



# A Summary of the Malaysian Clinical Practice Guidelines: Management of Type 2 Diabetes Mellitus (4<sup>th</sup> Edition) 2009

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#### Introduction

There were three previous Clinical Practice Guidelines (CPG) on the Management of Type 2 Diabetes Mellitus, the 1<sup>st</sup> edition published in 1992, followed by the 2<sup>nd</sup> edition (1996) and the 3<sup>rd</sup> edition (2004). This 4<sup>th</sup> edition was deemed necessary due to the tremendous body of new evidence that has become available in the last 4 to 5 years that has major impact on the management of Type 2 Diabetes, including new targets for control, new classes of pharmacological agents targeting novel pathways, as well as major outcome studies.

The main objective of this guideline is to provide evidence-based recommendations to assist health care providers in the identification, diagnosis and management of people with type 2 diabetes mellitus (T2DM). It seeks to answer four main clinical questions i.e., (i) How can diabetes be prevented? (ii) How to screen for glucose intolerance? (iii) How is diabetes diagnosed? and (iv) How can people with diabetes be managed?

This guideline is divided into six main sections as follows: Section 1 - Diabetes: The Disease; Section 2 - Screening and Diagnosis; Section 3 - Management of Type 2 Diabetes Mellitus; Section 4 - Metabolic Syndrome; Section 5 - Management of Chronic Complications; and lastly, Section 6 - Prevention of Type 2 Diabetes Mellitus. In addition, the appendices contain the following information (i) carbohydrate content of common Malaysian foods; (ii) glycaemic index of foods; (iii) examples of physical activity; (iv) food exchange list; (v) the 5-item version of the International Index of Erectile Function; (vi) dosage of anti-diabetic agents in renal failure; and lastly (vii) clinical monitoring protocol.

# **Guideline Development**

In Malaysia, the development of clinical practice guidelines is coordinated by the CPG Secretariat, Health

Technology Assessment Section, Medical Development Division, Ministry of Health (MOH). Malaysia already has in place standard operating procedures (SOPs) for the development of new CPGs or the revision of existing CPGs. For this guideline, the Guideline Development Task Force was formed in 2008, consisting of endocrinologists, a nephrologist, an ophthalmologist, two family medicine specialists, a general physician, a neurologist, a paediatric endocrinologist, two public health specialists, a dietician and a diabetic nurse educator.

The clinical questions were divided into major subgroups and members of the CPG Task Force were assigned individual topics within these subgroups. Literature search was carried out on PUBMED, Medline, Cochrane Databases of Systemic Reviews, and via the OVID search engine. References were also made on existing guidelines on the management of Type 2 diabetes, including American Diabetes Association (ADA) Position Statement on Standards of Medical Care in Diabetes 2008; American Association of Clinical Endocrinologists (AACE) Medical Guidelines for Clinical Practice for the Management of Diabetes Mellitus 2007; International Diabetes Federation (IDF) Global Guideline for Type 2 Diabetes 2005; American Diabetes Association (ADA) and European Association for the Study of Diabetes (EASD) Management of Hyperglycaemia in Type 2 Diabetes: A Consensus Algorithm for the Initiation and Adjustment of Therapy 2006; Malaysian CPG on Management of Obesity 2004; Canadian Clinical Practice Guidelines 2003; and Medical Nutrition Therapy Guidelines for Type 2 Diabetes, Malaysian Dietitian Association 2005.

All literature retrieved were critically appraised, presented and discussed during group meetings. The articles were graded using the criteria used by the United States/Canadian Preventive Services Task Force, while the grading of recommendation in this guideline was modified from the Scottish Intercollegiate Guidelines

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Corresponding author: Feisul Idzwan Mustapha, MD Disease Control Division (NCD Section), Ministry of Health, Malaysia, Level 6, Block E10, Parcel E, 62590 Putrajaya, Malaysia Email: dr.feisul@moh.gov.my Network (SIGN). All statements and recommendations formulated were agreed by the CPG Task Force members. Where the evidence was insufficient, the recommendations were derived by group consensus.

