SEMDSA guidelines for the diagnosis and management of type 2 diabetes mellitus for primary health care

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Criteria for diagnosis of diabetes mellitus

Patient has symptoms of diabetes[a]

Plus:

- Casual/random plasma glucose (PG) ≥ 11.1 mmol/l;[b] or
- Fasting plasma glucose (FPG) ≥ 7.0 mmol/l;[c] or
- Two-hour plasma glucose (2hPG) ≥ 11.1 mmol/l during oral glucose tolerance test (OGTT).[d]

[a] The classic symptoms of diabetes include polyuria, polydipsia and weight loss.
[b] "Casual" is defined as any time of day, withot regard to time of last meal.
[c] "Fasting" is defined as no caloric intake for at least eight hours.
[d] The test should be performed as described by the World Health Organization (WHO), using a glucose load containing the equivalent of 75 g anhydrous glucose dissolved in 250 ml water over five minutes.

Acute metabolic decompensation

In the absence of unequivocal hyperglycaemia accompanied by acute metabolic decompensation, a confirmatory laboratory glucose test (casual/random PG, FPG, or 2hPG during 75 g OGTT) must be done in all cases on another day. Different criteria are used to diagnose gestational diabetes in pregnant women.

Patient is asymptomatic

75 g OGTT is indicated in the following patients:

- Asymptomatic, high-risk individuals.
- FPG is ≥ 5.6 but < 7.0 mmol/l in detection/screening programmes.
- Casual/random PG ≥ 5.6 but < 11.1 on screening.[e]

[e] Or, do FPG.

- The WHO 1998/2006 criteria should be used to diagnose diabetes. The importance of not diagnosing diabetes on the basis of a single laboratory measurement, in the absence of symptoms, should be emphasised.
- The diagnosis should be based on laboratory plasma glucose (preferred), or capillary plasma glucose.

Conversion factor

Plasma glucose (mmol/l) = 0.102 + 1.066 x capillary blood glucose

Glycaemic targets for control[f]

Glycated haemoglobin (HBA_{1c}) < 7%[g]

Capillary (finger-prick) PG:

- Preprandial: 4-7 mmol/l
- Postprandial: 5-8 mmol/l[h]

[f] For non-pregnant adults.
[g] Referenced to non-diabetic range of 4-6% using a Diabetes Control and Complications Trial- (DCCT-) based assay (DCCT-aligned).
[h] Peak postprandial levels in people with diabetes are generally one to two hours after the beginning of a meal.

Key concepts in setting glycaemic targets

- HbA_{1c} is the primary target for glycaemic control. More stringent glycaemic goals (i.e. HbA_{1c} < 6.5%) may further lower the risk of microvascular complications (e.g. nephropathy), but at the cost of increased risk of hypoglycaemia and increased mortality in patients who are at elevated risk of cardiovascular disease (CVD).
- Postprandial glucose should be targeted if HbA_{1c} goals are not met, despite reaching the preprandial goal.
- Goals should be individualised based on duration of diabetes, co-morbid conditions, pregnancy status, hypoglycaemia unawareness, age, and individual patient considerations.

Body mass index, waist circumferences, lipid and blood pressure goals

Body mass index

Body mass index (BMI) < 25 kg/m^2

Waist circumference

Men < 94 cm [i]
Women < 80 cm

Blood pressure [j]

Systolic < 130 mmHg
Diastolic < 80 mmHg

[i] In men of South Asian descent, waist circumference goal < 90 cm.
[j] In diabetic nephropathy, blood pressure goals are systolic ≤ 120 mmHg and diastolic ≤ 70 mmHg.

Lipid goals

Total cholesterol < 4.5 mmol/l
Low-density lipoprotein (LDL) cholesterol < 2.5 mmol/l [k]
High-density lipoprotein (HDL) cholesterol
- Men > 1.0 mmol/l
- Women > 1.2 mmol/l

Triglycerides < 1.7 mmol/l

[k] In the presence of clinically manifest vascular disease (ischaemic heart disease, cerebrovascular disease or peripheral vascular disease), LDL cholesterol goal < 1.8 mmol/l.

