



## Complete Summary

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### GUIDELINE TITLE

Diabetes mellitus.

### BIBLIOGRAPHIC SOURCE(S)

Singapore Ministry of Health. Diabetes mellitus. Singapore: Singapore Ministry of Health; 2006 Jun. 161 p. [260 references]

### GUIDELINE STATUS

This is the current release of the guideline.

It updates a previously published version: Singapore Ministry of Health. Diabetes mellitus. Singapore: Singapore Ministry of Health; 1999.

## COMPLETE SUMMARY CONTENT

SCOPE  
METHODOLOGY - including Rating Scheme and Cost Analysis  
RECOMMENDATIONS  
EVIDENCE SUPPORTING THE RECOMMENDATIONS  
BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS  
CONTRAINDICATIONS  
QUALIFYING STATEMENTS  
IMPLEMENTATION OF THE GUIDELINE  
INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT  
CATEGORIES  
IDENTIFYING INFORMATION AND AVAILABILITY  
DISCLAIMER

## SCOPE

### DISEASE/CONDITION(S)

- Diabetes mellitus (type 1, type 2, and gestational)
- Cardiovascular disease in diabetes mellitus (including hypertension, dyslipidaemia)
- Diabetic nephropathy
- Diabetes-related eye complications (including retinopathy, macular oedema)
- Diabetes-related foot complications
- Diabetes-related pregnancy complications

### GUIDELINE CATEGORY

Diagnosis  
Evaluation  
Management  
Prevention  
Risk Assessment  
Screening  
Treatment

#### CLINICAL SPECIALTY

Cardiology  
Endocrinology  
Family Practice  
Internal Medicine  
Nephrology  
Nutrition  
Obstetrics and Gynecology  
Ophthalmology  
Pediatrics  
Preventive Medicine

#### INTENDED USERS

Advanced Practice Nurses  
Allied Health Personnel  
Nurses  
Physician Assistants  
Physicians

#### GUIDELINE OBJECTIVE(S)

To help physicians make sound clinical decisions about diabetes mellitus by presenting up-to-date information about diagnosis, classification, treatment, outcomes, and follow-up

#### TARGET POPULATION

Children, adolescents, and adults in Singapore with diabetes mellitus (DM) or at risk for DM and diabetes-related complications

#### INTERVENTIONS AND PRACTICES CONSIDERED

Diagnosis, Evaluation, and Screening

1. Testing of plasma glucose levels
2. Oral glucose tolerance test
3. Testing for ketones in the urine
4. Testing for plasma levels of glycated haemoglobin (HbA<sub>1c</sub>)
5. Medical history and physical exam to assess risk for cardiovascular disease
6. Blood pressure testing

7. Measurement of fasting serum lipids, including low density lipoprotein, high density lipoprotein, and triglycerides
8. Screening for albuminuria and testing of creatinine and potassium levels to assess for diabetic nephropathy

#### Treatment and Management

1. Lifestyle modifications
  - Implementation of nutrition therapy and tailored exercise program
  - Discouraging patients with diabetes from smoking
  - Discouraging patients with poor glycaemic control or dyslipidaemia from drinking alcohol
2. Patient education
3. Use of oral antihyperglycaemic agents
4. Use of insulin therapy
5. Use of combination therapy of one or more agents (including insulin)
6. Use of self monitoring of blood glucose
7. Use of electrocardiogram
8. Use of antihypertensive agents
9. Use of fibrate therapy and/or statins for dyslipidaemia
10. Use of antiplatelet agents, including aspirin
11. Use of a low protein diet in patients with overt nephropathy
12. Administration of regular visual acuity assessment and eye examinations by trained personnel
13. Use of laser photocoagulation in patients with severe and proliferative diabetic retinopathy
14. Administration of annual foot examination
15. Pre-pregnancy counseling and management of diabetes during and following pregnancy
16. Glucose monitoring of infants of diabetic mothers

#### MAJOR OUTCOMES CONSIDERED

##### Diagnosis and Evaluation

- Accuracy of diagnosis of diabetes mellitus
- Specificity and sensitivity of detection of diabetes-related complications

##### Treatment and Management

- Plasma glucose levels
- Plasma levels of glycated haemoglobin (HbA<sub>1c</sub>)
- Presence of ketones in the urine
- Blood pressure levels
- Serum lipid levels
- Serum creatinine and potassium levels
- Presence of albuminuria
- Incidence and severity of:
  - Cardiovascular disease
  - Stroke
  - Peripheral arterial disease
  - Diabetic nephropathy

- Diabetic retinopathy
- Diabetic foot complications
- Diabetes-related pregnancy complications
- Perinatal morality and morbidity for infants of diabetic mothers
- Mortality from diabetes-related complications

## METHODOLOGY

### METHODS USED TO COLLECT/SELECT EVIDENCE

Searches of Electronic Databases

### DESCRIPTION OF METHODS USED TO COLLECT/SELECT THE EVIDENCE

Not stated

### NUMBER OF SOURCE DOCUMENTS

Not stated

### METHODS USED TO ASSESS THE QUALITY AND STRENGTH OF THE EVIDENCE

Weighting According to a Rating Scheme (Scheme Given)

### RATING SCHEME FOR THE STRENGTH OF THE EVIDENCE

Level I a Evidence obtained from meta-analysis of randomised controlled trials

Level I b Evidence obtained from at least one randomised controlled trial

Level II a Evidence obtained from at least one well-designed controlled study without randomisation

Level II b Evidence obtained from at least one other type of well-designed quasiexperimental study

Level III Evidence obtained from well-designed non-experimental descriptive studies, such as comparative studies, correlation studies and case studies

Level IV Evidence obtained from expert committee reports or opinions and/or clinical experiences of respected authorities

### METHODS USED TO ANALYZE THE EVIDENCE

Systematic Review

### DESCRIPTION OF THE METHODS USED TO ANALYZE THE EVIDENCE

Not stated

## METHODS USED TO FORMULATE THE RECOMMENDATIONS

Expert Consensus

## DESCRIPTION OF METHODS USED TO FORMULATE THE RECOMMENDATIONS

The first edition of the Ministry of Health (MOH) clinical practice guidelines on diabetes mellitus for Singapore was published in 1999. Since that time, more facts about this important condition have emerged, not only with regard to its diagnosis and treatment, but also about whether or not type 2 diabetes may be prevented, and, if so, how this may be achieved.

