

## SEMDSA Guidelines for Diagnosis and Management of Type 2 Diabetes Mellitus for Primary Health Care – 2009



### Criteria for diagnosis of diabetes mellitus

A. Symptoms <sup>a</sup> of diabetes	B. If asymptomatic
<p style="text-align: center;"><b>PLUS</b></p> <ul style="list-style-type: none"> <li>• Casual/random plasma glucose <math>\geq 11.1</math> mmol/l<sup>b</sup></li> </ul> <p style="text-align: center;"><b>Or</b></p> <ul style="list-style-type: none"> <li>• Fasting plasma glucose (FPG) <math>\geq 7.0</math> mmol/l<sup>c</sup></li> </ul> <p style="text-align: center;"><b>Or</b></p> <ul style="list-style-type: none"> <li>• 2 hr plasma glucose (2PG) <math>\geq 11.1</math> mmol/l during OGTT<sup>d</sup></li> </ul>	<p>The 75 g OGTT is indicated in the following:</p> <ul style="list-style-type: none"> <li>• In the asymptomatic high-risk individuals</li> <li>• If FPG is <math>\geq 5.6 - &lt; 7.0</math> mmol/l (in detection/screening programmes)</li> </ul> <p>If random plasma glucose <math>\geq 5.6 - &lt; 11.1</math><sup>†</sup> (on screening)</p>
<p><sup>a</sup> The classic symptoms of diabetes include polyuria, polydipsia and weight loss</p> <p><sup>b</sup> Casual is defined as any time of day without regard to time of last meal</p> <p><sup>c</sup> Fasting is defined as no caloric intake for at least 8 hr</p> <p><sup>d</sup> The test should be performed as described by the World Health Organisation using a glucose load containing the equivalent of 75 g anhydrous glucose dissolved in 250 ml water over 5 minutes</p> <p><b>Note: Acute metabolic decompensation</b> In the absence of unequivocal hyperglycaemia accompanied by acute metabolic decompensation a confirmatory laboratory glucose test (a FPG, a casual PG or a 2hPG in a 75-g OGTT) must be done in all cases on another day. Different criteria are used to diagnose gestational diabetes in pregnant women.</p>	<p><sup>†</sup> or do FPG</p> <ul style="list-style-type: none"> <li>– WHO 1998/2006 criteria should be used to diagnose diabetes, including the importance of not diagnosing diabetes on the basis of a single laboratory measurement in the absence of symptoms.</li> <li>– Diagnosis should be based on laboratory plasma glucose (preferred) or capillary plasma glucose.</li> <li>– Conversion factor: plasma glucose (mmol/l) = 0.102 + 1.066 x capillary blood glucose.</li> </ul>

### Glycaemic targets for control<sup>a</sup>

Glycated haemoglobin (HbA1c) (%) <sup>b</sup>	< 7
Capillary (finger-prick) plasma glucose (mmol/l):	4–7
Pre-prandial	5–8
Post-prandial <sup>c</sup>	

<sup>a</sup> for non-pregnant adults, <sup>b</sup> referenced to non diabetic range of 4–6% using a DCCT-based assay (DCCT-aligned), <sup>c</sup> peak post-prandial levels in people with diabetes are generally 1–2 hr after the beginning of a meal.

#### Key concepts in setting glycaemic targets:

- HbA1c is the primary target for glycaemic control, more stringent glycaemic goals (i.e. HbA1c < 6.5%) may further lower the risk of microvascular complications viz nephropathy, but at the cost of increased risk of hypoglycaemia and increased mortality in patients who are at elevated risk of cardiovascular disease (CVD).
- Post prandial glucose should be targeted if HbA1c goals are not met despite reaching pre-prandial goal.
- Goals should be individualised based on: duration of diabetes, comorbid conditions, pregnancy status, hypoglycaemia unawareness, age, individual patient considerations.

### BMI, Waist, Lipid and Blood Pressure Goals

<p><b>BMI and Waist</b></p> <p>BMI &lt; 25 kg/m<sup>2</sup></p> <p>Waist &lt; 94 cm men**</p> <p style="padding-left: 20px;">&lt; 80 cm women</p>	<p><b>Lipid goals</b></p> <p>Total cholesterol &lt; 4.5 mmol/l</p> <p>LDL cholesterol &lt; 2.5 mmol/l+</p> <p>HDL cholesterol &gt; 1.0 mmol/l (men)</p> <p style="padding-left: 20px;">&gt; 1.2 mmol/l (women)</p> <p>Triglycerides &lt; 1.7 mmol/l</p>
<p><b>Blood Pressure ++</b></p> <p>Systolic &lt; 130 mmHg</p> <p>Diastolic &lt; 80 mmHg</p>	
<p>** &lt; 90 cm in men of South Asian descent.</p> <p>+ In the presence of clinically manifest vascular disease (ischaemic heart disease, cerebrovascular disease or peripheral vascular disease) the target should be a LDL cholesterol &lt; 1.8 mmol/l.</p> <p>++ The target blood pressure in diabetic nephropathy is systolic <math>\leq 120</math> mmHg and diastolic <math>\leq 70</math> mmHg.</p>	

