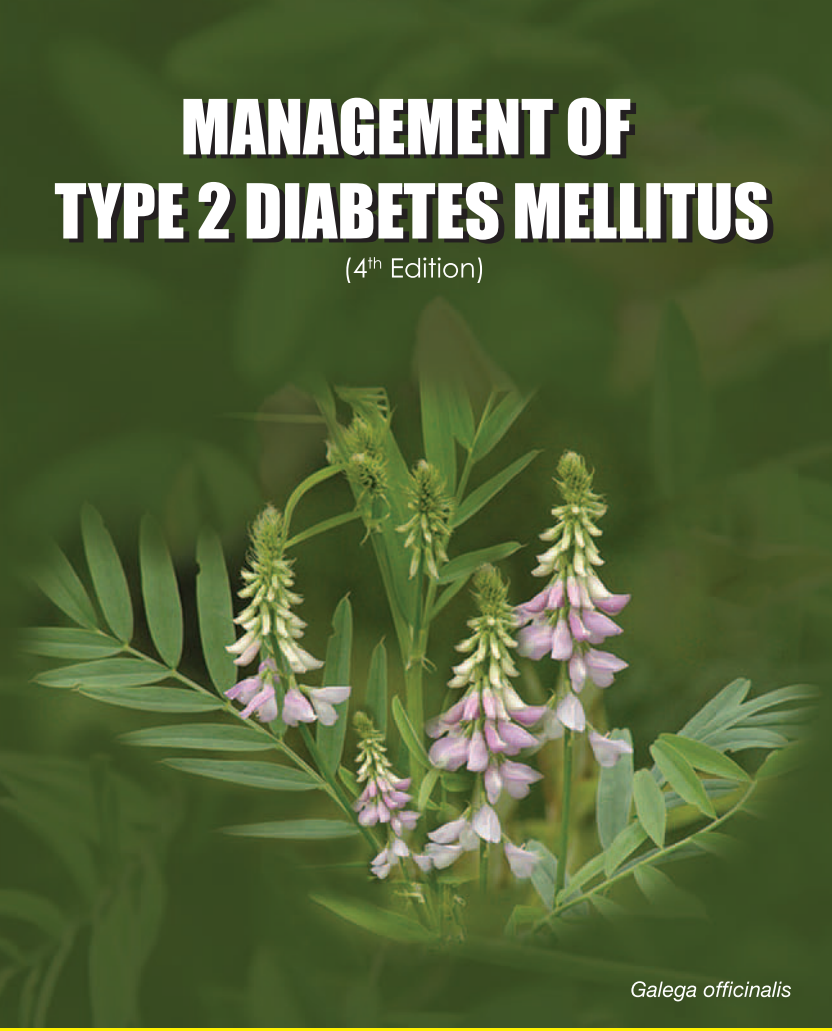
MANAGEMENT OF TYPE 2 DIABETES MELLITUS

(4th Edition)



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QUICK REFERENCE FOR HEALTH CARE PROVIDERS

MALAYSIAN ENDOCRINE & METABOLIC SOCIETY

MINISTRY OF HEALTH MALAYSIA

ACADEMY OF MEDICINE MALAYSIA

PERSATUAN DIABETES MALAYSIA

KEY MESSAGES

1. Diabetes is a chronic and progressive disease.

2. Perform screening for diabetes in those with risk factors annually.

3. Measure HbA_{1c} every 3-6 months. Monitor other risk factors and complications annually.

4. Individualise glycaemic targets. In most patients, $HbA_{1c} < 6.5\%$ is recommended.

5. Diabetes education is important and is effective in improving clinical outcomes and quality of life. Educate patients to practice self-care.

6. Non-pharmacological therapy such as behavioural modification, diet and exercise is essential.

7. Early treatment and intensification with combination of OAD agents and insulin will improve and sustain good glycaemic control.

This Quick Reference provides key messages and a summary of the main recommendations in the Clinical Practice Guidelines (CPG) Management of Type 2 Diabetes Mellitus, 4th Edition (2009).