As diabetes mellitus has great public health significance in developed countries and developing nations alike, managing it properly involves a consideration, not just of clinical issues, but also of health economics. This second edition of the guidelines attempts to address some of these complex issues wherever evidence-based information pertaining to them is available.

The workgroup closely examined the recommendations of the American Diabetes Association (ADA), and the World Health Organization (WHO), the European Diabetes Epidemiology Group and the International Diabetes Federation. In addition, the workgroup took into account data derived from the Singapore population.

## RATING SCHEME FOR THE STRENGTH OF THE RECOMMENDATIONS

Grade A (evidence levels Ia, Ib) Requires at least one randomised controlled trial, as part of the body of literature of overall good quality and consistency, addressing the specific recommendation

Grade B (evidence levels IIa, IIb, III) Requires availability of well conducted clinical studies, but no randomised clinical trials on the topic of recommendation

Grade C (evidence level IV) Requires evidence obtained from expert committee reports or opinions, and/or clinical experiences of respected authorities. Indicates absence of directly applicable clinical studies of good quality

GPP (good practice points) Recommended best practice based on the clinical experience of the guideline development group

## COST ANALYSIS

Diabetes mellitus is a costly condition, not just to the individual who has it, but also to healthcare systems with finite resources. Macrovascular disease is the major component of the costs in type 2 diabetes, and this component is incurred much earlier than those accruing from managing microvascular complications. In the US, 52% of costs incurred may be attributed to the management of macrovascular disease, while nephropathy accounts for 21%, neuropathy 17%,

and retinopathy 10%. Reducing the risks of macrovascular complications should ease the costs of diabetes mellitus. Whether this results in net savings for the individual or the healthcare system concerned would then depend on the cost of the treatment used to achieve the lower risks.

Data concerning the cost and benefit of any treatment may be derived from either empirical studies, or from modelling studies of simulated populations. Modelling uses a set of formulae based on assumptions about the accuracy of screening methods, rates of disease progression to endstage complications or death with and without a particular intervention, and the treatment costs. In chronic diseases like diabetes, empirical studies of interventions, for which outcomes would not be evident for many years, are seldom performed because of high costs and time delays. Much of current information comes from modelling studies which generate results rapidly, but are highly influenced by assumptions, and represent predictions rather than observations.

### Improved Glycaemic Control

#### Type 1 Diabetes

The Diabetes Control and Complications Trial (DCCT) demonstrated that improved glycaemic control intended to achieve near-normoglycaemia, compared with standard treatment in type 1 diabetes, could delay the progression of retinopathy, nephropathy, and neuropathy by about 50%. An economic analysis by the DCCT Research Group concluded that for type 1 diabetes, the cost-effectiveness of improved glycaemic control is within the range considered to represent a good value.

#### Type 2 Diabetes

In a US economic analysis of improved glycaemic control for type 2 diabetes, intended to achieve normoglycaemia by keeping the HbA1c at < 7.2%, it was found that, for type 2 diabetes, the cost-effectiveness of improved glycaemic control is within the range of interventions that is generally considered cost-effective.

#### Other Interventions

Blood pressure control, blood lipid control, smoking cessation and exercise are four widely practised interventions to prevent cardiovascular disease. Economic analyses have shown that, for the general population, such practices are clearly cost-effective. For diabetic patients, however, cost-benefit analyses have not been reported, but it is not unreasonable to expect that these interventions would also be cost-effective.

### METHOD OF GUIDELINE VALIDATION

Not stated

### DESCRIPTION OF METHOD OF GUIDELINE VALIDATION

Not applicable

## RECOMMENDATIONS

### MAJOR RECOMMENDATIONS

The recommendations that follow are those from the guideline's executive summary; detailed recommendations can be found in the original guideline document. Each recommendation is rated based on the level of the evidence and the classes of the recommendation. Definitions of the levels of the evidence (A, B, C, and Good Practice Point [GPP]) and classes of the recommendations (Level I through Level IV) are presented at the end of the "Major Recommendations" field.

Note from the National Guidelines Clearinghouse (NGC): These guidelines were updated by the developer in March 2006. Following are major changes or additions that have been made to the 1999 version of the guidelines, followed by a summary of the guidelines. Please refer to the original guideline document for further details.

The following is a list of the major revisions and additions to the previous guidelines:

- The diagnosis of diabetes mellitus and other categories of glucose tolerance underwent a significant change in 1997/1998. In late 2003, the American Diabetes Association proposed another new modification to the diagnostic criterion for impaired fasting glucose. Chapter 2 addresses this, and presents an update on how clinicians should diagnose and screen for diabetes and glucose intolerance.
- Chapter 5 on pharmacotherapy in diabetes mellitus has been updated to take into account recent clinical trial evidence of the efficacy of the newer classes of antidiabetes drugs.
- Chapter 7 on prevention of cardiovascular disease in diabetes mellitus has been extensively revised to address clinical targets for blood pressure and lipids. Recommendations on decision-making in the area of therapeutics have also been updated.
- Chapter 8 on prevention and management of diabetic nephropathy has been revised to present recent clinical trial evidence regarding the efficacy of, and indications for, the use of angiotensin converting enzyme inhibitors and angiotensin receptor blockers.
- Chapter 9 on the prevention and management of eye complications has been updated. Additionally, the new guidelines include a set of colour plates of retinal photographs (Annex 1, page 151 of the original guideline document). The authors hope the visual information these plates present would help physicians recognize diabetic retinal disease more readily, and take the appropriate clinical actions.
- Chapter 11 on pregestational and gestational diabetes mellitus has been updated.
- Chapter 12 on childhood and adolescent diabetes mellitus has new data on the appropriate use of biguanides in these patient groups.

