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SPECIAL REPORT

Type 2 diabetes management guidance

2021 Recommendations from the NZSSD

Making Education Easy 2021

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Abbreviations used in this review
ACEi = angiotensin converting enzyme inhibitor
ARB = angiotensin receptor blocker
BGL = blood glucose level
BMI = body mass index
BP = blood pressure
CCB = calcium channel blocker
CV = cardiovascular
DPPIV = dipeptidyl peptidase-IV
eGFR = estimated glomerular filtration rate
FBG = fasting blood glucose
GAD = glutamic acid decarboxylase
GI = glycaemic index
GLP1RA = glucagon-like peptide-1 receptor agonist
GTT = glucose tolerance test
HbA1c = haemoglobin A_{1c}
IA2 = islet-cell
LDL = low-density lipoprotein
NSAID = non-steroidal anti-inflammatory drugs
PCOS = polycystic ovarian syndrome
RBC = red blood cell
SGLT2i = sodium glucose co-transporter 2 inhibitor
SMBG = self-monitoring of blood glucose
T1D = type 1 diabetes
T2D = type 2 diabetes
UACR = urinary albumin:creatinine ratio
ZnT8 = zinc transporter 8

ABOUT RESEARCH REVIEW

Research Review is an independent medical publishing organisation producing electronic publications in a wide variety of specialist areas.

Publications are free to receive for health care professionals, keeping them up to date with their chosen clinical area.

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This review is as an educational resource for primary healthcare professionals. It provides a commentary and summary of the 2021 Type 2 Diabetes Management Guidance published by the NZSSD. The guidelines offer concise, pragmatic and evidence-based guidance on the management of type 2 diabetes and were developed in response to the urgent need to:

- Reduce clinical inertia
- Reduce inequities and standardise diabetes care across New Zealand
- Introduce best practice for newly funded medicines and reinforce the role of existing treatments
- Incorporate management focused on reducing CV risk
- Address ongoing challenges, e.g. insulin treatment, acting on abnormal findings in the annual review

What's new in the guidelines?

The major changes in guidance that clinicians should be aware of include:

1. Screening and diagnosis

- Screening for T2D is now recommended in high-risk individuals from 15 years of age
- A diagnosis of T2D should be confirmed without delay; on the same or next day if possible – waiting three months is no longer advised

2. Management

- Lifestyle management and metformin remain the first-line for managing T2D and should be started together at diagnosis
- Consider starting metformin and a second-line medicine at diagnosis if the HbA1c is > 64 mmol/mol
- SGLT2i and GLP1RA are the preferred second-line medicines for most patients with T2D
- All patients with T2D and diabetic renal disease and/or CV disease and/or five-year CV risk > 15% should be prescribed an SGLT2i and/or GLP1RA, regardless of glycaemic control and other glucose-lowering treatments
- Sulfonylureas are now a third or fourth-line class agent for managing T2D

3. Insulin

- Insulin should be initiated if at any time symptoms of insulin deficiency develop and/or HbA1c is > 90 mmol/mol
- Initiate basal insulin with weight-based dosing. Introduce prandial insulin once doses reach 0.5 units/kg/day if HbA1c is above target.

4. HbA1c testing

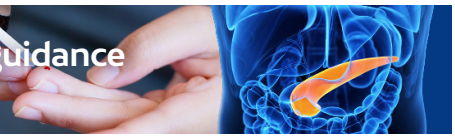
- The target HbA1c for most patients is 53 mmol/mol; guidance is provided when tighter control, e.g. < 48 mmol/mol, or more relaxed targets, e.g. 54-70 mmol/mol, are appropriate
- Repeat HbA1c testing every three months and escalate treatment if the target is not met; once the target is met, test every six months

5. Complications

- ACE inhibitors and ARBs do not prevent diabetic renal disease but are beneficial once it is established
- Aspirin is no longer recommended for the primary prevention of CV disease in patients with diabetes unless their five-year risk > 15% and there is a low risk of bleeding
- Hypoglycaemia is managed with either 30 g of rapid acting carbohydrate or weight-based dosing

Other key points in the guidelines include:

- How to differentiate between the different types of diabetes
- How to initiate and titrate basal and prandial insulin and whether to choose premixed or bolus insulin
- Self-funding of SGLT2i and GLP1RA if patients do not meet Special Authority criteria
- Guidance on diabetes and pregnancy and diabetes and driving
- Management of prediabetes
- Management of diabetic complications including neuropathic pain



Screening and diagnosis of type 2 diabetes

All people aged over 15 years with two or more risk factors for T2D should have an HbA1c performed at least every three years. Risk factors for T2D include:

- Non-European ethnicity
- Obesity
- Previous prediabetes or T2D in remission
- A first-degree relative with T2D < 40 years of age
- Features of insulin resistance, e.g. PCOS, acanthosis nigricans, hypertension, dyslipidaemia
- CV disease
- Current long-term corticosteroid or antipsychotic treatment
- Post-transplant

HbA1c testing should be routinely included in all CV risk assessments, beginning at age 45 years for men and age 55 years for women. CV assessments should start at age 30 years for males and 40 years for females of Māori, Pacific or Indo-Asian ethnicity.