Details of the evidence supporting these recommendations can be found in the above CPG, available on the following websites:

Ministry of Health Malaysia : http://www.moh.gov.my
Academy of Medicine : http://www.acadmed.org.my

SCREENING CRITERIA

a. Individual with symptoms suggestive of Diabetes

b. Asymptomatic overweight individuals (**age ≥ 30 years**) with BMI > 23 kg/m^2 or WC ≥ 80 cm (women)/WC ≥ 90 cm (men) with any of the following risk factors:
- Dyslipidaemia either HDL < 0.9 mmol/L or TG > 1.7 mmol/L
- History of cardiovascular disease
- Hypertension
- IGT or IFG on previous testing
- First-degree relative with diabetes
- Physical inactivity
- Other clinical conditions associated with insulin resistance (e.g. acanthosis nigricans)
- Women with polycystic ovarian syndrome (PCOS)

Note: *Screening should be done annually*

c. Pregnant women with any of the following risk factors:
- BMI > 27 kg/m^2
- Previous macrosomic baby (weighing ≥ 4 kg)
- Previous GDM
- First-degree relative with diabetes
- Bad obstetric history
- Glycosuria at the first prenatal visit
- Current obstetric problems (hypertensive disease in pregnancy, polyhydramnios and current use of steroids)
- Age > 25 years

Note: *Women with history of GDM should be screened annually*

d. Overweight children and adolescents (BMI > 85th percentile for age and sex, or weight > 120% of ideal) with any two of the following risk factors:
- Family history of T2DM in first- or second-degree relative
- Maternal history of GDM
- Ethnicity (esp. Indian ethnic background)
- Signs of insulin resistance (acanthosis nigricans, hypertension, dyslipidaemia, PCOS)

Note: *Screen every two years starting at the age of 10 years old or at onset of puberty if it occurs at a younger age*

VALUES FOR DIAGNOSIS

DIAGNOSIS FOR T2DM

	Fasting	Random
Venous Plasma Glucose (mmol/L)	≥ 7.0	≥ 11.1

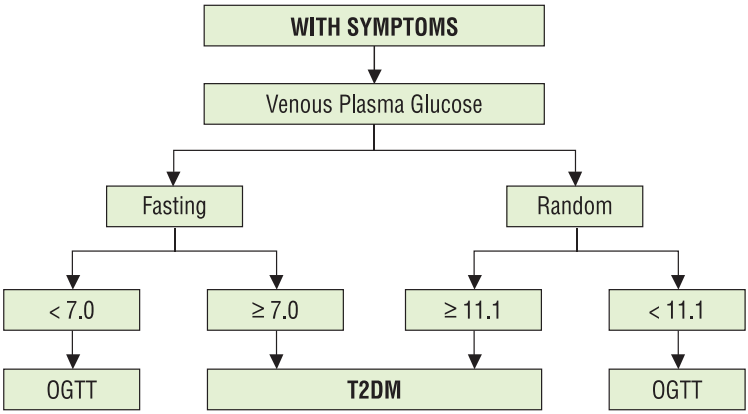
- In the symptomatic individual, one abnormal glucose value is diagnostic.
- In the asymptomatic individual, 2 abnormal glucose values are required.

DIAGNOSTIC VALUES OF OGTT

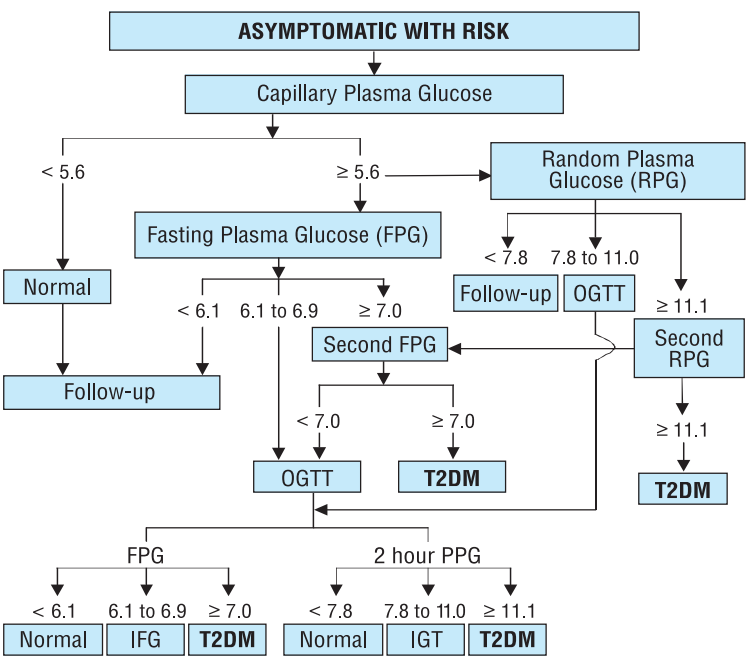
OGTT Plasma Glucose Values (mmol/L)		
Category	**Fasting**	**2-hour**
Normal	< 6.1	< 7.8
IFG (isolated)	6.1-6.9	< 7.8
IGT (isolated)	< 6.1	7.8-11.1
IFG & IGT (combined)	6.1-6.9	7.8-11.1
DM	≥ 7.0	> 11.1