- Chapter 13 is a new chapter that addresses prevention of type 2 diabetes mellitus. It reviews important information arising out of recent clinical trials designed to find out if type 2 diabetes mellitus could be prevented.
- Chapter 14 addresses cost-benefit issues in diabetes mellitus.
- Chapter 15 provides an update on clinical quality indicators for diabetes. Patients with diabetes are categorised into 'at risk' and 'high risk' individuals and recommended frequency to measure different quality indicators is specified for each category e.g. glycated haemoglobin (HbA<sub>1c</sub>) should be measured 6 monthly for 'at risk' and 3-4 monthly for 'high risk' diabetes patients.
- A new section on self-assessment containing 10 multiple choice questions has been added.

### Diagnosis and Screening of Diabetes Mellitus in Singapore

B In subjects with unequivocal hyperglycaemia with acute metabolic decompensation diabetes mellitus can be diagnosed without further testing. (Grade B, Level III)

B In patients with typical symptoms, diabetes mellitus can be diagnosed if any one of the following is present:

1. Casual plasma glucose  $\geq 11.1$  mmol/l
2. Fasting plasma glucose  $\geq 7.0$  mmol/l
3. 2-hour post-challenge glucose  $\geq 11.1$  mmol/l

Other individuals should have a repeat test on a subsequent day. (Grade B, Level III)

B Fasting plasma glucose measured in an accredited laboratory is the preferred test for the diagnosis of diabetes mellitus. (Grade B, Level III)

B Intermediate states of glucose metabolism termed impaired fasting glycaemia and impaired glucose tolerance should be recognized in accordance with the report of the World Health Organization consultation. (Grade B, Level III)

B All subjects with fasting plasma glucose from 6.1 to 6.9 mmol/l should undergo a 75 g oral glucose tolerance test to determine if they have impaired glucose tolerance or diabetes mellitus. (Grade B, Level III)

C Screening of asymptomatic individuals for diabetes mellitus should be carried out in accordance with the Ministry of Health Clinical Practice Guidelines for Health Screening (6/2003). (Grade C, Level IV)

N.B. The workgroup recommends lowering the cut-off value of triglycerides at which the individual is considered at increased risk of diabetes from 2.82 in Ministry of Health Clinical Practice Guidelines on Health Screening to 2.30 mmol/l.

### Lifestyle Modification

B Lifestyle modification is a cornerstone of diabetes management. Medical nutrition therapy and exercise prescription should be the initial therapy in obese (body mass index [BMI]  $\geq 30$ ) and overweight (BMI  $\geq 25$ ) type 2 diabetic patients unless they are symptomatic or severely hyperglycaemic. (Grade B, Level II a)

C Medical nutrition therapy should be individualized. Saturated fat intake should not exceed 10%, with carbohydrates making up 50 to 60% and proteins 15 to 20% of total calorie intake. Diet should include foods from each of the basic food groups. (Grade C, Level IV)

C An exercise programme tailored to suit the individual's age, fitness, aptitude and interest should be prescribed. (Grade C, Level IV)

C A pre-exercise evaluation to identify macrovascular, microvascular and neurological complications is recommended. (Grade C, Level IV)

C Individuals with diabetes, especially those on insulin treatment, should receive specific education on the prevention of exercise-induced hypoglycaemia. (Grade C, Level IV)

C Individuals with diabetic neuropathy should avoid exercises associated with repetitive foot trauma. (Grade C, Level IV)

C Individuals with severe diabetic proliferative retinopathy should avoid activities that dramatically elevate blood pressure. (Grade C, Level IV)

B Individuals with diabetes should be discouraged from smoking. (Grade B, Level III)

B Diabetic patients with poor glycaemic control or dyslipidaemia should be discouraged from consuming alcohol. (Grade B, Level II b)

### Pharmacotherapy in Diabetes Mellitus

A Type 2 diabetic patients may initially be treated with lifestyle modification (diet and exercise) for 2 to 4 months unless they are symptomatic or severely hyperglycaemic (i.e. random blood glucose  $> 15$  mmol/l or fasting blood glucose  $> 10$  mmol/l). Oral antihyperglycaemic agents should be started if glycaemic targets are not achieved. Insulin therapy should be started, if optimal combination therapy fails to attain target control (i.e. 2 consecutive HbA<sub>1c</sub> values failed to reach  $\leq 8\%$  over 3 to 6 months interval). (Grade A, Level I a)

A Type 2 diabetes is a progressive condition in which beta-cell function deteriorates with increasing duration of diabetes. Stepwise therapy with multiple pharmacological therapies is often needed over time to maintain target glucose control. Two or more oral agents, or insulin therapy either alone or in combination with oral agents, may be required. (Grade A, Level I a)

A All type 1 diabetic patients must receive insulin. Multiple daily injections (3 or more) or the use of continuous subcutaneous insulin infusion (CSII or insulin

pump therapy) may be required to achieve target glucose levels. (Grade A, Level I b)

### Glycaemic Control: Assessment and Targets

GPP Health care professionals should be familiar with the practical use of glucometers. (GPP)

