2017 SEMDSA DIABETES MANAGEMENT GUIDELINES

The updated 2017 South African guidelines for the management of type 2 diabetes mellitus were launched on 5 May at the 52nd congress of the Society of Endocrinology, Metabolism and Diabetes of South Africa (SEMDSA) in Johannesburg. This is the fourth edition of the guidelines, which were last updated in 2012. The 2017 edition has been completely revised and updated using the most recent clinical science, with contributions from more than 45 local experts in various aspects of diabetes management. It is a comprehensive document, consisting of 29 chapters covering epidemiology; definitions; diagnosis; screening and organisation; lifestyle interventions; glucose management; comorbidities and complications (weight management, cardiovascular risk, hypertension, diabetic kidney disease, diabetic eye disease and diabetic foot); along with type 2 diabetes management in special patient populations (pregnant women, children and adolescents, the elderly, those with HIV, those observing Ramadan, drivers and men with sexual dysfunction).

The guideline has been written with the clinician in mind and is practical and easy to use. Recommendations are summarised in table form at the beginning of each chapter and information relating to support for the recommendations is included in appendices at the end of the document.

The following is a brief summary of general recommendations and highlights information that is new or where recommendations from past editions of the guideline have been updated.

KEY MESSAGES

- It is estimated that as many as one in four South African adults older than 45 years may have type 2 diabetes
- More than half of those with type 2 diabetes remain undiagnosed
- The diabetes epidemic is largely driven by modifiable risk factors, in particular overweight and obesity
- Type 2 diabetes mellitus is a diagnosis of exclusion following careful investigation for an aetiology
- In symptomatic patients, diagnosis is confirmed by random plasma glucose ≥11mmol/l, fasting plasma glucose ≥7mmol/l, or HbA_{1c} ≥6.5%
- All patients should receive ongoing diabetes education and support to enable self-management and lifestyle change
- The target HbA_{1c} for most treated patients is ≤7%
- If it is not contraindicated and if it is tolerated, the initial pharmacotherapeutic choice is metformin, titrated to an appropriate dose for the individual
- In patients with diabetes that is inadequately controlled with monotherapy, the choice of add-on therapy should be individualised, with particular attention paid to glycaemic target, risks of hypoglycaemia and weight gain, comorbidities and patient preferences and capabilities
- Statins are recommended for all patients with cardiovascular risk factors
- Low-dose aspirin is not recommended for primary cardiovascular protection (in those who have not yet had a cardiovascular event).

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Epidemiology of type 2 diabetes

Based on the 2015 statistics from the International Diabetes Federation (IDF), there are approximately 2.3 million adults aged between 20 and 79 years with type 2 diabetes in South Africa, of whom approximately 60% remain undiagnosed. According to the 2012 South African National Health and Nutrition Examination Survey (SANHANES) the estimated prevalence of type 2 diabetes in South Africans older than 15 years was 9.5%, with a further 9% having impaired glucose regulation (HbA_{1c} 6.0-6.4%). However, in individuals older than 45 years, the prevalence of type 2 diabetes may be as high as 25%. Type 2 diabetes is most common among the Asian (30%) and coloured (13%) populations, with equal prevalence in blacks and whites (8%). It occurs in all sectors of society, with a similar prevalence in rural informal dwellers and urban formal dwellers.

Worldwide, the number of people who die annually from type 2 diabetes exceeds the combined mortality from HIV/AIDS, tuberculosis and malaria, and that is expected to rise. For example, by 2040, it is anticipated that the number of people in Africa with type 2 diabetes will have increased by 140%.

The diabetes epidemic is driven by interrelated risk factors, including positive family history, psychosocial factors, overweight and obesity, and insufficient physical exercise. Nevertheless, the rising prevalence of type 2 diabetes is predominantly associated with modifiable risk factors. The most important of these, and one that demands urgent attention, is the increasing prevalence of obesity. According to SANHANES, half of all South African males and three-quarters of females between the ages of 45 and 54 years are overweight or obese (body mass index (BMI) ≥25kg/m^2).

Definition and classification of diabetes

Diabetes mellitus is defined as '*a metabolic disorder with heterogeneous aetiologies, which is characterised by chronic hyperglycaemia and disturbances of carbohydrate, fat and protein metabolism resulting from defects in insulin secretion, insulin action or both*'.