Diagnosing T2D in an asymptomatic person requires two abnormal tests (HbA1c ≥ 50 mmol/mol or fasting glucose ≥ 7 mmol/L) either on the same day or without delay. Pre-diabetes is defined as either HbA1c 41-49 mmol/mol (single measurement if the patient is otherwise well), fasting glucose 6.1-6.9 mmol/L or 2-hour glucose 7.8-11 mmol/L on 75 g glucose tolerance test (GTT).

Practice point: Do not wait three months to confirm a T2D diagnosis, particularly since lifestyle management and metformin should also be used to treat high-risk prediabetes.

People with prediabetes or females with a history of gestational diabetes should have their HbA1c tested at least annually. An HbA1c test is not appropriate for patients with altered RBC turnover or those in the second or third trimester of pregnancy; perform a fasting glucose or 75 g GTT in these situations.

Testing symptomatic people

An HbA1c and fasting or random glucose test should be requested for all patients with symptoms of hyperglycaemia, i.e. polyuria, polydipsia, weight loss, recurrent fungal, skin or genitourinary infections. Diabetes in symptomatic patients is confirmed following a single HbA1c > 50 mmol/mol or a fasting glucose ≥ 7 mmol/L or a random glucose ≥ 11.1 mmol/L.

Determining the type of diabetes

At least 5% of adult-onset diabetes is not T2D. Therefore, other causes of diabetes should always be considered since this alters management, e.g. all patients with T1D require insulin and should be screened for other autoimmune diseases. T1D may develop at any age with an insidious onset and many patients are now overweight at diagnosis due to the prevalence of diabetes in the general population. A positive anti-GAD, anti-IA2 or anti-ZnT8 antibody titre or low C-peptide, e.g. < 250 pmol/L fasting or < 600 pmol/L post meal if glucose is > 8 mmol/L, at diagnosis is suggestive of T1D. Suspicion of T1D, diabetes due to pancreatic failure or monogenic diabetes should be discussed with secondary care.

Further information on the screening and diagnosis of T2D is available from the NZSSD guidelines

Glycaemic monitoring and HbA1c targets

Glycaemic targets should be individualised and reassessed at least yearly, including as part of the annual diabetes review. **HbA1c testing is preferred for assessing glycaemic control and should be performed every three months until the patient is to target, then every six months once at target**.

Many NZ health care professionals believe the target HbA1c for most T2D patients is < 64 mmol/mol because this remains a performance target for many Primary Health Organisations and the Ministry of Health. However, **the target HbA1c for most people with diabetes is < 53 mmol/mol** because microvascular complications exponentially increase from this point.

More aggressive targets, e.g. HbA1c < 48 mmol/mol, are often appropriate for patients with a low risk of hypoglycaemia who are either:

- Young
- Considering pregnancy or pregnant
- Have microvascular complications, especially retinopathy and nephropathy

A more relaxed target, e.g. HbA1c 54-70 mmol/mol, is more appropriate if the risks of hypoglycaemia are greater than the benefits of tight control. For example, patients with:

- Reduced life expectancy due to non-diabetic co-morbidities
- A history of severe hypoglycaemia
- Significant hypoglycaemic unawareness
- Old age and frailty or cognitive impairment
- Functional dependency

Practice point: Hypoglycaemia is rare in patients who are not taking insulin and/or sulfonylureas. Consequently, patients with T2D can be treated with metformin, vildagliptin, SGLT2i, GLP1RA and pioglitazone, alone or in combination with each other, without causing hypoglycaemia or needing to routinely self-monitor blood glucose (SMBG). An HbA1c < 45 mmol/mol is not concerning in these patients, but medications that do not reduce CV or renal disease, such as vildagliptin may be stopped. SMBG is recommended for patients considering or taking a sulfonylurea or insulin, or during preconception or pregnancy, for those who are acutely unwell or concerned about hypoglycaemia and patients unable to return reliable HbA1c results. SMBG can also be an educational tool for patients that helps them to understand the impact their lifestyle changes and medication regimen have on their glycaemic control.

Reducing cardiovascular and renal disease

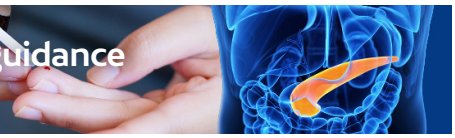
Most of the morbidity and mortality associated with T2D is caused by CV and renal disease and this is especially true for Māori and Pacific peoples. The focus for T2D management therefore now includes reducing CV and renal risk alongside glycaemic control. Although all glucose-lowering medicines reduce CV and renal risk by improving glycaemic control, metformin, SGLT2i and GLP1RA also reduce CV and/or renal risk independently of their effect on glucose levels. Metformin therefore remains the first line pharmacological intervention and SGLT2i and GLP1RA are now generally the preferred second-line interventions since becoming available in NZ.