B Self-monitoring of blood glucose (SMBG) should be initiated in most patients with diabetes, especially in insulin-treated subjects, in pregnant women with preexisting diabetes or gestational diabetes, and in patients who are at increased risk of developing hypoglycaemia. (Grade B, Level II a)

GPP The visual method of self-monitoring of blood glucose is not recommended. (GPP)

A Besides receiving proper training in the use of blood glucometers, patients must be educated on the interpretation of the results and, where possible, taught to modify treatment according to blood glucose levels. (Grade A, Level I b)

C Testing for glucose in urine is not recommended for monitoring of glycaemic status. (Grade C, Level IV)

C Testing for ketones in the urine is recommended in patients with type 1 diabetes, pregnant women with pre-existing and gestational diabetes, if there is (American Diabetes Association, 2004):

- Acute illness or stress
- Persistent elevation of blood glucose (>16.7 mmol/l)
- Any symptom suggestive of ketoacidosis (nausea, vomiting, abdominal pain or acetone breath). (Grade C, Level IV)

GPP Routine monitoring of blood ketones is not recommended for type 1 or type 2 diabetic patients. (GPP)

C HbA<sub>1c</sub> testing should be performed routinely in all patients with diabetes. The frequency of testing for any individual patient may vary according to the treatment regimen used and the status of glycaemic control. (Grade C, Level IV)

C The following schedule is recommended for glycated haemoglobin testing (Goldstein et al., 1995):

- 3- to 4-monthly in patients with unstable glycaemic control, failure to meet treatment goals, recent adjustment in therapy, or intensive insulin therapy.
- 6-monthly in patients who have stable glycaemic control and who are meeting treatment goals. (Grade C, Level IV)

C The targets of glycaemic control should be defined for each patient, with patient participation in the process. (Grade C, Level IV)

A "Optimal" glucose control should be the target for the majority of patients with diabetes. This refers to glucose levels that approach the normal range (HbA<sub>1c</sub> 6.5 to 7.0%; preprandial glucose 6.1 to 8.0 mmol/l) and is associated with a low risk of developing microvascular complications. (Grade A, Level I b)

A "Suboptimal" glucose control (HbA<sub>1c</sub> 7.1 to 8.0%; preprandial glucose 8.1 to 10.0 mmol/l) may be the target in special subsets of patients who are vulnerable to injury from the increased risk of severe hypoglycaemia associated with "optimal" glucose control. (Grade A, Level I b)

### Prevention of Cardiovascular Disease in Diabetes Mellitus

GPP The assessment of cardiovascular risk in persons with type 2 diabetes mellitus should include:

1. Medical history, which should include:
  - a. A smoking history
  - b. A history of hypertension and/or medication taken for the treatment of hypertension
  - c. A history of pre-existing cardiovascular disease (CVD) to include angina pectoris, myocardial infarction, stroke, or peripheral vascular disease
2. A physical examination which should include an assessment of peripheral pulses.
3. Blood pressure should be measured each time a patient with type 2 diabetes mellitus is seen in the clinic.
4. Fasting serum lipids should be measured at the time of diagnosis and at least once a year if they are in the optimal range.
5. Assessment of urine for microalbuminuria or proteinuria should be carried out at the time of diagnosis and at least once a year in all patients.
6. In view of the fact that persons with type 2 diabetes mellitus are more likely to experience atypical symptoms of coronary heart disease (CHD), a routine resting electrocardiogram (ECG) is recommended at baseline. Subsequent ECG may be performed when clinically indicated. Specific abnormalities which may suggest CHD should be assessed by a cardiologist for appropriate risk stratification. (GPP)

B The primary prevention of CVD should form one of the major goals of therapy in the management of type 2 diabetes mellitus. (Grade B, Level III)

B Type 2 diabetes mellitus should be considered a coronary CHD risk equivalent. (Grade B, Level III)

C An assessment of the CVD risk factors present is recommended for all persons with type 2 diabetes mellitus in order that appropriate therapy be instituted. (Grade C, Level IV)

A The prevention of CVD in persons with type 2 diabetes mellitus must take a global approach with intervention targeting all aspects of the disease. (Grade A, Level I b)

C Therapeutic lifestyle modification (through modulation of diet and physical activity) should form the mainstay of strategies to reduce cardiovascular risk associated with type 2 diabetes mellitus. (Grade C, Level IV)

B All possible efforts should be taken to encourage persons with type 2 diabetes mellitus to stop smoking. (Grade B, Level III)

### Hypertension in Patients with Diabetes Mellitus

A The target of hypertension treatment in type 2 diabetes mellitus should be <130/80 mmHg. (Grade A, Level I b)

A Lifestyle modification and drug therapy should be instituted for all subjects with blood pressure >130/80 mmHg. (Grade A, Level I b)

A The choice of first line therapy can include (a) diuretics (b) beta-blockers (c) angiotensin converting enzyme (ACE) inhibitors (ACEI) (d) calcium channel blockers (CCB) (e) angiotensin II receptor blockers (ARB) and should be based on the cost of the drug and any compelling indications and contraindications for its use. (Grade A, Level I b)

### Dyslipidaemia in Patients with Diabetes Mellitus

A For the prevention of CVD, the first priority is optimization of the low density lipoprotein (LDL) cholesterol. This is followed by high density lipoprotein (HDL)-cholesterol and then triglyceride (TG). (Grade A, Level I a)

C The exception is in individuals with levels of TG >4.5 mmol/l (400 mg/dl) who have an increased risk of acute pancreatitis. In these patients, the first priority is to reduce the TG level to prevent acute pancreatitis. (Grade C, Level IV)