Type 2 diabetes is associated with specific long-term adverse health consequences, including retinopathy, nephropathy, neuropathy and cardio-, cerebro- and peripheral vascular diseases.

The clinical stages of hyperglycaemia include intermediate hyperglycaemia (impaired fasting glucose and impaired glucose tolerance), which represents a high-risk state for development of future diabetes and cardiovascular disease.

When assessing a patient with diabetes, a wide array of potential aetiologies needs to be considered. Type 2 diabetes is a diagnosis of exclusion after careful investigation for and exclusion of other causes (Table 1).

Table 1. Aetiological classification of diabetes mellitus

I.	Type I diabetes
II.	Type II diabetes
III.	Specific aetiologies
a.	Genetic defects of β-cell function
b.	Genetic defects in insulin action
c.	Diseases of the exocrine pancreas (e.g. pancreatitis, trauma, neoplasia, haemochromatosis)
d.	Endocrinopathies (e.g. acromegaly, Cushing's syndrome, hyperthyroidism)
e.	Drug or chemical induced (e.g. glucocorticoids, nicotinic acid, thiazides, atypical antipsychotics, antiretroviral therapy)
f.	Infections
g.	Uncommon forms of immune-mediated diabetes
h.	Other genetic syndromes sometimes associated with diabetes (e.g. Down's syndrome)

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Screening and diagnosis

In patients with symptoms of type 2 diabetes (polyuria, polydipsia, blurred vision, weight loss) or metabolic decompensation (diabetic keto-acidosis or hyperosmolar non-ketotic state), the diagnosis is confirmed if one or more of the following are present:

- Random plasma glucose ≥11mmol/l or fasting plasma glucose (FPG) ≥7mmol/l
- HbA_{1c} ≥6.5%

Type 2 diabetes is diagnosed in asymptomatic patients by any one of the following tests, which must be confirmed on separate days within a two-week period:

- FPG ≥7mmol/l
- Two-hour post-load plasma glucose (oral glucose tolerance test [OGTT]) ≥11mmol/l
- HbA_{1c} ≥6.5%

Bedside or point-of-care devices (HbA_{1c} or glucose) should not be used to make the diagnosis.

Impaired fasting glucose and impaired glucose tolerance (prediabetes) are present when two consecutive tests on different days confirm FPG 6.1-6.9mmol/l or two-hour post-load plasma glucose 7.8-11.0mmol/l, respectively.

Asymptomatic individuals at high risk for diabetes should be screened using FPG, OGTT (preferred) or HbA_{1c} at least every three years, or more frequently if initial screening results are abnormal, or if they are at very high risk. This includes all adults who are overweight (BMI >25kg/m^2 or >23kg/m^2 in Asians), and have one or more of the following risk factors: physical inactivity, hypertension, a first-degree relative with diabetes, dyslipidaemia, polycystic ovarian syndrome, high-risk race/ethnicity, history of cardiovascular disease, gestational diabetes or baby >4kg, previous impaired FPG or OGTT, or other conditions associated with insulin resistance (severe obesity, acanthosis nigricans).

Management

1. Diabetes self-management education and support (DSME)

All people with diabetes and their families should be provided with the education and support for self-management so that they can effectively manage the disease at home themselves. DSME has been shown to be associated with better glycaemic control and is one of the strongest predictors of disease progression and development of diabetes complications.

2. Lifestyle change and medical nutrition therapy (MNT)

Behaviour change, physical activity (aerobic and resistance exercise) and healthy nutritional choices can achieve modest weight loss and improve outcomes in overweight and obese individuals with type 2 diabetes and prediabetes, and are the essential foundation of every patient's management programme. MNT can reduce HbA_{1c} by up to 2%. Nutritional recommendations should be individualised, aiming at a high-quality diet consistent with metabolic goals and sensitive to ethnic, cultural and socio-economic needs, so that it is sustainable. There is no one recommended diet that is considered superior, or ideal in respect of which percentage of calories should come from carbohydrates, fat or protein. Macronutrient distribution should be individualised to suit the patient. Refined carbohydrates high in sugar, fats and sodium should be replaced with whole grains, legumes, milk, vegetables and fruit. Monounsaturated fats are preferred to saturated fats and foods rich in long-chain omega-3 fatty acids, such as fatty fish, nuts and seeds, are recommended for cardiovascular risk prevention. Processed and fatty red meats should be limited. The long-term health risks associated with high-fat, low-carbohydrate and very-low-calorie diets are uncertain and these diets are not recommended. Whole foods are the best source of micronutrients and unless there are specific clinical indications, vitamins and supplements are not recommended.

