MANAGEMENT OF TYPE 2 DIABETES MELLITUS
(4th Edition)
Training Module For Health Care Providers
CLINICAL PRACTICE GUIDELINES TASK FORCE

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INTRODUCTION

The Clinical Practice Guidelines: Management of Type 2 Diabetes Mellitus (4th Edition) was published in May 2009. This Training Module is produced to assist the ‘trainers’ in delivering all of the components relating to the implementation of the new T2DM CPG systematically and effectively.

This document contains the following:

1. CD-ROM containing the powerpoint presentations
2. The outline for each topic
3. Case studies at the end of each topic
4. Template for the training program/schedule
5. Pre-test and post-test questionnaire

Target Audience:

All health care providers involved with the care of diabetes patients in both primary health care and secondary health care settings.

Table 1  Summary of Training Module Content

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<th>Duration (minutes)</th>
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<td>15</td>
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<td>Medical Nutrition Therapy</td>
<td>45</td>
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<td>7.</td>
<td>Insulin Therapy</td>
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<td>8.</td>
<td>Diabetes with Hypertension &amp; Dyslipidaemia</td>
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<td>Diabetes during Acute Illness, Emergencies &amp; Surgery</td>
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<td>45</td>
</tr>
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<td>11.</td>
<td>Screening &amp; Diagnosis of Diabetes Complications</td>
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Total 465 285
OVERVIEW OF THE T2DM CPG
MANAGEMENT OF TYPE 2 DIABETES MELLITUS
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Training Module For Health Care Providers
Slide 1

Diabetes: The Disease

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

Slide 2

Prevalence of Diabetes in Malaysia (1986-2006)

<table>
<thead>
<tr>
<th></th>
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<tr>
<td>≥35 years</td>
<td>6.3%</td>
<td>8.3%</td>
<td>11.6%</td>
<td>14.9%</td>
</tr>
<tr>
<td>≥30 years</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>≥18 years</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>≥30 years</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Prevalence

- Known diabetes
  - 4.5%
  - 6.5%
  - 7.0%
  - 9.5%

- Newly diagnosed
  - 1.8%
  - 1.8%
  - 4.5%
  - 5.4%

- Impaired Glucose Tolerance * / Impaired Fasting Glucose **
  - 4.8% *
  - 4.3% *
  - 4.2% **
  - 4.7% **

In 2006, there is an estimated 1.5 million Malaysians age 18 years and above living with diabetes.

Slide 2 - Notes

NHMS: National Health and Morbidity Survey

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Smoking</td>
<td>24.8%</td>
<td>N.A.</td>
<td>25.5%</td>
<td>21.5%</td>
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<tr>
<td>Physically Inactive</td>
<td>88.4%</td>
<td>85.6%*</td>
<td>60.1%</td>
<td>43.7%</td>
</tr>
<tr>
<td>Unhealthy Diet</td>
<td>N.A.</td>
<td>N.A.</td>
<td>72.8</td>
<td>N.A.</td>
</tr>
<tr>
<td>Overweight (BMI ≥25 &amp; &lt;30 kg/m²)</td>
<td>16.6%</td>
<td>27.4%</td>
<td>30.9%</td>
<td>29.1%</td>
</tr>
<tr>
<td>Obesity (BMI ≥30 kg/m²)</td>
<td>4.4%</td>
<td>12.7%</td>
<td>16.3%</td>
<td>14.0%</td>
</tr>
<tr>
<td>Hypercholesterolaemia</td>
<td>N.A.</td>
<td>N.A.</td>
<td>53.5%</td>
<td>20.6%</td>
</tr>
</tbody>
</table>

In 2006, there is an estimated 2.8 million Malaysians age 18 years and above are current smokers, 5.5 million physically inactive, 3.6 million overweight and 1.7 million Malaysians obese.

**Slide 3 - Notes**

NHMS : National Health and Morbidity Survey
MANS : Malaysian Adult Nutrition Survey, 2003
MyNCDS : Malaysian Non-Communicable Diseases Risk Factor Survey, 2005
People with type 2 diabetes have a higher risk of CVD events relative to people without diabetes.

- In the Framingham Heart Study, diabetes predisposed subjects to all of the major atherosclerotic diseases. CHD was the most common and most lethal.
- The chart shows the age-adjusted relative risk of CVD for diabetics versus non-diabetics (16 year follow-up after the tenth biennial examination of the Framingham Cohort Study). It is based on 554 men (46 with diabetes) and 760 women (43 with diabetes) who were free of CVD at examination.
- The risk for individuals without diabetes is represented by the line at a risk ratio of one. The risk of CVD is greater for those with diabetes compared with those without.

The mortality rate in men with diabetes is twice as great as that in patients without diabetes.

- The 20-year mortality of the men aged 44–55 years in the Whitehall, Paris Prospective and Helsinki Policemen studies was analysed.
- 75% of the deaths in the Helsinki study were from CVD, compared with 56% in Whitehall and 31% in France.
- In each study, the mortality rate from all causes was found to be twice as great in patients with diabetes.
- Diabetes was associated with an increased non-cardiovascular mortality in addition to excess cardiovascular mortality.

Better Control Equals Reduced Risk of Complications

Every 1% decrease in HbA1c was associated with clinically important reductions in the incidence of:

- diabetes-related death (-21%)
- myocardial infarction (-14%)
- microvascular complications (-37%)
- peripheral vascular disease (-43%)

There is no lower limit beyond which reductions in HbA1c cease to be of benefit. Taking diabetes-related death as an example, this means that:

- a reduction in HbA1c of 2% delivers a 42% reduction in risk
- a reduction in HbA1c of 3% delivers a 63% reduction in risk
- and so on.

Therefore, the greater the reduction in HbA1c, the greater the protection against complications.

Slide 8

Evidence that shaped our past guidelines and practice

- T2DM CPG 1996 – Pre-UKPDS
  - OAD monotherapy, Stepped care
  - SU, Metformin, Insulin
- Introduction of newer class of OADs (TZDs, Meglitinides, Alpha-glucosidase inhibitors)
- T2DM CPG 2003/4 – Post-UKPDS
  - Eventual monotherapy failure
  - Favoured Metformin for CV benefits
  - Addressed therapeutic inertia
  - Early combination therapy
  - However still “Stepped” approach

Slide 7 - Notes

| Diabcare Asia | Outcomes on Control and Complications in Type 1 and Type 2 Diabetic Asian Patients |
| IHM, MOH Audit | A Study on the Adequacy of Outpatient Management of Type 2 Diabetes Mellitus Cases in MOH Hospitals and Health Centres, IHM, MOH |
Algorithm 4: Medication for Type 2 Diabetes

Type 2 Diabetes

Success

Diet & Physical Activity††

Failure

Success

Overweight/Obese
Metformin ± Acarbose ± TZDs

Failure

Non-Obese
Metformin Or Insulin Secretagogues

Success

Metformin ± Acarbose ± TZDs ± Insulin Secretagogues

Failure

Metformin ± Insulin Secretagogues ± TZDs ± Acarbose

Success

Insulin ± Insulin Sensitisers

*Start medication at presentation if:
- Symptomatic
- HbA₁c > 8%
- FPG ≥ 11.1 mmol/L
- RPG > 14.0 mmol/L

*Combination OAD therapy should be considered at the outset in patients with HbA₁c > 10%

• Diet, physical activity and compliance must be emphasised at all levels
• Initiate screening for complications
Algorithm 5: Oral Anti-Diabetic Agents Failure And Subsequent Insulin Therapy

OAD Failure

- Confirm OAD Failure
- Suggest Insulin Therapy

Criteria:
- FPG > 7.0 mmol/L
- HbA1c > 8.5%
- On maximal dose of OAD

- Exclude intercurrent illness, e.g. TB
- If there is unexplained weight loss or patient is non-obese

[Flowchart Diagram]

- Acceptance Insulin Therapy
  - BIDS Regimen

- Diabetes Controlled
  - Continue OAD
  - Intermediate / long-acting insulin after 10pm
  - Initial dose 0.2 U/kg
  - Monitor FPG
  - Adjust insulin by 2-4 units after at least 3 days
  - Aim for FPG 4-8 mmol/L (individualised)

- Diabetes Uncontrolled
  - Continue BIDS
  - Replacement Insulin Therapy ± Insulin Sensitisers

- Refusal
  - Counselling

- Refusal
  - Counselling
MANAGEMENT OF TYPE 2 DIABETES MELLITUS
(4th Edition)

Galega officinalis

TRAINING MODULE FOR HEALTH CARE PROVIDERS

MERS
MINISTRY OF HEALTb MALAYSIA
ACADEMY OF MEDICINE MALAYSIA
RASIKAN DIABETES MALAYSIA
Preface

...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 required 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. ........

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- Section 1: Diabetes: The Disease
- Section 2: Screening and Diagnosis
- Section 3: Management for T2DM
- Section 4: Metabolic Syndrome
- Section 5: Management of Chronic Complications
- Section 6: Prevention of T2DM
TOPIC 2

SCREENING & DIAGNOSIS

MANAGEMENT OF TYPE 2 DIABETES MELLITUS

(4th Edition)

Training Module For Health Care Providers
Slide 1

Objective Of Presentation

- Why screen?
- Objective of screening
- Indications
- Screening methods
- Summary

Slide 2

Prevalence of Diabetes among Malaysian Adults (Age >30 years), comparison NHMS II & III

Slide 3

Screening & Diagnosis

Objective

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

Strategy

- Screening for high risk group
- Selective screening according to criteria
Slide 4

Who should be screened?
Symptomatic

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

Slide 5

Who should be screened?:
Asymptomatic

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

Slide 6

Who should be screened?
Asymptomatic

- Screening should begin at age ≥ 30 years.
Screening: Children and Adolescent

- 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)
Prevalence of Diabetes by Race, Aged ≥ 18 yrs

<table>
<thead>
<tr>
<th>Race</th>
<th>Prevalence (Number)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Indian</td>
<td>21,000 (19.9%)</td>
</tr>
<tr>
<td>Malay</td>
<td>23,000 (11.9%)</td>
</tr>
<tr>
<td>Chinese</td>
<td>14,000 (11.4%)</td>
</tr>
<tr>
<td>Other Bumi</td>
<td>8,000 (6.0%)</td>
</tr>
<tr>
<td>Other</td>
<td>4,000 (4.5%)</td>
</tr>
</tbody>
</table>

National Prevalence: 11.5%

Slide 10

Screening Schedule

- Screening should be done annually for adults.
- 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.

Slide 11

Screening: Pregnant Women

Pregnant women should be screened if they have any of the following risk factors:

- BMI > 27 kg/m²
- Previous macrosomic baby weighing 4 kg 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 years
Slide 12

Screening: Pregnant Women

- Screening is done using the 75 g 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

Slide 13

Values for Diagnosis

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

Slide 14

Diagnostic Values - OGTT

<table>
<thead>
<tr>
<th>Category</th>
<th>0-hour</th>
<th>2-hour</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal</td>
<td>≤ 6.1</td>
<td>&lt; 7.8</td>
</tr>
<tr>
<td>IFG</td>
<td>6.2 – 6.9</td>
<td>-</td>
</tr>
<tr>
<td>IGT</td>
<td>-</td>
<td>7.8 – 11.0</td>
</tr>
<tr>
<td>DM</td>
<td>≥ 7.0</td>
<td>≥ 11.1</td>
</tr>
</tbody>
</table>

Slide 15

Screening Test

- Screening can be done by measuring random blood glucose (capillary blood), using glucose meters and strips.
- In children and adolescents, follow the same screening procedure.
Slide 16

Algorithm: Screening for T2DM at Primary Care Level – With Symptoms

WITH SYMPTOMS

Venous Plasma Glucose

Fasting

< 7.0

OGTT

≥ 7.0

Random

≥ 11.1

Type 2 Diabetes Mellitus

< 11.1

OGTT

* All values in mmol/L

Slide 17

Algorithm: Screening for T2DM at Primary Care Level – Without Symptoms

ASYMPTOMATIC WITH RISK

Capillary Plasma Glucose

< 5.6

NORMAL

Follow-up

≥ 5.6

Random Plasma Glucose (RPG)

< 7.8

7.8 to 11.0

Follow-up OGTT

≥ 11.1

Second RPG

< 7.0

≥ 7.0

Second FPG

OGTT

DM

≥ 11.1

DM

PG

< 6.1

6.1 to 6.9

≥ 7.0

NORMAL IFG DM

2 hour PPG

< 7.8

≥ 7.8

≥ 11.1

Normal IFG DM

* All values in mmol/L
Slide 18

Summary

- Screening for diabetes should be performed annually in those with risk factors and those ≥ 30 years.
- 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.
- More frequent and/or earlier testing with either a FPG or 2-hour plasma glucose in a 75 g OGTT should be considered in people with additional risk factors for diabetes.
- Testing with a 75 g OGTT should be considered in individuals with an FPG of ≥ 6.1 to 6.9 mmol/L in order to identify individuals with IGT or diabetes. A glucose load of 1.75 g/kg body weight (max. 75 g) is used for children and adolescents.
- 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.
Case Study: Screening & Diagnosis

Management of Type 2 Diabetes Mellitus
(4th Edition)
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Slide 1

Introduction

- Mr. K.Y., 51 y.o. Malay man who presents for a routine evaluation
- No known medical problem till his 44th birthday – Started to gain weight about 2 to 3 kg/year.
- Sedentary lifestyle at work (bank officer)
- Current weight: 75 kg
- Current height: 165 cm
- Waist circumference: 100 cm

Slide 2

Questions

- Is he at high risk?
- What is his BMI?
- What are his risk factors?