C Fibrate therapy should be considered as first line therapy in those with TG >4.5 mmol/l (400 mg/dl) to prevent acute pancreatitis. (Grade C, Level IV)

A For all other patients with type 2 diabetes mellitus and LDL cholesterol >2.6 mmol/l (100 mg/dl), the treatment of choice is an 3-hydroxy-3-methylglutaryl coenzyme A (HMG CoA) reductase inhibitor (statin). (Grade A, Level I a)

A For patients with LDL cholesterol <2.6 mmol/l (100 mg/dl) and low HDL cholesterol (<40 mg/dl), a fibrate can be started as the initial lipid lowering therapy. (Grade A, Level I b)

C If HDL cholesterol remains low (<1 mmol/l or 40 mg/dl) after achieving the LDL goal with a statin, combination therapy can be considered in selected high risk patients, such as those with type 2 diabetes mellitus and existing CHD). (Grade C, Level IV)

B When combining a statin with a fibrate, gemfibrozil should not be used. (Grade B, Level III)

### Anti-Thrombotic Agents in Patients with Diabetes Mellitus

A All patients with type 2 diabetes mellitus over the age of 45 years or who have concomitant hypertension, dyslipidaemia or pre-existing cardiovascular disease (CHD, stroke or peripheral arterial disease) should be treated with aspirin 75 to 100 mg per day. In the presence of contraindications for aspirin therapy, other antiplatelet agents such as clopidogrel may be a reasonable alternative for patients with high risk. (Grade A, Level I a)

### Prevention and Treatment of Diabetic Nephropathy

C Screening for albuminuria should begin at 5 years after the diagnosis of type 1 diabetes; it should, however, begin immediately with the diagnosis of type 2 diabetes. Thereafter, screening for albuminuria should be done annually (Molitch et al., 2004; American Diabetes Association, 2002). (Grade C, Level IV)

GPP Serum creatinine should be measured at least annually. (GPP)

C The blood pressure target in all diabetic persons should be less than 130/80 mmHg. Diabetic patients with proteinuria levels exceeding 1 gram should try to have their blood pressure (BP) lowered to less than 125/75 mmHg ("The sixth report of the Joint National Committee," 1997). (Grade C, Level IV)

A In the absence of microalbuminuria or overt nephropathy, the principal intent is that of reducing the risk of a cardiovascular event. There is evidence for the initial antihypertensive agent to be from one of these classes: ACE inhibitors, ARBs, beta-blockers, diuretics, calcium channel blockers. (Grade A, Level I b)

A In the presence of microalbuminuria, both ACE inhibitors and ARBs can be used. (Grade A, Level I b)

A In the presence of overt nephropathy in type 1 diabetes, there is evidence that an ACE inhibitor can retard the progression of otherwise progressive renal disease (Lewis et al., 1993). (Grade A, Level I b)

A In type 2 diabetes with overt nephropathy, either an ACE inhibitor or an ARB may be used to retard the progression of renal disease (Brenner et al., 2001; Lewis et al., 2001; Barnett et al., 2004). (Grade A, Level I b)

GPP The serum creatinine and potassium should be checked within 4 weeks of initiation of treatment to detect any rise in the serum creatinine or hyperkalaemia. (GPP)

GPP Progressive but non-continuous rise in the serum creatinine may be seen over 2 to 3 months after starting on ACE inhibitor or ARB. A short-term rise of less than 30% in the serum creatinine should not necessitate withdrawing the ACE inhibitor or ARB. Nevertheless, the possibility that there may be critical renal artery stenosis should be considered, especially in the presence of a renal artery bruit or refractory hypertension or asymmetric kidney sizes on ultrasound. (GPP)

GPP Therapy should aim to reduce albuminuria as much as possible, and it is reasonable to aim for a proteinuria target of less than 1 g/day or at least 50% of the pre-treatment value. (GPP)

GPP Type 1 diabetic patients with overt nephropathy should be maintained on a low protein diet of 0.8 g/kg/day. (GPP)

GPP A nephrology referral is recommended when there are unexpected or rapid decline in renal function, difficulties with hyperkalaemia, atypical features e.g. haematuria, presence of casts in the urine sediment, presence of a renal bruit, difficult BP control, nephrotic range proteinuria (>3/day), and absence of retinopathy. (GPP)

### Prevention and Management of Eye Complications

#### Screening

C All patients diagnosed with diabetes require regular visual acuity assessment and eye examinations by trained personnel to screen for diabetic retinopathy using a test of adequate sensitivity. (Grade C, Level IV)

C Type 1 diabetic patients should be examined 3 to 5 years after diagnosis of diabetes, and at least once yearly subsequently. Type 2 diabetic patients should have an ocular assessment at the time of diagnosis and at least once yearly subsequently. (Grade C, Level IV)

C Retinal screening preferably using retinal photography, or direct ophthalmoscopy (if retinal photography is not available) through dilated pupils is recommended. (Grade C, Level IV)

#### Management of Systemic Risk Factors

A Good glycaemic control (HbA<sub>1c</sub> preferably 6.5 to 7.5%) should be instituted to reduce the risk of retinopathy. (Grade A, Level I b)

A Good control of blood pressure at or below 130/80 mmHg should be instituted to reduce the progression of diabetic retinopathy. (Grade A, Level I b)

C Significant hyperlipidaemia should be treated to retard diabetic retinopathy. (Grade C, Level IV)

#### Referrals

GPP Diabetic patients found to have diabetic retinopathy by their physicians should be referred for further ophthalmological assessment. (GPP)

A Timely laser therapy should be offered to patients with proliferative diabetic retinopathy and diabetic macular oedema. Panretinal and focal/grid laser treatment results in at least a 50% reduction in the risk of visual loss. (Grade A, Level I b)