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3. Glycaemic targets

In most patients, management should aim to achieve and maintain HbA_{1c} ≤7% (self-monitored plasma glucose [SMPG] fasting or preprandial 4-7mmol/l and post-prandial 5-10mmol/l). In newly diagnosed patients who are in good health, as long as it can be achieved safely, target HbA_{1c} ≤6.5% can prevent further retinopathy and nephropathy. In elderly patients and those with limited life expectancy, multiple comorbidities, severe vascular disease, advanced chronic kidney disease, recurrent severe hypoglycaemia or hypoglycaemia unawareness, HbA_{1c} 7.1-8.5% is acceptable.

4. Pharmacotherapy for type 2 diabetes

When added to metformin, most drug options for type 2 diabetes are equally efficacious at lowering blood glucose with reductions in HbA_{1c} of approximately 0.8-1.2%. However, in clinical practice the response to individual drugs varies widely between patients, with some responding well and others not at all. Implementation and intensification of lifestyle modifications also affect drug efficacy. Therefore, drug selection should be individualised, based not only on glycaemic targets, but also taking into consideration hypoglycaemia risk, risk of treatment-associated weight gain and other side effects, individual patient characteristics, treatment complexity and cost. Maximum glucose lowering is usually evident by six months.

Guidelines for step-wise pharmacotherapy for stable patients with type 2 diabetes with suboptimal glycaemic control, who are being managed at primary care facilities, are shown in Table 2. Intensification (step-up) of treatment may be considered if the HbA_{1c} target is not achieved after three months or if HbA_{1c} rises after initiating new therapy. Patients with metabolic decompensation who have severe symptomatic hyperglycaemia and those with severe micro- or macrovascular complications should be managed under specialist supervision.

Unless it is contraindicated, metformin is the drug of first choice and, as long as it is tolerated, should be continued indefinitely. Most patients will require titration to 1000-2550mg in two or three divided doses and the optimal dose for cardiovascular benefit in obese patients is 2550mg/day (850mg TDS). If tolerability is poor, consideration should be given to switching to the extended-release (XR) formulation.

Because of its low rate of hypoglycaemia and cardiovascular safety relative to other sulphonylureas, and its proven benefits in terms of microvascular outcomes, the sulphonylurea of choice is gliclazide modified release (MR). Glibenclamide should not be used.

Table 2. Guidelines for management of type 2 diabetes in nonpregnant adults without metabolic decompensation or cardiovascular disease

	Preferred	Alternative options without motivation*	Not recommended if HbA_{1c} target is attainable with other agents
1. Monotherapy	Metformin/XR	DPP4i Gliclazide MR Pioglitazone	GLP-1a Insulin SGLT2i
2. Dual therapy	Metformin/XR DPP4i Gliclazide MR	Pioglitazone SGLT2i	GLP-1a Insulin
3. Triple therapy	Metformin/XR DPP4i Gliclazide MR Pioglitazone	GLP1a Insulin (basal) SGLT2i	
4. Complex therapy	Metformin/XR + insulin (premix or basal)	Oral therapy + basal insulin + GLP1a	

DPP4i: dipeptidyl peptidase-4 inhibitor; SGLT2i: sodium glucose cotransporter-2 inhibitor; GLP-1a: glucagon-like peptide-1 receptor agonist

*These alternatives do not require motivation to funders as they offer similar benefits and are selected for the individual circumstances based on clinical judgement.

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In patients with symptomatic hyperglycaemia and HbA_{1c} >9% at diagnosis, initial dual therapy with metformin plus gliclazide MR should be considered. After optimisation of metformin dose and lifestyle modification it may be appropriate to discontinue the sulphonylurea.

Figure 1 provides additional advice for triple therapy and initiating insulin. When selecting additional therapies, consideration should be given to patient preference, comorbidities, the individual properties of each of the pharmacological options and access to medicines. Expected HbA_{1c} reductions are similar when adding a GLP-1 receptor agonist or titrated basal insulin, which are both slightly superior to triple oral therapy. Insulin initiation must be accompanied by ongoing patient education, appropriate SMBG, self-titration of insulin doses, frequent review (initially) and counselling regarding hypoglycaemia. In the absence of appropriate support for insulin therapy, a third oral agent is preferred.

