This is a revised and updated Clinical Practice Guidelines (CPG) on Management of Type 2 Diabetes Mellitus (T2DM). This CPG supersedes the previous CPG on Management T2DM (2004).

STATEMENT OF INTENT

This guideline is meant to be a guide for clinical practice, based on the best available evidence at the time of development. Adherence to this guideline may not necessarily guarantee the best outcome in every case. Every health care provider is responsible for the management of his/her unique patient based on the clinical picture presented by the patient and the management options available locally.

REVIEW OF THE GUIDELINE

This guideline was issued in May 2009 and will be reviewed in May 2013 or sooner if new evidence becomes available.

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Ministry of Health Malaysia
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Electronic version is available on the following websites:
http://www.moh.gov.my
http://www.acadmed.org.my
http://www.endocrine.my
http://www.diabetes.org.my
FOREWORD

Despite significant advances in Medicine, Diabetes Mellitus remains a major medical challenge in the 21st century.

It is common knowledge that urbanised lifestyle coupled with physical inactivity, together with a higher intake of saturated fats have impacted our population which appears to be genetically predisposed to Type 2 Diabetes. In Malaysia, the prevalence of diabetes continues to rise. What is even more worrying is the fact that almost half of our population with diabetes is unaware that they have the disease.

Diabetes is much easier to treat in its early stages, which underscores the critical need for screening at the primary care level. Lifestyle modification including weight loss, changes in diet and increased physical activity also plays a major role in controlling the disease. As more and more novel pharmacological anti-diabetic agents come into the market, we should not lose sight of the importance of patient empowerment to achieve behavioural modification.

I wish to congratulate all members of this committee for their hard work in producing the 4th edition of this Clinical Practice Guideline. This document will be an invaluable tool for all health practitioners in improving the delivery of care for our diabetic patients, particularly at the primary care level.

Thank you.

Tan Sri Dato’ Seri Dr. Hj. Mohd. Ismail b. Merican
Director-General of Health,
Ministry of Health, Malaysia
PREFACE

The prevalence of T2DM continues to rise in an exponential rate around the world and much of the global burden of this disease is expected to come from the Western-Pacific as well as the South-East Asia regions. In Malaysia, the Third National Health and Morbidity Survey (3rd NHMS) showed that the prevalence of the T2DM for adults aged 30 years old and above now stood at a staggering 14.9% T2DM, upped by almost 79.5% in the space of 10 years from 1996 to 2006. The prevalence of T2DM is the highest among Indian ethnic at 19.9% for those aged 30 years and above.

The Clinical Practice Guidelines (CPG) was developed to provide a clear and concise approach to all health care providers on the current concepts in the management of T2DM. Since T2DM is managed by various health care professionals in Malaysia, attempts were made to ensure the different stakeholders will benefit from this CPG. This is reflected by the representation of the committee members which developed the guideline.

There were three previous guidelines on the Management of T2DM; in 1992, 1996 and 2004. This edition is the Fourth in the series and was deemed necessary due to the tremendous body of new evidence that has become available in the last 4-5 years that has major impact on T2DM management including new targets for control, new classes of pharmacological agents targeting novel pathways as well as major outcome studies. All these have changed the algorithms for the management of T2DM. This new edition of the CPG will address many of these changes. In addition, the emphasis and recognition that a cluster of cardiovascular risk factors that make up the metabolic syndrome in which T2DM is the cornerstone of this syndrome is vital. As such, the management of T2DM requires an integrated and holistic approach that also involves the management of hypertension, dyslipidaemia and overweight/obesity in order to reduce the risk of macrovascular complications. Furthermore, recent major outcome studies showed that early and aggressive reduction in blood glucose level to target decrease the risk of complications thereby reducing healthcare cost.

I hope this latest edition of the CPG for T2DM will help to address the current shortfalls in the management of T2DM and it will be fully utilized by all relevant health care professionals. Last but not least, I would like to express my gratitude to everyone involved in the development of this guideline and especially to the task force members for their immense support and contribution towards this guideline.

Professor Dato’ Paduka Dr. Wan Mohamad Wan Bebakar
Chairperson
Clinical Practice Guideline Task Force
GUIDELINE DEVELOPMENT AND OBJECTIVES

Guideline Development
The guideline development task force consisted of endocrinologists, a nephrologist, an ophthalmologist, two family medicine specialists, a general physician, a neurologist, a paediatric endocrinologist, two public health physicians, a dietitian and a diabetic nurse educator.

The previous edition of the CPG for Management of T2DM (2004) was used as the basis for the development of this present guideline.

Literature search was carried out at the following electronic databases: PUBMED, Medline, Cochrane Databases of Systemic Reviews (CDSR), Journal full text via OVID search engine. In addition, the reference lists of all relevant articles retrieved were searched to identify further studies.

Reference was also made to other guidelines on the management of T2DM 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 Diabetes Association 2008 Clinical Practice Guidelines for the Prevention and Management of Diabetes in Canada; Medical Nutrition Therapy Guidelines for Type 2 Diabetes, Malaysian Dietitian Association, 2005.

This guideline is based largely on the findings of systemic reviews and meta-analyses in the literature, taking into consideration local practices.

The clinical questions were divided into major subgroups and members of the task force were assigned individual topics within these subgroups. The task force met a total of 9 times throughout the development of the guideline. All literature retrieved were critically appraised, presented and discussed during group meetings. All statements and recommendations formulated were agreed by the task force members. Where the evidence was insufficient, the recommendations were derived by consensus of the task force members.

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 Network (SIGN).

The draft guideline was posted on the Ministry of Health Malaysia website for comment and feedback. This guideline had also been presented to the Technical Advisory Committee for Clinical Practice Guidelines and the Health Technology Assessment and Clinical Practice Guidelines Council, Ministry of Health Malaysia for review and approval.
Objectives
The aim of the guideline is to provide evidence-based recommendations to assist health care providers in the identification, diagnosis and management of people with T2DM. It also includes a section on pre-diabetes and prevention of progression in the high-risk population and Metabolic Syndrome.

Clinical Questions
The clinical questions of these guidelines are:
1. How can diabetes be prevented?
2. How to screen for glucose intolerance?
3. How is diabetes diagnosed?
4. How can people with diabetes be managed?

Target Population
This guideline is applicable to children, adolescents and adults with T2DM and also diabetes in pregnancy as well as those at risk of developing diabetes.

Target Group
This guideline is meant for all health care professionals involved in treating patients with T2DM which includes: medical officers, family medicine specialists, general practitioners, public health personnel, general physicians, endocrinologists, cardiologists, nephrologists, neurologists, geriatricians, obstetricians and gynaecologists, paediatricians, ophthalmologists, nurses, assistant medical officers, podiatrists, pharmacists, dietitians as well as diabetic nurse educators.

CLINICAL INDICATOR FOR QUALITY MANAGEMENT

Proportion of people with diabetes with HbA1c < 6.5%

Numerator: Number of people with diabetes with HbA1c < 6.5%
Denominator: Total number of people with diabetes on treatment sampled

The optimum achievable standard: ≥30% for each facility
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SECTION 1  DIABETES: THE DISEASE

a) It is a common chronic disorder
b) There is chronic hyperglycaemia together with other metabolic abnormalities
c) It is due to insulin resistance and/or deficiency as well as increased hepatic glucose output
d) It is a risk factor for CVD
e) Currently there is no known cure but the disease can be controlled enabling the person to lead a healthy and productive life
f) The aim of management is directed at reducing complications (microvascular & macrovascular)

Symptoms of Diabetes
Fourty eight percent (48%) of patients above the age of 30 years old are not aware that they have diabetes. The majority are asymptomatic.

Acute Complications
a) Hypoglycaemia
b) Hyperglycaemia

Patients should be made aware of:
• Symptoms: Common symptoms include polyuria, polydipsia, tiredness and weight loss
• Precipitating factors (e.g. infection, intercurrent illness)
• Simple measures to avoid and manage the above

Chronic Complications
a) Macrovascular
   (e.g. Cardiovascular, Cerebrovascular, Peripheral vascular systems)
b) Microvascular
   (e.g. Nephropathy, Neuropathy and Retinopathy)
Inform patients regarding:
• Symptoms
• Preventive measures
• Coping strategies

Lifestyle Measures
Diet and physical activity form an integral part of the management of diabetes. Education on lifestyle modification should be initiated at diagnosis and reinforced regularly.

Medication
Emphasize that diet and physical activity are the mainstay of treatment. Medication can be given at diagnosis for appropriate patients.

Self-Care
Patients should be educated to practice self-care. This allows the patient to assume responsibility and control of his/her own diabetes management. Self-care should include:
• Blood glucose monitoring
• Body weight monitoring
• Foot-care
• Personal hygiene
• Healthy lifestyle/diet and physical activity
• Identify targets for control
• Stop smoking
• Alcohol intake
SECTION 2    SCREENING AND DIAGNOSIS

2.1 Objective
To detect pre-diabetes and diabetes in specific high risk population groups and to ensure timely and appropriate management.

2.2 Strategy
- Screening for high risk group
- Selective screening according to criteria

2.3 Who should be screened
a. Any individual who has symptoms suggestive of DM (tiredness, lethargy, polyuria, polydipsia, polyphagia, weight loss, pruritis vulvae, balanitis) must be screened. 2

b. Criteria for testing for pre-diabetes and diabetes in asymptomatic adult individuals

Testing should be considered in all adults who are overweight [body mass index (BMI) >23 kg/m² or waist circumference (WC) ≥80 cm for women & ≥90 cm for men] and have additional risk factors:
- Dyslipidaemia either high density lipoprotein (HDL) cholesterol <0.9 mmol/L or triglycerides (TG) >1.7 mmol/L
- History of cardiovascular disease (CVD)
- Hypertension (≥140/90 mmHg or on therapy for hypertension)
- Impaired Glucose Tolerance (IGT) or Impaired Fasting Glucose (IFG) on previous testing
- First-degree relative with diabetes
- Other clinical conditions associated with insulin resistance (e.g. severe obesity and acanthosis nigricans)
- Physical inactivity
- Women with polycystic ovarian syndrome (PCOS)

Adapted from American Diabetes Association (ADA). Position Statement on Standards of Medical Care in Diabetes – 2009 2

c. Pregnant women should be screened if they have any of the following risk factors:
- BMI >27kg/m²
- Previous macrosomic baby weighing 4kg or above
- Previous gestational diabetes mellitus (GDM)
- First-degree relative with diabetes
- Bad obstetric history
- Glycosuria at the first prenatal visit
- Current obstetric problems (essential hypertension, pregnancy induced hypertension, polyhydramnios and current use of steroids)
- Age above 25 ²
Screening is done using the 75g OGTT and performed at least once at ≥24 weeks of gestation. Screening at an earlier stage of gestation depends on the degree of suspicion and at the physician’s/obstetrician’s request.

d. Women with history of gestational diabetes should be screened for diabetes annually.  

e. In the absence of the above criteria, testing should begin at age ≥30 years.  

f. Children and adolescents who are overweight (BMI >85th percentile for age and sex, or weight >120% of ideal) and have any two of the following risk factors should be screened for pre-diabetes and diabetes.
   • Family history of T2DM in first- or second- degree relative
   • Maternal history of GDM
   • Ethnicity (those of Indian ethnic background are at higher risks of developing T2DM)  
   • Signs of insulin resistance or conditions associated with insulin resistance (acanthosis nigricans, hypertension, dyslipidaemia, PCOS) 

2.4 Schedule
Screening should be done annually.

In children and adolescents, screen every two years starting at the age of 10 years old or at onset of puberty if puberty occurs at a younger age.

2.5 Screening Test
Screening can be done by measuring random blood glucose (capillary blood), using glucose meters and strips.

Screening process is shown in Flow Chart 1 (Algorithm 1) and Flow Chart 2 (Algorithm 2)

In children and adolescents, follow the same screening procedure.

2.6 Diagnosis
Diagnosis must be confirmed by measurement of venous plasma glucose.

Venous sample for plasma glucose should be taken prior to initiating therapy.
Table 1: Values for Diagnosis

<table>
<thead>
<tr>
<th></th>
<th>Fasting</th>
<th>Random</th>
</tr>
</thead>
<tbody>
<tr>
<td>Venous Plasma Glucose</td>
<td>$\geq 7.0$ mmol/L</td>
<td>$\geq 11.1$ mmol/L</td>
</tr>
</tbody>
</table>

In the symptomatic individual, one abnormal glucose value is diagnostic.

In the asymptomatic individual, 2 abnormal glucose values are required.

Table 2: Diagnostic values for Type 2 Diabetes Mellitus/Glucose Intolerance – oral glucose tolerance test (OGTT) [IDF 2005] 5 (Level III)

<table>
<thead>
<tr>
<th>OGGT Plasma Glucose Values (mmol/L)</th>
<th>Category</th>
<th>0-hour</th>
<th>2-hour</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal</td>
<td>&lt; 6.1*</td>
<td>&lt; 7.8</td>
<td></td>
</tr>
<tr>
<td>IFG</td>
<td>6.1* – 6.9</td>
<td>-</td>
<td></td>
</tr>
<tr>
<td>IGT</td>
<td>-</td>
<td>7.8 – 11.0</td>
<td></td>
</tr>
<tr>
<td>DM</td>
<td>$\geq 7.0$</td>
<td>$\geq 11.1$</td>
<td></td>
</tr>
</tbody>
</table>

* ADA uses 5.6 mmol/L ²

In children and adolescents, the glucose load in OGGT is based on body weight (1.75g per kg body weight, maximum of 75g).

Recommendations: Screening and Diagnosis

1. Screening for diabetes using fasting plasma glucose (FPG) should be performed annually in those with risk factors and those $\geq 30$ years. [Grade C]

2. In children and adolescents at risk of developing diabetes, screening should be initiated at 10 years old or at onset of puberty if puberty occurs at a younger age. Screening is performed every two years. [Grade C]

3. More frequent and/or earlier testing with either a FPG or 2-hour plasma glucose in a 75g OGGT should be considered in people with additional risk factors for diabetes. [Grade C]

4. Testing with a 75g OGGT should be considered in individuals with a FPG of $\geq 6.1$ to 6.9 mmol/L in order to identify individuals with IGT or diabetes. [Grade C] A glucose load of 1.75g/kg body weight (max. 75g) is used for children and adolescents.

5. ALL newly diagnosed T2DM need to be reviewed by a medical doctor in which screening for other cardiovascular risk need to be done or planned. [Grade C]
2.7 Screening Process

Algorithm 1: Screening for type 2 diabetes mellitus at primary care level – with symptoms

- All values in mmol/L. Capillary whole blood reading is 12% lower than venous plasma glucose.
Algorithm 2: Screening for type 2 diabetes mellitus at primary care level – without symptoms

- If FPG $\geq 7.0$ mmol/L or 2 hour PPG $\geq 11.1$ mmol/L, repeat OGTT is required to make the diagnosis of diabetes.
- All values in mmol/L. Capillary whole blood reading is 12% lower than venous plasma glucose.
- For diagnosis of T2DM, venous plasma glucose value is required.
3.1 Initial Assessment
At diagnosis a detailed history, physical examination (including fundoscopy) must be done to assess the risk factors and complications of diabetes. The following baseline investigations should be performed:

FPG
Glycosylated Haemoglobin (HbA1c)
Renal profile
Lipid profile
Urine analysis particularly for albuminuria
Electrocardiogram (ECG)

Management should be based on the initial assessment and baseline investigations.

Diabetes management involves lifestyle modification, medication and patient education to encourage self care. 6, 7 (Level III), 8, 9 (Level I)

Assessment includes appraisal of cardiovascular risks and presence of end-organ damage.

A detailed assessment needs to be made at first diagnosis.