Slide 2 - Notes

Key Points
- His risk factors
  - Age over 30 years
  - BMI = 27.5 kg/m² - obese
  - WC > 90 (for men) – central obesity
  - Sedentary lifestyle
- Combination of several NCD risk factors - he is at high risk.
Slide 3

Lab Results

- Fasting plasma glucose: 8.1 mmol/L
- HbA₁c: 6.6%
- Total cholesterol: 7.4 mmol/L
- LDL-C: 3.9 mmol/L
- HDL-C: 0.9 mmol/L
- Triglycerides: 2.9 mmol/L
- Creatinine: 63 µmol/L

Slide 4

Questions

- Comment on his lab results.

Slide 4 - Notes

Key Points
- Elevated fasting glucose, HbA₁c, total cholesterol, LDL cholesterol and triglycerides, and low HDL cholesterol.
- His creatinine levels are in the normal range.

Slide 5

Review of Medical Notes

- You notice that 3 years ago, Mr. K.Y.’s fasting plasma glucose level was measured prior to a minor procedure was 6.4 mmol/L

Slide 5 - Notes

Key Point
- A review of Mr. K.Y.’s chart indicates that his fasting plasma glucose level was already elevated 18 months ago.
Slide 6

Question

• Should Mr. K.Y. have been screened for diabetes/pre-diabetes even prior to the procedure lab testing?
• Why, or why not?

Slide 6 - Notes

Question
• Ask the participants if they believe Mr. K.Y. should have been screened for diabetes or pre-diabetes even prior to his pre-operative assessment 3 years ago, and to elaborate on their answers.
• Ask if their answers are age-dependent.

Key Points
• These questions are meant to encourage participants to talk about their own clinical practices.
• At this point the participants should already some idea on indication for screening in asymptomatic subjects.
• The CPG recommendation on screening should now be discussed.

Slide 7

Question

• Should you be concerned about Mr. K.Y.’s cardiovascular risk?

Slide 7 - Notes

Question
• Ask the participants if they are concerned about Mr. K.Y.’s CVD risk.

Key Points
• This question is meant to encourage participants to talk about their own clinical practices.
• At this point participants should not only be concerned on hyperglycemia but also other CVD risk present in this patient.
Slide 8

Question

- Based on evidence, what interventions should have been recommended 3 years ago to prevent the onset of diabetes?

Key Points

- Life-style interventions
- Pharmacological
- Need to determine the presence of other NCD risk factors

Slide 9

Question

- Would you run any additional tests for Mr. K.Y or do you feel you have enough to make a diagnosis?

Questions

- Ask the participants if they would run additional tests for Mr. K.Y or if they feel they have enough information to make a diagnosis.
- RECALL: Mr. K.Y’s fasting plasma glucose is 8.1 mmol/l his HbA1c is 6.6% and he is asymptomatic.

Key Points

- The CPG recommendations on diagnosis of diabetes should be reviewed.
Slide 10

First Line Treatment

- You recommend.....
  Follow-up scheduled in 3 months

Slide 10 - Notes

Question
- Ask the participants what would their recommendations be for first line treatment.

Key Points
- You recommend that Mr. K.Y. increase his level of physical activity and begin a weight loss diet.
- You also begin metformin treatment.
- Follow-up is scheduled for 3 months from now.

Slide 11

Three Months Later...

- Mr. K.Y.'s HbA1c has increased further to 7.9%.
- What second-line agent would you recommend at this time?

Slide 11 - Notes

Key Point
- This topic (Management of T2DM) has not been discussed yet, this question is just to stimulate discussions for the next topic to be presented.
TOPIC 3

PREVENTION OF DIABETES

MANAGEMENT OF TYPE 2 DIABETES MELLITUS

(4th Edition)

Training Module For Health Care Providers
Slide 1

Scientific Evidence

- There is evidence that interventions can reduce the conversion of IFG/IGT to frank T2DM
  - Da Qing IGT & Diabetes Study (China)
  - Diabetes Prevention Study (Finland)
  - Diabetes Prevention Program (USA)
  - STOP NIDDM (Europe, Canada)
  - Troglitazone in the Prevention of Diabetes / TRIPOD (USA)

Slide 2

Scientific Evidence (cont.)

<table>
<thead>
<tr>
<th>Study</th>
<th>Reduction in Risk (%)</th>
<th>Reduction in Risk (%)</th>
</tr>
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<td></td>
<td></td>
</tr>
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<td>Da Qing</td>
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</tr>
<tr>
<td>DPS</td>
<td>58</td>
<td>-</td>
</tr>
<tr>
<td>DPP</td>
<td>58</td>
<td>31</td>
</tr>
<tr>
<td>Stop NIDDM</td>
<td>-</td>
<td>25</td>
</tr>
<tr>
<td>TRIPOD</td>
<td>-</td>
<td>55</td>
</tr>
</tbody>
</table>

Slide 3

Intervention

- Diet and physical activity are the mainstay of therapy.
- Weight loss remains a priority in prevention of T2DM
- In addition, Metformin should be considered:
  - Those at very high risk (combined IFG & IGT, plus other risk factors)
  - Fail lifestyle therapy after 6 months
Slide 4

Intervention (cont.)

- Other pharmacological agents than can be used:
  - Acarbose
  - Orlistat
  - Rosiglitazone
- All the above drugs – off label use
- Use of other agents (ACE-Is, ARBs and statins are not recommended solely for the purpose of primary prevention.)

Slide 5

Individual at risk

Those at risk include those with IGT or IFG but also those with:
- Family history of diabetes (1st degree relatives)
- GDM
- Hypertension
- Vascular disease
- Dyslipidaemia
- Obesity/overweight with central obesity
- PCOS

Slide 6

Summary

- 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.
MEDICAL NUTRITION THERAPY

MANAGEMENT OF TYPE 2 DIABETES MELLITUS

(4th Edition)

Training Module For Health Care Providers
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.
Slide 3

Medical Nutrition Therapy: General recommendations

1. Nutrition counselling by a dietician is recommended
2. Dietary counselling should be individualised according to:
   - Nutritional needs
   - Severity of disease
   - Cultural preferences and
   - Willingness to change

Slide 4

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

Slide 5

MNT: Management of Diabetes

1. Regular meals and synchronised with medication time actions
2. Monitor the total daily carbohydrate intake (by carbohydrate exchange) to achieve glycaemic control
3. Choose Low Glycemic Index foods while keeping to the calories and carbohydrate prescription. There are limited databases on the GI and load of local foods
4. Sucrose (e.g. table sugar) intake must be counted as part of the total carbohydrate intake. Excess sucrose intake contributes to calories and may cause weight gain. Artificial sweeteners (aspartame, acesulfame K) are allowed
Slide 6

MNT: Management of Diabetes (cont.)

5. Limit intake of saturated fatty acids, trans fatty acids, and cholesterol to reduce risk of CVD
6. Reduced sodium intake a diet high with fruits, vegetables, and low-fat dairy products lowers blood pressure
7. There is no clear evidence of benefit from the use of antioxidant vitamins A,C,E, selenium and herbs in diabetes management.

Slide 7

CHO Foods to monitor via exchange/count

- Rice, bread, cereals, flour
- Starchy vegetables
- Legumes & pulses
- Fruits
- Milk & milk products
- Sugars, sweets, cakes, kuihs

1 CHO exchange = 15 g CHO, 75 kcal, Foods with fewer than 20 calories and 5 grams of carbohydrate are considered "free." (Appendix 1 of Diabetes CPG)

Slide 8

1 CHO exchange = 15 g CHO, 75 kcal

- Rice (cooked) 50 g Household measure: 1/2 cup
- Rice Porridge Household measure: 1 cup
- Noodle (wet) 30 g Household measure: 1/3 cup
- Rice Noodle (Kuhl-teow) 50 g Household measure: 1/2 cup
- Pasta Household measure: 1/3 cup
- Cornflakes Household measure: 3/4 cup
- Cream Crackers Biscuit 20 g Household measure: 3 pieces
- White Bread 30 g Household measure: 1 slice
- Putu Mayam 45 g Household measure: 1 piece
Slide 9

1 CHO exchange = 15 g CHO, 75 kcal

- Chickpea (uncooked) 25 g Household measure: 1/4 cup
- Dhal (yellow) (uncooked) 25 g Household measure: 1/4 cup
- Tubers: 1/4 - 1/2 piece Potato: 1 medium
- Baked Bean (Canned) 95 g Household measure: 1/2 cup

Slide 10

1 CHO exchange = 15 g CHO, 60 kcal

- Apple (red) 160 g Household measure: 1 whole, medium
- Banana (Pisang Mas) 65 g Household measure: 1 small
- Green Apple 165 g Household measure: 1 whole, big
- Carambola /Star-fruit 300 g Household measure: 1 medium
- Guava 150 g Household measure: 1/2 whole, big (without skin/seeds)
- Mango 105 g Household measure: 1 small

Slide 11

1 CHO exchange = 10-15 g CHO, 90-150 kcal

Milk & dairy products

- Milk powder 30 g Household measure: 4 rounded dessertspoon
- Milk (low fat/skim/full cream) Household measure: 1 glass (240 ml)
- Yogurt plain 150 g Household measure: 3/4 cup
- Evaporated milk Household measure: 1/2 cup (120 ml)
Slide 12

1 CHO exchange = 15 g CHO, 65 kcal

Sugars/syrups/sweets
- Honey: 1 tablespoon (21 g)
- Kaya: 3 tbsp (30 g)
- Jam: 1 tablespoon (21 g)
- Sweets: 1-2 pieces
- Sugar (brown): 3 1/2 tsp (18 g)
- Sugar (white): 3 tsp (15 g)
- Rose syrup: 3 1/2 tsp (18 g)
- Condensed milk: 2 tablespoon (30 g)
- Cocoa/malt-based powder: 1 1/2 tablespoon

Slide 13

Glycaemic Index (GI)

What is it?
- The glycaemic index of food is a ranking of foods based on their immediate effect on blood glucose (blood sugar) levels.
- Carbohydrate foods that breakdown quickly during digestion have the highest glycaemic indexes.
- Their blood sugar response is fast and high. Carbohydrates that breakdown slowly, releasing glucose gradually into the blood stream, have low glycaemic indexes.

Slide 14

What is the significance of Glycemic Index?
- Low GI means a smaller rise in blood sugar and can help control established diabetes.
- Low GI diets can help people lose weight and lower blood lipids.
- Low GI diets can improve the body’s sensitivity to insulin.
- High GI foods can help re-fuel carbohydrate stores after exercise.
**Slide 15**

**GI in Diabetes**

- GI may be used to guide food choices while keeping to the calories and carbohydrate prescription but it is not recommended as the primary strategy in meal planning.
- Foods with a high glycaemic index are associated with greater increases in blood sugar than are foods with a low glycaemic index.
- But low-index foods aren’t necessarily healthier. Foods that are high in fat tend to have lower glycemic index values than do some healthier options.

**Slide 16**

**High GI**

- Potato
- White rice
- Kurma
- Riped banana
- Breakfast cereal
- Rasin
- White bread
- Sport drink
- Jelly

**Moderate GI**

- Basmati rice & brown
- Nasi lemak, roti canai
- Banana half riped
- Fried rice
- Whole meal bread
- Pineapple, mango
- Meehoon
- Jam, honey

**Low GI**

- Apple, pear, peach
- Soya, lentil, pea
- Citrus (orange, mandarin, lemon)
- Honey dew, plum
- Oat, bran, muesli
- Baked beans
- Vegetables

**Summary**

Diabetes Diet
- Timing of meals
- Food portions
- Choice and distribution of carbohydrates
Case Study: Medical Nutrition Therapy

Management of Type 2 Diabetes Mellitus
(4th Edition)
Training Module For Health care Providers

Slide 1

Introduction

- Mr C is a 30 y.o. man who works as finance manager
- Family history of diabetes: mother & 1 sibling
- Seen by GP: Metformin prescribed
- Investigations:
  - BP 130/90
  - Fasting blood glucose 7.8 mmol/l
  - Total chol 5.9 mmol/L; HDL chol 1.77; LDL chol 4.0; Triglycerides 1.5
  - BMI 28.7, weight 85 kg, height 1.72 m
  - Waist 105 cm

Slide 2

Lifestyle Behaviour

- Exercise
  - None, don’t intend to start because no time.

- Food habits; Have been:
  - Avoiding egg yolks and seafood for past 1 month.
  - Increasing vegetables intake past 1 month.
  - Reducing sweet foods and sugars in drinks past 1 month.
  - Claims to have regular meal timings
Slide 3

Diet History

<table>
<thead>
<tr>
<th>Time</th>
<th>Food</th>
<th>Remarks</th>
</tr>
</thead>
<tbody>
<tr>
<td>Breakfast 7 am</td>
<td>Raw oats 6 tbsp + condensed milk 2 tbsp + Milo 3-in-1, 1 packet</td>
<td>Tries to eat oats most days for 6 months now</td>
</tr>
<tr>
<td>10 am</td>
<td>Tomyam soup noodles 1 medium bowl OR Fried noodles with gravy 1 large plate</td>
<td>Weekends, eats out with family</td>
</tr>
<tr>
<td>Lunch</td>
<td>Skips if he eats breakfast late</td>
<td></td>
</tr>
<tr>
<td>Afternoon 2 pm</td>
<td>Rice 1 Chinese bowl Chicken/ beef dishes 1 palm size Vegetables 1 small bowl Chinese tea</td>
<td></td>
</tr>
<tr>
<td>Dinner 8 pm</td>
<td>Rice 1 bowl Vegetables 2 cups</td>
<td>Wife cooks vegetables only for him at home</td>
</tr>
<tr>
<td>Supper 11 pm</td>
<td>Milo 3-in-1, 1 packet OR Oats + condensed milk 1 bowl</td>
<td>Sometimes if hungry</td>
</tr>
</tbody>
</table>

Total calories: 2,000 kcal/day
Total carbohydrate: 300 g/day, 60-65% energy, 18-20 exchanges CHO

Slide 4

Questions

- Interpret the BMI and waist circumference of this patient.
- How would you interpret his other lab investigation results and his lifestyle habits?