Key initial processes of care	
Tests/procedures	**Frequency**
HbA_{1c}	At least twice a year, if stable Quarterly, if treatment changes or not meeting goals
Lipid profile	Annually, or more frequently, if lipids are high and after treatment has been initiated
Blood pressure	Measure at every routine diabetes visit
Weight, BMI and waist	Weigh and measure waist at each regular diabetes visit BMI annually
Comprehensive foot examination	Annually, or more often in patients with high-risk foot conditions
Micro-albumin	Annually if no persistent dipstick proteinuria
Serum creatinine	Annually
Eye examination for retinopathy	Annually, or more frequently if significant retinopathy present
Referral to diabetes nurse educator and/or dietitian	Annually, or whenever needed

Patient education

Patient education is the cornerstone of effective diabetes care, and sufficient time and resources should be made available in order to perform this function this effectively.

General principles

- An evidence-based, structured education programme should be offered to all patients at the time of diagnosis, and consolidated at regular intervals thereafter. The aim is to *promote patient self-management.*
- The programme should be presented by an appropriately trained educator.
- Ensure that education is available to all people with diabetes, irrespective of language, ethnicity, culture, educational level or socioeconomic status.
- Small group education is the most cost-effective option.
- Ensure that *active learning* is taking place.
- A regular audit of the programme and the effect on outcomes is advised.

Topics to be covered

- Basic knowledge of diabetes.
- Importance of good, comprehensive control.
- Methods to achieve good control:
  - Nutrition therapy, including weight loss in the overweight and obese.
  - Exercise: value, type and frequency.
  - Medication.
  - Insulin injection technique and sites of injection.
  - Self-monitoring of blood glucose.
- Recognition and management of acute complications, e.g. hypoglycaemia.
- Recognition and management of chronic complications.
- Foot care.
- Smoking and alcohol.
- Pregnancy.
- Psychosocial issues.
- When and where to get help.
- Identification disc or bracelet.

Children with type 2 diabetes

Type 2 diabetes does occur in children with increasing frequency, and is becoming a problem. All children should be referred for specialist assessment.

Lifestyle modifications

- Weight loss is recommended for all overweight (BMI 25–29.9 kg/m^2) or obese (BMI ≥ 30 kg/m^2) individuals who have diabetes.
- It is important to set a weight-loss goal that is *achievable* and *maintainable.*
- Moderate weight loss of 5% of body weight can produce significant health benefits, and may be a reasonable initial goal for most patients.
- For weight loss, either low-carbohydrate or low-fat calorie-restricted diets may be effective in the short term (up to one year).
- Regular physical activity helps to maintain weight loss and prevent weight regain.
- Regular exercise and aerobic fitness also improve insulin sensitivity, the lipid profile, and glycaemic and blood pressure control.
- Thirty to forty-five minutes of moderate-intensity aerobic physical activity, three to five days per week initially, gradually increasing the duration and frequency, is recommended.
- The value of screening asymptomatic diabetic patients for coronary artery disease remains uncertain, and clinical judgment is called for in this area.

Self-monitoring of blood glucose

- Self-monitoring of blood glucose (SMBG) results must be used for the purpose of attaining and maintaining glycaemic targets, by guiding self- and practitioner adjustment of therapy and to provide evidence on hypoglycaemia.
- SMBG should be carried out three or more times daily for patients using multiple (two or more) daily injections of insulin.

- SMBG should be carried out up to once daily for patients using a single daily injection of insulin, either alone or in combination with oral agents.
- SMBG can be considered in patients using oral agents (e.g. for assessing if additional treatment is required, or to confirm hypoglycaemia if symptomatic), but *not* regularly and indefinitely.
- Perform SMBG more frequently in the following cases:
  - Acute illness;
  - Periods of poor glycaemic control;
  - Frequent hypoglycaemic episodes;
  - Pregnancy;
  - After any adjustment to therapy