- If FPG ≥ 7.0 mmol/L or 2PPG ≥ 11.1 mmol/l, repeat OGTT is required to make diagnosis of T2DM.

SCREENING ALGORITHM FOR T2DM AT PRIMARY CARE LEVEL – WITH SYMPTOMS



SCREENING ALGORITHM FOR T2DM AT PRIMARY CARE LEVEL – WITHOUT SYMPTOMS



MANAGEMENT OF T2DM

- At diagnosis, a detailed history, physical examination (including fundoscopy) and investigation must be done to assess the risk factors and complications of diabetes.
- Assessment includes appraisal of cardiovascular risks and presence of end-organ damage.

CLINICAL MONITORING PROTOCOL

Test	Initial visit	Follow-up visit	Quarterly visit	Annual visit
Weight	✓	✓	✓	✓
BMI	✓			✓
Blood Pressure	✓	✓	✓	✓
Eye : visual acuity fundoscopy	✓			✓
Feet : pulses neuropathy	✓		✓	✓
Blood Glucose	✓	✓	✓	✓
HbA_{1c}	✓		✓	✓
Cholesterol/HDL cholesterol	✓		★	✓
Triglycerides	✓		★	✓
Albuminuria*	✓		★	✓
Creatinine/BUN	✓		★	✓
ECG	✓			✓
Urine microscopy	✓			✓

✓ *Conduct test* ☐ *No test required* ★ *Conduct test if result is abnormal in first visit*

** Microalbuminuria if resources are available*

TARGETS FOR T2DM

	Levels
Glycaemic Control*	
Fasting	4.4 - 6.1 mmol/L
Non-fasting	4.4 - 8.0 mmol/L
HbA_{1c}	< 6.5 %
Lipids	
Triglycerides	≤ 1.7 mmol/L
HDL cholesterol	≥ 1.1 mmol/L
LDL cholesterol	≤ 2.6 mmol/L#
Blood Pressure	
Normal renal function	≤ 130/80 mmHg§
Renal impairment/gross proteinuria	≤ 120/75 mmHg
Exercise	150 mins / week

* Glycaemic target should be individualised to minimise risk of hypoglycaemia.
\# In Individuals with overt CVD, LDL cholesterol target is < 1.8 mmol/L.
§ In children and adolescents, blood pressure (BP) should be < 95th percentile for age and sex.

RECOMMENDATIONS FOR PHARMACOLOGICAL THERAPY

ORAL AGENT MONOTHERAPY

1. If glycaemic targets are not achieved (HbA_{1c} < 6.5%, FPG < 6 mmol/L) with lifestyle modification within 3 months, OAD agents should be initiated.
2. In the presence of marked hyperglycaemia in newly diagnosed T2DM (HbA_{1c} 6.5-8%, FPG 6-10 mmol/L), OAD agents should be considered at the outset together with lifestyle modification.

COMBINATION OF ORAL AGENTS

Combination of oral agents is indicated in:
- Newly diagnosed patients with HbA_{1c} 8-10%, FPG 10-13 mmol/L.
- Patients who are not reaching targets (HbA_{1c} < 6.5%) after 3-6 months on monotherapy.