Slide 4 - Notes

Key Points
- Mr. C is obese + has central obesity
- Also has dyslipidaemia
- Sedentary lifestyle
Questions

- Based on the diet recall, identify the food choices and practices which are detrimental to his medical conditions.

Slide 5 - Notes

Key Points
- Show the participants slide number 4 for discussion.
- Slide number 6 contains the answers.

Slide 6

<table>
<thead>
<tr>
<th>Time</th>
<th>Food</th>
<th>Remarks</th>
</tr>
</thead>
<tbody>
<tr>
<td>7 am</td>
<td>Raw oats 6 tbsp + condensed milk 2 tbsp +</td>
<td>Tries to eat oats most days for 6 mths now</td>
</tr>
<tr>
<td></td>
<td>Milo 3-in-1, 1 packet</td>
<td></td>
</tr>
<tr>
<td>10 am</td>
<td>Tomyam soup noodles 1 medium bowl</td>
<td>Weekends, eats out with family</td>
</tr>
<tr>
<td></td>
<td>OR</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Fried noodles with gravy 1 large plate</td>
<td></td>
</tr>
<tr>
<td></td>
<td><strong>Meal Skipping</strong></td>
<td></td>
</tr>
<tr>
<td>Lunch</td>
<td>Skips if he eats breakfast late</td>
<td></td>
</tr>
<tr>
<td>2 pm</td>
<td>Rice 1 Chinese bowl</td>
<td><strong>CHO Intake: Big Potion Size, Refined CHO, Low Fiber</strong></td>
</tr>
<tr>
<td></td>
<td>Chicken/ beef dishes 1 palm size</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Vegetables 1 small bowl Chinese tea</td>
<td></td>
</tr>
<tr>
<td>Afternoon</td>
<td>No Protein Source</td>
<td><strong>Supper With Refined CHO</strong></td>
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<tr>
<td>8 pm</td>
<td>Rice 1 bowl</td>
<td>Wife cooks vegetables only for him at home</td>
</tr>
<tr>
<td></td>
<td>Vegetables 2 cups</td>
<td></td>
</tr>
<tr>
<td>Dinner</td>
<td></td>
<td></td>
</tr>
<tr>
<td>11 pm</td>
<td>Milo 3-in-1, 1 packet OR Oats + condensed milk 1 bowl</td>
<td>Sometimes if hungry</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Total calories: approx. 2,000 kcal/day. Total carbohydrate intake: High. (300 g/day 60-65% energy, 18-20 exchanges CHO)
Slide 7

Questions

• What kind of diet would you recommend to this patient?
• Suggest some suitable food choices and practices he can adopt.

Slide 7 - Notes

Key Points
• Slide number 8 & 9 contains the answers

Slide 8

Diet Advice

• Weight loss: 4 kg in 3 months. Calories: 1,500 kcal/day
• Regular meals: no skipping lunch: 3 main meals + 1 snack
• Count carbohydrate intake: distribute evenly into meals.
  - eat rice at lunch, not afternoon tea
  - smaller servings of rice & noodles
  - use brown rice to add fiber
• Balanced diet
  - add protein in dinner
  - add low GI fruits
• Reduce sugars/refined CHO:
  - switch condensed milk to low fat milk + oats
  - No 3-in-1 drinks: use plain powder
  - Use artificial sweetener
• Low fat dishes & low saturated fat foods: eat more fish & poultry, less fried foods

<table>
<thead>
<tr>
<th>Exchanges</th>
<th>Cereals</th>
<th>Fruit</th>
<th>Fish/ Poultry</th>
<th>Milk</th>
<th>Fat</th>
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<tr>
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<td>3</td>
<td>1</td>
<td>2</td>
<td>-</td>
<td>2</td>
</tr>
<tr>
<td>Afternoon snack</td>
<td>1</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dinner</td>
<td>3</td>
<td>1</td>
<td>2</td>
<td>-</td>
<td>2</td>
</tr>
</tbody>
</table>

1,500 kcal/day 55% en carbs, <30% en fat, 10-15% en protein. Total carb exchanges = 14 exchanges/day
Slide 9

Diet Modification

<table>
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<th>Food</th>
<th>Remarks</th>
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<tbody>
<tr>
<td>7 am</td>
<td>Raw oats 6 tbsp/ 1/4 cup + low fat milk 1/2 glass</td>
<td>Oats + low fat milk is low GI food</td>
</tr>
<tr>
<td></td>
<td>Fruit: guava/apple</td>
<td>Low GI fruits</td>
</tr>
<tr>
<td>10 am</td>
<td>Rice 1 cup / 3 scoops level</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Chicken/ fish dishes 1 palm size (low fat)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Vegetables 2 servings (1 bowl)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Papaya / pineapple 1 slice</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Chinese tea</td>
<td></td>
</tr>
<tr>
<td>Lunch</td>
<td></td>
<td></td>
</tr>
<tr>
<td>12 pm</td>
<td>Rice 1 cup / 3 scoops level</td>
<td>Low fat cooking method</td>
</tr>
<tr>
<td></td>
<td>Chicken/ fish dishes 1 palm size (low fat)</td>
<td>Add vegetables</td>
</tr>
<tr>
<td></td>
<td>Vegetables 2 servings (1 bowl)</td>
<td>Add low GI fruit</td>
</tr>
<tr>
<td></td>
<td>Papaya / pineapple 1 slice</td>
<td></td>
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<tr>
<td></td>
<td>Chinese tea</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Afternoon snack</td>
<td>Unsweetened wholemeal</td>
<td>Sometimes only if hungry</td>
</tr>
<tr>
<td>4 pm</td>
<td>biscuits 2 pieces</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Tea + low fat milk + artificial sweetener</td>
<td></td>
</tr>
<tr>
<td>Dinner</td>
<td>Rice 1 cup / 3 scoops level</td>
<td>Mix with brown rice to increase fiber content</td>
</tr>
<tr>
<td>7 pm</td>
<td>Fish/ chicken 1 palm size (low fat)</td>
<td>Add vegetables</td>
</tr>
<tr>
<td></td>
<td>Vegetables 2 cups</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Orange 1 medium</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Plain water</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Mix with brown rice to increase fiber</td>
<td></td>
</tr>
<tr>
<td></td>
<td>content</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Add vegetables</td>
<td></td>
</tr>
</tbody>
</table>

Slide 10

Questions

- What other lifestyle changes can he make?

Slide 4 - Notes

Key Points
- Increase physical activity or exercise

Slide 11

Physical Activity

- Make time for exercise: late evenings/after work, weekends
- Brisk walking 20 minutes most days of the week, gradually build up to 30-45 minutes
- Increase daily activities: use stairs, wash car, help in housework, wear pedometer to monitor increasing steps taken/day (aim 10,000 steps/day)
TOPIC 5

PHYSICAL ACTIVITY

MANAGEMENT OF TYPE 2 DIABETES MELLITUS
(4th Edition)

Training Module For Health Care Providers
Slide 1

Physical Activity

- Increased physical activity can improve glycaemic control, assist with weight maintenance and reduce risk of CVD.
- Before beginning a program more vigorous than brisk walking:
  - Assess for complications (CVD, retinopathy, neuropathy and foot injury)
  - Patient’s age and previous physical activity level should be considered

Slide 2

Treatment Algorithm for the Management of T2DM

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

* Consider metformin/AGI/other insulin sensitiser 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.
Slide 3

 Targets for Control

<table>
<thead>
<tr>
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<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>
<tr>
<td><strong>Lipids</strong></td>
<td></td>
</tr>
<tr>
<td>Triglycerides</td>
<td>≤ 1.7 mmol/l</td>
</tr>
<tr>
<td>HDL cholesterol</td>
<td>≥ 1.1 mmol/l</td>
</tr>
<tr>
<td>LDL cholesterol</td>
<td>≤ 2.6 mmol/l</td>
</tr>
<tr>
<td><strong>Exercise</strong></td>
<td></td>
</tr>
<tr>
<td></td>
<td>150 mins / week</td>
</tr>
<tr>
<td><strong>Blood Pressure</strong></td>
<td></td>
</tr>
<tr>
<td>Normal Renal Function</td>
<td>≤ 130/80 mmHg§</td>
</tr>
<tr>
<td>Renal Impairment / Gross Proteinuria</td>
<td>≤ 120/75 mmHg</td>
</tr>
</tbody>
</table>

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

Slide 3 - Notes

General Recommendations

- Individuals should exercise 5 days a week, preferably most days of the week and with no more than 2 consecutive days without physical activity.
- Brisk walking is recommended for all.
- 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.
- Overweight and obese individuals should gradually increase physical activity to 60-90 minutes/day for long term major weight loss.
- Any increase in daily energy expenditure is beneficial.
- In order to prevent hypoglycaemia, medication doses can be reduced or extra carbohydrate can be consumed before or during physical activity.
Case Study: Physical Activity

Management of Type 2 Diabetes Mellitus

(4th Edition)

Training Module For Health care Providers

Slide 1

Introduction

• Mr. G, 45 y.o. Malay man
• Diagnosed with T2DM three years ago
• His father died of heart attack at age 45 and his younger brother also has diabetes
• Height 165 cm, weighs 80 kg
• Currently on T. Metformin 500 mg BD and T. Gliclazide 80 mg daily

Slide 2

• As a businessman who deals direct with clients, he spends a great deal of time on travelling in which his diet fluctuates according to the spends place where he goes.
• He takes 1-2 carbonated drinks at a time. He can’t give up carbonated drink when he has business dinner or lunch.
• He hardly exercises and his excuse is ‘no time’ to think about it.

Slide 3

Question

• Explain how you are going to manage this patient.

Slide 3 - Notes

Key Points
• Take complete relevant history.
• Perform relevant physical examination.
• Assess blood glucose control.
• Assess target organ complications and CVD risk assessment.
• Assess knowledge on diabetes, particularly on patient’s knowledge on benefit of exercise and how to initiate exercise program.
• Assess readiness for exercise.
Key Points: Before Initiating an Exercise Program
- Exercise is an important component in the management of type 2 diabetes. It has been shown to substantially improve metabolic control and to promote weight loss.
- Before initiating an exercise program, each patient should be evaluated to ensure the patient's safety. The level of glycemic control should be determined and the patient's cardiovascular status evaluated on an individual basis, depending on the patient and level of exercise.
- Assessments for neuropathy, retinopathy, and nephropathy also should be performed.
- The exercise prescription itself should be designed to accommodate the clinical status of the patient and specify the type and intensity of activity as well as duration and frequency. High-intensity or strenuous activity should be discouraged in patients with nephropathy unless blood pressure is closely monitored during the activity.

Exercise Prescription
- Step 1: Patient Evaluation
  Physical Examination and Medical History
  Stress Test (if necessary)
- Step 2: Goal Setting
  Weight Loss
  Glucose levels
  Target exercise heart rate
  Caloric expenditure
  Lipid level
  Blood Pressure
- Step 3: Determination of appropriate exercise parameters for patient
  Duration - how long are you going to exercise
  Mode - type of exercise
  Frequency - how often is the exercise
  Intensity - how easy/hard the exercise
  Timing - when are you going to exercise
- Step 4: Determination of necessary exercise precautions

Question
- How do you start him on exercise program?
- How do you prescribe the exercise program for him?
Key Points

- How do you ensure that he sustains the exercise?
- What do you think the most challenging aspect of initiating and sustaining an exercise program?

Hints:
- Choose activities that you like
- Small changes – physical activity becomes part of your daily routine
- Check with medical professionals if you develop sudden pain, shortness of breath or ill feeling
- Exercise with a group
- Be realistic

Question

How do you measure effectiveness?