Pharmacological treatment of blood glucose

- Pharmacological therapy should always be accompanied by ongoing lifestyle modifications.
- From diagnosis, inform patients that a *progressive increase in the dose and number of medications is the rule,* given the natural history of type 2 diabetes and that insulin therapy is almost invariably required.
- Aim to achieve and maintain HbA_{1c} < 7%, or as close to normal as is safely possible.
- *HbA_{1c} > 7% must serve as a call to action* on the part of the practitioner; medication must be increased at this level of HbA_{1c}, except if the risk of severe hypoglycaemia is unacceptable.
- The following therapies have been proven, in long-term randomised clinical trials, to reduce the micro- and/or macrovascular complications of type 2 diabetes mellitus. These drugs, therefore, form the backbone of diabetes management:
  - Metformin;
  - Glibenclamide;
  - Gliclazide (including modified-release formulation);
  - Glimepiride; and
  - Insulin.

Metformin

- Metformin is the initial therapy of choice and should be initiated at the time of diagnosis in all patients (both overweight and of normal weight), unless specifically contraindicated. It is recommended that metformin therapy be continued even when other classes of antidiabetic agents, including insulin, are added subsequently.
- Metformin can be added as a second-line agent in patients in whom treatment has been initiated with any other class of oral antidiabetic drug.
- In the presence of heart failure, peripheral vascular disease, chronic obstructive pulmonary disease, or if the serum creatinine exceeds 135 µmol/l, metformin can only be used under specialist supervision
- The minimum effective daily dose is 1 500 mg, and the maximum dose should rarely exceed 2 550 mg. The dose should be escalated gradually over one to two months to minimise gastrointestinal side-effects. Consider extended-release tablets when gastrointestinal side-effects prevent continuation of metformin therapy.
- Metformin reduces HbA_{1c} by 1–2%. Monotherapy does not usually cause hypoglycaemia.

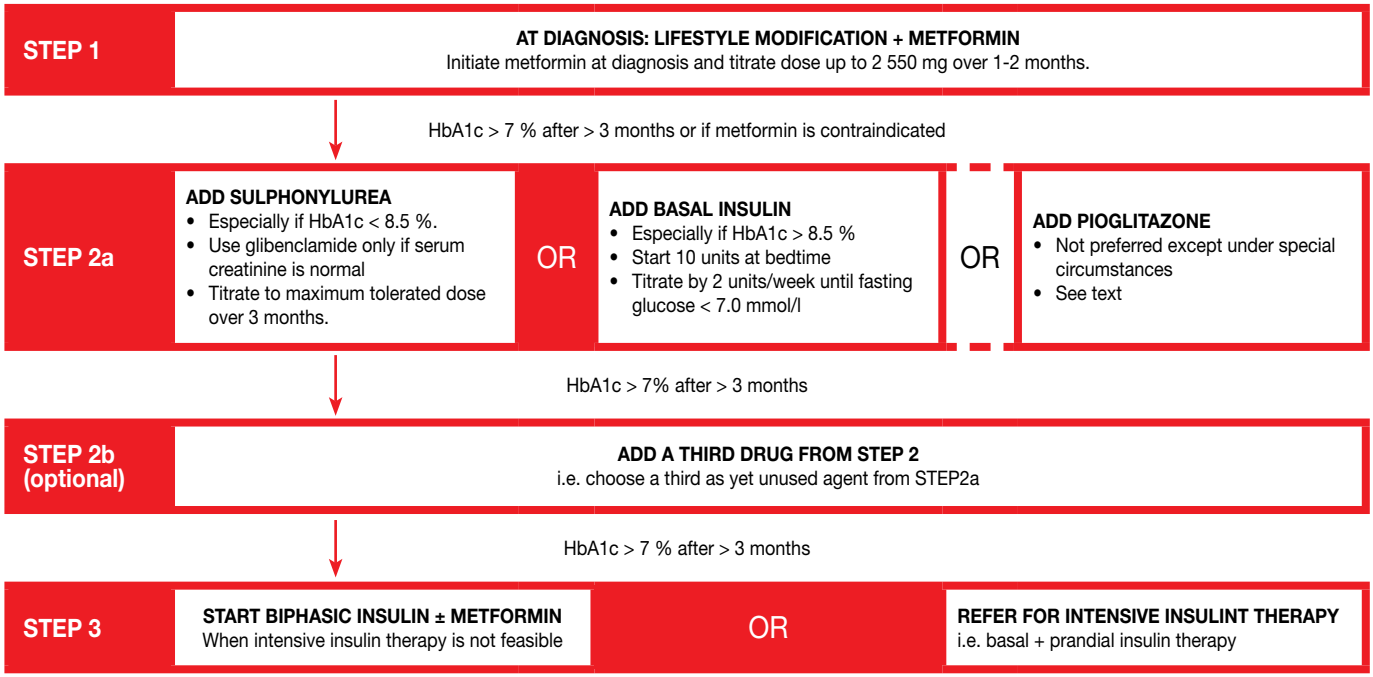
Sulphonylureas: glibenclamide, gliclazide and glimepiride