Key processes of care (all initially)	
Tests/ procedures	Frequency
HbA1c	At least 2 times/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/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
Microalbumin	Annually if no persistent dipstick proteinuria
Serum creatinine	Annually
Eye examination for retinopathy	Annual or more frequent if significant retinopathy present
Referral to diabetes nurse educator and/or dietician	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 do 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 given by an appropriately trained educator(s).
- Ensure that education is available to all people with diabetes irrespective of language, ethnicity, culture, educational level, socioeconomic status.
- Small group education is the most cost-effective option.
- Ensure that **active** learning is taking place.
- Regular audit of the programme and its effect on outcomes is advised.

#### Topics to be covered

- Basic knowledge of diabetes.
- The importance of good comprehensive control.
- Methods to achieve good control:
  - Nutrition therapy including weight loss in the overweight/obese.
  - Exercise (value, type, 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

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

### Lifestyle

- Weight loss is recommended for all overweight (BMI 25–29.9 kg/m<sup>2</sup>) or obese (BMI ≥ 30 kg/m<sup>2</sup>) individuals who have diabetes.
- It is important to set a weight-loss goal that is *achievable* and *can be maintained*.
- 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 1 year).
- Regular physical activity helps to maintain weight loss and prevent weight regain.
- Regular exercise and aerobic fitness also improve insulin sensitivity, lipid profile, glycaemic and blood pressure control.
- 30–45 min of moderate-intensity aerobic physical activity (3–5 days per week initially, gradually increasing the duration and frequency is recommended).
- Screening asymptomatic diabetic patients for CAD remains unclear and clinical judgment is called for in this area.

### Self Monitoring of Blood Glucose (SMBG)

- 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 (≥ 2) 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 Rx is required; to confirm hypoglycaemia if symptomatic), but NOT regularly and indefinitely.
- Perform SMBG more frequently in setting of:
  1. Acute illness
  2. Periods of poor glycaemic control
  3. Frequent hypoglycaemic episodes
  4. Pregnancy
  5. Any adjustment to therapy

### Pharmacological treatment of blood glucose

- Pharmacological therapy should always be accompanied by ongoing lifestyle modification.
- 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 the  $HbA_{1c} < 7\%$ , or as close to normal as is safely possible.
- An  $HbA_{1c} > 7\%$  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 macro-vascular complications of type 2 diabetes mellitus; these drugs therefore form the backbone of diabetes management: metformin, glibenclamide, gliclazide (including modified-release) and insulin.

### 1. Metformin

- Is the initial therapy of choice and should be started at the time of diagnosis in all patients (overweight and normal weight) unless specifically contra-indicated. It is recommended that metformin therapy continue even when other classes of anti-diabetic agents (including insulin) are added subsequently.
- Can be added as a second-line agent in patients where treatment has been initiated with any other class of oral anti-diabetic drug (OAD).
- Can only be used under specialist supervision in the presence of heart failure, peripheral vascular disease, chronic obstructive pulmonary disease or if the serum creatinine exceeds  $135 \mu\text{mol/l}$ .
- The minimum effective daily dose is 1500 mg and the maximum dose should rarely exceed 2550 mg. The dose should be escalated gradually over 1–2 months to minimise gastrointestinal side effects\*.
- Reduces  $HbA_{1c}$  by 1–2%. Monotherapy does not usually cause hypoglycaemia.  
\* Consider extended-release tablets when GI side effects prevent continuation of metformin therapy.

### 2. Sulphonylureas (glibenclamide and gliclazide)

- 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.
- Can be added to metformin or thiazolidenediones as a second-line agent when  $HbA_{1c}$  is above target.
- Common adverse events are hypoglycaemia and weight gain ( $\pm 2$  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  $< 150 \mu\text{mol/l}$ .
- Reduce  $HbA_{1c}$  by 1–2%.

### 3. Thiazolidenediones (pioglitazone, rosiglitazone)

- Generic agents are preferred because of cost-effectiveness.
- Can be used as first-line therapy in obese individuals who cannot tolerate metformin.
- May be added as second-line agents where treatment has been initiated with either metformin or a sulphonylurea.
- May be added as a third oral agent (to metformin and sulphonylurea) instead of insulin, when insulin therapy is not desirable or acceptable.
- May be useful in limiting the insulin dose when insulin requirements are unusually high ( $> 2 \mu\text{kg}$ ), 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.
- Does not usually cause hypoglycaemia when used alone or in combination with insulin.
- Reduces  $HbA_{1c}$  by 0.5–1.4%.