Key Points

- Body weight
- Diabetes control
- BP control
- Sense of well being/Quality of life
TOPIC 6

ORAL ANTI-DIABETIC AGENTS

MANAGEMENT OF TYPE 2 DIABETES MELLITUS

(4th Edition)

Training Module For Health Care Providers
Slide 1

Patients achieving target HbA1c

<table>
<thead>
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<th>IHM, MOH Audit</th>
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Slide 1 - Notes

Diabcare Asia: Outcomes on Control and Complications in Type 1 and Type 2 Diabetic Asian Patients
IHM, MOH Audit: A Study on the Adequacy of Outpatient Management of Type 2 Diabetes Mellitus Cases in MOH Hospitals and Health Centres, IHM, MOH

Slide 2

MOH Audit 2005: Medications prescribed

<table>
<thead>
<tr>
<th>Medication</th>
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</tr>
</thead>
<tbody>
<tr>
<td>TLC only</td>
<td>50</td>
<td>1.4</td>
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<tr>
<td>Biguanides</td>
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<tr>
<td>Sulphonylureas</td>
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<tr>
<td>Acarbose</td>
<td>201</td>
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<tr>
<td>Metiglinides</td>
<td>11</td>
<td>0.3</td>
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<tr>
<td>Glitazones (TZD)</td>
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<tr>
<td>Insulin</td>
<td>467</td>
<td>13.3</td>
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IHM, MOH 2005
## Slide 3

**Targets for Control**

<table>
<thead>
<tr>
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<th>Levels</th>
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<tbody>
<tr>
<td><strong>Glycaemic Control</strong></td>
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<tr>
<td>Fasting</td>
<td>4.4 – 6.1 mmol/l</td>
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<tr>
<td>Non-fasting</td>
<td>4.4 – 8.0 mmol/l</td>
</tr>
<tr>
<td>HbA1c</td>
<td>&lt; 6.5 %</td>
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<tr>
<td><strong>Lipids</strong></td>
<td></td>
</tr>
<tr>
<td>Triglycerides</td>
<td>≤ 1.7 mmol/l</td>
</tr>
<tr>
<td>HDL cholesterol</td>
<td>≥ 1.1 mmol/l</td>
</tr>
<tr>
<td>LDL cholesterol</td>
<td>≤ 2.6 mmol/l</td>
</tr>
<tr>
<td><strong>Exercise</strong></td>
<td></td>
</tr>
<tr>
<td></td>
<td>150 mins / week</td>
</tr>
<tr>
<td><strong>Blood Pressure</strong></td>
<td></td>
</tr>
<tr>
<td>Normal Renal Function</td>
<td>≤ 130/80 mmHg⁵</td>
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<tr>
<td>Renal Impairment / Gross Proteinuria</td>
<td>≤ 120/75 mmHg</td>
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</table>
Diabetes Education

**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, educational needs

**CONTENTS**
- Diet
- Exercise
- Medication
- Complications (acute and chronic)
- Self-care/SSGM/foot care
- Stop smoking
- Problem solving skills
- Psychosocial adaptation to diabetes
Treatment Algorithm for the Management of T2DM

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

- **HbA1c < 5.5% OR FPG < 6 mmol/L**
  - LIFESTYLE APPROACH
  - Follow-up with HbA1c after 3 months.
  - If HbA1c ≤ 5.5% continue with LIFESTYLE Approach.
  - If HbA1c > 5.5% on follow-up, consider OAD MONOTHERAPY.

- **HbA1c 6.5-8.0% OR FPG 6-<10 mmol/L**
  - OAD MONOTHERAPY
  - Metformin**
  - OR
  - DPP-4 Inhibitor / GLP-1 Agonist / SGLT-2i.
  - Optimize dose of OAD agent in 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 (DPP-4 Inhibitor / GLP-1 Agonist / SGLT-2i / SU / T2D) or with insulin.
  - Optimize dose of OAD agents in 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.

---

**Slide 5 - Notes**

- If symptomatic (weight loss, polyuria, etc) at any HbA1c and FPG level, consider insulin therapy.
- * Consider metformin/AGI/other insulin sensitiser 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.

---

**Slide 6**

Proactive management of glycaemia: Early combination approach

- **HbA1c %**
  - Diet
  - OAD monotherapy
  - OAD combinations
  - OADs up-titration
  - OAD + basal insulin
  - OAD + multiple daily insulin injections

- **Duration of diabetes**
Slide 7

Oral Agent Monotherapy: Recommendations

- If glycaemic targets are not achieved (HbA1c <6.5%, FPG <6 mmol/L) with lifestyle modification within 3 months, OAD agents should be initiated.
- 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.
- 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.
- As first line therapy:
  - Metformin is the preferred choice.
  - Use of TZDs as first line has been found to have greater durability in glycaemic control compared to metformin and sulphonylurea.
  - If monotherapy fails, combination of other agents is recommended.

Slide 8

Combination Oral Agents: Recommendations

- Newly diagnosed patients with HbA1c 8 – <10%, FPG 10 – <13 mmol/L.
- Patients who are not reaching targets (HbA1c <6.5%) after 3-6 months on monotherapy.

Slide 9

Combination Oral Agents & Insulin: Recommendations

- Newly diagnosed patients with HbA1c >10%, FPG >13 mmol/L.
- Patients who are not reaching targets (HbA1c <6.5%) after 3-6 months on optimal doses of combination therapy.
Slide 10

Oral Anti-Diabetic (OAD) Agents

There are currently five classes of OAD agents:
- Alpha-glucosidase inhibitor (AGIs)
- Biguanides
- Dipeptidyl peptidase-4 (DPP-4) Inhibitors
- Insulin Secretagogues
- Sulphonylureas
- Non-SUs or Meglitinides
- Thiazolidinediones (TZDs)

Slide 11

Alpha-glucosidase inhibitor (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%
- They can have synergistic effects when used with other OAD agents and may be combined with insulin

Slide 12

Alpha-glucosidase inhibitor (AGIs) (cont.)

- 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, diarrhoea and flatulence

<table>
<thead>
<tr>
<th>Formulation</th>
<th>Minimum Dose</th>
<th>Maximum Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acarbose</td>
<td>Initial dose 50 mg OD</td>
<td>Maximum dose 100 mg TDS</td>
</tr>
<tr>
<td>50 mg / 100 mg tablet</td>
<td>Usual dose 50-100 mg during main meals</td>
<td></td>
</tr>
</tbody>
</table>
Slide 13

**Biguanides (Metformin)**

- Metformin does not stimulate insulin secretion, and lowers 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

Slide 14

**Biguanides (Metformin)**

- Generally well tolerated. Most common adverse effects are nausea, anorexia and diarrhoea. 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)
- The major non-glycaemic 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
- Avoid if creatinine >150 umol/l or creatinine clearance <30 mL/min

Slide 15

**Biguanides (Metformin)**

<table>
<thead>
<tr>
<th>Formulation</th>
<th>Minimum Dose</th>
<th>Maximum Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Metformin 500 mg tablet</td>
<td>Initial dose 500 mg OD</td>
<td>Maximum dose 1,000 mg BD</td>
</tr>
<tr>
<td></td>
<td>Usual dose 600 mg TDS</td>
<td></td>
</tr>
<tr>
<td>Metformin Retard 850 mg tablet</td>
<td>Initial dose 850 mg OD</td>
<td>Maximum dose 1,700 mg OM / 805 mg ON</td>
</tr>
<tr>
<td></td>
<td>Usual dose 850 mg BD</td>
<td></td>
</tr>
<tr>
<td>Metformin extended release 500 mg tablet</td>
<td>Initial dose 500 mg OD</td>
<td>Maximum dose 2,000 mg OD</td>
</tr>
<tr>
<td>Gilbenclamide and metformin fixed dose combination</td>
<td>Initial dose one 1.25mg / 250mg tablet OD or BD</td>
<td>Maximum dose two 5 mg / 500 mg tablets BD</td>
</tr>
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</table>
Slide 16

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 insulinotropic 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 enhancers) and GLP-1 analogue or GLP-1 receptor agonist (incretin mimetics)

Slide 17

DPP-4 Inhibitor (Sitagliptin)

- It lowers HbA$_1c$ by 0.5-0.8%, its efficacy improves when used at higher HbA$_1c$ 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 is 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 (25 to 50 mg)
- It is generally well tolerated

Slide 18

DPP-4 Inhibitor (Sitagliptin) (cont.)

<table>
<thead>
<tr>
<th>Formulation</th>
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<th>Maximum Dose</th>
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</thead>
<tbody>
<tr>
<td>Sitagliptin</td>
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<td>100 mg OD</td>
</tr>
<tr>
<td>100 / 50 / 25 mg tablet</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sitagliptin and metformin fixed dose combination</td>
<td>50 mg / 500 mg BD</td>
<td>50 mg / 1,000 mg BD</td>
</tr>
<tr>
<td>50 mg / 500 mg tablet</td>
<td></td>
<td></td>
</tr>
<tr>
<td>50 mg / 850 mg tablet</td>
<td></td>
<td></td>
</tr>
<tr>
<td>50 mg / 1,000 mg tablet</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
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

Insulin Secretagogues (SUs) (cont.)

- SUs should be taken 30 minutes before meals, except Glimepiride and Gliclazide MR which can be taken just before the meal
- Combining two different SUs / insulin secretagogues is not recommended
- Side effects are rare and include hepatitis, syndrome of inappropriate antidiuretic hormone (SIADH), blood dyscrasias

Insulin Secretagogues (SUs) (cont.)

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<th>Formulation</th>
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<tr>
<td>Glibenclamide 5 mg tablet</td>
<td>2.5 mg OM</td>
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<td>Glibenclamide 80 mg tablet</td>
<td>40 mg OM</td>
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</tr>
<tr>
<td>Glibenclamide MR 30 mg tablet</td>
<td>30 mg OM</td>
<td>120 mg OM</td>
</tr>
<tr>
<td>Glipizide 5 mg tablet</td>
<td>12.5 mg OM</td>
<td>60 mg BD</td>
</tr>
<tr>
<td>Glimepiride 2 mg / 3 mg tablet</td>
<td>1 mg OM</td>
<td>6 mg OM</td>
</tr>
</tbody>
</table>
**Slide 22**

**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

**Slide 23**

**Insulin Secretagogues – Non-SUs or Meglitinides (cont.)**

- 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

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

**Slide 24**

**Thiazolidinediones (TZDs)**

- TZDs 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
- 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.
Thiazolidinediones (TZDs) (cont.)

- 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.
- TZDs are contraindicated in patients with CCF and liver failure.
- Use of TZDs with insulin is not recommended.

<table>
<thead>
<tr>
<th>Formulation</th>
<th>Minimum Dose</th>
<th>Maximum Dose</th>
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</thead>
<tbody>
<tr>
<td>Rosiglitazone 4 / 8 mg tablet</td>
<td>4 mg OD</td>
<td>4 mg BD</td>
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<tr>
<td>Rosiglitazone and Metformin fixed dose combination tablet</td>
<td>2 mg / 500 mg BD</td>
<td>4 mg / 1,000 mg BD</td>
</tr>
<tr>
<td>Pioglitazone 15 / 30 mg tablet</td>
<td>15 mg OD</td>
<td>45 mg OD</td>
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</table>

GLP-1 Analogue (Exenatide)

- It is given parenterally, just before breakfast and dinner
- It reduces HbA1c by 0.5-1.0%, sustained efficacy over 2 years
- It can be added to metformin and/or SU if glycaemic targets are not achieved
- Progressive weight loss is seen in a proportion of patients – because of its effect on satiety and delay in gastric emptying

<table>
<thead>
<tr>
<th>Formulation</th>
<th>Minimum Dose</th>
<th>Maximum Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Exenatide</td>
<td>5 µg / 20 µg / 10 µg / 40 µg pre-filled pen</td>
<td>5 µg BD</td>
</tr>
</tbody>
</table>
Proactive management of glycaemia: Early combination approach

- The early, aggressive approach to type 2 diabetes management avoids the risk of early treatment failure by adopting an intensive therapeutic strategy immediately upon diagnosis.
- Combinations of agents with complementary modes of action targeting the dual defects underlying type 2 diabetes (IR and β-cell dysfunction) are most likely to support tight, long-term glycaemic control.
- Furthermore, combination therapy with OADs (oral antidiabetics), should be considered earlier in the regimen to provide additional glycaemic control.


General Guidelines for Use of OAD Agents

- 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 individualised.
- When indicated, start with a minimal dose of OAD agent, while reemphasising 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.
Slide 30

Treatment strategy

• Choice of monotherapy – durability of drug, fit the phenotype
• More aggressive strategy – combination therapy for those with more severe hyperglycemia at diagnosis
• Earlier intensification of treatment
• Rational use of drugs with complementary mechanisms of action
• Ongoing patient education – adherence to lifestyle interventions and pharmacotherapy

Slide 31

Summary

• Current glycaemic management of diabetes is inadequate
  - Too few patients are achieving targets for HbA1c
  - New approaches are needed to improve outcomes
• Need to intervene early & more aggressively.
• Treat to goal, treat to phenotype, individualised.
• Early combination therapy but keep regimens simple. Early insulin initiation – start simply with bed-time insulin, then optimise.
• Achieve effective and sustained glycaemic control.
• Address underlying cardiovascular risk factors.
• Continuous strong multidisciplinary patient support and education.
TOPIC 7

INSULIN THERAPY

MANAGEMENT OF TYPE 2 DIABETES MELLITUS
(4th Edition)

Training Module For Health Care Providers
### Slide 1

#### Targets for Control

<table>
<thead>
<tr>
<th>Glycaemic Control *</th>
<th>Levels</th>
</tr>
</thead>
<tbody>
<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>HbA(_1c)</td>
<td>&lt; 6.5 %</td>
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</table>

<table>
<thead>
<tr>
<th>Lipids</th>
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<tbody>
<tr>
<td>Triglycerides</td>
</tr>
<tr>
<td>HDL cholesterol</td>
</tr>
<tr>
<td>LDL cholesterol</td>
</tr>
<tr>
<td>Exercise</td>
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<table>
<thead>
<tr>
<th>Blood Pressure</th>
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</thead>
<tbody>
<tr>
<td>Normal Renal Function</td>
</tr>
<tr>
<td>Renal Impairment / Gross Proteinuria</td>
</tr>
</tbody>
</table>

* Glycaemic target should be individualised to minimise risk of hypoglycaemia.