The benefits of metformin, SGLT2i and GLP1RA in reducing CV disease are synergistic and also typically lead to weight loss without hypoglycaemia unless combined with insulin and/or sulfonylureas. Therefore, **all patients with T2D and either diabetic renal disease (UACR > 3 mg/mmol and/or eGFR < 60 mL/min) OR heart failure OR CV disease OR five-year CV risk > 15% should ideally be on metformin, an SGLT2i and GLP1RA regardless of their glycaemic control or other glucose-lowering therapies**.

Notably, the benefits of SGLT2i and GLP1RA in reducing CV disease and renal risk are additional to the likely more significant reductions with statin and ACEi/ARB therapy. Thus, **unless contraindicated, all patients with T2D and renal disease and/or CV disease should be taking a statin and those with renal disease and/or heart failure should also be taking a ACEi/ARB unless contraindicated or not tolerated.**

The target LDL concentration continues to be < 1.8 mmol/L and the target systolic BP is < 130 mmHg and diastolic BP < 80 mmHg in this high-risk group, if tolerated.

If renal disease is present, ACEi or ARB dosing (not in combination) should ideally be maximised before adding another antihypertensive. As it is now known that ACEi/ARBs do not prevent diabetic renal disease, if a patient has a normal UACR and eGFR either a CCB, thiazide or ACEi/ARB can be used to treat hypertension. In patients with no microvascular or macrovascular complications and a five-year CV risk < 15%, a target systolic BP < 140 mmHg and diastolic BP < 90 mmHg is reasonable. All patients with a previous vascular event should take aspirin for secondary prevention, unless contraindicated. Aspirin is now no longer generally used for primary prevention in patients with diabetes because the benefits are reduced and the bleeding risk increased, compared to patients without diabetes. Smoking cessation is, as always, important.



Reducing clinical inertia

Clinical inertia is likely the largest barrier to effective diabetes management in NZ and worldwide. Indeed, despite suboptimal management being largely attributed to patient barriers, 99% of patients with diabetes in Auckland are enrolled with a GP practice and over 90% are attending this practice at least twice a year.[1] In patients with the poorest glycaemic control (HbA1c > 75 mmol/mol), more than 75% attend their practice at least twice a year and at least 85% attend their annual diabetes review and regularly receive scripts for glucose-lowering therapy.[1] Therefore, **the key to reducing clinical inertia is to proactively optimise diabetes management at every opportunity.** Action is important as almost all patients with an HbA1c > 75 mmol/mol have an HbA1c test at least once per year, but approximately two-thirds have a similar level for the next 12 months.[1]

The most important changes in the new guidance aimed at reducing clinical inertia are:

1. Confirm T2D diagnosis in asymptomatic patients as early as possible.
2. Start lifestyle management and metformin together at diagnosis to delay progression of T2D, reduce CV risk and assist weight loss. Commencing metformin should not, however, diminish the importance of lifestyle management.
3. Strongly consider starting a second-line agent with metformin at diagnosis if the patient's HbA1c > 64 mmol/mol as the majority of these will not reach an HbA1c target < 53 mmol/mol with metformin alone.
4. Repeat HbA1c testing every three months with intensification of treatment until the target is met, HbA1c testing is then every six months. Ideally, patients should have their blood pressure and lipids assessed at the same time with escalation of appropriate treatment as required.
5. Start weight-based basal insulin (rather than the traditional 6-10 unit starting dose) and add in prandial insulin once basal insulin doses reach 0.5 units/kg/day. Strong consideration should also be given to starting insulin immediately if the HbA1c is > 90 mmol/mol at any time, as these patients typically will not reach their glycaemic targets despite lifestyle management and all other glucose-lowering therapies.

The new 'algorithm' for managing T2D

The availability of SGLT2i and GLP1RA and the shift towards reducing CV and renal risk and obesity, in addition to improving glycaemic control, has led to major changes to T2D management in Aotearoa New Zealand (**Figure 1**). Lifestyle management and metformin remain the first-line interventions for all patients with T2D.