The draft guideline was submitted to external reviewers consisting of senior consultants of various relevant specialties. In addition, the draft guideline was also posted on the MOH website for comments and feedback. Finally in May 2009, the final guideline received the approval of the Health Technology Assessment and Clinical Practice Guidelines Council, MOH. It was officially launched by the Director General of Health Malaysia in Putrajaya, Malaysia in August 2009.

# **Screening and Diagnosis**

The guideline recommendations on screening are divided into four main categories: (i) for symptomatic individuals; (ii) asymptomatic adults; (iii) pregnant women; and (iv) children and adolescents. The indications for screening are consistent with current international guidelines and were mostly adapted from ADA recommendations. One major exception is the age cut-off point of 30 years for screening in the general population. The decision was based on the results of the Third National Health and Morbidity Survey (NMHS III) 2006, which showed a sharp increase in age-specific prevalence after the age of 30 years. (Figure 1)

The screening algorithm for symptomatic individuals is shown in Figure 2, while for asymptomatic individuals in Figure 3. Screening for diabetes using fasting plasma glucose (FPG) should be performed annually in those with risk factors and those ≥30 years. For children and adolescents at risk of developing diabetes, screening every 2 years should be initiated at 10 years old or at onset of puberty if puberty occurs at a younger age. In addition, more frequent or earlier testing with either a FPG or 2-hour plasma glucose in a 75g oral glucose tolerance test (OGTT) should be considered in people with additional risk factors for diabetes. For diagnosis using OGTT, Malaysia used 6.1 mmol/L as the cut-off point at 0-hour, instead of ADA's 5.6 mmol/L (Table 1), consistent with IDF recommendations.<sup>3</sup>

# Management of Type 2 Diabetes Mellitus

The CPG Task Force has created a unique treatment algorithm for Malaysia for the management of T2DM in relation to diagnosis and glycaemic targets. (Figure 4) The initial treatment regime is determined by the HbA1c level at diagnosis. However, taking into account that the coverage of HbA1c testing in Malaysia is not universal, particularly within the public health sector where over 70% of diabetes patients are on active follow-up, the CPG Task Force also included the corresponding fasting plasma glucose levels as well. The treatment targets are modified from the IDF Western Pacific Region (IDF-WPR) Type 2 Diabetes Practical Targets and Treatment as shown in Table 2.3 In particular, the CPG Task Force has adopted HbA<sub>1c</sub> of <6.5% as optimum glycaemic control. Targets for control are applicable for all age groups. However, in patients with co-morbidities or elderly patients, targets should be individualised.

<b>Table 1.</b> Values for (OGTT)	Oral G	lucose	Tolerance	Test			
OGTT Plasma Glucose Values (mmol/L)							
Category	0-hour		2-hour				
Normal	< 6.1*		< 7.8				
Impaired Fasting Glucose 6.1* – 6.9		)	-				
Impaire Glucose Tolerance	-		7.8 - 11.0				
Diabetes Mellitus	≥ 7.0		≥ 11.1				
* ADA uses 5.6 mmol/L							

Glycaemic Control* Fasting Non-fasting	4.4 – 6.1 mmol/L			
Non-fasting				
6				
	4.4 – 8.0 mmol/L			
HbA₁c	<6.5 %			
Lipids				
Triglycerides	≤1.7 mmol/L			
HDL cholesterol	≥1.1 mmol/L			
LDL cholesterol	≤2.6 mmol/L <sup>#</sup>			
Exercise	150 mins/week			
Blood Pressure				
Normal Renal Function	≤130/80 mmHg <sup>§</sup>			
Renal Impairment/Gross Proteinuria	≤125/75 mmHg			
* Glycaemic target should be individualised to minimize risk of				