<table>
<thead>
<tr>
<th>Specific symptoms</th>
<th>Polyuria, Polydipsia, Polyphagia, Weight loss, Nocturia, Hyperglycaemia, Malaise/fatigue, Altered vision</th>
</tr>
</thead>
<tbody>
<tr>
<td>Predisposition to diabetes</td>
<td>Age over 35, Family history, Ethnic group, Overweight, Physical inactivity, Hypertension, Obstetric history of large babies or Gestational diabetes, Medication causing hyperglycaemia, autoimmune disease (personal and/or family history of other autoimmune diseases e.g: hypo or hyperthyroidism)</td>
</tr>
<tr>
<td>Risk factors for complications</td>
<td>Personal or family history of CVD, Smoking, Hypertension, Dyslipidaemia</td>
</tr>
<tr>
<td>General symptoms review</td>
<td>Cardiovascular symptoms, Neurological symptoms, Bladder and sexual dysfunction, Foot and toe problems, Recurrent infections (especially urinary and skin)</td>
</tr>
<tr>
<td>Lifestyle issues</td>
<td>Smoking, Alcohol, Occupation, Eating and physical activity</td>
</tr>
</tbody>
</table>

In children and adolescents, predisposing factors to T2DM include low birth weight (LBW), small for gestational age (SGA), large for gestational age (LGA), maternal diabetes during pregnancy, childhood obesity, sedentary lifestyle, increased calorie and fat intake, onset of puberty, ethnicity, insulin resistance, PCOS, T2DM in first- and second- degree relatives. 10-13

Symptoms include pruritis vulvae in girls, enuresis, polyuria, polydipsia, lethargy and weight loss. The majority of T2DM in children and adolescents are diagnosed incidentally.
Examination

<table>
<thead>
<tr>
<th>Weight/waist</th>
<th>BMI = weight (kg) divided by height$^2$ (m$^2$), WC</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cardiovascular</td>
<td>Blood pressure (lying and standing), Peripheral neck and abdominal system vessels</td>
</tr>
<tr>
<td>Eye</td>
<td>Visual acuity (with corrected vision), Cataract, Retinopathy (examine with pupils dilated)</td>
</tr>
<tr>
<td>Feet</td>
<td>Sensation and circulation, Skin condition, Pressure areas, Interdigital problems, Abnormal bony architecture</td>
</tr>
<tr>
<td>Peripheral Nerves</td>
<td>Tendon reflexes, Sensation: touch (e.g: with 10G monofilament), vibration (e.g: with 128Hz tuning fork)</td>
</tr>
</tbody>
</table>

Investigations

| Baseline           | Urinalysis: albumin, microalbuminuria |
|--------------------| Renal profile: plasma urea and creatinine |
|                    | Lipids: Low density lipoprotein (LDL) cholesterol, HDL cholesterol, total cholesterol, triglyceride |
|                    | Glycaemia: FPG, HbA1c |
| Others             | ECG |
|                    | Thyroid function tests if there is a family history or clinical suspicion |

Plan of continuing care

- Relief of acute symptoms
- Optimize control of glycaemia and other risk factors for complications
- Treat existing complications

Priorities of management

Patient and carer counselling includes identifying and addressing concerns which may be causing distress and adversely affecting management.

If the patient is symptomatic then treatment for hyperglycaemia needs to be prompt but if the patient is asymptomatic initial treatment can be less urgent.

Control of blood pressure is as important as glycaemic control in preventing complications. For example the United Kingdom Prospective Diabetes Study (UKPDS) indicates that every 10mmHg reduction in systolic blood pressure accounted for a 15% reduction in diabetes related deaths. 14 (Level I)

The overall aims of management are to improve quality of life and prevent premature death:

**Short term:**
- Relief of symptoms and acute complications

**Long term:**
- Achievement of appropriate glycaemia
- Reduction of concurrent risk factors
- Identification and treatment of chronic complications
The team approach

• Consider referral to diabetes educator and dietitian for consolidation of education

In the team management of diabetes the patient is the central member.

For the patient to accept responsibility for self care they must understand the condition, its effect on health and the practicalities of management. Good communication between team members is important so that advice is consistent and not confusing for the patient.

The following professionals are important team members in the management of diabetes:

Primary Care Practitioner
Primary care practitioner plays a central role in coordinating management of person with diabetes and in providing patient education as well as counselling. Primary care practitioner is the point of first contact with people with diabetes and usually assumes the responsibility for their overall management.

In some instances where the diabetes educator or dietitian is not available primary care practitioner and/or the paramedics must undertake the responsibility to give detailed education to the patient.

Diabetes Educator
The diabetes educator can often spend more time than the primary care practitioner in facilitating knowledge and skills regarding healthy eating, physical activity, self-monitoring, medication usage, setting goal, problem solving, risk reduction practices such as foot care, smoking cessation and keeping with medical appointment.

Dietitian
The role of the dietitian in the management of diabetes is paramount. Lifestyle changes alone (healthy food and regular exercise with ensuing weight loss) are sufficient for glycaemic control in the majority of patients with newly diagnosed T2DM. Recommendation should be individualized to maximize cooperation. Referral to a dietitian is desirable to ensure detailed education on this important aspect of management. The other team members must understand the principles of dietary advice to reinforce the dietary recommendations for the patient.

Physician/Endocrinologist/Diabetologist
The advice of a specialist physician may be valuable for people with complicated problems related to diabetes. A shared care approach by the primary care practitioner and specialist will provide the best combination of expertise and continuity of care to the patient.

Ophthalmologist/optometrist
Referral to an ophthalmologist/optometrist is required for further assessment and management of retinopathy and other eye problems.

Oral health professional
Dental and periodontal problems are common in people with diabetes who need to see a dentist regularly.
### 3.2 Targets for Control

#### Table 3: Targets for Type 2 Diabetes Mellitus

<table>
<thead>
<tr>
<th></th>
<th>Levels</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Glycaemic Control</strong></td>
<td></td>
</tr>
<tr>
<td>Fasting</td>
<td>4.4 – 6.1 mmol/L</td>
</tr>
<tr>
<td>Non-fasting</td>
<td>4.4 – 8.0 mmol/L</td>
</tr>
<tr>
<td>HbA1c</td>
<td>&lt;6.5 %</td>
</tr>
</tbody>
</table>

| **Lipids**             |                                    |
| Triglycerides          | ≤1.7 mmol/L                        |
| HDL cholesterol        | ≥1.1 mmol/L                        |
| LDL cholesterol        | ≤2.6 mmol/L #                      |

| **Exercise**           | 150 mins/week                      |

| **Blood Pressure**     |                                    |
| Normal Renal Function  | ≤130/80 mmHg §                     |
| Renal Impairment/Gross Proteinuria | ≤125/75 mmHg §                  |

* Glycaemic target should be individualized to minimize risk of hypoglycaemia. 17 (Level I) The taskforce acknowledges the increased CVD death in the intensive group of the ACCORD study. 17 (Level I) However, the taskforce believes it is due to the overall treatment strategies that were employed to achieve the HbA1c target rather than the reduction in HbA1c. This is also collaborated by the ADVANCE study. 18 (Level I)

# 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. 19 (Level III)

Modified from the International Diabetes Federation Western Pacific Region (IDF-WPR) Type 2 Diabetes Practical Targets and Treatment, Fourth Edition, 2005. 20
3.3 Diabetes Education

Diabetes education is effective for improving clinical outcomes and quality of life. Hence it should be advocated to all patients with T2DM regardless of treatment mode. 21-23 (Level I)

Algorithm 3: Education Strategies

DOCTOR: Clinical Evaluation

Review for Medication

EDUCATOR

Doctor, Nurse, Assistant Medical Officer, Health Education Officer, Dietitian and others

OBJECTIVE
- To reassure and alleviate anxiety
- To understand the disease, its management and complication
- To promote compliance and self-care

EDUCATION PLAN
Assess knowledge, skill, attitude, health beliefs, psychosocial barriers, education needs 5 (Level III), 8, 9 (Level I)

CONTENTS 5 (Level II-2), 6, 24-25 (Level I), 26 (Level II-2), 27-28 (Level III)

Diabetes
- Diet
- Exercise
- Medication
- Complications (acute and chronic)
- Self-care/SBGM/foot care
- Stop smoking
- Problem solving skills
- Psychosocial adaptation to diabetes

Health education, diet therapy and exercise must be reinforced at follow-up. 8, 23 (Level I)
3.4 Lifestyle Modification

3.4.1 Medical Nutrition Therapy

Medical nutrition therapy (MNT) is important in preventing diabetes, managing existing diabetes, and delaying complications. Proper diet is crucial at any stage of management of diabetes including those on medication.

The goals of MNT together with medication are to attain and maintain blood glucose, blood pressure and lipid profile as close to normal as safely as possible. These goals can be achieved through healthy food choices.

General recommendations:

1. Nutrition counseling by a dietitian is recommended. 29 (Level I)

2. Dietary counseling should be individualized according to nutritional needs, severity of disease, cultural preferences and willingness to change. 30 (Level III)

Specific recommendations

A. Prevention of diabetes:

1. Weight loss of 5 to 10% of initial body weight over a 6 month period is recommended for all overweight or obese individuals who have or are at risk for diabetes. 31, 32 (Level I)

   This can be achieved by:
   
   - a reduced calorie diet (20-25 kcal/kg body weight)
   - increasing physical activity (at least 150 mins/week), and
   - behavioural modification

2. A balanced diet consisting of 50-60% energy from carbohydrate, 15-20% energy from protein and 25-30% energy from fats are encouraged. 30 (Level III) These recommendations must be individualized based on glucose and lipid goals. However, total caloric intake must be appropriate for weight management goals.

3. A high fibre diet (20-30g fibre/day or 5-7 servings/day) consisting of vegetables, fruits, legumes and whole grain cereals is encouraged. 33 (Level II-2)

In children and adolescents: maintenance of weight is associated with a reduction in BMI (as height increases), significant improvement in body composition, insulin resistance and inflammatory markers. 34 (Level I)
B. Management of Diabetes

In addition to the above recommendations:

1. Meal timings should be regular (avoid missing meals) and synchronised with medication time actions.

2. The diet should consist of carbohydrate from cereals (preferably whole grain), fruits, vegetables, legumes, and low-fat or skimmed milk. Total carbohydrate intake should be consistent and evenly distributed throughout the day i.e. 3 main meals with 1 or 2 snacks in between without incurring any excess calorie intake. (Please refer to APPENDIX 1)

3. Monitoring the total daily carbohydrate intake (by carbohydrate exchange) is the primary strategy in achieving glycaemic control. 35 (Level I)

4. The use of glycaemic index (GI) and load of foods may provide additional benefit in modulating postprandial response 36 (Level I) but is not recommended as the primary strategy in meal planning. GI may be used to guide food choices while keeping to the calories and carbohydrate prescription. There are limited databases on the GI and load of local foods. (Please refer to APPENDIX 2)

5. Sucrose (e.g. table sugar) intake must be counted as part of the total carbohydrate intake. 37 (Level III) Excess sucrose intake contributes to calories and may cause weight gain. 38 (Level I)

Artificial sweeteners (aspartame, acesulfane K) are allowed.

6. Individuals with diabetes should be encouraged to test pre- and postprandial glucose in order to evaluate and achieve postprandial glucose goals with a variety of foods.

7. Individuals with diabetes should limit intake of saturated fatty acids, trans fatty acids, and cholesterol 39 (Level I) to reduce risk of CVD. Saturated fats are usually found in animal fats (skin of poultry, fatty meats, full cream dairy products) and coconut milk.

8. In normotensive and hypertensive individuals, a reduced sodium intake (<2,400 mg sodium/day or 6 g of salt a day) with a diet high in fruits, vegetables, and low-fat dairy products lowers blood pressure. 40 (Level I)

Sodium restriction can be achieved through avoiding high sodium foods (soya sauce, ketchup & other sauces, pre-mixed cooking paste, monosodium glutamate, salt preserved foods and processed foods), reducing the frequency of eating out and limiting salt in cooking to ¼ to ½ teaspoonful of salt per person per day. 40 (Level I)

9. Individuals with diabetes have the same vitamin & mineral requirements as the general population. There is no clear evidence of benefit from the use of antioxidant vitamins A, C, E, selenium and herbs in diabetes management. 41 (Level I)
3.4.2 Physical Activity

Increased physical activity can improve glycaemic control, assist with weight maintenance, and reduce the risk of CVD. 25 (Level I)

Before beginning a program of physical activity more vigorous than brisk walking, people with diabetes should be assessed for complications that may preclude vigorous exercise (CVD, retinopathy, neuropathy and foot injury). The patient’s age and previous physical activity level should be considered.

General recommendations:
1. Individuals should exercise 5 days a week, preferably most days of the week and with no more than 2 consecutive days without physical activity.
2. Brisk walking is recommended for all.
3. The duration of exercise should be at least 150 min/week of moderate-intensity aerobic physical activity and/or at least 90 min/week of vigorous aerobic. Please refer to APPENDIX 3 for examples of exercise.
4. Overweight and obese individuals should gradually increase physical activity to 60 – 90 minutes per day for long term major weight loss.
5. Any increase in daily energy expenditure is beneficial e.g. gardening, walking up stairs, washing the car, mopping the floor.
6. In order to prevent hypoglycaemia, medication doses can be reduced or extra carbohydrate can be consumed before or during physical activity.

3.5 Non-Achievement of Glycaemic Target with Lifestyle Modification Therapy

If glycaemic targets are not achieved (HbA1c <6.5%, FPG <6 mmol/L) with lifestyle modification within 3 months, ORAL ANTI-DIABETIC (OAD) agents should be initiated. 42 (Level I)
### 3.6 Medication

#### 3.6.1 Oral Agent Monotherapy

**Recommendations: Oral Agent Monotherapy**

<table>
<thead>
<tr>
<th>1. If glycaemic targets are not achieved (HbA1c &lt; 6.5%, FPG &lt; 6 mmol/L) with lifestyle modification within 3 months, OAD agents should be initiated. [Grade A]</th>
</tr>
</thead>
<tbody>
<tr>
<td>2. In the presence of marked hyperglycaemia in newly diagnosed T2DM (HbA1c 6.5 – 8%, FPG 6 – 10 mmol/L), OAD agents should be considered at the outset together with lifestyle modification. [Grade C]</td>
</tr>
<tr>
<td>3. Patients should be follow-up within 2-4 weeks to monitor the symptoms, to assess the compliance and side effects of OAD and review the blood investigations including fasting lipid profile. [Grade C]</td>
</tr>
</tbody>
</table>

As first line therapy:

- Metformin is the preferred choice. [43 (Level III)] Other OAD agents are acceptable alternatives.
- Use of thiazolidinediones (TZDs) as first line has been found to have greater durability in glycaemic control compared to metformin and sulphonylurea (SU). [44 (Level I)]
- If monotherapy fails, combination of other agents is recommended. [45-50 (Level I, III)]

#### 3.6.2 Combination of Oral Agents

**Recommendation: Combination of Oral Agents**

<table>
<thead>
<tr>
<th>1. Combination of oral agents is indicated in:</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Newly diagnosed patients with HbA1c 8 – 10%, FPG 10 – 13 mmol/L. [Grade C]</td>
</tr>
<tr>
<td>• Patients who are not reaching targets (HbA1c &lt;6.5%) after 3 – 6 months on monotherapy. [Grade C]</td>
</tr>
</tbody>
</table>

#### 3.6.3 Combination of Oral Agents and Insulin

Combining insulin and the following OAD agents has been shown to be effective in people with T2DM:

- Biguanide (metformin). [51-53 (Level I)]
- Insulin secretagogues (SUs). [54 (Level I)]
- Insulin sensitizers (TZDs) [55 (Level I)] (the combination of a TZD plus insulin is not a recommended indication).
- α-glucosidase inhibitor (AGI). [56-57 (Level I)]

Insulin dosage can be increased until target FPG is achieved. If HbA1c targets are not achieved despite of normal FPG, then monitor post-prandial plasma glucose (PPG). In children and adolescents: Long-acting or intermediate acting insulin may be added at a dose of 0.5u/kg at bed-time. [11,58]

**Recommendation: Combination of Oral Agents and Insulin**

<table>
<thead>
<tr>
<th>1. Combination of oral agents and insulin is indicated in:</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Newly diagnosed patients with HbA1c &gt;10%, FPG &gt; 13 mmol/L. [Grade C]</td>
</tr>
<tr>
<td>• Patients who are not reaching targets (HbA1c &lt;6.5%) after 3 – 6 months on optimal doses of combination therapy. [Grade C]</td>
</tr>
</tbody>
</table>
3.6.4 General Guidelines for Use of Oral Anti-Diabetic (OAD) Agents in Diabetes

- In elderly non-obese patients, short acting insulin secretagogues can be started but long acting SUs are to be avoided. Renal function should be monitored.
- Compliance may be improved with daily dosing OAD agents.
- OAD agents are not recommended for diabetes in pregnancy.
- OAD agents are usually not the first line therapy in diabetes diagnosed during stress, such as infections. Insulin therapy is recommended.
- Targets for control are applicable for all age groups. However, in patients with comorbidities, targets are individualized.
- When indicated, start with a minimal dose of OAD agent, while reemphasizing diet and physical activity. An appropriate duration of time (2 – 16 weeks depending on agents used) between increments should be given to allow achievement of steady state blood glucose control.