#### Treatment

A Laser photocoagulation should be instituted for severe and proliferative retinopathy as it produces a 50% reduction in risk for severe visual loss and need for vitrectomy. (Grade A, Level I b)

### Prevention of Diabetic Foot Complications

B All individuals with diabetes should receive an annual foot examination to identify high-risk foot conditions (Mayfield et al., 2003). (Grade B, Level II b)

B The assessment of the feet involves risk identification, treatment and patient education appropriate to the level of risk (Litzelman et al., 1993; Edmunds, Foster & Watkins, 1998). (Grade B, Level II a)

A All patients, regardless of risk category, should receive ongoing education on foot care and footwear advice (Scottish Intercollegiate Guidelines Network, 1997). (Grade A, Level I b)

B Patients identified with foot-related risk conditions should have access to a specialized foot care team which should include diabetes specialist, podiatrist, physiotherapist trained in diabetes, diabetes nurse educator and vascular and orthopaedic surgeon (Scottish Intercollegiate Guidelines Network, 1997). (Grade B, Level III)

A Urgent referral to a specialized foot care team is needed in the presence of ulcerations, severe foot infection and gangrene (Scottish Intercollegiate Guidelines Network, 1997). (Grade A, Level I b)

### Management of Women with Pregestational and Gestational Diabetes Mellitus

#### Preconception Care

B All diabetic women in the reproductive age group should receive prepregnancy counselling, particularly before starting a family. (Grade B, Level II a)

#### Screening and Diagnosis

B Women at high-risk for gestational diabetes (GDM) should undergo an oral glucose tolerance test (OGTT) as early in pregnancy as feasible. Re-evaluation may be necessary at 28 weeks if glucose intolerance is not present at the early screen. (Grade B, Level II a)

B In all other patients, urine for glucose should be obtained at each antenatal visit and random blood sugar levels ascertained when there is  $\geq 1+$  glycosuria. A diagnostic test is necessary if the random plasma blood glucose  $> 6.6$  mmol/l more than 2 hours after a meal, or  $> 7.0$  mmol/l within 2 hours of a meal. (Grade B, Level III)

#### Antenatal Care

B In GDM, dietary control should be used in the first instance to attain glycaemic goals. If nutritional therapy does not consistently maintain a fasting or pre-meal capillary blood glucose of <5.5 mmol/l and/or a 2-hour postprandial capillary blood glucose of <6.7 mmol/l on two or more occasions within a 1-2 week interval, insulin therapy should be considered. (Grade B, Level IIa)

B In established diabetics (pregestational diabetes), intensive insulin treatment is often necessary to maintain target blood glucose. (Grade B, Level IIb)

B Maintain maternal capillary blood glucose concentrations as near normal as possible at <5.5 mmol/l in the fasting or premeal state, and/or <7.8 mmol/l 1 hour after meals, and/or <6.7 mmol/l 2 hours after meals. (Grade B, Level III)

B All women diagnosed with GDM and pregestational diabetes mellitus (DM) should receive specialized care. (Grade B, Level III)

#### Infants of Diabetic Mothers

B Close monitoring of blood glucose levels is necessary within the first 48 hours of the baby's life. Infants of diabetic mothers should be fed early. (Grade B, Level III)

#### Postnatal Management

B Breastfeeding is not contraindicated in women with diabetes. (Grade B, Level III)

B An OGTT should be performed at least 6 weeks postpartum and the patient reclassified and counselled according to criteria accepted in the non-pregnant state. (Grade B, Level IIb)

#### Contraception

B Low dose oestrogen-progestin oral contraceptives and the intra-uterine contraceptive devices are not contraindicated in women with previous GDM. (Grade B, Level III)

B Oestrogen-progestogen contraceptives should be avoided in women with complications of diabetes and those at risk of vascular disease. (Grade B, Level III)

#### Management of the Child and Adolescent with Diabetes Mellitus

B In childhood type 1 diabetes mellitus, the aims of treatment are:

- a. Normal physical growth and pubertal development.
- b. Normal psychosocial development and full participation in age-appropriate activities.
- c. Good glycaemic control with minimal hypoglycaemia.
- d. Absence of diabetic ketoacidosis.

e. Minimization and early detection and treatment of complications. (Grade B, Level II a)

B The care of diabetes in childhood and adolescence, whether type 1 or type 2, is best accomplished by a multi-disciplinary team in an institutional setting. (Grade B, Level II a)

B Screening for diabetes should be considered for children and adolescents who are overweight, have a strong family history of diabetes and have acanthosis nigricans, hypertension, dyslipidaemia or the polycystic ovarian syndrome. Testing in these individuals should be done at least every 2 years starting from age 10 years or at the onset of puberty, if the latter occurs at a younger age. (Grade B, Level II a)

C Children and adolescents with impaired glucose tolerance and obesity should be managed with diet and exercise. (Grade C, Level IV)

C Children with type 2 diabetes mellitus may initially be treated with lifestyle modifications (diet and exercise), unless they are symptomatic or severely hyperglycaemic. (Grade C, Level IV)

C Oral hypoglycaemic agents may be started in children with type 2 diabetes if glycaemic targets are not achieved. Insulin therapy should be started if oral agents fail to attain target control. (Grade C, Level IV)

#### Prevention of Type 2 Diabetes

A Individuals at high risk for developing diabetes should be made aware of the benefits of even modest weight loss and participating in regular physical activity. (Grade A, Level I b)

B Screening for high risk individuals should be done opportunistically, with either a fasting plasma glucose test, or a 2-hour OGTT. (Grade B, Level II b)

A Persons with impaired glucose tolerance or impaired fasting glucose should be given counselling about weight loss as well as instructions on how to increase physical activity. (Grade A, Level I b)