### 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.

### 5. Other anti-diabetic agents

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

#### *Anti-diabetic agents not for use in primary care*

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

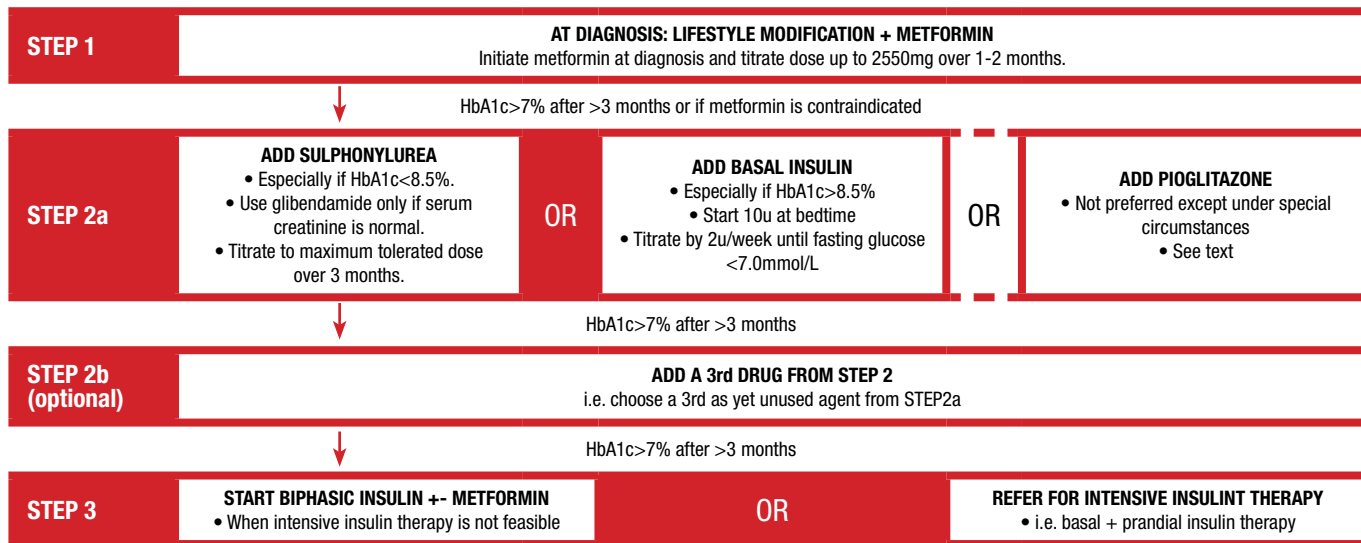
### 6. Insulin

- Consider insulin as first-line therapy in the setting of severely uncontrolled diabetes with catabolism. This includes patients with either:
  - fasting plasma glucose levels  $> 14 \text{ mmol/l}$ , random glucose levels consistently  $> 16.7 \text{ mmol/l}$ ,  $HbA_{1c} > 10\%$ , 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 acting (NPH) or long-acting insulin at bedtime, and titrating by 2 units every 3 to 7 days until the fasting glucose is 4–7 mmol/l. Continue metformin and SU 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 u/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 SU 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 recommendations

- Diagnosis of hypertension is made if BP  $\geq 130$  mmHg systolic or  $\geq 80$  mmHg diastolic on 2 separate days.
- Pharmacological therapy as well as advice on healthy lifestyle intervention should be instituted at the outset.

Glycaemic management of type 2 diabetes in non-pregnant adults



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

**Lipid treatment recommendations**

- 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 LDL cholesterol target with statins. However, these patients should be referred for specialist assessment).
- Statin therapy should be added to lifestyle therapy, regardless of baseline lipid levels, for all type 2 diabetic patients:
  - with existing cardiovascular disease
  - older than 40 years of age and who have one or more additional cardiovascular risk factor
 For diabetic patients at lower risk (without established cardiovascular disease or 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.
- 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 SA) as a secondary prevention strategy in those with diabetes with a history of CVD.
- Use aspirin therapy (75–162 mg/day) (150 mg in SA) as 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 (family history of CVD, hypertension, smoking, dyslipidaemia, or albuminuria).
- Aspirin therapy is not recommended in people under 30 years of age, due to lack of evidence of benefit, and is contraindicated in patients under the age of 21 years 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 alone for patients with CVD and documented aspirin allergy.
- For patients with CVD and documented aspirin allergy, clopidogrel (75 mg/day) should be used.

**Key references**

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**Guideline Committee**

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