3.6.5 Oral Anti-Diabetic (OAD) Agents

There are currently five classes of OAD agents:

a) AGIs
b) Biguanides
c) Dipeptidyl peptidase-4 (DPP-4) Inhibitors
d) Insulin Secretagogues – SUs
   - Non-SUs or Meglitinides
e) Thiazolidinediones (TZDs)

a) α-glucosidase inhibitors (AGIs)
   - AGIs e.g. acarbose, act at the gut epithelium, to reduce the rate of digestion of polysaccharides in the proximal small intestine by inhibiting α-glucosidase enzymes. They should be taken with main meals.
   - AGIs primarily lower postprandial glucose without causing hypoglycaemia.
   - They are less effective in lowering glycaemia than metformin or SU, reducing HbA1c by 0.5–0.8%.56 (Level I)
   - They can have synergistic effects when used with other OAD agents and may be combined with insulin.
   - If hypoglycaemia occurs when used in combination with SUs or insulin, advise patients to take monosaccharides, e.g. glucose.
   - The commonest side effects are bloating, abdominal discomfort, diarrhea and flatulence.

Dosage

<table>
<thead>
<tr>
<th>Formulation</th>
<th>Minimum Dose</th>
<th>Maximum Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acarbose 50mg / 100mg tablet</td>
<td>Initial dose 50mg OD</td>
<td>Maximum dose 100mg TDS</td>
</tr>
<tr>
<td></td>
<td>Usual dose 50mg – 100mg during main meals</td>
<td></td>
</tr>
</tbody>
</table>
b) Biguanides (Metformin)

- Metformin does not stimulate insulin secretion, and lowers blood glucose by decreasing hepatic glucose production.
- Metformin monotherapy is usually not accompanied by hypoglycaemia.
- It can lower plasma glucose by up to 20% as first line drug treatment especially in overweight/obese patients.
- Metformin monotherapy will lower HbA1c by about 1.5%.
- Metformin used in combination with other OAD agents have a synergistic effect to further reduce blood glucose. Metformin can increase insulin sensitivity and reduce insulin requirements.
- Generally well tolerated. Most common adverse effects are nausea, anorexia and diarrhea. These adverse effects are significantly less with the use of metformin extended release formulation.
- Lactic acidosis is quite rare (<one case per 100,000 treated patients). 59 (Level I)
- The major nonglycaemic effect of metformin is either weight stability or modest weight loss, in contrast to many of the other blood glucose-lowering medications.
- The UKPDS demonstrated a beneficial effect of metformin therapy on CVD outcomes. 60 (Level I)

## Dosage

<table>
<thead>
<tr>
<th>Formulation</th>
<th>Minimum Dose</th>
<th>Maximum Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Metformin 500mg tablet</td>
<td>Initial dose 500mg OD&lt;br&gt;Usual dose 500mg TDS&lt;br&gt;The side effects can be further reduced by taking it with food</td>
<td>Maximum dose 1000mg BD</td>
</tr>
<tr>
<td>Metformin retard 850 mg tablet (slow release formulation)</td>
<td>Initial dose 850mg OD&lt;br&gt;Usual dose 850mg BD</td>
<td>Maximum dose 1700mg OM / 850 mg ON</td>
</tr>
<tr>
<td>Metformin extended release 500mg tablet</td>
<td>Initial dose 500mg OD</td>
<td>Maximum dose 2000mg OD</td>
</tr>
<tr>
<td>Glibenclamide and metformin fixed dose combination 1.25mg / 250mg tablet 2.5mg / 500mg tablet 5mg / 500mg tablet</td>
<td>Initial dose one 1.25mg / 250mg tablet OD or BD</td>
<td>Maximum dose two 5mg / 250mg tablets BD</td>
</tr>
</tbody>
</table>

**Caution:**

- Should not be used in patients with impaired renal function (serum creatinine >150 µmol/l or creatinine clearance <30 mL/min), liver cirrhosis, congestive cardiac failure (CCF), recent myocardial infarction, chronic respiratory disease, vascular disease and severe infections or any conditions that can cause lactic acid accumulation.
- Vitamin B12 deficiency may occur if metformin is given to patients who have had partial gastrectomy and terminal ileal disease.
Incretins

- The incretin effect is markedly decreased in T2DM, resulting in delayed and reduced insulin release as well as lack of suppression of glucagon release, after a meal.
- After meals, incretins [glucagon-like peptide 1 (GLP-1) and glucose-dependent insulinoective polypeptide (GIP)] are released; these augment glucose-induced insulin secretion and glucagon release is suppressed, reducing hepatic glucose output - in a glucose dependent manner, i.e. normoglycaemia does not stimulate insulin secretion and glucagon release resumes.
- Agents that increase the effect of incretins have been proven to improve glucose control - 2 classes of drugs have recently been developed: DPP-4 inhibitor (incretin enhancer) and GLP-1 analogue or GLP-1 receptor agonist (incretin mimetic).

c) Dipeptidyl peptidase-4 (DPP-4) Inhibitor (Sitagliptin)

- It lowers HbA1c by 0.5 – 0.8%, its efficacy improves when used at higher HbA1c baselines.
- It can be combined with cumulative efficacy with other OAD agents e.g. metformin, TZDs, and SU.
- Data comparing it with glipizide suggest equivalent glycaemic efficacy.
- Other benefits include the minimal risk of hypoglycaemia and weight neutrality.
- It is excreted unchanged by the kidneys and a reduction of dose is recommended with renal impairment (25mg to 50mg).
- It is generally well tolerated.

<table>
<thead>
<tr>
<th>Formulation</th>
<th>Minimum dose</th>
<th>Maximum dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sitagliptin 100mg / 50mg / 25mg tablet</td>
<td>100mg OD</td>
<td>100mg OD</td>
</tr>
<tr>
<td>Sitagliptin and metformin fixed dose combination</td>
<td>50mg / 500 mg BD</td>
<td>50mg / 1000mg BD</td>
</tr>
<tr>
<td>50mg / 500mg tablet</td>
<td></td>
<td></td>
</tr>
<tr>
<td>50mg / 850mg tablet</td>
<td></td>
<td></td>
</tr>
<tr>
<td>50mg / 1000mg tablet</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

d) Insulin Secretagogues – SUs

- SUs lower plasma glucose by increasing insulin secretion. They can lower plasma glucose by up to 25% and lower HbA1c by about 1.5%.
- The major adverse side effect is hypoglycaemia. The risk is higher in renal impairment, liver cirrhosis and the elderly.
- Second generation SUs (glimepiride, gliclazide MR) cause less risk of hypoglycaemia and less weight gain.
- SUs can be combined with other OAD agents or insulin to improve glucose control, if indicated.
- SUs should be taken 30 minutes before meals, except glimepiride and gliclazide MR which can be taken just before the meal.
- Combining 2 different SUs / insulin secretagogues is not recommended.
- Side effects are rare and include hepatitis, syndrome of inappropriate antidiuretic hormone (SIADH), blood dyscrasias.
# Dosage

<table>
<thead>
<tr>
<th>Formulation</th>
<th>Minimum dose</th>
<th>Maximum dose</th>
<th>Duration</th>
</tr>
</thead>
<tbody>
<tr>
<td>Glibenclamide 5mg tablet</td>
<td>2.5mg OM</td>
<td>10mg BD</td>
<td>Long</td>
</tr>
<tr>
<td>Glibenclamide and Metformin Fixed Dose Combination</td>
<td>Initial dose one 1.25mg / 250mg tablet OD or BD</td>
<td>Maximum dose two 5mg / 500mg tablets BD</td>
<td>Long</td>
</tr>
<tr>
<td>1.25mg / 250mg tablet</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2.5mg / 500mg tablet</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>5mg / 500mg tablet</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Gliclazide 80mg tablet</td>
<td>40mg OM</td>
<td>160mg BD</td>
<td>Medium</td>
</tr>
<tr>
<td>Gliclazide MR 30mg tablet</td>
<td>30mg OM</td>
<td>120mg OM</td>
<td>Long</td>
</tr>
<tr>
<td>Glipizide 5mg tablet</td>
<td>2.5mg OM</td>
<td>10mg BD</td>
<td>Medium</td>
</tr>
<tr>
<td>Glimepiride 2mg / 3mg tablet</td>
<td>1mg OM</td>
<td>6mg OM</td>
<td>Long</td>
</tr>
</tbody>
</table>

**Note:**
- Glibenclamide is metabolised by the liver but its metabolites are active and excreted by the kidney. The drug should be stopped if renal impairment develops and should not be used in the elderly (>65 years). Other second generation SUs (glimepiride, gliclazide and glipizide) may still be used with caution.
- First line treatment with glibenclamide results in earlier monotherapy failure compared to metformin and rosiglitazone. **44 (Level I)**

**Caution:**
- SUs increase insulin secretion and therefore, increase the risk of hypoglycaemia. SUs increase appetite and promote weight gain. A weight gain of about 2kg is common with initiation of SUs therapy.
- SUs should be used with caution in patients known to be allergic to sulpha drugs.
- SUs are highly protein bound. Administration of drugs that can displace them (e.g. non-steroidal anti-inflammatory drugs (NSAIDs), antithyroid drugs, sulpha drugs, anticoagulants and -blockers) can increase the risk of hypoglycaemia.
- All patients taking SUs must be taught to recognize symptoms of hypoglycaemia and its management.

**Insulin Secretagogues – Non-SUs or Meglitinides**

- These are short acting insulin secretagogues which stimulate insulin secretion, although they bind to a different site within the SU receptor.
- It has a shorter circulating half life than SUs, and is rapidly absorbed from the GI tract with peak level 1-hour post administration and eliminated within 4 – 6 hours.
- It must be administered more frequently.
- It should be taken within 10 minutes before main meals.
- It can be combined with metformin, TZDs or AGIs, when indicated.
- It is associated with a similar risk of weight gain as the SUs but hypoglycaemia may be less frequent.
- It may be useful to control PPG.
Dosage

<table>
<thead>
<tr>
<th>Formulation</th>
<th>Minimum dose</th>
<th>Maximum dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Repaglinide 0.5mg / 1mg / 2mg tablet</td>
<td>0.5mg with main meals</td>
<td>4mg with main meals (not exceeding 16mg daily)</td>
</tr>
<tr>
<td>Nateglinide 120mg tablet</td>
<td>60mg with main meals</td>
<td>120mg with main meals (not exceeding 360mg daily)</td>
</tr>
</tbody>
</table>

Caution:
There is a higher risk of prolonged hypoglycaemia when repaglinide is combined with gemfibrozil. 73 (Level I) This combination is contraindicated.

e) Thiazolidinediones (TZDs)
- Thiazolidinediones are peroxisome proliferator-activated receptor-gamma (PPAR-γ) agonists and act primarily by increasing insulin sensitivity of muscle, adipose tissue and liver to endogenous and exogenous insulin (insulin sensitizers).
- When used as monotherapy, TZDs have demonstrated a 0.5–1.4% decrease in HbA1c.
- Improvement in glycaemic control may only be seen after six weeks and maximal effect up to six months.
- They can be combined with other OAD agents (SUs, metformin or DPP-4 inhibitors) to improve glucose control, when indicated.
- Side effects include an increase in adiposity, largely subcutaneous (S/C), with redistribution of body fat, weight gain, fluid retention, and haemodilution. The fluid retention usually manifests as peripheral oedema, although new or worsened heart failure can occur.
- Recent long term studies have found that both TZDs have been associated with an increased risk of fractures, particularly in women. The majority of these fractures were in the distal upper or lower limb, as opposed to the classic sites of osteoporotic fractures. 44 (Level I), 74 (Level II-2)
- TZDs are contraindicated in patients with CCF 75 and liver failure.
- Use of TZDs with insulin is not recommended.

Dosage

<table>
<thead>
<tr>
<th>Formulation</th>
<th>Minimum dose</th>
<th>Maximum dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rosiglitazone 4mg / 8mg tablet</td>
<td>4 mg OD</td>
<td>4mg BD</td>
</tr>
<tr>
<td>Rosiglitazone and Metformin fixed dose combination</td>
<td>2mg / 500mg BD</td>
<td>4mg / 1000mg BD</td>
</tr>
<tr>
<td>2mg / 1000mg tablet</td>
<td></td>
<td></td>
</tr>
<tr>
<td>4mg / 500mg tablet</td>
<td></td>
<td></td>
</tr>
<tr>
<td>4mg / 1000mg tablet</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pioglitazone 15mg / 30mg tablet</td>
<td>15 mg OD</td>
<td>45 mg OD</td>
</tr>
</tbody>
</table>
3.6.6 GLP-1 Analogue (Exenatide)

- It is given parenterally, just before breakfast and dinner. 76-77 (Level I)
- It reduces HbA1c by 0.5 – 1.0%, sustained efficacy over 2 years. 76-77 (Level I)
- It can be added to metformin 78 (Level I) and/or SU 79-80 (Level I) if glycaemic targets are not achieved.
- Progressive weight loss is seen in a proportion of patients 78-80 (Level I) – because of its effect on satiety and delay in gastric emptying.
- The main adverse effects are gastrointestinal symptom, notably nausea – this can be minimized by starting at a low dose with an increase of dose after 1 month. 84 (Level I)
- Starting dose is 5µg BD and should be increased to 10µg BD after 4 weeks. 76-77 (Level I)
- Incretin mimetic is not a substitute for insulin.

**Dosage**

<table>
<thead>
<tr>
<th>Formulation</th>
<th>Minimum Dose</th>
<th>Maximum Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Exenatide 5µg/20µL / 10µg/40µL</td>
<td>5µg BD</td>
<td>10µg BD</td>
</tr>
<tr>
<td>pre-filled pen for injection</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

3.6.7 Combination of Oral Agents and Insulin Therapy

Combining insulin and the following OAD agents has been shown to be effective in T2DM:

- Biguanide (metformin) 51-53 (Level I)
- Insulin secretagogues (SUs) 54 (Level I)
- Insulin sensitizers (TZDs) 55 (Level I) (the combination of a TZD plus insulin is not a recommended indication).
- AGI 56-57 (Level I)

If targets have not been reached after optimal OAD therapy, consider adding

- Pre-bed intermediate-acting or
- Pre-bed long-acting insulin or
- Pre-dinner premixed insulin

Dose of the above insulin can be increased every third or fourth day (2-4 units each time) until target FPG is achieved - *fix the fasting first*. Long-acting insulin can be injected at any time as long as it is the same time daily. If HbA1c target is not achieved in 3-6 months, intensify insulin regime by adding prandial insulin with the biggest meal initially or adding premixed insulin at breakfast. Insulin secretagogues should be stopped and metformin continued.
a) Reaching Glycaemic Targets

<table>
<thead>
<tr>
<th>To control</th>
<th>Adjust</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pre breakfast glucose</td>
<td>Pre bed intermediate acting insulin or long acting analogue or pre-dinner premixed</td>
</tr>
<tr>
<td>2 hour post breakfast</td>
<td>Breakfast intake or pre breakfast rapid acting or morning premixed insulin analogue</td>
</tr>
<tr>
<td>Pre lunch glucose</td>
<td>Morning tea or pre breakfast short acting insulin or morning premixed insulin</td>
</tr>
<tr>
<td>2 hour post lunch</td>
<td>Lunch intake or pre lunch rapid acting or morning premixed insulin</td>
</tr>
<tr>
<td>Pre dinner morning</td>
<td>Afternoon tea intake or pre lunch short acting insulin or premixed insulin</td>
</tr>
<tr>
<td>Post dinner/pre bed</td>
<td>Dinner intake or pre dinner rapid acting or pre dinner premixed analogue or pre dinner premixed insulin*</td>
</tr>
</tbody>
</table>

* may cause hypoglycaemia in the middle of sleep.

b) Types of Insulin Regimes
- OAD agents + basal insulin or premixed insulin once a day
- Metformin + premixed insulin more than once a day
- Metformin + basal insulin + prandial insulin

c) Short-term use of Insulin
Short-term insulin therapy should be considered in the following conditions:
- Acute illness, surgery, stress and emergencies (Please refer to page 28)
- Pregnancy (Please refer to page 29)
- Breast-feeding
- Insulin may be used as initial therapy in T2DM particularly in marked hyperglycaemia
- Severe metabolic decompensation (diabetic ketoacidosis, hyperosmolar hyperglycaemic state)

d) General Guidelines for Long-term Use of Insulin
Please refer to page 30.