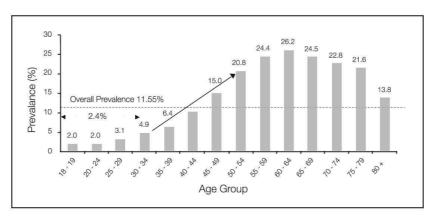


Figure 1. Prevalence of diabetes in Malaysia by age group, 2006

All T2DM patients are started on pharmacological treatment. As first-line therapy, metformin is the preferred choice; however other oral anti-diabetic (OAD) agents are acceptable alternatives. The algorithm also specifically states that sulphonylureas should preferably not be used as first-line. Second-line therapy after metformin is open to all classes of drugs. The CPG included references to five classes of OAD which are (i)  $\alpha$ -glucosidase inhibitors; (ii) biguanides; (iii) dipeptidyl peptidase-4 inhibitors; (iv) insulin secretagogues; and (v) thiazolidinediones. When indicated, start with a minimal dose of OAD agent, while re-emphasising diet and physical activity. An appropriate duration of time (2 to 16 weeks, depending on the OAD agent used) between increments are given to allow achievement of steady state blood glucose control.

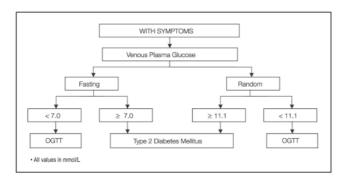


Figure 2. Screening algorithm for symptomatic individuals

Insulin may be used as initial therapy in T2DM particularly in marked hyperglycaemia or if targets have not been reached despite optimal OAD therapy. The CPG recommends starting with either pre-bed intermediate-acting, or pre-bed long-acting insulin or pre-dinner premixed insulin. The 'fix the fasting first' principle is applied in optimising the insulin dose. In children and adolescents, long-acting or intermediate-acting insulin may be added at a dose of 0.5u/kg at bed-time. In addition, short-term insulin therapy should be considered in (i) acute illness, surgery, stress and emergencies; (ii)

pregnancy; (iii) breast-feeding; and (iv) severe metabolic decompensation. Upon diagnosis, all patients are advised on lifestyle modification, medication and patient education to encourage self-care. It is recommended that all individuals with diabetes receive diet counseling by a dietitian. Diet counseling should be individualised according to nutrient needs, severity of disease, cultural preferences and willingness to change. The primary strategy recommended is monitoring of carbohydrate intake by carbohydrate exchanges. Total carbohydrate intake should be consistent and evenly distributed throughout the day with regular meal timings and synchronised with medication time actions. Glycemic index (GI) may be used to guide food choices while keeping to calories and carbohydrate prescription. Excessive intake of sucrose is discouraged as it may lead to weight gain and sucrose intake must be counted as part of the total carbohydrate allowance for the day. Artificial sweeteners such as aspartame are allowed. Other dietary recommendations include reducing saturated fat and cholesterol intake and limiting sodium intake.4

For physical activity, it is recommended that individuals should exercise 5 days a week and brisk walking is recommended for all. The duration of exercise should be at least 150 mins/week of moderate intensity activities. For overweight and obese individuals, physical activity should gradually be increased to 60 to 90 minutes per day for long term weight loss. Any increase in daily energy expenditure such as gardening, walking up stairs, or washing the car is beneficial.

# Management of T2DM in Pregnancy

The recommendations for this section are mostly adapted from the National Institute for Health and Clinical Excellence (NICE), Diabetes in Pregnancy.<sup>5</sup> The CPG emphasises on pre-pregnancy euglycaemia with early referral to physician or endocrinologist, counselling and target HbA<sub>1c</sub><6.5% with insulin therapy if necessary. The