- Sulphonylureas are an option for first-line therapy when the HbA_{1c} is above target and:
  - The patient is normal weight; or
  - The patient is intolerant of metformin; or
  - Rapid control of hyperglycaemic symptoms is needed.
- A sulphonylurea can be added to metformin or thiazolidenediones as a second-line agent when HbA_{1c} is above target.
- Common adverse events include hypoglycaemia and weight gain (± 2 kg).
- Glibenclamide is absolutely contraindicated when the serum creatinine is abnormal, because of the risk of severe prolonged hypoglycaemia. Gliclazide and glimepiride can be used when the serum creatinine is < 150 µmol/l.
- Sulphonylureas reduce HbA_{1c} by 1–2%.

Thiazolidenediones: pioglitazone and rosiglitazone

- Generic agents are preferred, because of cost-effectiveness.
- Thiazolidenediones can be used as first-line therapy in obese individuals who cannot tolerate metformin.
- Thiazolidenediones may be added as second-line agents where treatment has been initiated with either metformin or a sulphonylurea.
- A thiazolidinedione may be added as a third oral agent (after metformin and a sulphonylurea) instead of insulin, when insulin therapy is not desirable or acceptable.
- Thiazolidenediones may be useful in limiting the insulin dose when insulin requirements are unusually high (> 2 units/kg), but this is not always effective and must be balanced against the increased risk of adverse effects.
- The main adverse effects are weight gain, oedema and fluid retention (especially severe when combined with insulin). Therefore, do not use in the presence of heart failure (overt or incipient), or renal failure. Controversy exists over the apparent increase in cardiovascular events with rosiglitazone.

Glycaemic management of type 2 diabetes in non-pregnant adults



- Thiazolidenediones do not usually cause hypoglycaemia when used alone or in combination with insulin.
- Thiazolidenediones reduce HbA_{1c} by 0.5–1.4%.

Combination oral therapy

Consideration should be given to the earlier initiation or addition of combinations of oral agents from different classes in patients with high glycaemic levels (HbA_{1c} > 9%), as a single agent is unlikely to achieve the target.

Other antidiabetic agents

- Alpha-glucosidase inhibitors (acarbose).
- Rapid-acting insulin secretagogues (e.g. nateglinide and repaglinide).
- Dipeptidyl peptidase intravenous inhibitors (e.g. vildagliptin, sitagliptin).

Anti-diabetic agents not for use in primary care

- Glucagon-like peptide-1 mimetics (e.g. exenatide and liraglutide).

