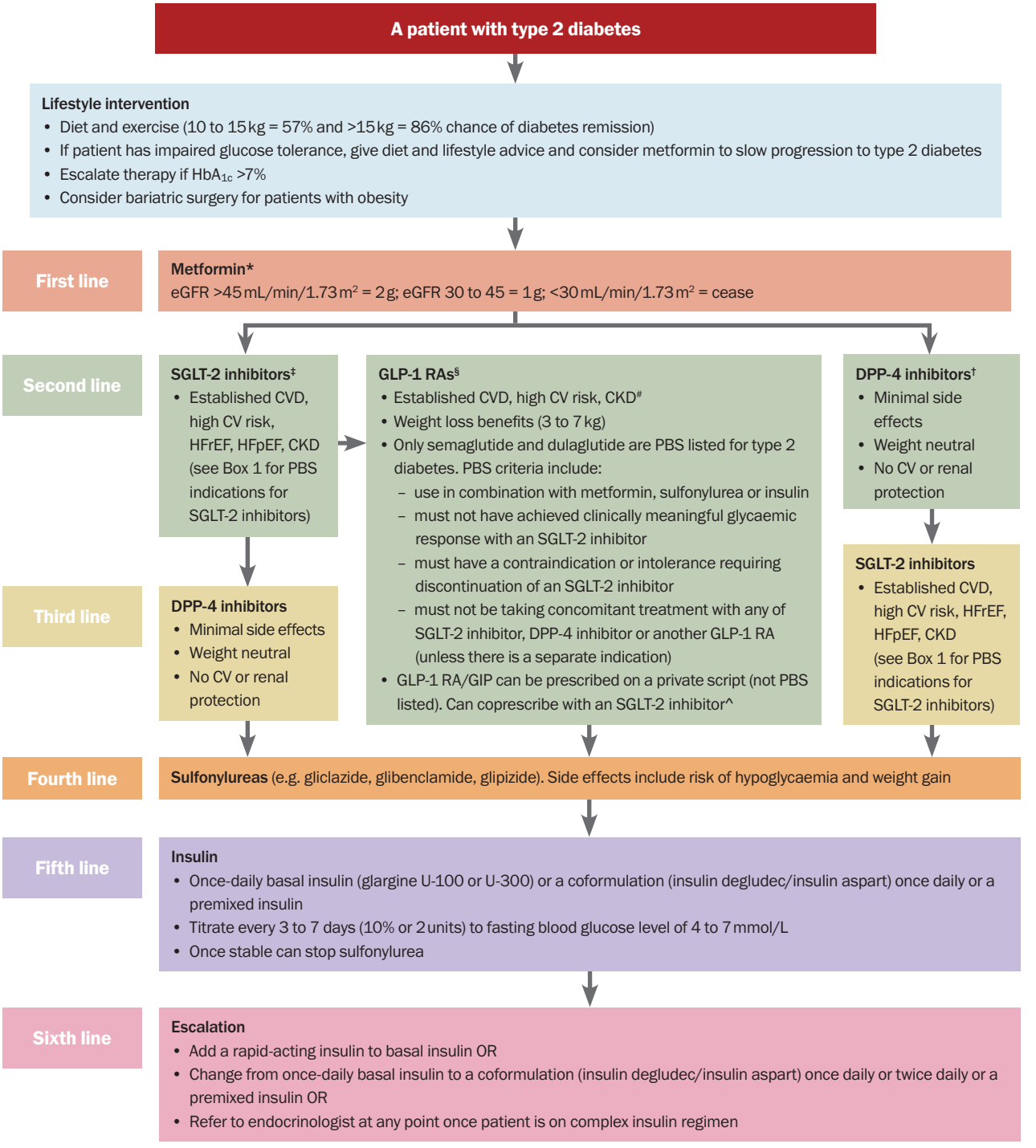
## A practical guide for the management of type 2 diabetes




Abbreviations: CKD = chronic kidney disease; CV = cardiovascular; CVD = cardiovascular disease; DPP-4 = dipeptidyl peptidase-4 inhibitors eGFR = estimated glomerular filtration rate; GIP = glucose-dependent insulinotropic polypeptide; GLP-1 = glucagon-like peptide-1; $HbA_{1c}$ = glycated haemoglobin; HFrEF = heart failure with reduced ejection fraction; HFpEF = heart failure with preserved ejection fraction SGLT-2 = sodium-glucose cotransporter-2.

* Metformin: immediate release must be twice daily; extended release can be once daily.

† DPP-4 inhibitors: sitagliptin, linagliptin, alogliptin, vildagliptin, saxagliptin. All except linagliptin need to be renally adjusted.

‡ SGLT-2 inhibitors: empaglifozin and dapagliflozin. Initiate when eGFR >25 mL/min/1.73 m² (PBS criteria). General advice is to continue treatment if eGFR <25 mL/min/1.73 m² but seek nephrology advice. Note: an acceptable drop in eGFR after initiation is <25%.

§ GLP-1 RAs: of the GLP-1 RAs, only semaglutide and dulaglutide are PBS listed for type 2 diabetes. Semagltide: recommended eGFR is >30 mL/min/1.73 m ²; dulaglutide: recommended eGFR >15 mL/min/1.73 m².

# Only semaglutide is currently proven to slow progression of CKD.

^ Tirzepatide is TGA approved for patients with insufficiently controlled type 2 diabetes (not on PBS). Note: DPP-4 inhibitors and GLP-1 RAs are the same class, therefore do not combine.