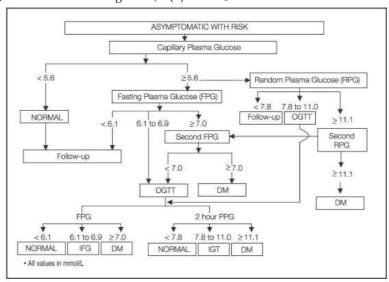


Figure 3. Screening algorithm for asymptomatic individuals

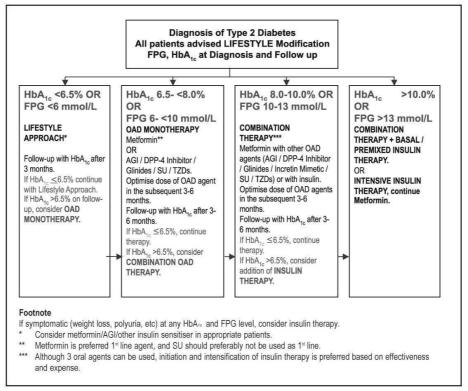


Figure 4. Treatment algorithm

glycaemic targets during pregnancy are shown in Table 3, with individualised monitoring recommended as follows:

- Diet therapy: pre-breakfast,1 hour post prandial glucose (PPG) levels (weekly to fortnightly);
- Insulin therapy: pre-meals and pre-bed glucose levels (weekly to fortnightly). Test PPG after pre-meal targets are achieved.
- HbA<sub>1c</sub> (4 to 6 weekly)

Table 3. Glycaemic Targets During Pregnancy				
Timing Glucose Level (mmol/L)				
Pre-breakfast	3.5 – 5.9			
Pre-prandial	3.5 - 5.9			
1-hour post prandial	< 7.8			
2-hour post prandial	4.4 - 6.7			
0200 – 0400 hours	> 3.9			

All insulin including rapid acting insulin is safe. Metformin and glibenclamide are not recommended during pregnancy. In addition, Glucose-Insulin-Potassium (GIK) regimen can be used during delivery or caesarean section. During post-partum period, insulin dosage must be reduced as insulin requirement drops immediately after delivery by 60-75%. For breast-feeding patients insulin therapy should be continued at a lower dose if necessary. In non-breast-feeding patients, OAD agents can be continued.

# Hypertension and T2DM

The CPG recommends initiation of treatment in diabetics with blood pressure (BP) >130/80 mmHg and they should

be screened for proteinuria or microalbuminuria.<sup>6</sup> Tight BP control (<130/80 mmHg) should take precedence over the class of anti-hypertensive drug used. In the presence of proteinuria of >1g/24 hours, the target BP is ≤125/75 mmHg. The treatment of hypertension in diabetes is recommended based on the Malaysian Clinical Practice Guidelines for the Management of Hypertension 2008.<sup>7</sup> This includes dietary counselling targeting optimal body weight and dietary sodium restriction.

Angiotensin converting enzyme inhibitors (ACEI) are the drug of choice for patients with diabetes, both with and without microalbuminuria or proteinuria, with angiotensin receptor blocker (ARBs) recommended for ACEI intolerant patients. Diuretics, calcium channel blockers (CCBs), beta-blockers and peripheral alpha blockers may be used as add-on therapy. A table which illustrates the choice of anti-hypertensive drugs in diabetes patients with concomitant conditions, adapted from the Malaysian Hypertension CPG is also included in the guideline.<sup>7</sup>

#### Dyslipidaemia and T2DM

The guideline emphasises LDL-C as the primary target. Without overt CVD patients >40 years old should be treated with a statin regardless of baseline LDL cholesterol levels. With overt CVD, all patients should be treated with a statin to a target LDL-C of 1.8mmol/L. The secondary targets are non-HDL-C, HDL-C and TG. The recommended medications are as follows:

- Lower LDL-C: Statin
- Increase HDL-C: Fibrate +/- Nicotinic Acid
- Lower TG: Fibrate +/- Statin

 Combined Hyperlipidaemia: Statins +/-Fibrate or Resin +Fibrate or Nicotinic Acid

Statin therapy is contraindicated in pregnancy. In children and adolescents lipid lowering medications should only be initiated in those >10 years old.