Insulin

- Consider insulin as first-line therapy in the setting of severely uncontrolled diabetes with catabolism. This includes patients with either:
  - FPG > 14 mmol/l, random glucose consistently > 16.7 mmol/l, HbA_{1c} > 10%, or the presence of ketonuria; or
  - Symptomatic diabetes with polyuria, polydipsia, and significant weight loss.
- Add insulin to oral agents, as second- or third-line therapy, when glycaemic targets are unmet. Add either:
  - *Basal insulin,* starting with 10 units of intermediate- (NPH) or long-acting insulin at bedtime, and titrating by two units every three to seven days until the fasting glucose is 4–6 mmol/l. Continue metformin and sulphonylurea therapy when adding basal insulin. Use analogue (glargine or detemir) insulin if nocturnal hypoglycaemia is problematic with NPH/Lente insulin.
  - *Biphasic insulin,* starting with a minimum total dose of 0.4 units/kg, with 2/3 initially administered before breakfast and 1/3 before supper. Titrate the morning dose according to pre-supper glucose levels, and the evening dose according to pre-breakfast glucose levels (target 4–7 mmol/l). Metformin therapy should be continued, but sulphonylurea therapy should be stopped.
- Patients should be provided with structured education and written instructions for insulin dose titration.
- If glycaemic targets are not met with basal or biphasic insulin, then intensive insulin therapy (with multiple daily injections) must be considered.
- Specialist referral is appropriate at any stage if glycaemic targets remain unmet.

Blood pressure treatment

- A diagnosis of hypertension is made if the blood pressure (BP) ≥ 130 mmHg systolic or ≥ 80 mmHg diastolic on two separate days.
- Pharmacological therapy, as well as advice on healthy

lifestyle interventions, should be instituted at the outset.

- An angiotensin-converting enzyme (ACE) inhibitor (or angiotensin receptor blocker [ARB], in the case of intolerance to the former) should be the drug of choice as initial therapy. In black patients, a low-dose thiazide diuretic is preferable as initial monotherapy.
- A low-dose thiazide or loop diuretic (if the estimated glomerular filtration rate ≥ 50 ml/minute) should be added if the BP target is not achieved.
- Two or more agents are often required to achieve BP targets.
- Avoid combinations of an ACE inhibitor and an ARB, or either one of these with spironolactone, as potassium levels can rise.
- Monitor serum potassium and creatinine in all patients, particularly if ACE inhibitors, diuretics or ARBs are prescribed.
- In the presence of microalbuminuria or macroalbuminuria, it is mandatory to use an ACE inhibitor (or ARB, if intolerant to ACE inhibitors).
- Beta blockers are only indicated if there is coexisting angina, in patients with a previous myocardial infarct or if hypertension is refractory to a combination of other classes.

Lipid treatment

- Achieving the recommended LDL cholesterol level is the primary goal of therapy.
- Statins are first-line agents for lowering LDL cholesterol in diabetic patients. The addition of a fibrate or another lipid-modifying drug may be considered if triglycerides remain > 2 mmol/l after reaching the LDL cholesterol target with statins. However, these patients should be referred for specialist assessment.
- Statin therapy should be accompanied by lifestyle modification, regardless of baseline lipid levels, for all type 2 diabetic patients who:
  - Have existing cardiovascular disease;
  - Are older than 40 years of age and have one or more additional cardiovascular risk factor.
- For diabetic patients at lower risk (i.e. without established cardiovascular disease or who are under 40 years of age) use a targeted approach. In these patients, statin therapy should be considered if the LDL cholesterol remains > 2.5 mmol/l, despite adequate glycaemic control and advice on lifestyle.
- Patients with triglycerides > 5 mmol/l in the controlled diabetic, or > 15 mmol/l before treatment, should be referred for specialist assessment.

Antiplatelet agents

- Use aspirin therapy (75–162 mg/day; 150 mg in South Africa) as a secondary prevention strategy in those with diabetes with a history of CVD.
- Use aspirin therapy (75–162 mg/day; 150 mg in South Africa) as a primary prevention strategy in those with type 1 or 2 diabetes at increased cardiovascular risk, including those who are > 40 years of age or who have additional risk factors (i.e. family history of CVD, hypertension, smoking, dyslipidaemia, or albuminuria).
- Aspirin therapy is not recommended in people < 30 years of age, because of lack of evidence of benefit, and is contraindicated in patients < 21 years of age, because of the associated risk of Reye's syndrome.
- Combination therapy with clopidogrel is reasonable for up to a year after an acute coronary syndrome or as monotherapy for patients with CVD and documented aspirin allergy.
- For patients with CVD and documented aspirin allergy, clopidogrel (75 mg/day) should be used.

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