COMBINATION OF ORAL AGENTS AND INSULIN

Combination of oral agents and insulin is indicated in:
- Newly diagnosed patients with HbA_{1c} > 10%, FPG > 13 mmol/L.
- Patients who are not reaching targets (HbA_{1c} < 6.5%) after 3-6 months on optimal doses of oral therapy.

ORAL ANTI-DIABETIC AGENTS (OAD)

Formulation	Minimum Dose	Maximum Dose	Remarks
α-glucosidase inhibitor (AGI)			
Acarbose 50/100 mg	Initial dose 50 mg OD Usual dose 50-100 mg TDS	100 mg TDS	• Should be taken with main meals. • Causes bloating, abdominal discomfort, diarrhoea and flatulence.
Biguanides (Metformin)			
Metformin 500 mg	Initial dose 500 mg OD Usual dose 500 mg TDS	1,000 mg BD	• May cause nausea, anorexia and diarrhoea. • Should **not** be used in patients with impaired renal function (serum creatinine > 150 μmol/l, creatinine clearance < 30ml/min), liver cirrhosis, CCF, recent MI or any conditions that can cause lactic acid accumulation.
Metformin retard 850 mg	Initial dose 850 mg OD Usual dose 850 mg BD	1,700 mg OM / 850 mg ON	
Metformin extended release 500 mg	Initial dose 500 mg OD	2,000 mg OD	
Insulin Secretagogues: Sulphonylureas (SUs)			
Glibenclamide	2.5 mg OM	10 mg BD	• Major adverse side effect is hypoglycaemia. Higher risk in renal impairment, liver cirrhosis and the elderly. • Combining 2 different SUs / insulin secretagogues is **not** recommended.
Glibenclamide and metformin fixed-dose combination	Initial dose one 1.25 mg / 250 mg OD or BD	Two 5 mg / 500 mg tablets BD	
Gliclazide	40 mg OM	160 mg BD	
Gliclazide MR	30 mg OM	120 mg OM	
Glipizide	2.5 mg OM	10 mg BD	
Insulin Secretagogues: Non-SUs or Meglitinides			
Repaglinide	0.5 mg	4 mg (not exceeding 16 mg OD)	• Take with main meals. • Higher risk of prolonged hypoglycaemia when repaglinide is combined with gemfibrozil. This combination is **contraindicated.**
Nateglinide	60 mg	120 mg (not exceeding 360 mg OD)	
Thiazolidinediones (TZDs)			
Rosiglitazone	4 mg OD	4 mg BD	• Side effects include weight gain, fluid retention, and haemodilution. • **Contraindicated** in patients with CCF and liver failure. • Use with insulin is **not** recommended.
Rosiglitazone and Metformin fixed dose combination	2 mg / 500 mg BD	4 mg / 500 mg BD	
Pioglitazone	15 mg OD	45 mg OD	
DPP-4 Inhibitor			
Sitagliptin 100 / 50 / 25 mg	100 mg OD	100 mg OD	• Minimal risk of hypoglycaemia and weight neutral. • Excreted unchanged by the kidneys and a reduction of dose is recommended with renal impairment (25 to 50 mg).
Sitagliptin and metformin fixed dose combination 50 mg / 500 mg 50 mg / 850 mg 50 mg / 1000mg	50 mg / 500 mg BD	50 mg / 1,000 mg BD	

GUIDELINES FOR INSULIN USE

- Insulin can be used if combination therapy of oral agents has not achieved target
- Types of insulin regimes:
  - OAD agents + pre-bed basal insulin or pre-dinner premixed insulin
  - Metformin + premixed insulin more than once a day
  - Metformin + basal insulin + prandial insulin
- Patient should be educated on:
  - injection technique
  - symptoms, treatment and prevention of hypoglycaemia
  - simple guidelines to self-adjust the insulin dose
  - self-monitoring of blood glucose

MANAGEMENT OF CONCOMITANT CO-MORBIDITIES&COMPLICATIONS

HYPERTENSION

1. ACE-Is are the agents of choice for patients with diabetes without microalbuminuria or proteinuria.
2. ARBs or ACE-Is are the agents of choice for patients with diabetes and microalbuminuria or proteinuria.