Lifestyle management

Lifestyle changes with healthy eating, physical activity, education and support continues to be the cornerstone of T2D management. Ideally, lifestyle modifications should target a 5-10% reduction in total bodyweight if the patient has a BMI > 30 kg/m^2 OR a BMI > 25 kg/m^2 and a waist circumference > 88 cm for females or > 102 cm for males. **Nutritional education from a registered dietitian is best practice at diagnosis and then annually for ongoing assessment, when starting prandial insulin or at any time if required.** Recent evidence suggests that low-energy, low-GI and modified macronutrient dietary approaches can be as effective as bariatric surgery in achieving weight loss and T2D remission. However, there is no conclusive evidence that one dietary strategy is more effective than another in achieving sustained weight loss and improved glycaemic control. In particular, meta-analyses show that the benefits of ketogenic diets are unlikely to be sustained. Consequently, the choice of dietary strategy will depend on factors including patient preference, tolerance, income, co-morbidities, cultural suitability and nutritional needs. Indeed, it is important to ensure adequate nutrition in young people, pregnant or lactating women or those considering pregnancy, and the elderly.

Dietary recommendations and activity guidelines are available from: www.health.govt.nz/our-work/eating-and-activity-guidelines. Patients who are unable to meet the recommended activity levels should be supported to complete as much exercise as they are able. Smoking cessation, reduced alcohol intake, a green prescription and screening for depression (e.g. PHQ-9) and referral for psychology input as required remain important components of lifestyle management.

Further information on T2D lifestyle management is available @ NZSSD guidelines

Metformin

Metformin remains the first-line pharmacological agent for patients with T2D because it reduces CV risk independently of glycaemic control. The mean maximal reduction in HbA1c with metformin monotherapy is 16 mmol/mol, but importantly this is associated with modest weight loss, without the risk of hypoglycaemia. **Many patients with gastrointestinal adverse effects are labelled 'intolerant to metformin', but most will tolerate it well when it is started at 250-500 mg, once or twice daily, with food and titrated up weekly.**

Anecdotally, patients tolerate metformin much better in combination tablets with vildagliptin or empagliflozin, compared to metformin alone. The therapeutic benefit of metformin > 2 g/day is minimal, but the risk of adverse effects is increased. Therefore, **the maximum recommended dose of metformin is 1 g, twice daily**. Doses of metformin need to be reduced if the eGFR is < 60 mL/min.

Escalation of therapy

The choice of second-line agent is dependent on co-morbidities, primarily CV and renal disease. All patients with T2D with either diabetic renal disease OR heart failure OR CV disease OR five-year CV disease risk > 15% should ideally be on metformin, an SGLT2i and GLP1RA regardless of their glycaemic control or other glucose-lowering therapies. The choice between an SGLT2i or GLP1RA can be difficult, but an SGLT2i is likely preferable if renal disease or heart failure predominates, and a GLP1RA is likely preferable if cerebrovascular disease predominates. If the HbA1c remains above target in this high-risk group then dual SGLT2i and GLP1RA therapy is recommended but not funded (see: Mismatch between recommendations and Special Authority criteria).

To date, the benefits of SGLT2i and GLP1RA in reducing CV and/or renal risk have almost exclusively been demonstrated in those with existing CV and/or renal disease and more evidence for their role in primary prevention is awaited, particularly the potential for dulaglutide to reduce CV events in those with multiple risk factors. Obesity and its complications are also very common and are major causes of morbidity. Therefore, **SGLT2i or GLP1RA are still the likely preferred second-line agents when escalation of metformin therapy is required in T2D patients without CV or renal disease who are overweight or obese.** This is because GLP1RA and SGLT2i both cause weight loss without hypoglycaemia, whilst vildagliptin is weight neutral and pioglitazone, sulfonylureas and insulin cause weight gain. GLP1RA typically lead to greater reductions in weight and glucose levels than SGLT2i, however only patients of Māori or Pacific ethnicity or those with early onset T2D, i.e. before age 40 years, will be eligible for funded treatment.

Vildagliptin is likely the preferred second-line agent when patients cannot afford to self-fund SGLT2i and/or GLP1RA therapy OR when escalation of metformin therapy is required in patients with T2D without CV or renal disease who are of normal weight. This is because vildagliptin is the only agent to date shown to delay the need for insulin, when used in combination with metformin, and it does not cause weight gain or hypoglycaemia. Pioglitazone, sulfonylureas and insulin are now third- and fourth-line agents due to the associated weight gain, risk of hypoglycaemia and the need to SMBG with insulin and sulfonylureas.

SGLT2 inhibitors

SGLT2i are a preferred second-line treatment for patients with T2D and CV disease, especially heart failure and renal disease, as they reduce CV mortality and progression of established renal disease independently of glycaemic control.[2–4] SGLT2i are associated with a 6-13 mmol/mol reduction in HbA1c.

How to prescribe SGLT2i: Empagliflozin is available in 10 mg and 25 mg tablets and in combination with metformin (5mg/500mg, 5mg/1000mg, 12.5mg/500mg, 12.5mg/1000mg). Empagliflozin is initiated at 10 mg, daily, with the patient's HbA1c, eGFR and blood pressure retested in three months and the dose increased to 25 mg, daily, if the HbA1c is above target and treatment is tolerated. Dose adjustments are not necessary for other glucose-lowering medicines unless sulfonylureas and/or insulin are prescribed.