**Recommendation: Combination of Oral Agents and Insulin Therapy**

1. Combination of insulin and OAD agents has been shown to improve glycaemic control in those not achieving target despite optimal OAD agents. [Grade A]
3.7 MONITORING
3.7.1 Self Blood Glucose Monitoring

Self blood glucose monitoring (SBGM) is the method of choice in monitoring glycaemic control. SBGM should be carried out for patients on insulin and is desirable for those on OAD agents. ²

Frequency of blood glucose testing depends on the glucose status, glucose goals and mode of treatment.

Although self blood glucose monitoring has not been shown to have a significant impact on outcome measures such as HbA1c and body weight, it is recommended as part of a wider educational strategy to promote self-care.

Monitoring provides information on the effects of therapy, diet and physical activity. The Position Statement from ADA, 2009 ² recommends:

- SBGM should be carried out 3 or 4 times daily for patients using multiple insulin injections or insulin pump therapy
- For patients using less frequent insulin injections, non-insulin therapies or MNT alone, SBGM may be useful in achieving glycaemic goals

To achieve postprandial glucose targets, postprandial SBGM may be appropriate.

Table 4: Recommendations for Self Blood Glucose Monitoring

<table>
<thead>
<tr>
<th>Mode of Treatment</th>
<th>Breakfast</th>
<th>Lunch</th>
<th>Dinner</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Pre</td>
<td>Post</td>
<td>Pre</td>
</tr>
<tr>
<td>Diet Only</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Oral anti-diabetic agent</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Insulin</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
</tbody>
</table>

Note:
✓ Recommended timing of SBGM
✓ Optional timing of SBGM
3.7.2 Insulin Treated
Those on replacement insulin therapy need to check glucose levels before each meal and before bed (10-11 pm) (Please refer to Targets for Control, page 10) [Pre-meal (breakfast, lunch, dinner) and pre-bed glucose levels]. Once pre-meal glucose levels are achieved, PPG testing is recommended for fine-tuning of insulin dose. This information will allow adjustments of insulin dosage after taking into account the effect of diet and physical activity.

Glucose Monitoring in Relation to Insulin Therapy

Oral Agents + Bedtime Insulin

- Values before breakfast give information about bedtime insulin (Refer to Figure 1a) or once daily basal long acting insulin (Refer to Figure 1b)

Note:
- Recommended timing of SBGM
Basal Bolus Insulin Regimen

Figure 2: Basal Bolus Insulin Regimen

- Values before breakfast give information about pre-dinner or pre-bed intermediate acting insulin.
- Insulin glargine or detemir may be used in place of neutral protamine hagedorn (NPH). Pre-breakfast values are used for dose titration.
- Values before other main meals (pre-lunch or pre-dinner) reflect short acting insulin taken at the previous meal.
- Once pre-meal glucose levels are achieved, PPG testing is recommended for fine-tuning of insulin dose.
- Values at pre-bed give information about short acting insulin given before dinner.
- Rapid acting insulin analogues can be given in place of the short acting insulin. It should be given at the start or immediately after the meal. 2-hour PPG values are used for dose titration.

Note:
- Recommended timing of SBGM
- Optional timing of SBGM

Twice Daily Premixed or Combination Intermediate Acting with Short Acting Insulin

Figure 3: Intermediate Acting with Short Acting Insulin

- Values before breakfast give information about pre-dinner or pre-bed intermediate or long acting insulin.
- Values at pre-lunch give information about short acting insulin given before breakfast.
- Values at pre-dinner give information about the intermediate acting insulin given before breakfast.
- Values at pre-bed give information about short acting insulin given before dinner.
- Once pre-meal glucose levels are achieved, PPG testing is recommended for fine-tuning of insulin dose.

Ideally these tests should be done on a daily basis or if possible at least one 24–hour cycle per week.

Note:
- Recommended timing of SBGM
- Optional timing of SBGM

* SBGM
Patients should be taught to use SBGM to adjust food, physical activity and insulin dosage.
3.7.3 Diet or Oral Anti-Diabetic (OAD) Agents
Those on OAD agents or diet need to check fasting and 2-hour PPG levels.

3.7.4 HbA1c
HbA1c should be measured approximately every 3 to 6 months to ensure that glycaemic targets are being met.

This reflects overall glucose control over a 3 month period with recommended target level of 6.5% (IDF 2005). 5

Glycaemic targets must be individualized. Therapy in most patients with T2DM should be targeted to achieve a HbA1c <6.5%. Reduction in HbA1c has been shown to decrease the risk of microvascular [Grade A] and macrovascular complications.

Recommendations: HbA1c Target

1. Glycaemic targets must be individualized. Therapy in most patients with T2DM should be targeted to achieve a HbA1c <6.5%. Reduction in HbA1c has been shown to decrease the risk of microvascular [Grade A] and macrovascular complications. [Grade C]

2. To achieve a HbA1c <6.5%, aim for FPG or pre-prandial plasma glucose targets of 4.4 to 6.1 mmol/L and 2-hour PPG targets of 4.4 to 8.0 mmol/L. [Grade B]

3.7.5 Monitoring of Other Risk Factors
• Blood pressure and body weight should be monitored at each visit.
• Fasting lipids and urine for albuminuria/microalbuminuria need to be checked annually.
• If cardiovascular or renal complications are present or patients are on lipid-lowering and/or anti-hypertensive therapy, lipids and renal function may need to be checked more often.
3.8 Treatment Algorithm for the Management of Type 2 Diabetes Mellitus

Algorithm 4:

---

**Diagnosis of Type 2 Diabetes**
All patients advised LIFESTYLE Modification
FPG, HbA1c at Diagnosis and Follow up

**HbA1c < 6.5% OR**
FPG < 6 mmol/L

LIFESTYLE APPROACH*

- Follow-up with HbA1c after 3 months
  - If HbA1c ≤ 6.5% continue with Lifestyle Approach.
  - If HbA1c > 6.5% on follow-up, consider OAD monotherapy

**HbA1c 6.5% – <8.0% OR**
FPG 6 - <10 mmol/L

OAD MONOTHERAPY
Metformin**
OR
AGI / DPP-4 Inhibitor / Glinides / SU / TZDs

- Optimize dose of OAD agent in the subsequent 3 – 6 months
- Follow-up with HbA1c after 3 – 6 months
  - If HbA1c ≤ 6.5%, continue therapy
  - If HbA1c > 6.5%, consider COMBINATION OAD Therapy

**HbA1c 8.0% – 10.0% OR**
FPG 10 - 13 mmol/L

COMBINATION THERAPY***
Metformin with other OAD agents (AGI / DPP-4 Inhibitor / Glinides / Incretin Mimetic / SU / TZDs) or with insulin

- Optimize dose of OAD agents in the subsequent 3 – 6 months
- Follow-up with HbA1c after 3 – 6 months
  - If HbA1c ≤ 6.5%, continue therapy
  - If HbA1c > 6.5%, consider addition of INSULIN THERAPY

**HbA1c > 10.0% OR**
FPG > 13 mmol/L

COMBINATION THERAPY + BASAL / PREMIXED INSULIN THERAPY
OR
INTENSIVE INSULIN THERAPY, continue Metformin

---

Footnote:
If symptomatic (weight loss, polyuria, etc) at any HbA1c and FPG level, consider insulin therapy

- Try to achieve as near normal glycaemia without causing hypoglycaemia
- * Consider metformin/AGI/other insulin sensitizer in appropriate patients
- ** Metformin is preferred 1st line agent, and SU 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
3.9 Management of Type 2 Diabetes Mellitus in Acute Illness, Surgery, Stress and Emergencies

- OAD agents may not be adequate in maintaining euglycaemia during stress and emergency situations (e.g. infection, myocardial infarction and surgery)
- In any form of stress, if glycaemic control is inadequate, OAD therapy should be replaced by insulin
- Diabetic ketoacidosis (DKA) may develop during stress
- OAD regimen may be resumed when stress has resolved
- If the patient develops DKA during stress and the patient is young, consider long term insulin therapy

Table 5: Management of Diabetes During Stress and Emergency Surgery

<table>
<thead>
<tr>
<th>Status of Control</th>
<th>Minor Surgery</th>
<th>Major surgery</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acceptable control</td>
<td>• Stop OAD agent</td>
<td>• Stop OAD agent</td>
</tr>
<tr>
<td>FPG &lt; 8.0 mmol/L</td>
<td>• Resume OAD agent post-op, once taking orally</td>
<td>• Glucose-Insulin-Potassium (GIK) regimen during op</td>
</tr>
<tr>
<td>RPG &lt; 11.0 mmol/L</td>
<td></td>
<td>• s/c insulin post-op, once taking orally</td>
</tr>
<tr>
<td>Poor Control</td>
<td>• Stop OAD agent</td>
<td>• GIK regimen (pre- and intra-op)</td>
</tr>
<tr>
<td>FPG ≥ 8.0 mmol/L</td>
<td>• GIK regimen post-op, once taking orally</td>
<td>• s/c insulin post-op, once taking orally</td>
</tr>
<tr>
<td>RPG ≥ 11.0 mmol/L</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

- In elective surgery, delay operation until glycaemic control is achieved. Control with insulin or OAD agents as indicated
- GIK regimen can be continued until food intake after surgery
- Maintain insulin therapy post-surgery until stress is resolved and satisfactory wound healing is achieved
**3.10 Management of Type 2 Diabetes Mellitus in Pregnancy**

Women with T2DM who are planning pregnancy should be referred to physician/diabetologist for further management.

**Pre-pregnancy:**
- Counseling is important
- Pregnancy should be planned
- Achieve good glycaemic control before conception, aim for HbA1c <6.5%
- Insulin therapy may be necessary before conception

**During Pregnancy:**
- Achieve and maintain ideal glucose levels (Refer to Table 6)
- Close SBGM is required (individualize frequency of monitoring)
  - On diet therapy: pre-breakfast, 1 hour PPG levels (weekly – fortnightly) \(^3\)
  - On insulin therapy: premeal (breakfast, lunch, dinner) and pre-bed glucose levels (weekly – fortnightly). Once premeal glucose levels are achieved, PPG testing is recommended for fine-tuning of insulin dose.
- HbA1c (4-6 weekly)
- Insulin therapy is indicated when diet fails. Insulin lispro and aspart may be used. Although published data suggests that metformin and glibenclamide are safe, OAD agents are not generally recommended as they are not registered for use during pregnancy. \(^3\)
- GIK regimen can be used during delivery/lower segment caesarean section (LSCS)

**Post-partum:**
- Insulin requirement drops immediately after delivery by 60 -75%
- In breast-feeding, if glycaemic control is inadequate with diet therapy alone, insulin therapy should be continued at a lower dose.
- In non-breast-feeding mothers, OAD agents can be continued.

**Table 6: Targets for Pregnant Women**

<table>
<thead>
<tr>
<th>Timing</th>
<th>Glucose Level* (mmol/L)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pre-breakfast</td>
<td>3.5 – 5.9</td>
</tr>
<tr>
<td>Pre-prandial</td>
<td>3.5 – 5.9</td>
</tr>
<tr>
<td>1 hour post prandial</td>
<td>&lt; 7.8</td>
</tr>
<tr>
<td>2 hour post prandial</td>
<td>4.4 – 6.7</td>
</tr>
<tr>
<td>0200 – 0400 hours</td>
<td>&gt; 3.9</td>
</tr>
</tbody>
</table>

* Plasma calibrated values (Capillary whole blood reading is 12% lower than venous plasma glucose)

Adapted from the National Institute for Health and Clinical Excellence (NICE), Diabetes in Pregnancy, March 2008 (revised reprint July 2008). \(^3\)
3.11 General Guidelines for Long-Term Use of Insulin

- Persistent hyperglycaemia in spite of optimal OAD agents with stable or loss of weight suggests beta cell failure. However, it is important to exclude chronic infections, malignancies or medications as cause of weight loss.
- The basal intermediate acting insulin should be administered pre-bed because of the risk of hypoglycaemia in the early hours of the morning if given earlier.
- It is not necessary to have an extra meal or snack after intermediate or long acting insulin.
- Requirements of high dose of insulin (>1.5 unit/kg per day) should prompt a search for an underlying cause/secondary problems such as non-compliance, incorrect dosing and administration timing, hypertrophy of injection area, inter meal hypoglycaemia with rebound hyperglycaemia pre meal, expired insulin or expired strips and occult infections.
- There is no limitation of insulin dose.
- The rate of absorption from the injections depend on the site and ‘exercise activity’ of the ‘site’. Patients should be encouraged to rotate all their injection sites in the abdomen region.
- Assessment of pancreatic reserve (e.g. glucagon stimulation test, insulin/C-peptide estimations) prior to insulin use is unnecessary.
### Table 7: Human Recombinant Insulins and Analogues

<table>
<thead>
<tr>
<th>Insulin Preparation</th>
<th>Onset of Action</th>
<th>Peak Action</th>
<th>Duration of Action</th>
<th>Timing of Insulin</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Fast Acting</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rapid Analogue</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Aspart (Novorapid)</td>
<td>5 – 15 minutes</td>
<td>1 – 2 hours</td>
<td>4 – 6 hours</td>
<td>5 to 15 minutes before or immediately after meals</td>
</tr>
<tr>
<td>Lispro (Humalog)</td>
<td>30 – 60 minutes</td>
<td>2 – 4 hours</td>
<td>6 – 10 hours</td>
<td>30 to 60 minutes before meals</td>
</tr>
<tr>
<td>Human Regular</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Actrapid</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Humulin R</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Intermediate Acting</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Human NPH Insulin</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Insulatard</td>
<td>1 – 2 hours</td>
<td>4 – 8 hours</td>
<td>10 – 16 hours</td>
<td>Pre-breakfast/Pre-bed</td>
</tr>
<tr>
<td>Humulin N</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Long Acting</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Basal Long Acting</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Analogue</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Glargine</td>
<td>1 – 2 hours</td>
<td>Flat</td>
<td>~ 24 hours</td>
<td>Same time everyday at anytime of the day</td>
</tr>
<tr>
<td>Detemir</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Premixed Insulins</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mixtard 30/70</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Humulin 30/70</td>
<td>Biphasic onset and peak</td>
<td>10 – 16 hours</td>
<td>30 – 60 minutes before meals</td>
<td></td>
</tr>
<tr>
<td>BIAsp 30/70</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Humalog mix 25/75</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Note:**
The time course of action may vary in different individuals, or at different times in the same individual. Because of these variations, time periods indicated above should be considered as general guidelines only. The higher the dose of the insulin, the longer is the duration of action.

The long acting insulin analogue (glargine<sup>86 (Level I)</sup> and detemir<sup>87 (Level I)</sup>) which are peakless have less hypoglycaemic episodes and less weight gain compared to conventional insulin. The new rapid acting insulin analogues (lispro and insulin aspart<sup>88-91 (Level II)</sup>) have the added advantage (besides the above) of the ability to inject immediately pre meal. In some patients at higher doses the long acting insulin may have a peak.