#### **Metabolic Syndrome**

The CPG recognises the metabolic syndrome based on the IDF definition, which includes central obesity (waist circumference of 90 cm for men and 80 cm for women) plus any two of the following: (i) raised TG level >1.7 mmol/L; (ii) low HDL-C (<1.0 mmol/L in men and <1.3 mmol/L in women); (iii) high BP  $\geq$ 130/85 mm Hg; (iv) raised FPG  $\geq$ 5.6 mmol/L or previously diagnosed T2DM.

The main aim of therapy is to reduce the risk of cardiovascular disease and the development of T2DM. Management includes lifestyle modification with pharmacological treatment of the individual components of the syndrome to target values as shown in Table 2. The recommended optimal weight loss is 1 to 2 kg/month in adults. The recommended anti-obesity agents in diabetics include orlistat and sibutramine. Bariatric surgery may be an option in patients with BMI >35 kg/m². Anti-obesity agents and bariatric surgery are not recommended in children.

# **Management of Chronic Complications**

People with T2DM should be screened for complications at diagnosis and thereafter at yearly intervals. The screening schedule is shown in Table 4. Achieving as well as maintaining tight glycaemic and blood pressure control is reiterated repeatedly for prevention of complications.

For retinopathy, health care professionals should refer patients to an ophthalmologist for (i) unexplained poor vision; (ii) diabetic retinopathy greater than occasional microaneurysms; and (iii) macular oedema or hard exudates within the macula. Urgent referral is required if there is (i) sudden visual deterioration; (ii) new vessels on fundoscopy; (iii) rubeosisiridis; (iv) vitreous haemorrhage; and (v) retinal detachment.

Annual screening for microalbuminuria is advocated as essential. Microalbuminuria is defined as a urinary albumin:creatinine ratio (ACR) >2.5 mg/mmol in men and >3.5 mg/mmol in women, or a urinary albumin concentration >20mg/l. Screening can be done initially with conventional dipstick on an early morning urine specimen if urine dipstick for proteinuria is negative. Two further tests within 3 to 6 months is required to confirm a positive microalbuminuria. In patients with proteinuria of >1 gram a day, the target BP is ≤125/75 mmHg. ACEI or ARB should be started unless contraindicated. Referral to a nephrologist should be made if (i) serum creatinine >200 µmol/L; (ii) haematuria; (iii) nephritic syndrome; (iv)

absence of retinopathy (where the diagnosis of diabetic nephropathy may be in doubt); (v) difficult to control blood pressure; and (vi) worsening renal function.

Table 4. Schedule for Screening for Complications						
Test	Initial visit	Follow-up visit	Quarterly visit	Annual visit		
Eye: visual acuity &						
funduscopy	✓			✓		
Feet: pulses &						
neuropathy	✓		✓	✓		
Weight	✓	✓	✓	✓		
ВМІ	✓			✓		
Blood pressure	✓	✓	✓	✓		
Blood glucose	✓	✓	✓	✓		
HbA <sub>1c</sub>	✓		✓	✓		
Cholesterol/HDL						
cholesterol	✓		*	✓		
Triglycerides	✓		*	✓		
Albuminuria*	✓		*	✓		
Creatinine/BUN	✓		*	✓		
ECG	✓			✓		
Urine microscopy	✓			✓		
✓ Conduct test						

- ★ Conduct test if abnormal first visit
- \* Microalbuminuria if resources are available

Diabetic peripheral neuropathy may be diagnosed by 10-g monofilament pressure sensation, 128 Hz tuning fork, ankle jerks (deep tendon reflexes) and pin prick test. Medical treatment for sensory symptoms of painful peripheral neuropathy includes: gabapentin, lamotrigine, carbamazepine or amitriptyline.