A GLP-1 receptor agonist may be preferred to other options under the following circumstances:

- For overweight and obese patients
- Weight gain or hypoglycaemia has been or is likely to be problematic with other treatment options (see section 5)
- HbA_{1c} is very high
- Patients with established cardiovascular disease (liraglutide benefit) who are to be managed with specialist level participation or responsibility.

Equally, these agents should not be the preferred option:

- In patients in whom weight loss is not desirable
- In patients with chronic gastrointestinal disorders
- In patients with a history of pancreatitis or pancreatic tumours.

The guidelines provide detailed considerations for use of the other agents, including pioglitazone, DPP-4 inhibitors and SGLT-2 inhibitors.

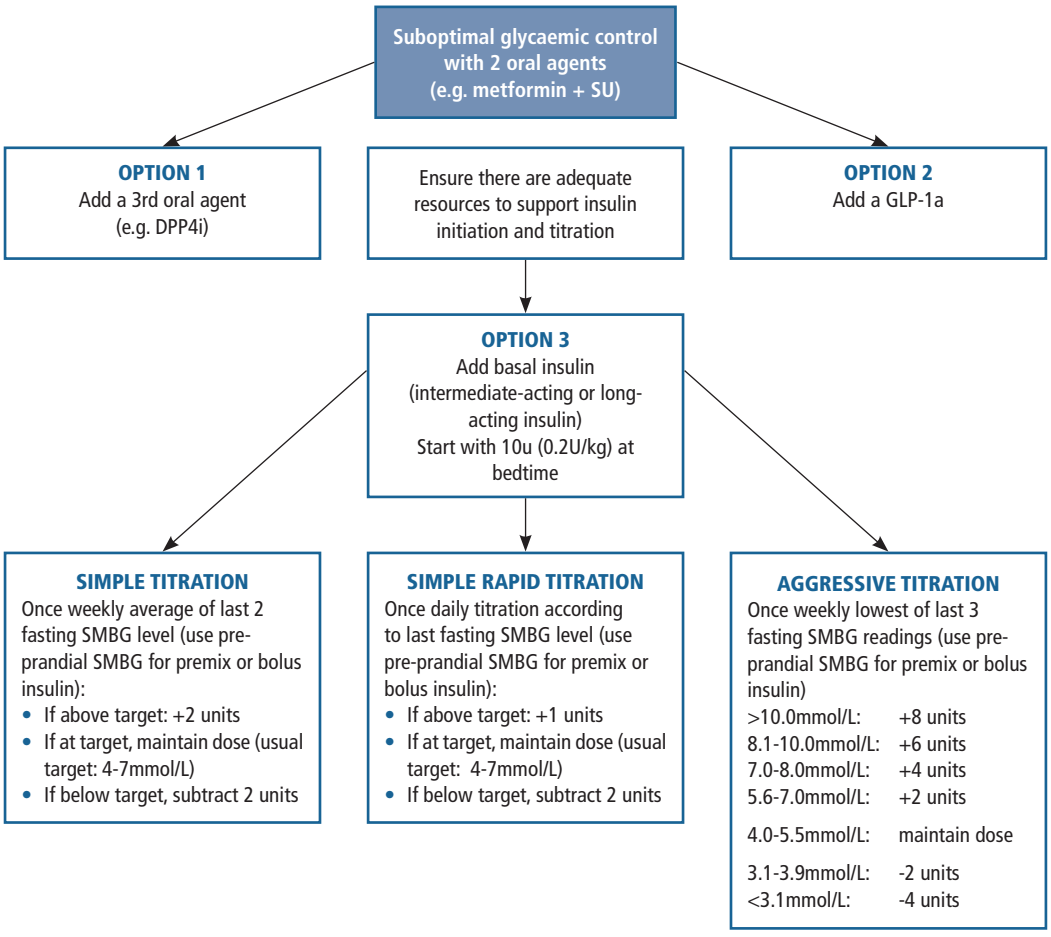


Figure 1. Initiating and titrating basal insulin therapy

SMBG: self-monitored blood glucose; DPP4i: dipeptidyl peptidase-4 inhibitor; GLP-1a: glucagon-like peptide-1 receptor agonist