This is a guide and is the personal opinion of Dr Thomas Dover and will not apply to all patients. For formal guidelines please see the Australian Diabetes Society *Type 2 Diabetes Glycaemic Management Algorithm* (current update June 2024; see: https://www.diabetessociety.com.au/guideline/australian-t2d-glycaemic-management-algorithm-june-2024/).



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treatment before initiation of finerenone. Both trials achieved significance, with the FIGARO-DKD trial demonstrating a 13% relative risk reduction in MACE and the FIDELIO-DKD trial demonstrating an 18% reduction in renal endpoints. Finerenone was ceased in 1.2% of patients in the FIGARO-DKD trial and 2.3% of patients in the FIDELIO-DKD trial because of hyperkalaemia (see Box 3 on finerenone dosing).

### Cardiovascular disease

Although aspirin for secondary prevention of cardiovascular disease is established practice, aspirin or other antiplatelet therapy is not recommended for the primary prevention of cardiovascular disease in patients with type 2 diabetes. Earlier studies of aspirin in the primary prevention setting were undertaken when the use of blood pressure and statin therapy was less widespread. A Study of Cardiovascular Events in Diabetes (ASCEND) evaluated the role of aspirin in the primary prevention of serious vascular events in people with type 2 diabetes, and although a modest reduction in MACE was observed, this was offset by an increase in major bleeding.[29]

Icosapent ethyl is a highly purified eicosapentaenoic acid ethyl ester (a component of fish oil) that demonstrated a significant 25% cardiovascular risk reduction for hypertriglyceridaemia.[30] It is TGA approved to reduce the risk of cardiovascular events in statin-treated patients at high cardiovascular risk with elevated triglyceride levels (≥1.7 mmol/L) and established cardiovascular disease or diabetes, and at least one other cardiovascular risk factor. It should become available for use in Australia later in 2024.

## Navigating the PBS and type 2 diabetes treatment algorithm

The pharmacological management of type 2 diabetes has changed dramatically over the past 20 years. In the 2000s, the thiazolidinediones (rosiglitazone and pioglitazone) entered the market, adding a third option to metformin and sulfonylureas. The DPP-4 inhibitors (initially sitagliptin, then saxagliptin, linagliptin, vildagliptin and alogliptin) soon followed. The PBS was relatively easy to navigate at this point. However, immediate-release exenatide entered the market in 2010, and the SGLT-2 inhibitors (dapagliflozin, followed by empagliflozin) in 2013, and it became complex. It seemed the PBS was being updated to reflect which DPP-4 inhibitor, SGLT-2 inhibitor, GLP-1 RA could be used in combination – without forgetting insulin. In the late 2010s, the new indications discussed in this article added further complexity. DPP-4 inhibitors should be ceased when GLP-1 RAs are prescribed as they have no therapeutic effect in this setting (act on same pathway). The PBS does not subsidise coprescription of GLP-1 RAs and SGLT-2 inhibitors for diabetes management; however, there is evidence to support the concomitant use of these agents.[31]

The GLP-1 RAs no longer have streamlined authority codes for new initiations. On 1 June 2024, changes were made to the restrictions of several medicines listed on the PBS for the treatment of type 2 diabetes to implement recommendations made by the Pharmaceutical Benefits Advisory Committee in March 2023, July 2023 and March 2024. These changes aim to simplify and clarify the PBS restrictions, ensure use in accordance with the PBS restrictions, and align the restrictions with current clinical guidelines while considering the cost effectiveness of comparative treatments. The restriction changes were recommended following PBAC consideration of a utilisation analysis examining the extent of use of type 2 diabetes medicines outside of the current PBS restrictions. Relevant consumer and prescriber groups and sponsor companies were consulted regarding the restriction changes.[32] It was reported that almost 60% of people prescribed GLP-1 RA appeared to be on a regimen inconsistent with PBS guidelines. GLP-1 RAs prescribing has risen from 7% (2017–18; cost about $37 million) to 26% (2021–22; cost $193 million), with GLP-1 RAs now the most expensive type 2 diabetes medication on the PBS.[32]

In summary, to prescribe a GLP-1 RA after metformin, the patient must trial an SGLT-2 inhibitor and not have a clinically meaningful glycaemic response or they must have a contraindication or intolerance to an SGLT-2 inhibitor. If the patient has a separate indication for a SGLT-2 inhibitor (e.g. heart failure or CKD as outlined above), then coprescription is allowed. The Australian Diabetes Society *Type 2 Diabetes Glycaemic Management Algorithm* is regularly updated (current update June 2024; see: https://www.diabetessociety.com.au/guideline/australian-t2d-glycaemic-management-algorithm-june-2024/) and the *Living Evidence Guidelines in Diabetes* aims to keep clinicians up to date with the latest changes.[33] A practical treatment guide from the use of metformin to insulin, taking into consideration patient factors and the PBS to guide prescribing, is shown in the Flowchart. This is not a replacement for the nationwide guidelines/algorithm, but an aid to simplify the common treatment approaches for GPs.

## Summary

A major paradigm shift has occurred in the management of type 2 diabetes. Remission has been shown with weight loss as a result of diet and lifestyle interventions and should always be the cornerstone of practice. Medications are now chosen based on patient characteristics and comorbidities (e.g. CKD, HFrEF, HFpEF, cardiovascular risk and weight) and the PBS indications. We have never been in a better position to help our patients with type 2 diabetes manage glycaemic control, risk factors and diabetes complications. **ET**

### References

A list of references is included in the online version of this article (www.endocrinologytoday.com.au).

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# Type 2 diabetes management

## What's new?

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