Both the long acting insulin analogues (glargine and detemir) have not been licensed for use in pregnancy.
3.12 Hypertension and Diabetes Mellitus

The prevalence of hypertension in T2DM is reported to be around 40-80%. Hypertension should be detected and treated early in the course of DM to prevent CVD and to delay the progression of renal disease and diabetic retinopathy.

Pharmacological treatment should be initiated in patients with diabetes when the BP is persistently >130 mmHg systolic and/or >80 mmHg diastolic. People with diabetes should also be screened for proteinuria or microalbuminuria. The presence of microalbuminuria strongly predicts overt nephropathy and CVD. The presence of microalbuminuria or overt proteinuria should be treated even if the BP is not elevated. An angiotensin converting enzyme inhibitor (ACEI) or angiotensin receptor blocker (ARB) is preferred. In a proportion of patients, microalbuminuria may be normalised by higher doses of ACEIs and ARBs. Normalisation of microalbuminuria is associated with a reduction in the rate of decline in glomerular filtration rate.

Tight BP control should take precedence over the class of antihypertensive drug used. This often will require combination therapy. There are suggestions that a lower target BP may be necessary to maximally protect against the development and progression of cardiovascular and diabetic renal disease. In general, the SBP should be targeted to <130 mmHg and diastolic pressure <80 mmHg. The BP should be lowered even further to ≤125/75 mmHg in the presence of proteinuria of >1g/24 hours.

The treatment of hypertension in diabetes should follow the guidelines for the treatment of hypertension in general (Malaysian Clinical Practice Guidelines for the Management of Hypertension 2008).

Non-pharmacological management cannot be over emphasised. Dietary counselling should target at optimal body weight and take into consideration glycaemic control and the management of concomitant dyslipidaemia. Moderate dietary sodium restriction is advisable. It enhances the effects of BP lowering drugs especially ACEIs and ARBs. Further sodium restriction, with or without a diuretic, may be necessary in the presence of nephropathy or when the BP is difficult to control.

Certain classes of antihypertensive drugs may be disadvantageous in diabetes. Please refer to Table 8.

ACEIs are drugs of choice based on extensive data. If an ACEI is not tolerated, an ARB should be considered. ARBs have been reported to be superior to conventional non-ACEI antihypertensive drugs in terms of slowing the progression of nephropathy at the microalbuminuric and overt nephropathy stage.

Diuretics, calcium channel blockers (CCBs), beta-blockers and peripheral alpha blockers may be used as add-on therapy.

**Recommendations: Hypertension and Diabetes Mellitus**

1. ACEIs are the agents of choice for patients with diabetes without microalbuminuria or proteinuria [Grade A]
2. ARBs or ACEIs are the agents of choice for patients with diabetes and microalbuminuria or proteinuria [Grade A]
Table 8: Choice of antihypertensive drugs in diabetes patients with concomitant conditions (Adapted from Malaysian Clinical Practice Guidelines for the Management of Hypertension 2008 111 (Level III))

<table>
<thead>
<tr>
<th>Concomitant Disease</th>
<th>Diuretics</th>
<th>β-blockers</th>
<th>ACEIs</th>
<th>CCBs</th>
<th>Peripheral α-blockers</th>
<th>ARBs</th>
</tr>
</thead>
<tbody>
<tr>
<td>DM (without nephropathy)</td>
<td>+</td>
<td>+/-</td>
<td>+++</td>
<td>+</td>
<td>+/-</td>
<td>++</td>
</tr>
<tr>
<td>DM (with nephropathy)</td>
<td>++</td>
<td>+/-</td>
<td>+++</td>
<td>+++*</td>
<td>+/-</td>
<td>+++</td>
</tr>
<tr>
<td>Gout</td>
<td>+/-</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Dyslipidaemia</td>
<td>+/-</td>
<td>+/-</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Coronary heart disease</td>
<td>+</td>
<td>+++</td>
<td>+++</td>
<td>++</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Heart failure</td>
<td>+++</td>
<td>+++#</td>
<td>+++</td>
<td>+@</td>
<td>+</td>
<td>+++</td>
</tr>
<tr>
<td>Asthma</td>
<td>+</td>
<td>-</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Peripheral vascular disease</td>
<td>+</td>
<td>+/-</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Non-diabetic renal impairment</td>
<td>++</td>
<td>+</td>
<td>+++</td>
<td>+*</td>
<td>+</td>
<td>++</td>
</tr>
<tr>
<td>Renal artery stenosis</td>
<td>+</td>
<td>+</td>
<td>+++$</td>
<td>+</td>
<td>+</td>
<td>++$</td>
</tr>
<tr>
<td>Elderly with no co-morbid conditions</td>
<td>+++</td>
<td>+</td>
<td>+</td>
<td>+++</td>
<td>+/-</td>
<td>+</td>
</tr>
</tbody>
</table>

The grading of recommendation from (+) to (+++) is based on increasing levels of evidence and/or current widely accepted practice

+/-  Use with care
-    Contraindicated
*    Only non-dihydropyridine CCB
#    Metoprolol, bisoprolol, carvedilol – dose needs to be gradually titrated
@    Current evidence available for amlodipine and felodipine only
$    Contraindicated in bilateral renal artery stenosis
3.13 Diabetic Dyslipidaemia

DM is a coronary heart disease (CHD) risk equivalent. Control of hyperglycaemia in T2DM has not been associated with significant decrease in CVD events\textsuperscript{17, 115, 116} (Level I) except in overweight people with diabetes who were given metformin\textsuperscript{60} (Level I). Thus, efforts must also be directed to control other risk factors such as dyslipidaemia, hypertension and other new emerging risk factors.

Screening

In adult patients, test for lipid disorders at least annually and more often if needed to achieve goals. In adults with low-risk lipid values (LDL cholesterol <2.6mmol/L, HDL cholesterol >1.0mmol/L in males and >1.3 mmol/L in females and TG <1.7mmol/L), lipid assessments may be repeated every year.

In people with diabetes:

a) Primary target: LDL cholesterol
   i) In individuals without overt CVD
   • All patients over the age of 40 years should be treated with a statin regardless of baseline LDL cholesterol levels.\textsuperscript{117-118} (Level I)

   ii) In individuals with overt CVD
   • All patients should be treated with a statin.\textsuperscript{119} (Level I)
   • The target of LDL cholesterol level is 1.8mmol/L.\textsuperscript{118-120} (Level I)

b) Secondary target: Non-HDL cholesterol, HDL cholesterol and TG
   i) Non-HDL cholesterol <3.4mmol/L (when TG >2.3mmol/L)
   ii) HDL cholesterol >1.0 mmol/L for males
       >1.2 mmol/L for females
   iii) TG <1.7 mmol/L

In children and adolescents with T2DM, screening for lipid disorders should be done at diagnosis after glycaemic control is achieved. If normal lipid values are obtained, screening should be repeated every TWO years.\textsuperscript{121-124}

Lifestyle modification focusing on the reduction of saturated fat, \textit{trans} fat, and cholesterol intake; weight loss (if indicated) and increased physical activity have been shown to improve the lipid profile in patients with diabetes.

Table 9: Drug Therapy for Diabetic Dyslipidaemia

<table>
<thead>
<tr>
<th>Lipid Goal</th>
<th>Initial Drug</th>
<th>Suggested Addition in Order of Preference</th>
</tr>
</thead>
<tbody>
<tr>
<td>1) Lower LDL cholesterol</td>
<td>Statins</td>
<td></td>
</tr>
<tr>
<td>2) Increase HDL cholesterol</td>
<td>Fibrate or Nicotinic Acid*</td>
<td></td>
</tr>
<tr>
<td>3) Lower TG</td>
<td>Fibrates</td>
<td>Statins**</td>
</tr>
<tr>
<td>4) Treat Combined Hyperlipidaemia</td>
<td>Statins**</td>
<td>Fibrates Resin plus Fibrates Nicotinic Acid</td>
</tr>
</tbody>
</table>

* with careful monitoring and keeping dose <1.5 g/day
** high dose may be required
In patients with very high TG, reduction of carbohydrate intake is emphasised.

Lowering TG in patients with clinical CVD and normal LDL cholesterol level with a fibrate is associated with a reduction in cardiovascular events. 125 (Level I)

Combination therapy using statins and other lipid-lowering agents may be necessary to achieve lipid targets but has not been evaluated in outcome studies for either CVD event reduction or safety. 126 (Level I)

Statin therapy is contraindicated in pregnancy.

Treatment strategies in children and adolescents are no different with regards to dietary and glycaemic control. Lipid lowering medications should only be initiated in those >10 years old. 121

<table>
<thead>
<tr>
<th>Recommendations: Diabetic Dyslipidaemia</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. All patients <em>without</em> overt CVD over the age of 40 years should be treated with a statin regardless of baseline LDL cholesterol levels. [<em>Grade A</em>]</td>
</tr>
<tr>
<td>2. All patients <em>with</em> overt CVD should be treated with a statin. [<em>Grade A</em>]</td>
</tr>
</tbody>
</table>
SECTION 4 Metabolic Syndrome

The metabolic syndrome is a clustering of features which puts an individual at high risk of cardiovascular disease and T2DM. 127-130 (Level I)

4.1 Definition

There have been various attempts to define the metabolic syndrome. The World Health Organisation (WHO) 1999 and the National Cholesterol Education Program (NCEP) (Adult Treatment Panel III) 2001 for instance, provide two different definitions. 122, 131 (Level III) This has led to confusion and the lack of applicability in different ethnic populations. 132 (Level III)

The IDF consensus worldwide definition of the metabolic syndrome 127 (Level III)

Based on the IDF definition, a person has the metabolic syndrome when they have:

Central obesity [defined as WC 90cm for men and 80cm for women (ethnicity specific values)]. A practical approach in the clinic would be to use the WC as a means of identifying those at risks of CVD and diabetes.

Plus any two of the following four factors:

- Raised TG level: >1.7 mmol/L, or specific treatment for this lipid abnormality
- Reduced HDL cholesterol: <1.0 mmol/L in males and <1.3 mmol/L in females, or specific treatment for this lipid abnormality
- Raised blood pressure: systolic BP ≥130 mmHg or diastolic BP ≥85 mmHg, or on treatment of previously diagnosed hypertension
- Raised FPG ≥5.6 mmol/L, or previously diagnosed T2DM. If FPG >5.6 mmol/L, OGTT is strongly recommended but is not necessary to define presence of the syndrome.

4.2 Management

The main aim of therapy is to reduce the risk of CVD and the development of T2DM. 127 (Level III) In those who have established T2DM, refer to appropriate section.

Management should encompass the following:

Lifestyle changes (Please refer to Lifestyle Modification section, pages 12-14)
In individuals who do not achieve targets (Please refer to Targets for Control, page 10) through lifestyle changes, individual component of the syndrome should be treated pharmacologically.

Obesity in Type 2 Diabetes Mellitus

In obese patients with diabetes, a weight loss of 5 – 10% of initial body weight improves insulin sensitivity, reduces blood pressure and improves dyslipidaemia. 133 (Level III), 134-137 (Level I)

The optimal rate of weight loss is 1 – 2 kg/month. 138 (Level I)

In children and adolescents who are still growing in stature, maintenance of weight results in reduction in BMI, insulin sensitivity and metabolic profile. However weight loss would be desirable if there are associated severe co-morbidities or obstructive sleep apnoea syndrome (OSAS).
Management should include the following:

a) *Lifestyle intervention* \(^{139-141}\) (Level I) (Please refer to Lifestyle Modification section, pages 12-14)

b) *Use of pharmacological agents if lifestyle measures fail to achieve the desired weight loss after an adequate trial of 3 to 6 months* \(^{127-128}\) (Level III)
   - **Appropriate choice of anti-diabetic agent**
     - Incretin mimetics/analogues usually cause weight loss \(^{76-80}\) (Level I)
     - Metformin, acarbose and DPP-4 inhibitors are weight neutral \(^{71,140-143}\) (Level I)
     - SUs, TZD and insulin can result in significant weight gain \(^{42,75}\) (Level I)
   - **Pharmacological treatment of obesity**
     - Can only be justified when combined with diet, lifestyle changes and behaviour modifications
     - Adjustments to OAD agents may be required as the individual with diabetes loses weight to reduce the risk of hypoglycaemia
   - **Anti-obesity agents proven for use in people with diabetes include orlistat* \(^{144}\) (Level I) and sibutramine* \(^{145}\) (Level I)

c) *Bariatric surgery may be an option in patients with BMI >35 kg/m\(^2\)*

Anti-obesity agents and bariatric surgery are not recommended in children.

**Recommendations: Metabolic syndrome**

1. The metabolic syndrome is a clustering of features, which puts an individual at high risk of cardiovascular disease and T2DM. [Grade A]
2. 5-10% body weight reduction reduces insulin resistance. [Grade C]
3. Individual components of the syndrome should be treated to target values. [Grade C]
4. T2DM should be managed to current recommended standards. [Grade A]
SECTION 5 MANAGEMENT OF CHRONIC COMPLICATIONS

5.1 Introduction
- People with diabetes should be screened for complications at diagnosis and thereafter at yearly intervals. 2
- The UKPDS data confirmed that in T2DM, improvement of glycaemic control by lowering the HbA1c lowers the risk of developing both macrovascular and microvascular complications. 42, 60 (Level I)

5.2 Detection and Treatment of Diabetes Complications

Microvascular complications

5.2.1 Retinopathy

Introduction
The initial assessment should be conducted at the time of diagnosis of T2DM and annually thereafter.

Pregnant women with T2DM (not gestational diabetes) should have retinal examination during each trimester. 146 (Level II-3)

Eye Examination
Visual acuity is assessed with a Snellen chart and any refractive error corrected with a pinhole in addition to asking the patient to wear his bifocals or glasses for presbyopia.

Fundus examination must be conducted through a dilated pupil (tropicamide 0.5% or 1.0%) by using a direct ophthalmoscope to improve sensitivity. Photography with a non-mydriatic fundus camera may be used to screen a large number of people with diabetes.

Treatment
Achieve and maintain tight glycaemic and blood pressure control. 42, 97, 147-150 (Level I)

Patients with pre-proliferative or proliferative retinopathy may experience a temporary worsening of retinopathy when the blood glucose level is rapidly lowered. 151 (Level I)

Referral to an ophthalmologist is necessary for the following situations: 152-153 (Level III)
1. Unexplained poor vision
2. Diabetic retinopathy greater than occasional microaneurysms
3. Macular oedema or hard exudates within the macula

Refer urgently to an ophthalmologist if the following findings are noted
1. Sudden visual deterioration
2. New vessels on fundoscopy
3. Rubeosis iridis
4. Vitreous haemorrhage
5. Retinal detachment

Recommendations: Retinopathy
1. The initial assessment should be conducted at the time of diagnosis of T2DM and annually thereafter. [Grade C]
2. Refer to ophthalmologist as indicated above. [Grade C]
5.2.2 Nephropathy

Introduction

Diabetic Nephropathy (DN) is a major cause of chronic kidney disease (CKD) contributing to 57% of new patients requiring dialysis in 2007 in Malaysia. 154 (Level III) DN is also a major risk factor for cardiovascular morbidity and mortality. The diagnosis of DN is made clinically by the presence of proteinuria (either microalbuminuria or overt proteinuria). Progression to end stage renal disease (ESRD) requiring renal replacement therapy occurs in the majority of patients, particularly those with poor diabetic and blood pressure control.

Screening

Screening allows early diagnosis and intervention.

Microalbuminuria refers to the presence of a small amount of albumin in the urine which cannot be detected with the usual urine dipstick. It 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. Microalbuminuria is the earliest sign of diabetic nephropathy and predicts increased cardiovascular mortality and morbidity and end-stage renal failure. 16, 155 (Level III)

Recommendations for Screening

1. Screening for proteinuria should be performed at diagnosis and annually. [Grade C]
2. Urine should be screened for proteinuria with conventional dipstick on an early morning urine specimen. [Grade C]
3. If urine dipstick for proteinuria is negative, screening for microalbuminuria should be performed on an early morning urine specimen. [Grade C]
4. If microalbuminuria is detected, confirmation should be made with 2 further tests within 3 to 6 months. [Grade C]
5. If microalbuminuria is not detected, re-screening should be performed annually. [Grade C]

Management

If proteinuria is detected a 24 hour urine collection for protein (or a urine protein-creatinine ratio) or overnight timed urine collection should be performed to rule out postural proteinuria.