# In Individuals with overt CVD, LDL cholesterol target is <1.8 mmol/L.

§ In children and adolescents, blood pressure should be <95\(^{th}\) percentile for age and sex.
Slide 2

Treatment Algorithm for the Management of T2DM

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

1. **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.

2. **HbA1c 6.5-<8.0% OR FPG 6-<10 mmol/L**
   - OAD MONOTHERAPY
   - Metformin
   - OR
   - DPP-4 Inhibitor / GLP-1 / 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.

3. **HbA1c 6.0-10.0% OR FPG 10-13 mmol/L**
   - COMBINATION THERAPY
   - Metformin with other OAD agents (GLP-1 / DPP-4 inibitor / GLP-1 / 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.

4. **HbA1c >10.0% OR FPG >13 mmol/L**
   - COMBINATION THERAPY + BASAL / PREMIXED INSULIN THERAPY.
   - OR
   - INTENSIVE INSULIN THERAPY, continue Metformin.

Slide 2 - Notes

- If symptomatic (weight loss, polyuria, etc) at any HbA1c and FPG level, consider insulin therapy.
  - Consider metformin/AGI/other insulin sensitiser 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.

Slide 3

Combination of Oral Agents & Insulin Therapy

- Combining insulin and the following OAD agents has been shown to be effective in T2DM:
  - Biguanides (Metformin)
  - Sulphonylureas
  - Alpha-glucosidase inhibitors

- Insulin can be used for short term and long term indications.
Short Term Use of Insulin

Short-term insulin therapy should be considered in the following conditions:

- Acute illness, surgery, stress and emergencies
- Pregnancy
- Breast-feeding
- Insulin may be used as initial therapy in T2DM particularly in marked hyperglycaemia
- Severe metabolic decompensation (e.g. DKA, HONK)

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.

Long Term Use of Insulin (cont.)

- 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.
Slide 7

Insulin Initiation

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

Slide 8

Insulin Optimisation

- Dose of insulin can be increased every 3rd or 4th day (2-4 units each time) till reach target – fix the fasting first
- Basal / bedtime insulin regimen -> titrate insulin till target pre-breakfast 4-6 mmol/L, adequate dose 0.4 U/kg/day
- Premixed insulin regimen – more difficult to optimise

Slide 9

Insulin Intensification

- Bedtime basal insulin -> premixed insulin daily / twice daily
- Bedtime basal insulin -> sequential addition of bolus insulin prmeals (BASAL PLUS)
- Bedtime basal insulin -> addition of three bolus insulin (BASAL BOLUS)
- Single premixed dose -> Twice then maybe thrice daily 1->2->3 (premixed analogue)

Slide 10

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
**Slide 11**

**Self Blood Glucose Monitoring**

- Method of choice in monitoring glycaemic control. SBGM should be carried out for patients on insulin and is desirable for those on OAD agents.
- Frequency of blood glucose testing depends on the glucose status, glucose goals and mode of treatment.
- Although SBGM has not been shown to have a significant impact on outcome measures such as HbA\(_1c\) and body weight, it is recommended as part of a wider educational strategy to promote self-care.
- SBGM should be carried out 3 or 4 times daily for patients using multiple insulin injections or insulin pump therapy.

**Slide 12**

**Monitoring - SBGM**

<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>
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<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>

- Recommended timing of SBGM
- Optional timing of SBGM

**Slide 13**

**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</td>
<td>Afternoon tea intake or pre lunch short acting insulin or morning 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>
Slide 14

Glucose Monitoring in Relation to Insulin Therapy

- Those on replacement insulin therapy need to check glucose levels before each meal and before bed (10-11 pm).
- 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.

Slide 15

Oral Agents + Bedtime Insulin

- Values before breakfast give information about bedtime insulin or once daily basal long acting insulin.

Figure 1a: Oral Agent(s) + Bedtime Insulin – Intermediate Acting Insulin

Slide 16

Oral Agents + Bedtime Insulin (cont.)

Recommended timing of SBGM

Figure 1b: Oral Agent(s) + Once Daily Basal Long Acting Insulin
Slide 17

Basal Bolus Insulin Regimen

Figure 2: Basal Bolus Insulin Regimen

---

Slide 18

Basal Bolus Insulin Regimen (cont.)

- 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.
Twice Daily Premixed or Combination Intermediate Acting with Short Acting Insulin

Figure 3: Intermediate Acting with Short Acting Insulin

Slide 20

Twice Daily Premixed or Combination Intermediate Acting with Short Acting Insulin (cont.)

- 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.

Slide 21

Keys to success with insulin

- Start early
- Start simply – easy regimen
- SBGM – monitor regularly
- Avoid hypos
- Review frequently
- Use enough insulin
- Modify insulin regimen with time
- Continuous patient education.
Case Study: OAD & Insulin Therapy

Management of Type 2 Diabetes Mellitus
(4th Edition)
Training Module For Health care Providers

Slide 1

Case 1: Mr. B.A.

Slide 2

Introduction

- 37 y.o. Indian man
- F/H of diabetes: +
- Polyuria and polydipsia of one week duration
- Weight 74 kg; BMI 28 kg/m²
- Recent weight loss.
- Physical examination: NAD
- Random blood glucose: 27 mmol/L

Slide 3

Questions

- Comment on this patient.
- How would you manage this patient?

Slide 3 - Notes

Key Points

- Has several risk factors i.e. Indian ethnicity, family history of diabetes, age over 30 years, obese
- Symptomatic
- Hyperglycaemia
- Screen for other risk factors & diabetes related complications
- HbA₁c will help decide on treatment regime
Slide 4

Treatment

- HbA1c was not done at diagnosis
- FBS 11.0 mmol/L
- Patient was started on:
  - Glibenclamide 2.5 mg BD
  - Metformin 500 mg BD
- After 3 months, HbA1c 8.3; FBS 6.0, 2PPG 7.0

Slide 5

Questions

- Any comments on the HbA1c of 8.3%?
- What would you do after this?

Slide 5 - Notes

Key Points

- HbA1c of 8.3% includes the period of hyperglycaemia at the time of diagnosis.
- HbA1c is an average of glucose over 3 months. Hence it can be predicted that the HbA1c will be less in the next few months.
- Furthermore there may be some improvement in pancreatic function as glucose toxicity to beta cells is reduced.
- Hence it may not be necessary to add extra medications just yet.

Slide 6

Case 2: Madam J.A.

Slide 7

Introduction

- 58 y.o. lady, housewife
- Weight 110 kg; BMI 47 kg/m²
- Duration of diabetes < 1 year
- History of hysterectomy
- F/H nil
- O/E: Acanthosis nigricans noted
Slide 8

- HbA₁c 12.2%
- FBS 15.9 mmol/L
- BP 140/79 mmHg
- Current treatment:
  - Metformin 1 gm TDS
  - Adalat & Prazocin

Slide 9

Questions

- Comment on her status?
- How would you manage this patient?

Key Points

- Severely obese
- Poor glycaemic control
- High BP
- Weight management is essential as insulin use may result in further weight gain.
- Refer obesity clinic
- Change to ACE-I or ARB & optimise anti-HPT. May consider adding thiazides

Slide 9 - Notes

Follow up 3 months later...

- BP now 106/55 mmHg
- HbA₁c 7.6; FBS 11.2
- Still on Metformin 1 gm TDS
- Rosiglitazone 4 mg OD was added during last follow-up

Slide 11

Question

- What would you do next?
Case 3: Madam R.M.

Introduction
- 48 y.o. Malay lady
- Weight 62 kg; BMI 27.3 kg/m²
- F/H: Nil
- Duration of DM: 11 years
- Already on gliclazide and metformin
- HbA₁c 7.9%
- Her weight is increasing

Questions
- How would you manage her?

Key Points
- Still not reaching glycaemic target
- Intensify OADs – may add on Rosiglitazone

On Follow-up...
- Current medications:
  - Metformin 750 mg TDS
  - Gliclazide 120 mg BD
  - Rosiglitazone 4 mg OD
- HbA₁c 7.4%
- Weight 65 kg
Slide 16

Questions

- What do you think is happening to this patient?
- What would you do next?

Key Points
- The addition of rosiglitazone did not give any benefit in this particular patient.
- The patient need to have more education on diet and exercise.
- The other options are DPP-4 inhibitor or Acarbose or Incretin mimetics – these options do not increase weight.

Slide 17

Case 4: Mr. D.K.

Slide 18

Introduction

- 50 y.o. Indian man
- Weight 64.5 kg; BMI 22.5 kg/m²
- Has family history of diabetes
- Duration of diabetes: 5 years
- HbA₁c, 8.6%
- Currently on Metformin 250 mg TDS and Gliclazide 80 mg BD

Slide 19

Questions

- What are your comments on the management of this patient initially?

Key Points
- Poor glycaemic control, not reaching target
- Increase dose of OADs
On Follow-up...
- At the last follow-up, the OADs doses were increased:
  - Metformin 1 gm BD
  - Gliclazide 120 mg BD
- Weight 68 kg
- HbA1c 6.7%

Subsequent Follow-ups...
- HbA1c remained < 7.0%
- Noted elevated post prandial blood glucose of 10-11 mol/L

Questions
- Do you want to do anything else?
- If yes, what would you do?

Key Points
- May increase dose of gliclazide
- May start acarbose to address the post prandial hyperglycaemia
- The other option other than acarbose would be DPP-4 inhibitors.

Case 5: Mr. T.V.
Slide 24

Introduction

- 45 y.o. Indian male, lorry driver
- T2DM for the last 5 years
- No complications detected so far
- Current treatment Glibenclamide 10 mg bd and Metformin 500 mg bd for the last 2 years
- Persistently raised FPG > 8; HbA1c > 9% in the last 2 years
- No symptoms to suggest hypoglycemia
- No SBGM

Slide 25

On Examination…

- Wt. 80 kg (was 75 kg at diagnosis);
- WC 90 cm
- BP 135/80 mmHg
- TG 2.8; LDL 2.5; HDL 1.0
- Urine microalbumin not detected

Slide 26

Questions

- Comment on his status?
- How would you optimise his glycemic control?

Slide 26 - Notes

Key Points

- Poor glycaemic control > 6 months
- Dyslipidaemia
- 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
- Metformin usually maintained
Slide 27

Case 6: Madam Z.R.

Slide 28

Introduction

- 45 y.o. Malay lady, executive officer
- T2DM 5 years, no complications
- Currently on Gliclazide 160 mg BD, Metformin 1 g BD, Acarbose 100 mg BD
- Usually has “lighter” breakfast and lunch; but tend to have late heavy dinner with family
- FPG > 9; HbA1c 10%
- SBGM pre-dinner > 9; 2PPG 12-15

Slide 29

On Follow-up...

- Wt. 80 kg (not much of change since diagnosis); WC 90 cm
- BP 140/90 mmHg
- TG 4.5; HDL 0.9 mmol/L
- She was re-counseled for change in lifestyle and insulin therapy
- She finally agreed for 1 injection per day
- What can we offer her?

Slide 30

Questions

- Comment on her status?
- What can we offer her?

Slide 30 - Notes

Key Points
- Poor glycaemic control despite maximum OADs combination
- Has dyslipidaemia
- Has central obesity
- BP also high
- High pre-dinner blood glucose
Case 7: Mr. M.Y.

Introduction
- 60 y.o. Chinese male, retired teacher
- T2DM for 10 years, complicated by peripheral neuropathy and immature cataract bilaterally
- Currently on Gliclazide 160 mg BD and Metformin 1 g BD; unable to tolerate Acarbose
- FBS > 13; HbA1C > 10%
- Stopped SBGM; disappointed with the results which were always in the teens
- Requesting for multivitamin to overcome lethargy and weight loss

On Examination...
- Wt. 55 kg (was 60 kg 5 years ago)
- WC 75 cm
- Clinically euthyroid; BP 150/80 mmHg
- Sensory loss in stocking distribution with no ulcer or wound or tinea pedis; dermopathy seen on the shins
- TG 1.8; LDL 3.4; HDL 1.3 mmol/L
- 24-hour urine protein 0.5 g per day

Comment on his status.
How will you optimise his condition?

Key Points
- Poor glycaemic control despite maximum OAD
- BP high
- Dyslipidaemia
- Weight loss may indicate pancreatic failure
- Need to start insulin therapy, while managing his other concomitant co-morbidities
TOPIC 8

DIABETES WITH HYPERTENSION & DYSLIPIDAEMIA

MANAGEMENT OF TYPE 2 DIABETES MELLITUS

(4th Edition)

Training Module For Health Care Providers
Slide 1

Hypertension & T2DM

- 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
  - Delay the progression of renal disease and diabetic retinopathy

Slide 2

Diagnosis

- BP >130/80 mmHg two reading 2-3 weeks apart
- Pharmacological treatment should be initiated in patients with diabetes when the BP is persistently >130 mmHg systolic and/or >80 mmHg diastolic

Slide 3

Treatment Goals & Targets

- In general, the target blood pressure should be
  - systolic < 130 mmHg
  - diastolic < 80 mmHg
- With proteinuria >1g/24 hrs, target is ≤125/75 mmHg
- Tight BP control should take precedence over the class of antihypertensive drug used.
- Combination therapy often required
- Lower BP target may be necessary to maximally protect against the development & progression of CV and renal disease.

Slide 4

Other assessments

- Screen for proteinuria or microalbuminuria
- Microalbuminuria / proteinuria +
  - Strongly predicts overt nephropathy and CVD
  - Should be treated even if the BP is not elevated
Other assessments (cont.)