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5. Hypoglycaemia

Hypoglycaemia is an important limitation in achieving optimal glycaemic control and is a significant risk factor for cardiovascular mortality and morbidity, especially in those with pre-existing cardiovascular disease. It is defined as SMBG <3.9mmol/l, with significant hypoglycaemia <3mmol/l. Severe hypoglycaemia is any low blood glucose value accompanied by cognitive dysfunction and the need for external assistance to correct the hypoglycaemia. Patients at risk of hypoglycaemia (Table 3) require education to recognise and treat hypoglycaemic episodes (with confirmation of hypoglycaemia with SMBG wherever possible). Oral glucose (15-20g) is the preferred treatment for non-severe episodes and IV 50% dextrose water for severe hypoglycaemia. In the event of no IV access, 1mg subcutaneous or intramuscular glucagon may be administered.

Any episode of severe hypoglycaemia or hypoglycaemia unawareness requires re-evaluation of the treatment regimen and patients. Patients with recurrent episodes should be referred to specialist care.

Table 3. Characteristics of patients at high risk of hypoglycaemia

• Treatment with insulin and/or insulin secretagogues (sulphonylurea and meglitinides)
• Intensive glucose control
• Use of ≥2 glucose-lowering drugs
• Older age
• Longer duration of diabetes
• Hypoglycaemia unawareness
• Impaired cognitive function
• Low body mass index
• Renal or hepatic impairment
• Microvascular complications
• Patients who exercise or skip meals
• Excessive alcohol intake
Adapted from SEMDSA 2017 Guidelines

6. Cardiovascular risk management

6.1. Statins are the first-line agents for lowering LDL-cholesterol in patients with type 2 diabetes. They should be added to lifestyle therapy regardless of baseline lipid levels in all patients with pre-existing cardiovascular disease, chronic kidney disease (eGFR <60ml/min/1.72m^2) and in those aged ≥40 years or with diabetes duration ≥10 years and with ≥1 additional cardiovascular risk factors.

6.2. Low-dose aspirin therapy is strongly recommended for secondary prevention of cardiovascular disease in patients with type 2 diabetes, but is not recommended for primary prevention in those who have not yet had a cardiovascular event.

6.3. Blood pressure (BP) should be measured at every routine visit to the healthcare professional. The threshold for treatment initiation is >140/90mmHg. The treatment targets for most patients are systolic BP 130-140mmHg and diastolic BP 80-90mmHg. Suitable initial choices in patients without albuminuria include an angiotensin-converting enzyme (ACE) inhibitor, angiotensin receptor blocker (ARB), thiazide-like diuretic (due to its widespread availability and low cost, indapamide is the preferred diuretic) or calcium channel blocker (CCB). Diuretics or CCBs are preferred in black patients. ACE inhibitors, ARBs, thiazide-like diuretics and nondihydropyridine CCBs have been shown to be of benefit in diabetic kidney disease. CCBs should be avoided in patients with heart failure and beta-blockers should be avoided in patients at high risk of stroke. ACE inhibitors and ARBs should not be used in combination.

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Additional information

The following practical tools and patient support aids are included in the appendices of the 2017 SEMDSA diabetes management guidelines:

Appendix 13a: Algorithm for the management of hyperglycaemic emergencies.
Appendix 13b: Diabetic coma chart.
Appendix 14: Treatment algorithm for in-hospital management of diabetes.
Appendix 21: Diabetes foot care patient checklist; diabetic foot screening assessment form; foot abnormalities and footwear illustrations; practical guide to neuropathy assessment; care pathway for people with diabetic foot problems.
Appendix 26: Examples of Ramadan-specific meal plans for South Africans.
Appendix 29: Assessment and treatment algorithm for sexual dysfunction in men with type 2 diabetes.

Reference

The Society of Endocrinology, Metabolism and Diabetes of South Africa Type 2 Diabetes Guidelines Expert Committee. The SEMDSA 2017 guidelines for the management of type 2 diabetes mellitus. *Journal of Endocrinology, Metabolism and Diabetes of South Africa* 2017; **22**(1): S1-S182.

The latest complete pdf version of the guideline is available at
http://www.jemdsa.co.za/index.php/JEMDSA/issue/view/42/showToc

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