Blood pressure and glycaemic control are crucial in preventing or retarding progression of diabetic nephropathy. 14, 85 (Level I)

In people with diabetes the target BP is ≤130 mmHg/80 mmHg 109 (Level III) but in patients with proteinuria of >1 gram a day, the target is ≤125 mmHg/75 mmHg 2, 96 (Level III), 97,110-111 (Level I)

Several anti-hypertensive agents will be needed to achieve these targets.

Renin-angiotensin blockers reduce microalbuminuria or proteinuria and slow the progression of diabetic nephropathy. These effects have been shown to be independent of their effects on BP control. Thus ACEIs or ARBs should be initiated unless contraindicated. 103-104 (Level I), 105 (Level III), 111, 156-157 (Level II-1)

Other measures include lipid control, stopping smoking, weight reduction and moderate protein and salt restriction.
Referral to Nephrologist

Referral should be made if the serum creatinine exceeds 200 µmol/L \(^{16}\) (Level III) and earlier in patients with haematuria, nephritic syndrome, absence of retinopathy (where the diagnosis of diabetic nephropathy may be in doubt), difficult to control blood pressure and worsening renal function.

### Recommendations: Nephropathy

1. Screening for proteinuria should be performed at diagnosis and annually. \([\text{Grade C}]\)
2. Referral to nephrologist should be made if the serum creatinine exceeds 200 µmol/L and earlier in patients with haematuria, nephritic syndrome, absence of retinopathy (where the diagnosis of diabetic nephropathy may be in doubt), difficult to control blood pressure and worsening renal function. \([\text{Grade C}]\)
3. Target BP in diabetics should be \(\leq 130/80\) and \(\leq 125/75\) in patients with proteinuria \(>1\)g/day. \([\text{Grade A}]\)
4. ACEIs or ARBs should be initiated in patients with microalbuminuria or proteinuria. \([\text{Grade A}]\)

### 5.2.3 Neuropathy

#### Introduction

Diabetic peripheral neuropathy may be defined as “the presence of symptoms and/or signs of peripheral nerve dysfunction in people with diabetes after the exclusion of other causes”. \(^{158}\) (Level III)

Diabetic peripheral neuropathy may be asymptomatic in a large proportion of cases (up to 50%) \(^{159}\) (Level III) and requires clinical examination to document/unveil its existence. It causes or contributes to significant morbidity and mortality. \(^{158-159}\) (Level III)

There are 5 neuropathies in diabetes: distal symmetrical polyneuropathy, proximal asymmetrical neuropathy (diabetic amyotrophy), autonomic neuropathy, radiculopathy and mononeuritis multiplex.

#### Screening

Diabetic peripheral neuropathy may be diagnosed reasonably accurately (>87% sensitivity) by bedside clinical methods namely: \(^{160}\) (Level II)

- a. 10-g Semmes-Weinstein monofilament pressure sensation
- b. 128 Hz tuning fork vibration perception (on-off or absolute)
- c. ankle jerks (deep tendon reflexes)
- d. pin prick

These bedside tests should be performed at least annually.

#### Prevention

Diabetic peripheral neuropathy can be prevented by maintaining good glycaemic control. \(^{161-162}\) (Level I)

#### Treatment

1. Relief of symptoms includes the use of anticonvulsant agents \(^{163}\) (Level II) e.g. gabapentin \(^{164}\) (Level I), lamotrigine \(^{165}\) (Level I), carbamazepine or tricyclic antidepressants e.g. amitriptyline \(^{166}\) (Level II).
2. Achieve tight glycaemic control.
**Recommendations: Neuropathy**

1. Assessment for peripheral neuropathy should be performed at diagnosis and annually.  
   *[Grade C]*

2. The sensory symptoms of painful diabetic peripheral neuropathy may be treated with anticonvulsants like gabapentin, lamotrigine, carbamazepine or tricyclic antidepressants like amitriptyline.  
   *[Grade B]*

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**Macrovascular complications**

**5.2.4 Coronary Heart Disease (CHD)**

**Introduction**

The major concern of T2DM is its increased risk (two to four fold) for CHD, manifested as angina, myocardial infarction (MI), CCF and sudden death. In addition T2DM, independent of CHD, may lead to diabetic cardiomyopathy. CHD accounts for up to two-third of deaths in T2DM. The increased risk of CHD in patients with diabetes is only partly explained by concomitant risk factors such as hypertension, obesity, dyslipidaemia, and smoking. It has been shown that hyperglycaemia itself and its consequences are very important for the increased risk for CHD and related mortality.\(^{151, 167, 168}\) (Level II-1), \(^{169, 170, 171}\) (Level I)

CHD in T2DM is characterized by its early onset, extensive disease at the time of diagnosis, and higher morbidity and mortality after MI. Angiographically the disease is more diffuse, involving multiple coronary arteries including small and distal vessels.\(^{169}\) (Level II-2), \(^{170, 171}\) (Level I)

The similar occurrence of MI in patients with T2DM and those without T2DM who had previous MI has given rise to the notion that T2DM is a CHD-defining disease. As such, we should manage cardio-metabolic risks associated with T2DM and CHD in T2DM aggressively. The challenge faced by doctors is to accurately identify patients with asymptomatic CHD.\(^{172, 173}\) (Level II-2)

**Screening**

Typical symptoms of CHD warrant a prompt referral to a cardiologist for further assessment. However it is quite common for patients with T2DM to have atypical symptoms or even ‘silent’ CHD. Atypical symptoms include dyspnoea, fatigue, and gastrointestinal symptoms associated with exertion.\(^{174}\) (Level II-1)

When it comes to screening asymptomatic patients with T2DM for CHD we propose the following approach:

A. Performance of a resting ECG \(^{175}\)

AND

B. Application of an established cardiovascular risk assessment tool (Framingham Risk Score \(^{176}\) or UKPDS Risk Engine \(^{177}\)) \(^{178, 179}\)

Patients with an abnormal resting ECG or those having high risk score based on either one of the two risk assessment tools should be referred to a cardiologist for further evaluation. It is important to note that a normal resting ECG does not exclude CHD.\(^{174}\) (Level II-1), \(^{180, 181}\) (Level I)
The cardiovascular risk assessment tools such as the Framingham Risk Score and NCEP III Risk Assessment Tool can be applied to persons with or without diabetes. Both these scores have been analysed in different populations and the conclusion is that, while the absolute risk may differ from population to population, the proportionate risk ranking provided by these scores is consistent across populations. 182, 183 (Level II-2)

On the other hand, the diagnosis of metabolic syndrome identifies people at a higher risk of CHD than those in the general population. However it does not provide a better or even equally good prediction of cardiovascular risk than the risk assessment tools mentioned above which are based on the major cardiovascular risk factors. 184 (Level III)

In addition, the following patients with T2DM should also be considered for screening for CHD:
1. Those with peripheral or cerebrovascular disease. 172, 173 (Level I)
2. Those leading a sedentary lifestyle, age ≥35 years and plan to begin a vigorous exercise program.
3. Those with two or more of the risk factors listed below. 185, 186 (Level I)
   a) Total cholesterol >4.0 mmol/L, LDL cholesterol >2.0 mmol/L, or HDL cholesterol <1.0 mmol/L for males and <1.2 mmol/L for females.
   b) Blood pressure >130/85 mmHg
   c) Smoking
   d) Family history of premature CHD
   e) Positive micro/macroalbuminuria test

**Recommendations: Coronary Heart Disease**

1. Normal resting ECG does not exclude CHD. [Grade B]
2. The risk stratification tools and ECG are part of risk assessment. [Grade B]
Aspirin for Primary Prevention of Cardiovascular Disease in People with Diabetes

There is strong evidence that aspirin is effective for secondary prevention of cardiovascular events. However, it is unclear whether it prevents primary cardiovascular events in people who are at high risk of CVD, such as those with T2DM.

The American Heart Association (AHA) and ADA guidelines recommended aspirin for primary prevention in diabetes based on a reduction of events in a mixed group of patients with and without CVD in the Early Treatment of Diabetic Retinopathy Study (ETDRS). The assumption is that the positive findings of aspirin in patients with symptomatic CVD can be extended to those high-risk patients without clinical evidence of CVD. However, six other well-controlled trials, including the Women’s Health Study and Physicians’ Health Study, have shown no benefit of aspirin in primary prevention even for at risk patients.

The two most recent randomised controlled trials which addressed this issue are the Prevention of Progression of Arterial Disease and Diabetes (POPADAD) and the Japanese Primary Prevention of Atherosclerosis with Aspirin for Diabetes (JPAD) studies, did not show any significant benefit.

In general, the decision to start patients on low dose aspirin as a primary prevention of CVD should be individualised. However, based on detailed examination of current evidence we recommend that asymptomatic people with diabetes who have a high risk of developing CVD based on the Framingham Risk Assessment Score (>10% risk over a 10 year period) be treated with low dose aspirin. In doing so, it is essential that the risk of gastrointestinal bleeding in individual patients be taken into consideration.

<table>
<thead>
<tr>
<th>Recommendation: Aspirin for Primary Prevention of Cardiovascular Disease in People with Diabetes</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Primary prevention of CVD with low dose aspirin (75mg-100mg) is not recommended in people with diabetes [Grade A] unless they are at high risk based on Framingham Risk Assessment Score [Grade C]</td>
</tr>
</tbody>
</table>
5.2.5 Cerebrovascular Disease
(Refer to Malaysian Clinical Practice Guidelines on the Management of Stroke, 2006)

[Note: The above guideline is also available electronically at the following websites: www.moh.gov.my; www.acadmed.org.my; www.neuro.org.my]

Combination of Micro- and Macrovascular complications

5.2.6 Diabetic Foot

Introduction

Foot ulcerations and amputations are major causes of morbidity and mortality in patients with diabetes. In the 2006 Third National Health Morbidity Survey, the prevalence of lower limb amputation among patients with diabetes was 4.3%. \(^1\) (Level III) Peripheral neuropathy predisposes to ulcerations and vasculopathy retards the healing process.

Prevention of foot ulcers:

Foot ulcers usually precede amputated digits and limbs. Hence preventing the first ulcer would reduce the incidence of amputations. Prevention starts with examination of the feet (shoes and socks removed) and identifying those at high risk of ulceration. Those patients at risk are then given relevant education to reduce the likelihood of future ulcers. The feet should be examined at least once annually or more often in the presence of risk factors. \(^193\) (Level III)

Risk factors for Foot Ulcers \(^194\) (Level III)
1) Previous amputation
2) Past foot ulcer history
3) Peripheral neuropathy
4) Foot deformity
5) Peripheral vascular disease
6) Visual impairment
7) Diabetic nephropathy (especially patients on dialysis)
8) Poor glycaemic control
9) Cigarette smoking

Neuropathy should be assessed with a 10g monofilament and one other modality i.e. pin prick, vibration sense using a 128Hz tuning fork, ankle reflexes or vibration perception threshold testing using a biothesiometer. Loss of protective sensation (LOPS) would be considered present if one or more of the tests are abnormal.

Vasculopathy is assessed by asking for symptoms of claudication and examining the dorsalis pedis and posterior tibial for pulses.

Relevant education for patients; \(^195\) (Level III)

- In the presence of feet with reduced sensation, look at feet daily using a mirror to detect early ulcerations.
- Wear flat, soft and well fitted shoes to avoid callousities.
- Ensure no foreign objects in the shoes before putting feet in.
- Have one pair of shoes for indoor use as well.

An ulcer in a patient with any of the above risk factors will warrant an early referral to a specialist for shared care. Ulcers with cellulitis will require antibiotics. Trauma induced ulcers with no other risk factors will require the standard wound care and close follow-up until full recovery.
Recommendations: Diabetic Foot

1. Examine feet of patients at least once every year to identify individuals who would then require intensive education on self care to avoid ulcers and amputations. [Grade B]
2. To detect clinically relevant neuropathy, at least use a 10g monofilament. [Grade C]

5.2.7 Erectile Dysfunction

Introduction
Erectile Dysfunction (ED) is defined as the consistent or recurrent inability of a male to attain and/or maintain a penile erection sufficient for sexual performance. ED affects approximately 34 to 45% of men with diabetes. ED results from vasculopathy and/or autonomic neuropathy and/or psychological factors. Risk factors include increasing age, increasing duration of diabetes, poor glycaemic control, smoking, hypertension, dyslipidaemia and CVD.

Screening
All adult males over the age of 40 should be asked about ED since they usually do not volunteer problems with ED. Preservation of early morning erection suggests a psychological cause. Screening can be done using the 5-item version of the International Index of Erectile Function (IIEF) questionnaire.

Treatment
Avoid medications (if possible) that may cause ED
- Antihypertensives (thiazides, beta blockers, methyldopa, spironolactone)
- Antidepressants and tranquilisers
- NSAIDS
- H2 antagonists (cimetidine)
- Narcotics
- Miscellaneous drugs (ketoconazole, anti-cancer agents)

Psychosexual counselling is recommended in functional ED.

Phosphodiesterase-5 (PDE-5) inhibitors e.g. sildenafil, tadalafil and vardenafil can be used to treat ED and should be offered as first-line therapy to men with diabetes wishing treatment. PDE-5 inhibitors are contraindicated in unstable angina, poor exercise tolerance or nitrate medication.

Referral to a urologist may be necessary for those not responding to PDE-5 inhibitors.

Other therapies include intracavernosal injections, intraurethral alprostadil, vacuum devices with constricting band and surgery.

Recommendations: Erectile Dysfunction

1. All adult males with diabetes over the age of 40 should be asked about ED. [Grade C]
2. PDE-5 inhibitor should be offered as first-line therapy if there are no contraindications. [Grade A]
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. [Grade C]
6.1 For healthy and people at risk
There are many risk factors that predispose an individual or population to developing glucose intolerance and finally diabetes. There is ample evidence that lifestyle related changes are the main factors influencing the explosion of diabetes in modern times. As diabetes is an endpoint in the glucose tolerance continuum in the general population, it is possible to halt this slide from normal to IGT and subsequently T2DM.

6.2 Prediabetes
There is evidence that interventions can reduce the conversion of IFG/IGT to frank T2DM.
- Diet and physical activity are the mainstay of therapy 5, 32, 214-216 (Level I)

In addition to lifestyle intervention, metformin should be considered for those at very high risk (combined IFG & IGT plus other risks factors) or for those who fail lifestyle therapy after 6 months. 2,32,217 (Level I)

Other pharmacological interventions listed below have also been shown to prevent/delay the onset of T2DM. 218-220 (Level I)
- Acarbose
- Orlistat
- Rosiglitazone

* All the above drugs including metformin have not yet been approved for the treatment of prediabetes. Use of these agents is at the discretion of the doctor as off label use.

The use of other agents like ACEIs, ARBs and statins are not recommended solely for the purpose of primary prevention.

It must be noted that most of the subjects in the studies above were either overweight or obese and were at high risk for developing DM. The reduced conversion rate from IGT to frank T2DM is associated with weight loss. Thus weight loss remains a priority in the prevention of DM. Those at risk include those with IGT or IFG but also those with a family history of diabetes (1st degree relatives), GDM, hypertension, vascular disease, dyslipidaemia, obesity or overweight with central obesity and PCOS.

It must be emphasised that while pharmaceutical intervention is available, lifestyle intervention programmes have greater efficacy 5 (Level I) and are practical and cost effective making its implementation possible in any primary health care setting. 2,5,133,214,215

Longstanding positive behavioural adaptation and lifestyle modification will provide the answers to our fight against the impending epidemic of T2DM.