The most common adverse effects of empagliflozin include polyuria (proportional to glucose levels and transient) volume depletion, a transient decrease in eGFR (up to 25% is acceptable), skin reactions and genitourinary infections, particularly vaginal thrush and balanitis.[5] Current recommendations for genital hygiene with empagliflozin use are for women to wash and change pads at least twice daily, and men to wash at least once daily. Very rare adverse effects include diabetic ketoacidosis (glucose levels may be normal) and necrotising fasciitis of the perineum (Fournier's gangrene).[5] Empagliflozin should not be prescribed to women who are pregnant or breastfeeding, patients aged < 18 years, patients with an eGFR < 30 mL/min or T1D and should be used with caution in those with recurrent genitourinary infections and/or are aged > 75 years.[5]

GLP-1 receptor agonists

GLP1RA are a preferred second-line medicine in patients with T2D and CV and renal disease because they reduce CV mortality and progression of diabetic renal disease, independently of glycaemic control.[6,7] GLP1RA are associated with greater reductions in glucose levels and weight than any other class of non-insulin glucose-lowering therapies, as well as reduced blood pressure, without causing hypoglycaemia in monotherapy.[8] As such, GLP1RA are a useful alternative to basal insulin.

How to prescribe GLP1RA: Dulaglutide is initiated at 1.5 mg subcutaneously, weekly, at any time of the day. Metformin and other glucose-lowering medicines should be continued, although vildagliptin should be withdrawn. Dose adjustments are not necessary for other glucose-lowering medicines unless sulfonylureas and/or insulin are prescribed.

Advise patients that the most common adverse effects of dulaglutide are gastrointestinal, e.g. nausea, diarrhoea and constipation, and mild injection site reactions, but these often resolve. Less common adverse effects include vomiting and rarely myalgia or muscle weakness, Stevens-Johnson's syndrome and thrombocytopenia. The patient's HbA1c, eGFR and blood pressure should be retested in three months and if the HbA1c is above target, other glucose-lowering treatments should be intensified. Dulaglutide should not be prescribed to women who are pregnant or breastfeeding, patients aged < 18 years, patients with an eGFR < 15 mL/min, T1D or those with severe gastrointestinal disease, previous pancreatitis or medullary thyroid carcinoma or history of MEN2 syndrome.

DPPIV inhibitors

DPPIV inhibitors are a second-line medicine that are weight neutral and do not cause hypoglycaemia in monotherapy. DPPIV inhibitors are well tolerated in older people and can be used safely in those with renal dysfunction. Vildagliptin is the only DPPIV inhibitor funded and is currently the only glucose-lowering therapy shown to delay the need for insulin therapy in T2D when combined with metformin.[10]

Sulfonylureas

Sulfonylureas are a third-line medicine that may cause weight gain and hypoglycaemia and do not reduce CV or renal disease independently of glycaemic control. Patients taking sulfonylureas need to SMBG levels and be educated about: hypoglycaemia management, how the medicine may affect driving ability, and sick day management.

Pioglitazone

Pioglitazone is a third or fourth-line medicine that is likely to reduce CV disease independently of glycaemic control and does not cause hypoglycaemia alone. However, the adverse effects of weight gain and increased risk of fractures limit its use. The greatest benefit of pioglitazone is likely to occur in obese patients with insulin resistance and fatty liver disease with the benefits likely to be increased in women.

Acarbose

Acarbose limits carbohydrate absorption and is weight neutral and will not cause hypoglycaemia in monotherapy. Significant GI adverse effects mean that acarbose is seldom used.

Mismatch between recommendations and Special Authority criteria

Approximately 33-50% of patients with T2D will meet the Special Authority funding criteria for empagliflozin (SGLT2i) or dulaglutide (GLP1RA) which is:

- T2D with an HbA1c > 53 mmol/mol, despite regularly using metformin and/or an alternative glucose-lowering medicine (except empagliflozin or dulaglutide) for at least three months **AND** any of the following:
  - Māori or Pacific ethnicity OR
  - Diabetic renal disease OR
  - Known CV disease (ischaemic heart disease, cerebrovascular event, peripheral vascular disease, congestive heart failure or familial hypercholesterolaemia) OR
  - Five-year CV risk > 15% OR
  - Diabetes onset in childhood or as a young adult