C Drug therapy should not be routinely used to prevent diabetes until more information, particularly in regard to cost-effectiveness, is available. (Grade C, Level IV)

#### Clinical Quality Indicators for Diabetes Mellitus

A Measures of process of diabetes care should include the initial and ongoing performance of medical indicators which have been proven to influence long term outcome. (Grade A, Level I b)

GPP Data to measure the outcomes of diabetes management should be obtained from the individual with diabetes. (GPP)

## Definitions:

### Levels of Evidence

Level I a Evidence obtained from meta-analysis of randomised controlled trials

Level I b Evidence obtained from at least one randomised controlled trial

Level II a Evidence obtained from at least one well-designed controlled study without randomisation

Level II b Evidence obtained from at least one other type of well-designed quasi-experimental study

Level III Evidence obtained from well-designed non-experimental descriptive studies, such as comparative studies, correlation studies and case studies

Level IV Evidence obtained from expert committee reports or opinions and/or clinical experiences of respected authorities

### Grades of Recommendations

Grade A (evidence levels I a, I b) Requires at least one randomised controlled trial, as part of the body of literature of overall good quality and consistency, addressing the specific recommendation

Grade B (evidence levels II a, II b, III) Requires availability of well conducted clinical studies, but no randomised clinical trials on the topic of recommendation

Grade C (evidence level IV) Requires evidence obtained from expert committee reports or opinions, and/or clinical experiences of respected authorities. Indicates absence of directly applicable clinical studies of good quality

GPP (good practice points) Recommended best practice based on the clinical experience of the guideline development group

### CLINICAL ALGORITHM(S)

Algorithms are provided in the original guideline document for:

- Diagnosis of diabetes mellitus
- Individuals suspected to have diabetes but whose fasting plasma glucose < 7 mmol/L
- Non-obese type 2 diabetes mellitus
- Obese type 2 diabetes mellitus

## EVIDENCE SUPPORTING THE RECOMMENDATIONS

### REFERENCES SUPPORTING THE RECOMMENDATIONS

[References open in a new window](#)

## TYPE OF EVIDENCE SUPPORTING THE RECOMMENDATIONS

The type of supporting evidence is identified and graded for each recommendation (see "Major Recommendations" field).

## BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS

### POTENTIAL BENEFITS

- Accurate diagnosis of diabetes mellitus
- Tight control of blood glucose and glycosylated haemoglobin levels
- Prevention, accurate diagnosis and, optimal management of:
  - Cardiovascular disease
  - Stroke
  - Peripheral artery disease
  - Diabetic nephropathy
  - Diabetic retinopathy
  - Diabetic foot complications
  - Complications during or following pregnancy
- Reduced morbidity and mortality from diabetes-related complications
- Prevention of type 2 diabetes

### POTENTIAL HARMS

- Combination therapy with one or more agents (including insulin) from other classes may be considered. However, one would need to monitor carefully for adverse events such as hypoglycaemia or fluid retention.
- The risks of medications are often increased with advancing age. For instance, decline in renal function is often not reflected in a measurable change in serum creatinine because of an accompanying decline in muscle mass. Metformin, which must be used with care in renal impairment, should hence be used with caution in elderly patients. In addition, decline in cardiac function and risks of volume overload in the elderly may become clinically apparent with the use of thiazolidinediones. In elderly patients, initiating therapy with low-dose, short-acting oral antihyperglycemic agents is recommended. Metformin is the only oral antihyperglycemic agents approved by the United States Food and Drug Administration for use in children with type 2 diabetes.
- The use of certain oral hypoglycaemic agents in renal impairment, especially long-acting drugs like glibenclamide and chlorpropamide, may increase the risk for hypoglycaemia. Thiazolidinediones may cause fluid retention, particularly in patients with renal dysfunction.
- Metformin must be used with care in the presence of co-morbid conditions which increase the risks of lactic acidosis (e.g. class III or IV cardiac failure). Thiazolidinediones need to be used with caution in subjects at risk of fluid retention (e.g. cardiac failure)
- Hepatic insufficiency increases the risks of lactic acidosis and hypoglycaemia and influences the metabolism of many oral antihyperglycemic agents.

- The mechanism of action, advantages and disadvantages of major classes of oral antihyperglycemic agents are shown in Table 3 of the original guideline document.
- The key to effective insulin therapy is an understanding of principles that, when implemented, can result in improved diabetes control. Unfortunately, tight glycaemic control is associated with a certain degree of risk of hypoglycaemia.
- The combination of a statin with a fibrate is associated with increased risk of myositis.

## CONTRAINDICATIONS

### CONTRAINDICATIONS

- Metformin is usually contraindicated in the presence of renal or hepatic insufficiency as it may cause lactic acidosis.
- Inhaled insulins have been in development for more than a decade. In early 2006, an inhaled form of human insulin, Exubera, was approved in Europe and the United States for the treatment of type 1 and 2 diabetes in adults. Both the United States Food and Drug Administration and the European Agency for the Evaluation of Medicinal Products have specified that the drug is contraindicated in smokers and in patients who have smoked in the preceding six months. It is not recommended in patients with asthma, bronchitis or emphysema. The drug's long term pulmonary safety is under study.
- For hypertension treatment:
  - Calcium channel blockers (verapamil or diltiazem) are contraindicated in patients with heart failure
  - Beta-blockers are contraindicated in patients with asthma & chronic obstructive pulmonary disease
  - Beta-blockers and calcium channel blockers are contraindicated in patients with heart block
  - Diuretics are contraindicated in patients with gout
  - Angiotensin-converting enzyme (ACE) inhibitors and angiotensin II receptor blockers are contraindicated in patients with bilateral renal artery stenosis
- ACE inhibitors are contraindicated in pregnancy and therefore should be used with caution in women of childbearing potential.
- Because of the concerns of lactic acidosis, metformin is contraindicated in children with impaired renal function and hepatic disease, and should be discontinued with any acute illness associated with dehydration or hypoxaemia.
- When combining a statin with a fibrate, gemfibrozil should not be used.
- Low-dose oestrogen-progestin oral should be avoided in women with complications of diabetes and those at risk for vascular disease.