**Recommendation: Prevention of Type 2 Diabetes Mellitus**

1. In individuals with IGT, a structured program of lifestyle modification that includes moderate weight loss and regular physical activity has been shown to reduce the risk of T2DM. **[Grade A]**
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58. Lorenz RA. Modern Insulin Therapy for Type 1 Diabetes Mellitus. *Primary Care: Clinics in Office Practice* 1999; 26: 917-929.


143. Scheen AJ. Is There a Role for -Glucosidase Inhibitors in the Prevention of Type 2 Diabetes Mellitus? *Drugs* 2003; 63: 933 – 951.


Randomized, Controlled Study. *Neurology* 2001; 57: 505 – 509.


### Carbohydrate Content of Common Malaysian Foods

<table>
<thead>
<tr>
<th>Foods</th>
<th>Serving</th>
<th>Calories (kcal)</th>
<th>Carbohydrate content (g)</th>
<th>Approx. Carbohydrate Exchanges*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cooked rice</td>
<td>1 bowl (159g)</td>
<td>207</td>
<td>48</td>
<td>3</td>
</tr>
<tr>
<td>Roti canai</td>
<td>1 piece (95g)</td>
<td>301</td>
<td>46</td>
<td>3</td>
</tr>
<tr>
<td>Chappati</td>
<td>1 piece (100g)</td>
<td>300</td>
<td>47</td>
<td>3</td>
</tr>
<tr>
<td>Curry mee</td>
<td>1 bowl (450g)</td>
<td>549</td>
<td>55</td>
<td>4</td>
</tr>
<tr>
<td>Fried noodles (mee/mee hoon)</td>
<td>1 plate (170g)</td>
<td>281</td>
<td>41</td>
<td>3</td>
</tr>
<tr>
<td>Bread (white/wholemeal)</td>
<td>1 slice (30g)</td>
<td>70</td>
<td>15</td>
<td>1</td>
</tr>
<tr>
<td>Biscuits, unsweetened</td>
<td>2 pieces (18g)</td>
<td>80</td>
<td>14</td>
<td>1</td>
</tr>
<tr>
<td>Curry puff</td>
<td>1 piece (40g)</td>
<td>128</td>
<td>17</td>
<td>&gt;1</td>
</tr>
<tr>
<td>Potato</td>
<td>1 medium (90g)</td>
<td>90</td>
<td>16</td>
<td>1</td>
</tr>
<tr>
<td>Dhall (raw)</td>
<td>½ cup (98g)</td>
<td>98</td>
<td>64</td>
<td>4</td>
</tr>
<tr>
<td>Full cream milk</td>
<td>1 cup (250 ml)</td>
<td>187</td>
<td>18</td>
<td>1</td>
</tr>
<tr>
<td>Low fat milk</td>
<td>1 cup (250 ml)</td>
<td>131</td>
<td>12</td>
<td>1</td>
</tr>
<tr>
<td>Skim milk powder</td>
<td>4 tablespoon (28g)</td>
<td>100</td>
<td>16</td>
<td>1</td>
</tr>
<tr>
<td>Condensed milk, sweetened</td>
<td>2 tablespoon (40g)</td>
<td>126</td>
<td>21</td>
<td>1.5</td>
</tr>
<tr>
<td>Apple/orange</td>
<td>1 medium (114g)</td>
<td>40</td>
<td>9</td>
<td>&lt;1</td>
</tr>
<tr>
<td>Banana (pisang mas)</td>
<td>1 small (50g)</td>
<td>40</td>
<td>9</td>
<td>&lt;1</td>
</tr>
<tr>
<td>Star fruit</td>
<td>1 medium (260g)</td>
<td>56</td>
<td>11</td>
<td>1</td>
</tr>
<tr>
<td>Durian local</td>
<td>5 small seeds (189g)</td>
<td>64</td>
<td>12</td>
<td>1</td>
</tr>
<tr>
<td>Langsat/grapes/longan</td>
<td>8 small (233 g)</td>
<td>52</td>
<td>12</td>
<td>1</td>
</tr>
<tr>
<td>Guava</td>
<td>½ fruit (100g)</td>
<td>50</td>
<td>11</td>
<td>1</td>
</tr>
<tr>
<td>Watermelon/papaya/pineapple</td>
<td>1 slice (160g)</td>
<td>56</td>
<td>11</td>
<td>1</td>
</tr>
<tr>
<td>Mango</td>
<td>1 small (100g)</td>
<td>50</td>
<td>11</td>
<td>1</td>
</tr>
<tr>
<td>Glycaemic Index of Foods</td>
<td>Low GI (&lt;55)</td>
<td>Intermediate GI (56-70)</td>
<td>High GI (&gt;70)</td>
<td></td>
</tr>
<tr>
<td>--------------------------</td>
<td>--------------</td>
<td>-------------------------</td>
<td>---------------</td>
<td></td>
</tr>
<tr>
<td>Sponge cake, plain</td>
<td>Pastry</td>
<td>Waffles, doughnut</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Unsweetened apple/carrot/orange juice</td>
<td>Soft drinks (carbonated &amp; sugar) Cordial drink</td>
<td>Sports drink</td>
<td></td>
<td></td>
</tr>
<tr>
<td>All bran breakfast cereal</td>
<td>Instant porridge Wheat biscuits</td>
<td>Cornflakes</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Brown rice</td>
<td>White rice</td>
<td>Jasmine rice</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Basmati rice</td>
<td>Glutinous rice</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Capati</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Idli</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Full fat milk</td>
<td>Ice cream</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Skim milk</td>
<td>Sweetened condensed milk</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Low fat milk</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yogurt</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Soymilk</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Apple</td>
<td>Papaya</td>
<td>Dates</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Banana</td>
<td>Pineapple</td>
<td>Lychee</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Grapes</td>
<td></td>
<td>Watermelon</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mango</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Baked beans</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Chickpeas</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lentils</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mung bean</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fructose</td>
<td>Honey</td>
<td>Glucose</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lactose</td>
<td>Sucrose</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
# Examples of Physical Activity

<table>
<thead>
<tr>
<th>Mild Activities</th>
<th>Moderate activities</th>
<th>Strenuous activities</th>
</tr>
</thead>
<tbody>
<tr>
<td>Brisk walking on flat surfaces</td>
<td>Faster walking</td>
<td>Jogging</td>
</tr>
<tr>
<td>Cycling on level surface</td>
<td>Walking down stairs</td>
<td>Climbing stairs</td>
</tr>
<tr>
<td>Gardening, weeding</td>
<td>Cycling</td>
<td>Football</td>
</tr>
<tr>
<td>House painting</td>
<td>Doing heavy laundry</td>
<td>Squash</td>
</tr>
<tr>
<td>Mopping the floor</td>
<td>Ballroom dancing (slow)</td>
<td>Swimming</td>
</tr>
<tr>
<td>Cleaning windows</td>
<td>Badminton (non-competitive)</td>
<td>Tennis</td>
</tr>
<tr>
<td>Golf – walking &amp; pulling</td>
<td>Aerobics (low impact)</td>
<td>Jumping rope</td>
</tr>
<tr>
<td>Bowling</td>
<td></td>
<td>Basketball</td>
</tr>
</tbody>
</table>
## Cereals, Grain Products and Starchy Vegetables (Each item contains 15g carbohydrate)

<table>
<thead>
<tr>
<th>Cereals, Grain &amp; Bread</th>
<th>Serving Size</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rice, white unpolished (cooked)</td>
<td>1/3 Chinese bowl or ½ cup</td>
</tr>
<tr>
<td>Rice porridge (thick)</td>
<td>2/3 Chinese bowl or 1 cup</td>
</tr>
<tr>
<td>Kuey teow</td>
<td></td>
</tr>
<tr>
<td>Mee hoon</td>
<td></td>
</tr>
<tr>
<td>Tang hoon</td>
<td>1/3 Chinese bowl or ½ cup</td>
</tr>
<tr>
<td>Spaghetti</td>
<td></td>
</tr>
<tr>
<td>Macaroni</td>
<td></td>
</tr>
<tr>
<td>Loh see fun</td>
<td></td>
</tr>
<tr>
<td>Yellow mee</td>
<td></td>
</tr>
<tr>
<td>Wanton Mee</td>
<td>1/3 piece</td>
</tr>
<tr>
<td>Egg noodle</td>
<td></td>
</tr>
<tr>
<td>Idli</td>
<td></td>
</tr>
<tr>
<td>Putu mayam</td>
<td>1 piece</td>
</tr>
<tr>
<td>Tosai</td>
<td>½ piece</td>
</tr>
<tr>
<td>Chappati</td>
<td>1/3 piece</td>
</tr>
<tr>
<td>Bread (wholemeal, high fiber, white/brown)</td>
<td>1 slice</td>
</tr>
<tr>
<td>Plain roll</td>
<td>1 small piece</td>
</tr>
<tr>
<td>Burger bun</td>
<td></td>
</tr>
<tr>
<td>Pita bread, diameter 6”</td>
<td>½ piece</td>
</tr>
<tr>
<td>Oatmeal, cooked</td>
<td></td>
</tr>
<tr>
<td>Oats, uncooked</td>
<td>¼ cup</td>
</tr>
<tr>
<td>Muesli</td>
<td></td>
</tr>
<tr>
<td>Flour (wheat, rice, atta)</td>
<td>3 rounded tablespoons</td>
</tr>
<tr>
<td>Biscuits (plain, unsweetened)</td>
<td>3 pieces</td>
</tr>
<tr>
<td>Small thin, salted biscuits (4.5X4.5cm)</td>
<td>6 pieces</td>
</tr>
</tbody>
</table>
## Starchy Vegetables

<table>
<thead>
<tr>
<th>Item</th>
<th>Serving Size</th>
</tr>
</thead>
<tbody>
<tr>
<td>* Baked beans, canned</td>
<td>1/3 Chinese bowl or ½ cup</td>
</tr>
<tr>
<td>* Lentils</td>
<td>2/3 Chinese bowl or 1 cup</td>
</tr>
<tr>
<td>* (Contains more protein than other foods in the list i.e. 5g/serve)</td>
<td></td>
</tr>
<tr>
<td>Corn kernel (fresh/canned)</td>
<td>½ cup</td>
</tr>
<tr>
<td>Peas (fresh/canned)</td>
<td>½ cup</td>
</tr>
<tr>
<td>Breadfruit (sukun)</td>
<td></td>
</tr>
<tr>
<td>Carrot</td>
<td></td>
</tr>
<tr>
<td>Sweet Potato</td>
<td>½ cup</td>
</tr>
<tr>
<td>Tapioca</td>
<td></td>
</tr>
<tr>
<td>Yam</td>
<td></td>
</tr>
<tr>
<td>Pumpkin</td>
<td>1 cup (100g) / ½ cup</td>
</tr>
<tr>
<td>Corn on the cob, 6 cm length</td>
<td>1 small</td>
</tr>
<tr>
<td>Potato</td>
<td>1 small or ½ cup</td>
</tr>
<tr>
<td>Waterchestnut</td>
<td>4 pieces</td>
</tr>
<tr>
<td>All other leafy vegetables can be freely eaten</td>
<td></td>
</tr>
</tbody>
</table>

## Fruits (Each item contain 15g carbohydrate)

<table>
<thead>
<tr>
<th>Fruit</th>
<th>Serving Size</th>
</tr>
</thead>
<tbody>
<tr>
<td>Apple</td>
<td></td>
</tr>
<tr>
<td>Custard apple (buah nona)</td>
<td></td>
</tr>
<tr>
<td>Orange</td>
<td></td>
</tr>
<tr>
<td>Star Fruit</td>
<td></td>
</tr>
<tr>
<td>Pear</td>
<td>1 medium</td>
</tr>
<tr>
<td>Peach</td>
<td></td>
</tr>
<tr>
<td>Persimmon</td>
<td></td>
</tr>
<tr>
<td>Sapodilla (ciku)</td>
<td></td>
</tr>
<tr>
<td>Kiwi</td>
<td></td>
</tr>
<tr>
<td>Banana (emas)</td>
<td>1 small</td>
</tr>
<tr>
<td>Banana (except for emas)</td>
<td>½ whole</td>
</tr>
<tr>
<td>Fruit</td>
<td>Quantity</td>
</tr>
<tr>
<td>------------------------------</td>
<td>--------------</td>
</tr>
<tr>
<td>Hog plum (kedondong)</td>
<td>6 whole</td>
</tr>
<tr>
<td>Mangosteen</td>
<td>2 small</td>
</tr>
<tr>
<td>Plum</td>
<td></td>
</tr>
<tr>
<td>Duku Langsat</td>
<td></td>
</tr>
<tr>
<td>Grapes</td>
<td></td>
</tr>
<tr>
<td>Langsat</td>
<td>8 pieces</td>
</tr>
<tr>
<td>Grapes</td>
<td></td>
</tr>
<tr>
<td>Langsat</td>
<td></td>
</tr>
<tr>
<td>Longan</td>
<td></td>
</tr>
<tr>
<td>Water apple (jambu air), small</td>
<td>4 whole</td>
</tr>
<tr>
<td>Water apple (jambu air), big</td>
<td></td>
</tr>
<tr>
<td>Lychee</td>
<td>5 whole</td>
</tr>
<tr>
<td>Rambutan</td>
<td></td>
</tr>
<tr>
<td>Pamelo</td>
<td>5 slices</td>
</tr>
<tr>
<td>Papaya</td>
<td></td>
</tr>
<tr>
<td>Pineapple</td>
<td>1 slice</td>
</tr>
<tr>
<td>Watermelon</td>
<td></td>
</tr>
<tr>
<td>Soursop (durian belanda)</td>
<td></td>
</tr>
<tr>
<td>Guava</td>
<td>½ whole</td>
</tr>
<tr>
<td>Jackfruit (cempedak)</td>
<td>4 pieces</td>
</tr>
<tr>
<td>Jack fruit (nangka)</td>
<td></td>
</tr>
<tr>
<td>Prunes</td>
<td>3 pieces</td>
</tr>
<tr>
<td>Dates (kurma), dried</td>
<td>2 pieces</td>
</tr>
<tr>
<td>Raisin</td>
<td>1 dessert spoon</td>
</tr>
<tr>
<td>Durian</td>
<td>2 medium seeds</td>
</tr>
<tr>
<td>Mango</td>
<td>½ small</td>
</tr>
<tr>
<td>Lean Meat</td>
<td></td>
</tr>
<tr>
<td>--------------------------------</td>
<td>---------</td>
</tr>
<tr>
<td>Chicken (raw, without skin)</td>
<td>½ drumstick</td>
</tr>
<tr>
<td>Lean meat (beef/mutton/pork etc)</td>
<td>1 matchbox size</td>
</tr>
<tr>
<td>Poultry (chicken/duck)</td>
<td>½ drumstick</td>
</tr>
<tr>
<td>Egg (hen)</td>
<td>1 medium</td>
</tr>
<tr>
<td>Soya bean curd (taukua)</td>
<td>½ piece (60g)</td>
</tr>
<tr>
<td>Soya bean curd (soft, tauhoo)</td>
<td>¾ piece (90g)</td>
</tr>
<tr>
<td>Soya bean curd, sheet (Fucok)</td>
<td>1 ½ sheets (30g)</td>
</tr>
<tr>
<td>Tempeh</td>
<td>1 piece (45g)</td>
</tr>
<tr>
<td>Cheese, cheddar</td>
<td>2 thin slices (30g)</td>
</tr>
<tr>
<td>Cottage cheese</td>
<td>¼ small cup</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Fish, Shellfish</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Fish (e.g. ikan kembong, selar)</td>
<td>½ piece</td>
</tr>
<tr>
<td>Fish cutlet</td>
<td>¼ piece</td>
</tr>
<tr>
<td>Squid</td>
<td>1 medium</td>
</tr>
<tr>
<td>Crab meat</td>
<td></td>
</tr>
<tr>
<td>Lobster meat</td>
<td>¼ cup</td>
</tr>
<tr>
<td>Prawn meat</td>
<td></td>
</tr>
<tr>
<td>Cockles</td>
<td>20 small</td>
</tr>
<tr>
<td>* Dried red bean/mug bean</td>
<td>1/3 cup cooked</td>
</tr>
<tr>
<td>* Dhal gravy</td>
<td>1 cup cooked</td>
</tr>
<tr>
<td>* Taukua (soya bean hard)</td>
<td>½ piece</td>
</tr>
<tr>
<td>* Soft tauhu</td>
<td>¾ piece</td>
</tr>
<tr>
<td>* Fucuk</td>
<td>1 ½ sheet</td>
</tr>
<tr>
<td>* Tempeh</td>
<td>1 piece</td>
</tr>
</tbody>
</table>