Proteinuria or microalbuminuria +
- Treatment recommendation
  - ACE-I or ARB is preferred
  - In a proportion of patients, microalbuminuria may be normalised by higher doses of ACE-Is and ARBs
  - Normalisation of microalbuminuria is associated with a reduction in the rate of decline in GFR

Non-Pharmacological Treatment

- Non-pharmacological management cannot be over emphasised.
- Dietary counselling
  - Target at optimal body weight
  - Consider glycaemia / dyslipidaemia control
- Moderate dietary sodium restriction is advisable - enhances the effects of ACE-Is and ARBs.
- Further sodium restriction, + diuretic, may be necessary in nephropathy or when the BP is difficult to control.

Pharmacologic Treatment

- If an ACEI is not tolerated, an ARB can be considered
- Diuretics, CCBs, β-blockers and α-blockers may be used as add-on Rx
- Certain classes of antihypertensive drugs may be disadvantageous in DM
### Slide 8

Table 8 (A): Choice of antihypertensive drugs in diabetes patients with concomitant conditions (Adapted from Malaysian CPG for Hypertension 2008)

<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>
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<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>
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<td>+</td>
<td>+</td>
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<td>+</td>
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<tr>
<td>Coronary heart disease</td>
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<td>+++</td>
<td>+++</td>
<td>++</td>
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<td>+</td>
</tr>
<tr>
<td>Heart failure</td>
<td>+++</td>
<td>+++@</td>
<td>+++</td>
<td>+</td>
<td>+</td>
<td>+++</td>
</tr>
</tbody>
</table>

Grading of recommendation (+) to (+++) is based on increasing levels of evidence + current widely accepted practice

* Use with care
* Contraindicated
* Only non-dihydropyridine CCBs
* Metoprolol, bisoprolol, carvedilol – dose needs to be gradually titrated
@ Current evidence available for amlodipine and felodipine only

### Slide 9

Table 8 (B): Choice of antihypertensive drugs in diabetes patients with concomitant conditions (Adapted from Malaysian CPG for Hypertension 2008)

<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>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-diab 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>

Grading of recommendation (+) to (+++) is based on increasing levels of evidence + current widely accepted practice

* Use with care
* Contraindicated
* Only non-dihydropyridine CCB
$ Contraindicated in bilateral renal artery stenosis
Recommendations

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

Summary

- Multi factorial approached needed for treatment patients with T2DM
- Treatment of BP more beneficial than blood glucose
- Choice of mono therapy of HPT should be individualised
- Fixed combination therapy preferred in patients required more than one agent

Introduction

- DM is a coronary heart disease (CHD) risk equivalent.
- Control of hyperglycaemia in T2DM has not been associated with significant decrease in CVD events, except in overweight people with diabetes who were given metformin.
- Efforts must be directed to control other risk factors such as dyslipidaemia, hypertension and other new emerging risk factors
- Treatment of hypertension in diabetes should follow the guidelines for the treatment of hypertension in general (Malaysian CPG for the Management of Hypertension 2008).
DM is a coronary heart disease (CHD) risk equivalent.


Slide 14 - Notes

Aim:
- To highlight the increased risk of cardiovascular disease in people with Type 2 diabetes.

Discussion:
- People with Type 2 diabetes have a higher risk of myocardial infarction (MI) than non-diabetic individuals.
- In one study, people with Type 2 diabetes who had never had an MI had as high a risk of having one as people without Type 2 diabetes with a history of MI.1
- This is of great importance in clinical practice. Remember – look at each person with Type 2 diabetes as if they have already had an MI.

DM is a coronary heart disease (CHD) risk equivalent. Control of hyperglycaemia in T2DM has not been associated with significant decrease in CVD events except in overweight people with diabetes who were given metformin. In other people with T2DM the effect of hyperglycaemia treatment on macrovascular complication can only be seen after 15-18 years early aggressive therapy. Thus, efforts must also be directed to control other risk factors such as dyslipidaemia, hypertension and other new emerging risk factors.

Reference
Slide 15

Dyslipidaemia & Diabetes: Screening

- In adult patients, test for lipid disorders at least annually
- More often if needed to achieve the goal
- 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

Slide 16

Primary target: LDL Cholesterol

- 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
- In individuals with overt CVD
  - All patients should be treated with a statin
- The target of LDL cholesterol: 1.8 mmol/L

Slide 17

Secondary Target: Non-HDL, HDL & TG

<table>
<thead>
<tr>
<th>Non-HDL cholesterol</th>
<th>&lt; 3.4 mmol/L (when TG &gt; 2.3 mmol/L)</th>
</tr>
</thead>
<tbody>
<tr>
<td>HDL cholesterol</td>
<td>&gt; 1.0 mmol/L for males</td>
</tr>
<tr>
<td></td>
<td>&gt; 1.2 mmol/L for females</td>
</tr>
<tr>
<td>TG</td>
<td>&lt; 1.7 mmol/L</td>
</tr>
</tbody>
</table>

Slide 18

Non-Pharmacological Treatment

- Lifestyle modification focusing on the reduction of saturated fat, trans fat and cholesterol intake.
- Weight loss (if indicated) and increased physical activity have been shown to improve the lipid profile.
Slide 19

Pharmacological Treatment

<table>
<thead>
<tr>
<th>Lipid Goal</th>
<th>Initial Drug</th>
<th>Suggested addition (in order of preference)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lower LDL cholesterol</td>
<td>Statins</td>
<td>-</td>
</tr>
<tr>
<td>Increase HDL cholesterol</td>
<td>Fibrate or Nicotinic Acid</td>
<td>-</td>
</tr>
<tr>
<td>Lower TG</td>
<td>Fibrates</td>
<td>Statins</td>
</tr>
<tr>
<td>Treat combined hyperlipidaemia</td>
<td>Statins</td>
<td>Fibrates Resin plus Fibrates Nicotinic Acid</td>
</tr>
</tbody>
</table>

Slide 20

Pharmacological Treatment (cont.)

- In T2DM with very high TG, reduction of carbohydrate intake is emphasised.
- Lowering TG in patients with clinical CVD and normal LDL-cholesterol with a fibrate is associated with a reduction in cardiovascular events.
- 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.

Slide 21

Pharmacological Treatment (cont.)

Special situations
- 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.

Slide 22

Recommendations

- All patients without overt CVD over the age of 40 years should be treated with a statin regardless of baseline LDL cholesterol levels.
- All patients with overt CVD should be treated with a statin.
Case Study: Diabetes with Hypertension & Dyslipidaemia

Management of Type 2 Diabetes Mellitus (4th Edition)

Training Module For Health care Providers

Slide 1

Case One: Mr. S.T.

Slide 2

Introduction

• Mr. S.T., a 45 y.o. Malay man
• Referred by his family physician for further management of diabetes and hypertension
• He is a case of T2DM diagnosed in last 6 years
• Currently treated with:
  - Metformin 1 gm
  - Gliclazide 160 mg twice daily
  - Amlodipine 10 mg daily

Slide 3

Examination & Investigation

• Weight 58 kg; Height 165 cm,
• BP 140/90 mmHg; PR 78 beats/min
• Fundus examination revealed mild non-proliferate retinopathy
• Other examination were normal
• Investigations:
  - FBS 8.0 mmol/L
  - HbA\sub{1c} 7.8%
  - Creatinine 96 µmol/L (6 months earlier)
Slide 4

Question

• What are your comments on the management of the referring doctor?

Slide 4 - Notes

Key Points

• HbA1c not at target despite on maximum doses of 2 OAD agents
• BP not at target
• Choice of anti HPT – ACE-I/ARB recommended for diabetes patients

Slide 5

Laboratory Results

• Total cholesterol 5.2 mmol/L
• HDL-Chol 0.8 mmol/L
• TG 1.7 mmol/L
• LDL-Chol 2.0 mmol/L
• Albustix - ve
• Microalbuminuria + ve
• 24hr. Urine protein 278 mg/24hrs
• S. Creatinine 89 µmol/l
• A1C 8.0 %
• FPG 7.9 mmol/L
• ECG LVH

Slide 6

Question

• Comment on the results
• What are the treatment issues that need to be discussed with the patients?
• Adding third oral agent? or insulin?
• What is the BP target?
**HOT Study**

- The Hypertension Optimal Treatment (HOT) Study enrolled 18,790 patients to assess the optimal target diastolic blood pressure for hypertensive patients over a period of 4.9 years (average follow-up 3.8 years)
- Patients were randomised to felodipine + placebo or felodipine + aspirin
- Principal aims of this study were to assess: the association between major cardiovascular events (non-fatal myocardial infarction, non-fatal stroke, and cardiovascular death) and the target BPs of <90 mmHg, <85 mmHg, and <80 mmHg; the association between major cardiovascular events and diastolic BP achieved during treatment; and the impact of the addition of acetylsalicylic acid to antihypertensive treatment on the rate of major cardiovascular events
- 1,501 patients had diabetes at baseline


![Slide 8](slide8.png)

**HOT Outcomes by Target Blood Pressure Group**

*The outcomes for different blood pressure groups were not statistically significant*

Mean fall in glomerular filtration rate (GFR) according to the degree of proteinuria in patients treated with usual blood pressure control (mean BP about 130/80) or with more aggressive antihypertensive therapy in which the mean BP was 4.7 mmHg lower over a three-year period. The rate of fall in GFR varied directly with protein excretion and the benefit of aggressive BP control was absent in the 420 patients excreting less than 1 g/day, modest in the 104 patients excreting between 1 and 3 g/day, and substantial (3.5 mL/min per year slower) and statistically significant in the 54 patients excreting at least 3 g/day. Data from Klahr, S, Levey, AS, Beck, GJ, et al, N Engl J Med 1994; 330:877.
**Slide 11**

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**Slide 12**

**Question**

- What are the choices for anti-hypertensive drugs?
- In microalbuminuric stage?
- In overt nephropathy?
- ACE-I or ARB?

**Slide 12 - Notes**

**Key Points**

- ACE-I as effective as ARB in nephropathy
- ARBs effect are more class related
- The choice between thiazide, CCB, Beta-blocker, ACE-I or ARB for initial monotherapy does not have great clinical relevance since combination therapy will be required in almost all patients with HT and DM to attain goal of BP values
IRMA 2 Study Design

- 590 patients with hypertension, type 2 diabetes, microalbuminuria (albumin excretion rate 20-200 µg/min), and normal renal function

<table>
<thead>
<tr>
<th>Screening/Enrollment</th>
<th>Control group*</th>
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<tr>
<td></td>
<td>Irbesartan 150 mg*</td>
</tr>
<tr>
<td></td>
<td>Irbesartan 300 mg*</td>
</tr>
</tbody>
</table>

Up to 5 weeks

Follow-up: 2 years

- Adjunctive antihypertensive therapies (excluding ACE inhibitors, angiotensin II receptor antagonists, and dihydropyridine calcium channel blockers) could be added to all groups to help achieve equal blood pressure levels.

IRMA 2 Primary Endpoint Time to Overt Proteinuria

- IRMA 2 is a positive study, demonstrating a 70% risk reduction for the primary endpoint (prevention or slowing of progression to overt diabetic nephropathy), independent of the effects of irbesartan on systemic blood pressure.
- A clear dose response is observed in IRMA 2 for the primary endpoint. The irbesartan 150 mg group demonstrates a 39% relative risk reduction (RRR) vs. the control group (placebo in addition to other non-excluded antihypertensive therapies) in the development of overt proteinuria (urinary albumin excretion rate [AER] > 200 mg/min, or 300 mg/day, and an increase of urinary AER from baseline by at least 30%), p=0.08. The irbesartan 300 mg group demonstrates a highly significant 70% RRR vs. the control group, p<0.001. The Kaplan-Meier curves separate at the first visit (at 3 months) and continue to diverge.
- After adjustment for the baseline level of microalbuminuria and the achieved blood pressure during the study, the benefits of irbesartan in slowing progression to overt proteinuria are still present: RRR of 44% for irbesartan 150 mg vs. the control group (p=0.05); RRR of 68% for irbesartan 300 mg vs. the control group (p<0.001).
IRMA 2 Primary Endpoint Development of Overt Proteinuria

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- A clear dose response is observed in IRMA 2 for the primary endpoint. The irbesartan 150 mg group demonstrates a 39% relative risk reduction (RRR) vs. the control group (placebo in addition to other non-excluded antihypertensive therapies) in the development of overt proteinuria (urinary albumin excretion rate [AER] > 200 mg/min, or 300 mg/day, and an increase of urinary AER from baseline by at least 30%), p=0.08. The irbesartan 300 mg group demonstrates a highly significant 70% RRR vs. the control group, p<0.001. The Kaplan-Meier curves separate at the first visit (at 3 months) and continue to diverge.

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Regression to normoalbuminuria (<20 mg/min, or <30 mg/day) at the last visit was more frequent in the patients treated with irbesartan 300 mg than in the control (placebo in addition to other non-excluded antihypertensive therapies) group (34% vs. 21%, respectively, p=0.006).
Multiple Antihypertensive Agents are Needed to Reach BP Goal

- Major clinical trials have demonstrated that patients typically needed treatment with multiple antihypertensive agents to get to, and stay at, BP goal.
- The number of antihypertensive agents required for BP control in many patients typically averages 2-4, with co-morbid conditions (such as kidney disease or diabetes mellitus) imposing greater drug requirement.
- For example, in the Hypertension Optimal Treatment (HOT) study, an average of 3.3 drugs were required to attain a diastolic BP goal of <80 mmHg, and in the Anglo Scandinavian Cardiac Outcomes Trial-Blood Pressure Lowering Arm (ASCOT-BPLA), most patients were taking at least two antihypertensive agents by the end of the trial.