## QUALIFYING STATEMENTS

### QUALIFYING STATEMENTS

- These guidelines are not intended to serve as a standard of medical care. Standards of medical care are determined on the basis of all clinical data

available for an individual case and are subject to change as scientific knowledge advances and patterns of care evolve.

- The contents of this publication are guidelines to clinical practice, based on the best available evidence at the time of development. Adherence to these guidelines may not ensure a successful outcome in every case. These guidelines should neither be construed as including all proper methods of care, nor exclude other acceptable methods of care. Each physician is ultimately responsible for the management of his/her unique patient, in the light of the clinical data presented by the patient and the diagnostic and treatment options available.

## IMPLEMENTATION OF THE GUIDELINE

### DESCRIPTION OF IMPLEMENTATION STRATEGY

#### Measurement of Quality Indicators

The workgroup has proposed the following schedule to allow patients and health care providers to better gauge their quality of care.

The care provided to each patient may be more adequately appropriated if he/she were categorised according to his/her risk of developing complications arising from diabetes. Two risk categories are proposed.

- An "at risk" individual may be defined as one who is stable and meeting targets of control as agreed by the patient and his primary care physician.
- A "high risk" individual may be defined as:
  1. One whose control has been unstable and failing to meet targets in the past 12 months
  2. Any pregnant female with diabetes
  3. One already with established diabetic complications
  4. One with psychosocial problems (including alcohol or substance abuse) that complicate management

#### Quality Indicators Recommended Frequency\*

Quality Indicators	Recommended Frequency
HbA <sub>1c</sub>	At risk: 6-monthly High risk: 3-4 monthly
Eye assessment	At risk: annual High risk: as clinically indicated
Foot assessment	At risk: annual High risk: as clinically indicated
Nephropathy assessment	At risk: annual High risk: as clinically indicated
Blood pressure	At risk: 3-4 monthly measurement

Quality Indicators	Recommended Frequency
	High risk: as clinically indicated
Weight and body mass index (BMI)	At risk: 3-4 monthly
	High risk: as clinically indicated
Lipid profile	At risk: annual
	High risk: as clinically indicated
Cardiac assessment	At risk: as clinically indicated
	High risk: as clinically indicated
Self-management education	At risk: annual
	High risk: as clinically indicated

\* includes a baseline assessment.

A sample of a patient care card is shown in Table 19 of the original guideline document to assist both the patient and his/her health care provider in the tracking of these indicators.

Monitoring of diabetes care quality indicators is an evolving and promising faculty. The precise value of some of the proposed measurements requires further research. Their implementation will require a concerted effort from all levels of health care providers.

## IMPLEMENTATION TOOLS

Audit Criteria/Indicators  
Chart Documentation/Checklists/Forms  
Clinical Algorithm  
Personal Digital Assistant (PDA) Downloads  
Quick Reference Guides/Physician Guides  
Slide Presentation  
Staff Training/Competency Material

For information about [availability](#), see the "Availability of Companion Documents" and "Patient Resources" fields below.

## INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES

### IOM CARE NEED

Living with Illness  
Staying Healthy

### IOM DOMAIN

Effectiveness  
Patient-centeredness

## IDENTIFYING INFORMATION AND AVAILABILITY

### BIBLIOGRAPHIC SOURCE(S)

Singapore Ministry of Health. Diabetes mellitus. Singapore: Singapore Ministry of Health; 2006 Jun. 161 p. [260 references]

### ADAPTATION

Not applicable: The guideline was not adapted from another source.

### DATE RELEASED

2006 Jun

### GUIDELINE DEVELOPER(S)

Singapore Ministry of Health - National Government Agency [Non-U.S.]

### SOURCE(S) OF FUNDING

Singapore Ministry of Health

### GUIDELINE COMMITTEE

Workgroup on Diabetes Mellitus

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### FINANCIAL DISCLOSURES/CONFLICTS OF INTEREST

Not stated

#### GUIDELINE STATUS

This is the current release of the guideline.

It updates a previously published version: Singapore Ministry of Health. Diabetes mellitus. Singapore: Singapore Ministry of Health; 1999.

#### GUIDELINE AVAILABILITY

Electronic copies: Available from the [Singapore Ministry of Health Web site](#).

Print copies: Available from the Singapore Ministry of Health, College of Medicine Building, Mezzanine Floor 16 College Rd, Singapore 169854.

#### AVAILABILITY OF COMPANION DOCUMENTS

The following are available:

- Diabetes mellitus clinical practice guideline. Available for personal digital assistant (PDA) download in ISilo and MsReader formats from the [Singapore Ministry of Health Web site](#).
- Diabetes mellitus summary card. Available in Portable Document Format (PDF) from the [Singapore Ministry of Health Web site](#). Also available for personal digital assistant (PDA) download in ISilo and MsReader formats.
- Slides and speeches. Available for download from the [Singapore Ministry of Health Web site](#).

Quality indicators, samples of patient care cards, and a continuing medical education (CME) self assessment are available in the [original guideline document](#).

Print copies: Available from the Singapore Ministry of Health, College of Medicine Building, Mezzanine Floor 16 College Rd, Singapore 169854.

#### PATIENT RESOURCES

None available

#### NGC STATUS

This NGC summary was completed by ECRI on September 20, 2006.

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