**Fat** (Each item contains 5g of fat. Nuts and seeds also contain small amount of carbohydrate and protein besides fat)

<table>
<thead>
<tr>
<th>Fat</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Oil (all types)</td>
<td>1 level teaspoon (5g)</td>
</tr>
<tr>
<td>Butter, margarine</td>
<td></td>
</tr>
<tr>
<td>Cooking oil (all types)</td>
<td></td>
</tr>
<tr>
<td>Ingredient</td>
<td>Measurement</td>
</tr>
<tr>
<td>------------------------------------------------</td>
<td>---------------------------------</td>
</tr>
<tr>
<td>Mayonnaise</td>
<td>1 level teaspoon</td>
</tr>
<tr>
<td>Shortening, lard</td>
<td></td>
</tr>
<tr>
<td>Peanut butter (smooth or crunchy)</td>
<td>2 level teaspoons</td>
</tr>
<tr>
<td>Cream, unwhipped (heavy)</td>
<td></td>
</tr>
<tr>
<td>Cream cheese</td>
<td>1 level tablespoon</td>
</tr>
<tr>
<td>Salad dressing</td>
<td></td>
</tr>
<tr>
<td>Cream, unwhipped (light)</td>
<td></td>
</tr>
<tr>
<td>Coconut, shredded</td>
<td></td>
</tr>
<tr>
<td>Coconut milk (santan)</td>
<td>2 level tablespoons</td>
</tr>
<tr>
<td>Non dairy creamer, powder</td>
<td></td>
</tr>
<tr>
<td>Almond</td>
<td></td>
</tr>
<tr>
<td>Cashew nut</td>
<td>6 whole</td>
</tr>
<tr>
<td>Walnut</td>
<td>1 whole</td>
</tr>
<tr>
<td>Peanut</td>
<td>20 small</td>
</tr>
<tr>
<td>Sesame seed</td>
<td>1 level tablespoon</td>
</tr>
<tr>
<td>Watermelon seed (kuaci with shell)</td>
<td>¼ cup</td>
</tr>
<tr>
<td>Milk</td>
<td>[These foods contain varying amount of carbohydrate (12 - 15g CHO per exchange)]</td>
</tr>
<tr>
<td>Fresh cow's milk</td>
<td></td>
</tr>
<tr>
<td>UHT fresh milk</td>
<td>1 cup (240 ml)</td>
</tr>
<tr>
<td>Powdered milk (skim, full cream)</td>
<td>4 rounded tablespoons or 1/3 cup</td>
</tr>
<tr>
<td>Yogurt (plain/low fat)</td>
<td>¾ cup</td>
</tr>
<tr>
<td>Evaporate (unsweetened)</td>
<td>½ cup</td>
</tr>
<tr>
<td>Cheese</td>
<td>2 slices</td>
</tr>
<tr>
<td>Grated cheese</td>
<td>2 tablespoon</td>
</tr>
</tbody>
</table>
The 5-Item Version of the International Index of Erectile Function (IIEF-5)\textsuperscript{209}

Please choose the appropriate column for each question about your sexual abilities over the past 4 weeks.

<table>
<thead>
<tr>
<th>1. How do you rate your confidence that you could get and keep an erection?</th>
<th>Very low</th>
<th>Low</th>
<th>Moderate</th>
<th>High</th>
<th>Very high</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>2. When you had erections with sexual stimulation, how often were your erections hard enough for penetration (entering your partner)?</th>
<th>No sexual activity</th>
<th>Never or almost never</th>
<th>A few times (much less than half the time)</th>
<th>Sometimes (about half the time)</th>
<th>Most times (much more than half the time)</th>
<th>Almost always or always</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>3. During sexual intercourse, how often were you able to maintain your erection after you had penetrated (entered) your partner?</th>
<th>Did not attempt intercourse</th>
<th>Never or almost never</th>
<th>A few times (much less than half the time)</th>
<th>Sometimes (about half the time)</th>
<th>Most times (much more than half the time)</th>
<th>Almost always or always</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>4. During sexual intercourse, how difficult was it to maintain your erection to completion of intercourse?</th>
<th>Did not attempt intercourse</th>
<th>Extremely difficult</th>
<th>Very difficult</th>
<th>Difficult</th>
<th>Slightly difficult</th>
<th>Not difficult</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>5. When you attempted intercourse, how always or was it satisfactory for you?</th>
<th>Did not attempt intercourse</th>
<th>Never or almost never</th>
<th>A few times (much less than half the time)</th>
<th>Sometimes (about half the time)</th>
<th>Most times (much more than half the time)</th>
<th>Almost often always</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
<td></td>
</tr>
</tbody>
</table>

- All questions are preceded by the phrase ‘Over the past 4 weeks’
- Add the scores for each item 1-5 (total possible score = 25). ED Severity Classification: Total score 1-7 (severe ED); 8-11 (moderate ED); 12-16 (mild to moderate ED) 17-21 (mild ED); 22-25 (no ED)
Indeks Fungsi Seks Antarabangsa (IIEF-5) 209

Soalan-soalan ini bertanya tentang kesan ke atas kehidupan seks (kemampuan seks) anda akibat masalah ketegangan zakar (kemaluan atau ‘batang’ keras) di sepanjang 4 minggu yang lalu. Sila jawab soalan-soalan berikut dengan sejujur dan sejelas mungkin. Bagi menjawab soalan-soalan itu, definisi berikut adalah berkaitan:

- **Kegiatan seks** meliputi persetubuhan, belaian (rabaan, usapan), cumbuan dan perlancapan
- **Persetubuhan** ditakrif sebagai kemasukan zakar (kemaluan) ke dalam faraj (pintu rahim) pasangan (zakar anda memasuki alat kelamin pasangan anda)
- **Rangsangan seks (naik nafsu seks)** meliputi keadaan seperti mencumbui pasangan, melihat gambar-gambar erotik atau lucah, yang menaikkan nafsu seks, dll.
- **Terpancut** pemancutan air mani daripada zakar (atau perasaan seolah-olah berlaku pemancutan)

<table>
<thead>
<tr>
<th>Soalan</th>
<th>Tinggi</th>
<th>Tinggi</th>
<th>Sederhana</th>
<th>Rendah</th>
<th>Sangat rendah</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Bagaimanakah anda menentukan kadar keyakinan yang kemaluan anda berfungsi dan dapat mengekalkan ketegangannya.</td>
<td>4</td>
<td>5</td>
<td>4</td>
<td>3</td>
<td>2</td>
</tr>
<tr>
<td>2. Apabila anda mengalami ketegangan zakar (kemaluan atau ‘batang’ keras) menerusi rangsangan seks, berapa kerap ketegangan itu cukup keras untuk persetubuhan?</td>
<td>4</td>
<td>5</td>
<td>4</td>
<td>3</td>
<td>2</td>
</tr>
<tr>
<td>3. Sewaktu bersetubuh, berapa kerap anda mencuba sukar untuk mengekalkan ketegangan kemaluan sehingga selesai persetubuhan?</td>
<td>4</td>
<td>5</td>
<td>4</td>
<td>3</td>
<td>2</td>
</tr>
<tr>
<td>4. Sewaktu bersetubuh, berapa sukarkah untuk mengekalkan ketegangan kemaluan sehingga selesai persetubuhan?</td>
<td>4</td>
<td>5</td>
<td>4</td>
<td>3</td>
<td>2</td>
</tr>
<tr>
<td>5. Apabila anda cuba melakukan persetubuhan, berapa kerap anda berasa puas hati?</td>
<td>4</td>
<td>5</td>
<td>4</td>
<td>3</td>
<td>2</td>
</tr>
</tbody>
</table>

- Semua soalan, bermula dengan “Disepanjang 4 minggu yang lalu,”
- Jumlahkan skor pada setiap item 1-5 (Jumlah skor yang mungkin = 25).
- Klasifikasi Keterukan ED : Jumlah skor 1-7 (sangat teruk); 8-11 (sederhana); 12-16 (ringan hingga sederhana); 17-21 (ringan); 22-25 (tidak ada masalah ED)
Dosage of Antidiabetic Agents in Renal Failure

<table>
<thead>
<tr>
<th>Generic Name</th>
<th>Usual Dose</th>
<th>Dose adjustment in renal failure</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Mild (GFR 60 - 90ml/min)</td>
</tr>
<tr>
<td>Sulphonylureas</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Chlopropamide</td>
<td>250mg od – 500mg od</td>
<td>Avoid</td>
</tr>
<tr>
<td>Glibenclamide</td>
<td>5mg od – 10mg bd</td>
<td>25-50%</td>
</tr>
<tr>
<td>Gliclazide</td>
<td>80mg od – 160mg bd</td>
<td>50-100%</td>
</tr>
<tr>
<td>Glimepiride</td>
<td>1mg od – 4mg od</td>
<td>100%</td>
</tr>
<tr>
<td>Glipizide</td>
<td>2.5mg od – 15mg od</td>
<td>100%</td>
</tr>
</tbody>
</table>

Others

|          |            |                                |                                |                        |
|----------|------------|---------------------------------|---------------------------------|                        |
| Acarbose | 25mg tds – 100mg tds | 50-100% | 50-100% | Avoid |
| Exenatide | 5mcg bd – 10 mcg bd | 100% | 100% | Avoid |
| Insulin | Variable | 100% | 75% | 50% |
| Metformin | 500mg bd – 1g bd | 50% | 25% | Avoid |
| Nateglinide | 120mg tds | 100% | 100% | 50-100% |
| Pioglitazone | 15mg od – 30mg od | 100% | 100% | 50-100% |
| Repaglinide | 0.5mg tds – 4mg tds | 100% | 100% | 50-100% |
| Rosiglitazone | 4 – 8 mg od | 100% | 100% | 50-100% |
| Sitagliptin | 100mg od | 100mg | 50mg | 25mg |

od = once daily; bd = twice daily; tds = three time daily

### Clinical Monitoring Protocol

<table>
<thead>
<tr>
<th>Test</th>
<th>Initial Visit</th>
<th>Follow-up visit</th>
<th>Quarterly visit</th>
<th>Annual visit</th>
</tr>
</thead>
<tbody>
<tr>
<td>Eye: visual acuity</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fundoscopy</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Feet: pulses</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Neuropathy</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Weight</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>BMI</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Blood Pressure</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Blood Glucose</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>HbA1c</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cholesterol/HDL cholesterol</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Triglycerides</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Albuminuria*</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Creatinine/BUN</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ECG</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Urine microscopy</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

= Conduct test  
= No test required  
= Conduct test if abnormal first visit

* Microalbuminuria if resources are available

Adapted from the International Diabetes Federation Western Pacific Region (IDF-WPR) Type 2 Diabetes Practical Targets and Treatment, Fourth Edition, 2005.
GLOSSARY OF TERMS

ACEI  Angiotensin Converting Enzyme Inhibitor
ADA  American Diabetes Association
AGI  $\alpha$-glucosidase inhibitor
AHA  American Heart Association
ARB  Angiotensin II Receptor Blocker
BD  Twice Daily (*Bis Die*)
BMI  Body Mass Index
BP  Blood Pressure
BUN  Blood Urea Nitrogen
CCB  Calcium Channel Blocker
CCF  Congestive Cardiac Failure
CHD  Coronary Heart Disease
CVD  Cardiovascular Disease
DCCT  Diabetes Control and Complications Trial
DKA  Diabetes Ketoacidosis
DM  Diabetes Mellitus
DN  Diabetic Nephropathy
DPP-4  Dipeptidyl peptidase-4
ECG  Electrocardiogram
ED  Erectile Dysfunction
ETDRS  Early Treatment of Diabetic Retinopathy Study
FPG  Fasting Plasma Glucose
GDM  Gestational Diabetes Mellitus
GI  Glycaemic Index
GIK  Glucose Insulin Potassium
GIP  Glucose-dependent Insulinotropic Polypeptide
GLP-1  Glucagon-like Peptide 1
HbA1c  Glycosylated Haemoglobin
HDL  High Density Lipoprotein
IDF  International Diabetes Federation
IFG  Impaired Fasting Glucose
IGT  Impaired Glucose Tolerance
JPAD  Japanese Primary Prevention of Atherosclerosis with Aspirin for Diabetes
LBW | Low Birth Weight
LDL | Low Density Lipoprotein
LGA | Large for Gestational Age
LPOS | Loss Of Protective Sensation
LSCS | Lower Segment Caesarean Section
MNT | Medical Nutrition Therapy
NCEP | National Cholesterol Education Program
NPH | Neutral Protamine Hagedorn
NSAIDs | Non-steroidal Anti-inflammatory Drugs
OAD | Oral Anti-diabetic
OD | Once Daily *(Omni Die)*
OGTT | Oral Glucose Tolerance Test
OM | On Morning *(Omni Mane)*
ON | On Night *(Omni Nocte)*
OSAS | Obstructive Sleep Apnoea Syndrome
PCOS | Polycystic Ovarian Syndrome
PDE-5 | Phospodiesterase-5
POPADAD | Prevention of Progression of Arterial Disease and Diabetes
PPAR-γ | Peroxisome Proliferator-Activated Receptor-Gamma
PPG | Post-prandial Plasma Glucose
RPG | Random Plasma Glucose
S/C | Subcutaneous
SBMG | Self Blood Monitoring Glucose
SGA | Small for Gestational Age
SIADH | Syndrome of Inappropriate Antidiuretic Hormone
SU | Sulphonylurea
T2DM | Type 2 Diabetes Mellitus
TDS | Three Times Daily *(Ter Die Sumendus)*
TG | Triglycerides
TZD | Thiazolidinedione
UKPDS | United Kingdom Prospective Diabetes Study
WC | Waist Circumference
WHO | World Health Organisation
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  Klinik Kesihatan Purun
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LEVELS OF EVIDENCE SCALE
The definition of types of evidence and the grading of recommendation used in this guideline originate from the U.S./Canadian Preventive Services Task Force and are set out in the following tables:

<table>
<thead>
<tr>
<th>LEVEL</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>Evidence obtained from at least one properly randomized controlled trial</td>
</tr>
<tr>
<td>II – 1</td>
<td>Evidence obtained from well-designed controlled trials without randomization</td>
</tr>
<tr>
<td>II – 2</td>
<td>Evidence obtained from well-designed cohort or case-control analytic studies, preferably from more than one centre or research group</td>
</tr>
<tr>
<td>II – 3</td>
<td>Evidence obtained from multiple time series with or without the intervention. Dramatic results in uncontrolled experiments (such as the results of the introduction of penicillin treatment in the 1940s) could also be regarded as this type of evidence</td>
</tr>
<tr>
<td>III</td>
<td>Opinions of respected authorities, based on clinical experience; descriptive studies and case reports; or reports of expert committees</td>
</tr>
</tbody>
</table>

SOURCE: U.S./CANADIAN PREVENTIVE SERVICES TASK FORCE

GRADES OF RECOMMENDATIONS

<table>
<thead>
<tr>
<th>GRADE</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>At least one meta analysis, systematic review, or RCT, or evidence rated as good and directly applicable to the target population</td>
</tr>
<tr>
<td>B</td>
<td>Evidence from well conducted clinical trials, directly applicable to the target population, and demonstrating overall consistency of results; or evidence extrapolated from meta analysis, systematic review, or RCT</td>
</tr>
<tr>
<td>C</td>
<td>Evidence from expert committee reports, or opinions and/or clinical experiences of respected authorities; indicates absence of directly applicable clinical studies of good quality</td>
</tr>
</tbody>
</table>

SOURCE: MODIFIED FROM SCOTTISH INTERCOLLEGIATE GUIDELINES NETWORK (SIGN)