Recommendations for Multiple-mechanism Therapy: What the Treatment Guidelines Say: JNC 7

- “Most patients with hypertension will require two or more antihypertensive agents to achieve their BP goals”
- “When BP is more than 20 mmHg above systolic goal or 10 mmHg above diastolic goal, consideration should be given to initiate therapy with 2 drugs, either as separate prescriptions or in fixed-dose combinations”

Slide 18 - Notes

- The JNC 7 guidelines also acknowledge that most patients with hypertension will require two or more antihypertensive medications with different and complementary mechanisms to achieve BP goal.
- Indeed, the guidelines state that initiation of drug therapy with more than one agent may increase the likelihood of patients achieving their BP goal in a more timely manner.
- This has important implications because a rapid achievement of target BP may reduce the risk of cardiovascular events.

Question

- Is there a need for lipid lowering agent?

Key Points

- Diabetic Patients with low LDL-CHOL: Benefit of statin treatment; Studies
  - HPS
  - CARE
  - CARDS
Impact of Simvastatin in Patients with Diabetes with Low LDL-C

In patients with diabetes and low baseline LDL-C (<3.0 mmol/L), simvastatin significantly reduced the risk of first major vascular events whether or not patients had prior cardiovascular disease. In all patients with diabetes and baseline LDL-C <3.0 mmol/L (116 mg/dl), simvastatin decreased the incidence of first major vascular events from 20.9% to 15.7%, a 27% risk reduction (p=0.0007). Patients with diabetes, low baseline LDL-C, and no prior cardiovascular disease also had a significant risk reduction with simvastatin (11.1% vs. 8.0%, 30% risk reduction, p=0.05).

Slide 20 - Notes

- In patients with diabetes and low baseline LDL-C (<3.0 mmol/L), simvastatin significantly reduced the risk of first major vascular events whether or not patients had prior cardiovascular disease. In all patients with diabetes and baseline LDL-C <3.0 mmol/L (116 mg/dl), simvastatin decreased the incidence of first major vascular events from 20.9% to 15.7%, a 27% risk reduction (p=0.0007). Patients with diabetes, low baseline LDL-C, and no prior cardiovascular disease also had a significant risk reduction with simvastatin (11.1% vs. 8.0%, 30% risk reduction, p=0.05)

Primary and Secondary Analyses

- Primary efficacy analysis - time to first primary end point
- Acute CHD death
- Non-fatal MI, including silent MI
- Unstable angina
- CABG or other coronary revascularisation
- Resuscitated cardiac arrest
- Stroke
- Secondary efficacy analyses
- All-cause mortality
- Time to first CV event
- Time to any CV event
- Lipid and lipoprotein changes

Slide 21 - Notes

- The primary end point was considered the first of any of the following: acute CHD event (MI including silent infarction, unstable angina, acute CHD death, resuscitated cardiac arrest), coronary revascularisation procedures, or stroke (fatal or non-fatal).
- Secondary end points included the incidence of death, time to first CV event, and lipid and lipoprotein changes.
- Major coronary events are deaths from acute MI; other acute CHD deaths; and non-fatal MI, including silent infarction.
- Coronary revascularisation procedures include coronary artery bypass grafting (CABG) or percutaneous transluminal coronary angioplasty (PTCA).
- Unstable angina is defined as ischemic symptoms accompanied by electrocardiogram (ECG) changes or a troponin rise insufficient to be labeled MI.
- Resuscitated cardiac arrests are those that involved direct current (DC) shock treatments.
- Stroke includes focal neurologic deficits of sudden onset lasting more than 24 hours and subarachnoid haemorrhage regardless of symptom duration.
Effect of Atorvastatin on the Primary End Point: Major CV Events Including Stroke

Relative Risk Reduction 37% (95% CI: 17-52)

P = 0.001

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</tr>
<tr>
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<tr>
<td>4.75</td>
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<td>328</td>
</tr>
</tbody>
</table>


Slide 22 - Notes

- The primary end point comprised the first of the following: acute CHD event (MI including silent infarction, unstable angina, acute CHD death, resuscitated cardiac arrest), coronary revascularisation procedures, or stroke (fatal or non-fatal). Treatment with atorvastatin 10 mg/day was associated with a highly significant 37% reduction in the incidence of the primary end point of major coronary events and stroke (P=0.001).
- Not all patients were completely compliant with their randomised treatment. Had all patients remained on the treatment to which they had been allocated, the observed 37% risk reduction is a conservative estimate. One might argue that with perfect compliance, a risk reduction of up to 46% in the primary end point might have been expected.
- The observed risk reduction is consistent with that seen in HPS and ASCOT. The 37% reduction in major CVD events in CARDS is the largest point estimate of the treatment effect seen among the three trials of lipid lowering for primary prevention in diabetes. In patients with diabetes and no clinically-evident CVD, HPS demonstrated a 33% risk reduction over 5 years (P=.0003) and ASCOT demonstrated a 23% risk reduction over 3.3 years (P<0.001).

References
Slide 23

Question

- Would you prescribe anti-platelets?

Slide 23 - Notes

Key Points

- Aspirin benefit as secondary prevention is similar in diabetic and non-diabetic population.
- Primary prevention study suggest that there little evidence that aspirin is beneficial.
- Aspirin at a dose of 75 mg should be targeted at those with existing CV disease.

Slide 24

Case 2: Mr. Y.M.

Slide 25

Introduction

- Mr. Y.M., 59 year y.o. Malay male
- T2DM for last 6 years
- Weight 70.0 kg; height 165 cm
- BP 130/70 mmHg
- HbA1c 6.4 %
- LDL-Chol 2.8 mmol/L
- HDL-Chol 0.8 mmol/L
- TG 2.0 mmol/l

Slide 26

Current Medications

- Metformin 1 gm BD
- NPH insulin 34 U at bed time
- Amlodipine 5 mg OD
- Aspirin 75 mg OD
Slide 27

Questions

- Identify the patient’s problems
- What are your further assessment?
- Comment on patient’s current management
- Describe your plan of management

Slide 28

Case 3: Madam M.S.

Slide 29

Introduction

- 57 y.o. Indian woman
- Non-smoker
- Hypertension since age 38 years
- T2DM since age 42 years, now on OAD

Slide 30

At Follow-up

- Height 150 cm, weight 68.6 kg, waist 93 cm; BMI 30.5
- BP 145-155 / 90-98 mmHg
- HbA1c 7.6%
- Current treatment:
  - OAD
  - Atenolol 100 mg OD
  - Nifedipine 10 mg BD
Slide 31

Question

- Identify her problems.
- What other investigations would you ask for?

Slide 31 - Notes

Key Points

- Poor BP control
- Obese
- Poor glycaemic control
- Request Renal Function Test + UFEME

Slide 32

Laboratory Investigations

- Renal function:
  - Urea 6.5 mmol/L
  - Na 138 mmol/L
  - K 4.9 mmol/L
  - Creatinine 100 umol/L
- Urine microscopy
  - Protein + (0.25)
  - RBC 5
  - WBC 3
  - Mucus +
  - Bacteria ++

Slide 33

Question

- What is your next step?
- Will you do a urine microalbumin?

Slide 33 - Notes

Key Points

- No, not to do urine microalbumin until urine properly collected. Repeat urine microscopy (mid-stream).
Slide 34

Results
- Repeat mid-stream urine:
  - Urine protein trace
  - Cells 0
  - Bacteria - negative

Slide 35

Question
- So, how now?
- What to do about the BP?

Slide 35 - Notes

Key Points
- Low salt diet
- Increase nifedipine
- Add thiazide
- Add ACE-I
- Add ARB
- Add $\alpha$-blocker

Slide 36

On Follow-up...
- Patient was started on Irbesartan 150 mg OD
- BP now 135 - 140 / 85 mmHg
Slide 37

Question

• Are you satisfied?
• If not, what would you do next?

Slide 37 - Notes

Key Points

• Increase dose of Irbesartan 300 mg OD
• Add Thiazide
• Add ACE-I

Slide 38

Next Follow-up...

• Dose of Irbesartan increased to 300 mg OD

Slide 39

Question

• If BP still not < 130 / 80 mmHg, what would you do?

Slide 39 - Notes

Key Points

• Add Thiazide, half dose
• Change CCB, from Nifedipine to Amlodipine
Slide 40

What about her lipids?

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<thead>
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<th>Date</th>
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<th>September 1999</th>
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<tr>
<td>TC</td>
<td>5.5</td>
<td>4.6</td>
<td>4.0</td>
</tr>
<tr>
<td>HDL</td>
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<td>0.7</td>
</tr>
<tr>
<td>LDL</td>
<td>1.9</td>
<td>2.6</td>
<td>2.1</td>
</tr>
</tbody>
</table>

Slide 41

Question

- Are you happy with her lipid profile?
- If not, what's wrong?
- Will you give her medication?
- If yes, what?

Slide 41 - Notes

Key Points
- Patient has dyslipidaemia
- Start on statins
Slide 1

Background

- OAD agents may not be adequate in maintaining euglycaemia during stress and emergency situations (e.g. infection, MI & surgery).
- In any form of stress, if glycaemic control is inadequate, OAD therapy should be replaced by insulin.
- DKA may develop during stress.
- OAD regimen may be resumed when stress has resolved.

Slide 2

During stress & emergency surgery

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

Slide 3

During stress & emergency surgery (cont.)

- 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.
TOPIC 10

PREGNANCY IN DIABETES

MANAGEMENT OF TYPE 2 DIABETES MELLITUS

(4th Edition)

Training Module For Health Care Providers
Slide 1

Diabetes in Pregnancy

Pregnancy related
- Gestational diabetes (GDM)

Pre-existing diabetes
- Type 1 DM
- Type 2 DM

Slide 2

GDM - Definition

- Any degree of glucose intolerance with onset or first recognition during pregnancy.
- Applies whether insulin or only diet modification is used for treatment and whether or not the condition persists after pregnancy.
- Does not exclude the possibility that unrecognised glucose intolerance may have antedated or begun concomitantly with the pregnancy.

Slide 3

Maternal complications in diabetic pregnancy

- Hypoglycemia, ketoacidosis
- Pregnancy-induced hypertension
- Pyelonephritis, other infections
- Polyhydramnios
- Preterm labor
- Worsening of chronic complications – retinopathy, nephropathy, neuropathy, cardiac disease

Slide 4

Complications for infants of mothers with DM

- Congenital malformations
- Macrosomia
- Birth injury
- Asphyxia
- Respiratory Distress Syndrome
- Perinatal mortality
- Metabolic abnormalities
  - Hypoglycaemia, hypokalemia, hypocalcemia, hyperbilirubinemia, erythrosis
Slide 5

Screening

- Pregnant women should be screened if they have any of the following risk factors:
  - BMI > 27kg/m²
  - Previous macrosomic baby weighing 4 kg or above
  - Previous 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 years

Slide 6

Screening (cont.)

- Pregnant women should be screened at least once at > 24 weeks of gestation, using 75 gm OGTT.
- Screening at an earlier stage of gestation depends on the degree of suspicion and at the physician’s / obstetrician’s request.

Slide 7

Pregnancy and Pre-existing T2DM

- Women with pre-existing T2DM who are planning pregnancy should be referred to physician/diabetologist for further management.
- Pregnancy should be planned.
- Achieve good glycaemic control before conception, aim for HbA1c < 6.5%.
- Insulin therapy may be necessary before conception to achieve good glycaemic control.
Pre-conception care

- The importance of avoiding unplanned pregnancy should be an essential component of diabetes education for women with diabetes in reproductive age group.
- Offer pre-conception care and advice to women with diabetes who are planning to become pregnant before discontinuing contraception.

Pre-conception care (cont.)

- Establishing good glycaemic control before conception and continuing this throughout pregnancy will reduce the risk of miscarriage, congenital malformation, stillbirth and neonatal death.
- It is important to explain that risks can be reduced but not eliminated.

During Pregnancy

- Achieve and maintain ideal glucose levels.
- Advise women with insulin-treated diabetes of the risks of hypoglycaemia and hypoglycaemia unawareness in pregnancy, particularly in the first trimester.
- HbA₁c (4-6 weekly)

Glycaemic targets in pregnancy

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<thead>
<tr>
<th>Timing</th>
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<td>Pre-breakfast</td>
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<tr>
<td>Pre-prandial</td>
<td>3.5 – 5.9</td>
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<tr>
<td>1 hour post prandial</td>
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<tr>
<td>2 hour post prandial</td>
<td>4.4 – 6.7</td>
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<tr>
<td>0200 – 0400 hours</td>
<td>&gt; 3.9</td>
</tr>
</tbody>
</table>
Slide 12

During Pregnancy (cont.)

Close SBGM is required (individualise frequency of monitoring):
• On diet therapy: pre-breakfast, 1 hour PPG levels (weekly-fortnightly)
• On insulin therapy: premeal (breakfast, lunch, dinner) and pre-bed (weekly-fortnightly).
  Once premeal glucose levels are achieved, PPG testing is recommended for fine-tuning of insulin dose

Slide 13

During Pregnancy (cont.)

• 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.