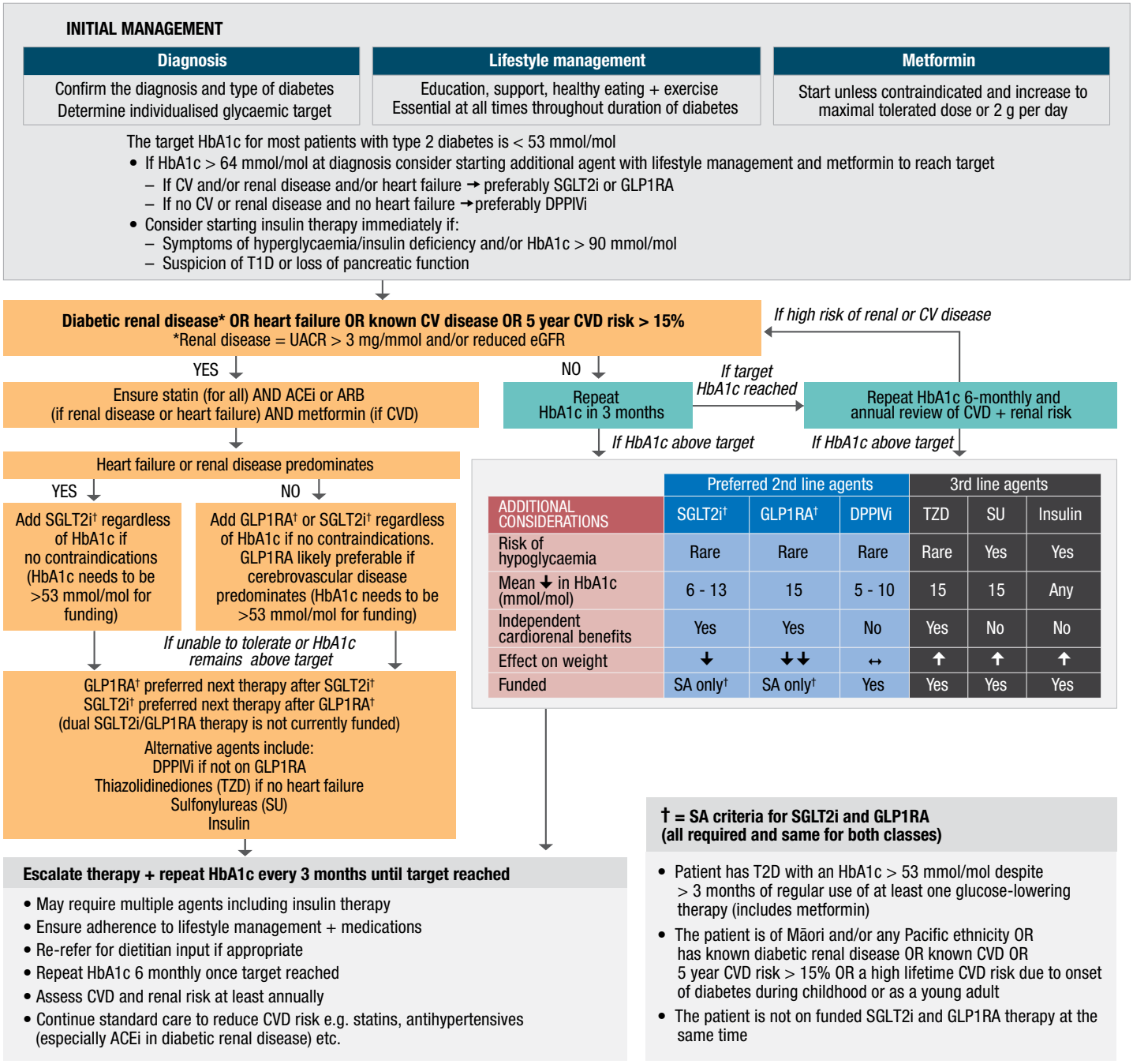
NB: The inclusion of the ethnicity and age-group clauses is to reduce barriers in these high-risk populations, but there is no evidence to date that these agents are more or less effective in these groups.

Patients cannot be on funded empagliflozin and dulaglutide at the same time, but this is only due to financial constraints. Dual SGLT2i/GLP1RA therapy leads to additional reductions in glucose levels and weight and likely provides additional benefit in reducing CV disease. **Therefore, the Special Authority does not fully match best practice**. Patients should be offered to self-fund empagliflozin and/or dulaglutide in the following situations:

- All patients who meet the Special Authority criteria, but who would benefit from dual SGLT2i/GLP1RA therapy
- Patients with diabetic renal disease and/or heart failure, and/or CV disease, and/or five-year CV risk > 15% with an HbA1c < 53 mmol/mol, i.e. do not qualify because HbA1c is to target
- Non-Māori non-Pacific patients without early onset diabetes who are overweight or obese with an HbA1c above target despite taking metformin or are intolerant to metformin
- Non-Māori non-Pacific patients without early onset diabetes of normal weight with an HbA1c above target who are taking metformin and vildagliptin or are intolerant to this combination
- All patients with an HbA1c at target where the adverse effects of a thiazolidinedione, sulfonylurea and/or insulin need to be avoided

It costs approximately $85 per month to self-fund empagliflozin, compared with the likely $300-500 for dulaglutide (price not yet released). Therefore, for dual SGLT2i/GLP1RA therapy, patients would be best to receive funded dulaglutide and pay for empagliflozin. Patients should be encouraged to compare pharmacy prices as the mark-up varies significantly and online pharmacies are often the cheapest.