DYSLIPIDAEMIA

1. All patients without overt CVD but over the age of 40 years should be treated with a statin regardless of baseline LDL cholesterol levels.
2. All patients with overt CVD should be treated with a statin.

CORONARY HEART DISEASE (CHD)

1. Normal resting ECG does not exclude CHD.
2. The risk stratification tools and ECG are part of risk assessment.
3. Primary prevention of CVD with low dose aspirin (75-100 mg) is **NOT** recommended in people with diabetes unless they are at high risk based on Framingham Risk Assessment Score.

NEPHROPATHY

1. Referral to nephrologist should be made if the serum creatinine exceeds 200 umol/L.
2. Target BP in diabetics should be less than 125/75 in patients with proteinuria > 1 g/day.
3. ACE-Is or ARBs should be initiated in patients with microalbuminuria or proteinuria.

RETINOPATHY

1. Refer to ophthalmologist if sudden worsening of vision, unexplained poor vision or diabetic retinopathy greater than occasional microaneurysms occurs.

NEUROPATHY

1. The sensory symptoms of painful diabetic peripheral neuropathy may be treated with anticonvulsants (e.g. gabapentin, lamotrigine, carbamazepine) or TCA (e.g. amitriptyline).

DIABETIC FOOT

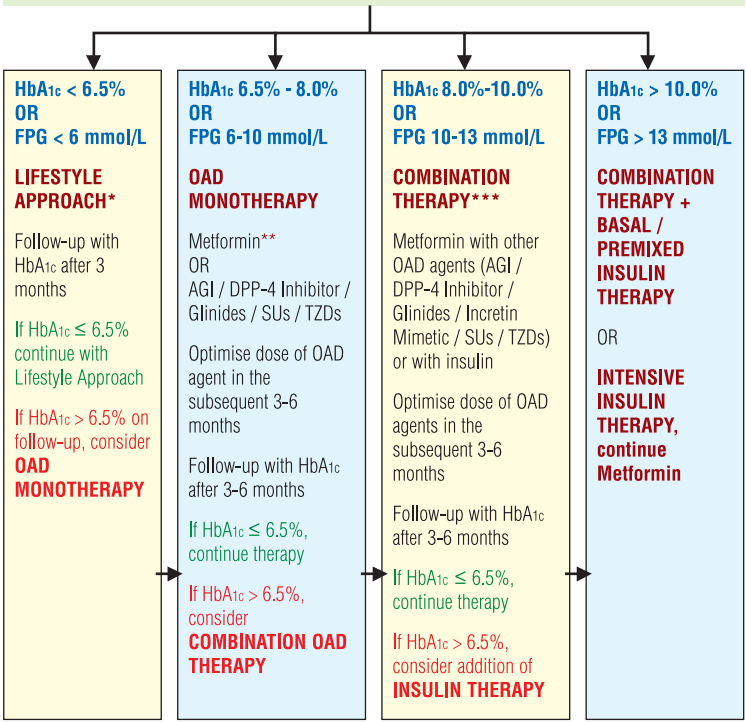
1. Patients with high risk of diabetic foot require extensive education on self care to avoid ulcers and amputations
2. To detect clinically relevant neuropathy, use at least a 10G monofilament.

ERECTILE DYSFUNCTION

1. All adult males with diabetes over the age of 40 should be asked about ED.
2. PDE-5 inhibitor should be offered as first-line therapy if there is no contraindication.
3. Referral to a specialist in ED should be considered for men who do not respond to PDE-5 inhibitors or for whom the use of PDE-5 inhibitors is contraindicated.

TREATMENT ALGORITHM FOR T2DM

MANAGEMENT OF T2DM
Lifestyle modification, pharmacotherapy, FPG and HbA_{1c} at Diagnosis and Follow Up



Footnote:

If symptomatic (weight loss, polyuria, etc.) at any HbA_{1c} and FPG level, consider insulin therapy. Try to achieve as near normal glycaemia without causing hypoglycaemia.

* *Consider metformin/AGI/other insulin sensitiser in appropriate patients.*

** *Metformin is preferred 1st line agent, and SUs should preferably not be used as 1st line.*

*** *Although 3 oral agents can be used, initiation and intensification of insulin therapy is preferred based on effectiveness and expense.*

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