To reduce the risk of coronary heart disease (CHD), patients with atypical symptoms or who are asymptomatic should be screened using a resting ECG and by applying an established cardiovascular risk assessment tool such as Framingham Risk Score or UKPDS Risk Engine. 8,9 Patients with an abnormal resting ECG or those having high risk should be referred to a cardiologist for further evaluation. Primary prevention with low dose aspirin is not generally recommended unless patients have high risk of developing CHD based on the Framingham Risk Assessment Score (>10% risk over a 10 year period).

All adult male T2DM patients over the age of 40 should be asked about erectile dysfunction (ED) and screened for ED by using the International Index of Erectile Function (IIEF) questionnaire. Medications which cause ED should be avoided if possible. Phosphodiesterase-5 (PDE-5) inhibitors can be used to treat ED in patients without contraindications. Urology referral may be necessary for those not responding; or for those with contraindications to PDE-5 inhibitors.

# **Prevention of Diabetes**

In addition to lifestyle modification to decrease the risk of conversion of IFG or IGT to frank T2DM, metformin should be considered as off-label use for those at very high risk (combined IFG and IGT plus other risk factors) or for those who fail lifestyle therapy after 6 months. The use of other agents like ACEIs, ARBs and statins are not

recommended solely for the purpose of primary prevention.

For prevention of diabetes, weight loss (5-10% of initial body weight), regular physical activity (150 min/week), with dietary strategies including reduced calories and behavior modification are recommended. A high fibre diet (20-30g/day with 5 to 7 servings/day) consisting of vegetables, fruits, legumes and whole grains is encouraged.<sup>4</sup>

#### **Dissemination of Information**

To support the dissemination of the recommendations contained in the CPG, the CPG Task Force also developed and published two supporting documents. The first document is the 'Quick Reference for Health Care Providers,' an 8-page pocket-size booklet which provides key messages and a summary of the main recommendations in the CPG Management of T2DM (4th edition) 2009. The main objective of this booklet is to provide an easy and quick reference for doctors, assistant medical officers and nurses involved in the management of T2DM patients, particularly at the primary care level.

The second document published is the 'Training Module for Health Care Providers.' This is a comprehensive document which also includes a CD containing powerpoint presentations of the various topics contained in the T2DM CPG together with relevant case studies. The main objective of this document is to provide a standardised training package to assist trainers in conducting training to disseminate the recommendations contained in the CPG to all health care providers involved in the management of T2DM particularly at the primary care level.

The CPG Task Force also undertook a series of training-of-trainers (TOT) workshops held in five different regions throughout Malaysia which was held from October 2009 until January 2010. A total 169 family medicine specialists, physicians and medical officers from various MOH health care facilities underwent this 2-full day training, which was conducted mostly by members of the CPG Task Force. The Training Module developed was used as the training material during the TOT and subsequent echo trainings held at the state, district and hospital level throughout 2010.

#### Summary

Publication of the T2DM CPG was only the first step in the process of disseminating the latest recommendations to further improve the quality of care of T2DM patients. It is an important tool, but it will only prove useful if health care providers are aware of its existence, have easy access, ease of retrieving the required information and have the opportunity to undergo training on the practical aspects of implementation. All of the documents mentioned in this

article were printed and distributed throughout Malaysia. They are also downloadable in pdf format from the MOH website, together with the powerpoint slides for the Training Module.

For the public primary health care facilities, Malaysia has in place an audit mechanism called the 'Diabetes Clinical Audit,' together with a National Quality Assurance (QA) Program entitled 'Quality of Diabetes Care at MOH Health Care Facilities: Glycaemic Control' which are implemented in all MOH health clinics throughout Malaysia involved in the management of T2DM patients since 2009. For the QA program, the current set optimum standard is ≥30% of T2DM patients achieving HbA₁c<6.5% for each health clinic. Compliance to the current T2DM CPG forms part of the shortfall in quality (SIQ) investigation within the QA program. Over the coming years, the CPG Task Force hopes to see a positive impact of the implementation of the recommendations contained in the CPG.

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The full document is available at the Malaysia Ministry of Health website at http://www.moh.gov.my/v/ed.

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