Figure 1: Management algorithm for T2D adapted from NZSSD[9]



Insulin

The progressive nature of T2D means many patients will require insulin in the advanced stages of disease, despite maximal doses of other glucose-lowering therapies. However, many patients fail to reach glycaemic targets on insulin therapy due to subtherapeutic dosing or ineffectual dose titration.

Patients starting insulin need clear instructions on how to administer and self-titrate doses and how to SMBG levels and to recognise and manage hypoglycaemia. Patients should be provided with a sick day management plan and referred to a dietitian.

Patients taking insulin need to understand their obligations if driving. Factors influencing fitness to drive include vision, peripheral vascular disease and neuropathy, risk of hypoglycaemia, cognitive impairment and other co-morbidities, e.g. obstructive sleep apnoea.

Further information about diabetes and driving is available from the NZSSD guidelines.

Prescribing insulin

Basal insulin is required by patients with any of the following:

- Likely or confirmed T1D
- Significant hyperglycaemia at any time, e.g. HbA1c > 90 mmol/mol (including at diagnosis)
- Symptoms of insulin deficiency, e.g. weight loss, polyuria, polydipsia
- Unable to meet glycaemic targets after lifestyle management and maximal oral/GLP1RA treatment
- Previous diabetic ketoacidosis or hyperosmolar hyperglycaemic syndrome

Figure 2: Insulin treatment algorithm adapted from NZSSD[9]

Start basal insulin. Continue lifestyle management + other hypoglycaemic agents. Refer for dietitian input.

Start isophane or glargine insulin at 0.1 – 0.2 units/kg nocte
Monitor FBG levels + educate on how to manage hypoglycaemia
If 3 consecutive FBG > 7 mmol/L then ↑ dose by 10% or 2 units (i.e. can ↑ dose every 3 days)
Stop uptitration of basal insulin if any of the following occurs: Hypoglycaemia (< 4 mmol/L) OR FBG < 7 mmol/L OR doses reach 0.5 units/kg/day

Repeat HbA1c in 3 months → *If target HbA1c reached* → Repeat HbA1c 6 monthly
If target HbA1c not reached ↓

Add bolus insulin OR switch to premixed insulin
Continue lifestyle management + other glucose lowering therapies • Consider stopping sulfonylureas once regimen established • Consider referral to dietitian to allow matching of insulin and carbohydrate intake • The choice of bolus or premixed insulin should be based on patient data + preference

Favours basal-bolus	Factors to consider	Favours premixed
Yes	Needs flexibility for work patterns, exercise etc	No
Yes	Prefers varied diet + timing of meals	No
Yes	Will likely need rapid intensification of insulin therapy	No
Good ability	Ability to inject (e.g. cognitive ability, dexterity, supervised environment)	Reduced ability
Comfortable with more frequent monitoring	Monitoring of glucose levels	Prefers less frequent monitoring
Comfortable with more frequent injections	Number of injections per day	Prefers fewer injections

Bolus (rapid-acting insulin) | Premixed

If predominately 1 large meal per day | If multiple meals per day

Add bolus insulin with largest meal – 'basal plus'
- Start rapid-acting insulin at 4 units or 10% of basal dose
- Monitor BGLs before + 2 hours after meal
- ↑ dose by 2 units if 3 x BGL checks with meal show increase > 3 mmol/L
- Consider early addition of bolus insulin at other meals
- Can add correction doses to treat pre-meal hyperglycaemia
- NB: Doses of basal insulin may need to be ↓ to prevent hypoglycaemia, especially if HbA1c < 64 mmol/mol

Start premixed insulin with largest meal
- Convert daily dose of basal insulin to premixed insulin before largest meal
- Monitor BGLs before + 2 hours meal
- ↑ dose by 10% if 3 x BGL checks with meal show increase > 3 mmol/L AND 3 x fasting BGLs are > 10 mmol/L

Start premixed insulin with breakfast + dinner
- Convert daily dose of insulin to premixed insulin with half the dose pre-breakfast + half pre-dinner
- Consider different ratio (e.g. 2/3rd to 1/3rd) if one meal larger than other
- Monitor BGLs before + 2 hours after breakfast and dinner
- ↑ Breakfast dose by 10% if 3 x BGL checks with meal show increase > 3mmol/L AND 3 x pre-dinner BGLs are > 10mmol/L
- ↑ Dinner dose by 10% if 3 x BGL checks with meal show increase > 3 mmol/L AND 3 x pre-breakfast BGLs are > 10 mmol/L

Repeat HbA1c in 3 months → *If target HbA1c reached* → Repeat HbA1c 6-monthly
If target HbA1c not reached ↓

Add bolus insulin with other meals
• Start rapid-acting insulin at 4 units or 10% of basal dose at other meals • Monitor BGLs before + 2 hours after meals • ↑ dose by 2 units every 3 days if BGL rise with meal is > 3 mmol/L

Repeat HbA1c in 3 months → *If target HbA1c reached* → Repeat HbA1c 6-monthly
If target HbA1c not reached ↓

Tips for insulin prescribing
- Use different coloured pens for different types of insulin
- BD fine 4-5 mm needles are associated with ↑ absorption + ↓ trauma
- Change needles regularly (at least every 2nd day)
- Premixed insulin needs to be mixed by gently inverting before each use
- Encourage patients to rotate their injection sites
- Premixed + bolus insulin should be injected before meals
- Ensure adherence + check injection technique before altering doses
- Provide clear instructions for patients on how to self-titrate insulin
- Pens that use 1/2 unit increments are useful in insulin sensitive patients
- Memory adjuncts (e.g. NovoPen Echo®, InsulCheck etc.) may be useful
- Doses of insulin may need to be reduced around exercise

If HbA1c remains above target
- Check insulin injection technique and injection sites
- Ensure adherence to all therapy including lifestyle management
- Optimise non-insulin glucose-lowering therapies NB: doses of insulin may need to be reduced to prevent hypoglycaemia
- Screen for depression
- Re-refer to dietitian and consider carbohydrate awareness
- Consider doses of rapid acting insulin with snacks
- An increase in basal insulin may be required if BGLs are ↑ overnight
- Consider correction doses of rapid acting insulin pre-meals
- Consider switching insulin regimens particularly if increases in premixed insulin are prevented by hypoglycaemia

Sick day management
- All patients on insulin should have a sick day management plan
- If reduced oral intake will likely need reduction/omission of bolus insulin and 20-30% reduction in basal + premixed insulin
- Patients should monitor their glucose levels at least 3-4 times per day
- Treatment for hypoglycaemia should be readily available
- Correction insulin can be used to treat hyperglycaemia
- High dose steroids often require a ~ 30%↑ in insulin doses during the day

Weight-based dosing of isophane or glargine is safe and effective and typically results in faster glycaemic control than the traditional starting dose of 6 – 10 units. Basal insulin is most effective when taken at night to offset hepatic glucogenesis. The recommended starting doses for weight-based basal insulin are:

- 0.1 units/kg daily if there are concerns over hypoglycaemia, e.g. HbA1c < 64 mmol/mol or BMI < 18 kg/m^2 or elderly or renal/liver failure; OR
- 0.2 units/kg daily if HbA1c > 64 mmol/mol and BMI > 18 kg/m^2

Safety remains paramount and regardless of the starting dose regular dose titration results in most patients reaching their glycaemic target. FBG should be monitored while taking basal insulin and if three consecutive levels > 7 mmol/L occur, increase the dose by 10% or 2 units.The dose should not be increased if any hypoglycaemia occurs OR the FBG < 7 mmol/L OR doses reach 0.5 units/kg/day. Doses of basal insulin above 0.5 units/kg/day typically do not reduce glucose levels further but lead to weight gain. Clinicians should confirm injection technique and adherence before adjusting insulin doses.

If a patient has not reached their glycaemic target on 0.5 units/kg/day of basal insulin they require prandial insulin with either premixed or bolus insulin. The choice of bolus or premixed insulin is based on the patient's clinical characteristics and preference (**Figure 2**). Premixed insulin is only appropriate for patients who eat regular meals.

Correction insulin involves adding doses of rapid-acting insulin to bolus insulin to correct pre-prandial hyperglycaemia. This is administered separately if the patient is taking basal or premixed insulin alone.

TAKE-HOME MESSAGES

- Screen for T2D in high-risk populations from age 15 years
- Confirm a diagnosis of T2D on the same or next day if possible; waiting three months is no longer advised.
- The target HbA1c for most patients with T2D is < 53 mmol/mol
- Start lifestyle management and metformin together at diagnosis
- Consider starting metformin and a second-line medicine at diagnosis if the HbA1c is > 64 mmol/mol; SGLT2i and GLP1RA are the preferred second-line medicines for most patients with T2D.
- Monitor HbA1c levels every three months and escalate treatment if the target is not met
- Prescribe an SGLT2i and/or GLP1RA to all patients with T2D and diabetic renal disease and/or CV disease and/or five-year CV risk > 15%, regardless of their glycaemic control
- Initiate insulin at any time if patients have symptoms of insulin deficiency, e.g. weight loss, polyuria, polydipsia, and/or an HbA1c > 90 mmol/mol
- Initiate basal insulin with weight-based dosing; introduce prandial insulin if doses reach 0.5 units/kg/day if the HbA1c is above target.

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