Slide 14

At Delivery

• GIK regimen can be used during delivery or lower segment Caesarean section (LSCS)
• Labour is exercise – need to reduce insulin dose
• Requires glucose substrate

Slide 15

Post-partum Care

• 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.
Slide 16

Postnatal Care

- Offer women who were diagnosed with GDM:
  - Lifestyle advice
  - OGTT

Slide 17

Summary

- Normoglycemia is the goal.
- Prevention of hypoglycemia is paramount especially during times of increased insulin sensitivity.
- To achieve goals: Increased glucose monitoring at peak postprandial glucose concentrations and at peak insulin levels.

Slide 18

Summary

- Normoglycemia is the goal.
- Prevention of hypoglycemia is paramount especially during times of increased insulin sensitivity.
- To achieve goals: Increased glucose monitoring at peak postprandial glucose concentrations and at peak insulin levels.
Case Study: Diabetes in Pregnancy

Management of Type 2 Diabetes Mellitus (4th Edition)

Training Module For Health Care Providers

Slide 1

Case 1: Madam B
Introduction: First Visit

- 35 y.o. Malay woman executive with history of T2DM for 3 years
- Recently married and wishes to start trying for a family immediately
- No other medical illness
- On OAD: Metformin 850 mg bd, Diamicron MR 2 tabs daily
- FPG 7.5 mmol/L, HbA1c 7.8%

Slide 2

Questions

- What should you do next?
- What general advice should she be given?

Slide 2 - Notes

Key Points
- Madam B is a 35-yr-old Malay woman, known T2DM for 3 years, on OAD and trying to conceive for the first time
- She has poor blood glucose control pre-conception
- She needs expert advice from Diabetologist or Physician (with interest in gestational diabetes)
- Madam B is in serious need of expert pre-pregnancy counselling. The importance of avoiding unplanned pregnancy should be an essential component of her diabetes education
- Establishing good glycaemic control before conception and continuing this throughout pregnancy will reduce the risk of miscarriage, congenital malformation, stillbirth and neonatal death.
- It is important to explain that risks can be reduced but not eliminated.
- Pregnancy should be planned. She should try to achieve good glycaemic control before conception, aim for HbA1c < 6.5%
- She will require Lifestyle modification advice and her OAD stopped, and started with insulin therapy at preconception
Slide 3

Questions

• How would you manage her blood glucose?
• How would you monitor her blood glucose?

Slide 3 - Notes

Key Points

• Madam B should try to achieve good glycaemic control for at least 3 months before conception, aim for \( \text{HbA}_1c \leq 6.5\% \)
• Monitor using \( \text{HbA}_1c \) two-monthly as well as frequent/individualise SBGM
• Her treatment should be changed to full insulin therapy and her OAD stopped
• She should get the go-ahead from her diabetologist/physician before trying to conceive

Slide 4

Case 2: Madam C
Introduction: First Visit

• 35 y.o. Indian woman executive recently married is seen at the antenatal clinic (ANC) at 15 weeks gestation
• No prior medical illness
• Her pre-conception BMI was 28 kg/m\(^2\)
• FH both parents have T2DM

Slide 5

Question

• At 15 weeks gestation, should you screen for GDM in her?

Slide 5 - Notes

Key Points

• She has risk factors for GDM (age, BMI, FH), so should be screened early for it
Slide 6

Laboratory Results

- OGTT results
- FPG 5.3 mmol/L
- 2PPG 7.9 mmol/L

Slide 7

Questions

- What is her glucose status?
- What management is required?

Slide 7 - Notes

Key Points

- OGTT showed normal FPG but abnormal 2PPG. So she has GDM.
- Her initial management is lifestyle modification advice and monitor blood glucose at fasting and post-prandial weekly or two-weekly. In third trimester monitor weekly.
- HbA₁c should be monitored monthly. Evidence is not strong because of dilutional effect of pregnancy on haemoglobin but consensus groups suggests that it is a helpful guide to have.

Slide 8

On Follow-up...

- At 30 weeks of gestation, her SBGM are:
  - FPG 5.8 mmol/L, 2PPG 7.1 mmol/L
  - HbA₁c is 7%
  - Fetal USG normal
Case 3: Madam D.D.

Introduction: First Visit

- 35 y.o. Chinese woman executive
- History of T2DM for 3 years
- Recently married and now pregnant at 11 weeks POA
- No other medical illness
- On OAD Metformin 850 mg daily, Diamicon 80 mg bd.
- Compliance to treatment suboptimal
- FPG 8.0 mmol/L, HbA1c 9.0%

Questions

- What is her glucose status?
- What management is required?
- How should her BG be monitored now?

Key Points

- Her SBGM are all elevated as is her HbA1c.
- She now require full insulin therapy for her blood glucose control as well as counselling from dietician and diabetes nurse educator.
- SBGM monitoring while on insulin is FPG and Pre-Prandial BG twice weekly or weekly.

Question

- What should you do next?

Key Points

- No previous counselling regarding pre-conception care in diabetes.
- She has poor blood glucose control currently.
- Madam D.D. needs to establish good glycaemic control ASAP to reduce the risk of miscarriage, stillbirth and neonatal death. Congenital malformation is no longer avoidable this late in the first trimester.
- It is important to explain that risks can be reduced but not eliminated.
- Her OAD should be stopped and insulin started.
Slide 13

Question

• How should she be managed at this stage?

Key Points

• Madam DD needs counselling on preconception care in diabetes to reduce the risk of miscarriage, congenital malformation, stillbirth and neonatal death. It is important to explain that risks can be reduced but not eliminated.
• If she wishes to get pregnant again soon, she should remain on full insulin therapy and not go back on OAD. Aim for good BG control from about 3 months before conceiving again.
• If she has no wish to get pregnant again soon, she may go back on OAD but try to maintain good BG control and practice lifestyle modification. She or her husband should practice contraception.
• When ready to conceive again, she should go back on Insulin therapy and achieve good BG control from about 3 months before conception.

Slide 14

Case 4: Madam E

Introduction: First Visit

• 35 y.o. Malay woman with history of T2DM for 3 years, G2 P0+2
• No other medical illness
• On OAD Metformin 850 mg daily, Diamicron 80mg bd
• Compliance to treatment good
• FPG 7.0 mmol/L, HbA1c 7.5%
• No proper preconception care previously
• Planning pregnancy again
Slide 15

Question

• What should you do next?

Slide 15 - Notes

Key Points
• Blood glucose control currently not optimal.
• Need to give preconception counselling.
• Madam E needs to establish good glycaemic control from about 3 months pre-conception to reduce the risk of miscarriage, congenital malformation, stillbirth and neonatal death. It is important to explain that risks can be reduced but not eliminated.
• Her OAD should be stopped and full insulin therapy started.

Slide 16

On Follow-up…

• After 6 months of pre-conception care, she is pregnant at 8 weeks POA
• Her latest HbA1c was 6.2%
• She’s on Mixtard 32u am, 26u pm

Slide 17

Question

• How would you continue to monitor her?

Slide 17 - Notes

Key Points
• Madam E is pregnant again but this time she had good preconception care. HbA1c at conception was 6.2%.
• Madam E needs to maintain good glycaemic control from now on to reduce the risk of miscarriage, stillbirth and neonatal death. The risk of congenital malformation associated with poor BG control should be low for her.
• Perform SBGM weekly or two weekly.
Slide 18

At 16 weeks...

- At 16 wks gestation her SBGM are as follows:
  - FPG 6.0
  - Pre-lunch 5.2
  - Pre-dinner 6.0
  - Pre-bed 5.8
- On Mixtard 44u am, 32u pm
- No hypoglycaemic attack

Slide 19

Question

- Comment on her current glucose control

Slide 19 - Notes

Key Points
- At 16 weeks POA her SBGM are not on target. The profile suggests that Mixtard is no longer suitable for her.
- She needs basal bolus regimen.
- Perform SBGM weekly or two weekly.

Slide 20

At 31 weeks...

- At 31 wks gestation, her SBGM are as follows:
  - FPG 8.8
  - Pre-lunch 4.2
  - Pre-dinner 5.0
  - Pre-bed 3.5
- On Actrapid 16, 20, 18; Insulatard 20 u
- Mild hypoglycaemic attack around 2 am
Slide 21

Questions

- Comment on her current glucose control
- How would you manage her?

Slide 21 - Notes

Key Points
- At 31 weeks POA her SBGM are generally good except hypoglycaemic attack at 2 am, low BG pre-bed and probably rebound high at pre-breakfast.
- Decrease her night Actrapid and Insulatard by 2 units each. Take snacks pre-bed.
- Perform SBGM weekly.

Slide 22

At 34 weeks...

- AT 34 wks gestation her SBGM are as follows:
  - FPG 5.1
  - Pre-lunch 4.2
  - Pre-dinner 4.8
  - Pre-bed 3.4
- On Actrapid 16, 20, 16; Insulatard 18 u
- Mild hypoglycaemic attack around pre-bed despite sufficient dinner and pre-bed snacks

Slide 23

Question

- Comment on her current glucose control
- How would you manage her?

Slide 23 - Notes

Key Points
- At 34 weeks POA her SBGM are generally good except hypoglycaemic attack at pre-bed only.
- Change her dinner insulin to aspart at 14 units. Maintain all other insulins. She should get less or no hypo attack at pre-dinner.
- Perform SBGM weekly.
- If baby ok, discuss delivery at term with O&G. Will need GIK regimen during labour.
TOPIC 11

SCREENING & DIAGNOSIS OF DIABETES COMPLICATIONS

MANAGEMENT OF TYPE 2 DIABETES MELLITUS

(4th Edition)

Training Module For Health Care Providers
Slide 1

Overview

Microvascular Complications:
• Retinopathy
• Nephropathy
• Neuropathy

Macrovascular Complications:
• Coronary Heart Disease
• Cerebrovascular Disease

Combination of Micro- and Macrovascular complications:
• Diabetic Foot
• Erectile Dysfunction

Slide 2

Retinopathy: Screening

• Initial assessment should be conducted at time of diagnosis of T2DM and annually thereafter.
• Pregnant women with T2DM (not gestational diabetes) should have retinal examination during each trimester.

Slide 3

Eye Examination

• Visual acuity assessed with Snellen chart and any refractive error corrected with pinhole in addition to asking patient to wear bifocals or glasses for presbyopia.
• Fundus examination must be conducted through dilated pupil (tropicamide 0.5% or 1.0%) using direct ophthalmoscope to improve sensitivity.
• Photography with non-mydriatic fundus camera may be used to screen large number of patients.
Retinopathy: Treatment

- Achieve and maintain tight glycaemic and blood pressure control.
- Patients with pre-proliferative or proliferative retinopathy may experience temporary worsening of retinopathy when blood glucose level rapidly lowered.

Referral to ophthalmologist

- Unexplained poor vision
- Diabetic retinopathy greater than occasional micro-aneurysms
- Macular oedema or hard exudates within the macula

Urgent referral to ophthalmologist

- Sudden visual deterioration
- New vessels on funduscopy
- Rubeosis iridis
- Vitreous haemorrhage
- Retinal detachment

Nephropathy: Introduction

- Major cause of chronic kidney disease (CKD) contributing to 57% of new patients requiring dialysis in 2007 in Malaysia.
- Also major risk factor for cardiovascular morbidity and mortality.
- Diagnosis made clinically by the presence of proteinuria (either microalbuminuria or overt proteinuria).
- Progression to ESRD requiring renal replacement therapy occurs in majority of patients, particularly those with poor diabetic and blood pressure control.
Slide 8

Nephropathy: Screening

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

Slide 9

Nephropathy: Management

- If proteinuria detected, 24-hour urine or overnight timed urine should be collected for protein (or a urine protein-creatinine ratio).
- BP and glycaemic control crucial in preventing or retarding progression of diabetic nephropathy.
- Target BP: < 130 / 80 mmHg, but in patients with proteinuria > 1 g/day, target is 125 / 75 mmHg. Several anti-hypertensive agents will be needed to achieve these targets.
- ACEIs or ARBs should be initiated unless contra-indicated to slow progression of diabetic nephropathy.
- Other measures: lipid control, stopping smoking, weight reduction and moderate protein and salt restriction.

Slide 10

Referral to nephrologist

- Serum creatinine > 200 µmol/L
- 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
  - worsening renal function
Neuropathy: Introduction

- Diabetic peripheral neuropathy - "the presence of symptoms and/or signs of peripheral nerve dysfunction in people with diabetes after the exclusion of other causes".
- Diabetic peripheral neuropathy may be asymptomatic in large proportion of cases (up to 50%).

Types of Diabetic Neuropathies

- Distal symmetrical polyneuropathy
- Proximal asymmetrical neuropathy (diabetic amyotrophy)
- Autonomic neuropathy
- Radiculopathy
- Mononeuritis multiplex

Neuropathy: Screening

- Diabetic peripheral neuropathy may be diagnosed by bedside clinical methods
  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.

Neuropathy

Prevention
- Diabetic peripheral neuropathy can be prevented by maintaining good glycaemic control.

Treatment
- Relief of symptoms includes the use of anticonvulsant agents e.g. gabapentin, lamotrigine, carbamazepine or tricyclic antidepressants e.g. amitriptyline.
- Achieve tight glycaemic control.
Slide 15

Coronary Heart Disease: Screening

- Typical symptoms of CHD warrant prompt referral to cardiologist for further assessment.
- Screening asymptomatic patients for CHD:
  - Performance of resting ECG
  - Application of an established cardiovascular risk assessment tool (Framingham Risk Score or UKPDS Risk Engine)

Slide 16

CHD: Screening (cont.)

- Those with peripheral or cerebrovascular disease
- Those leading a sedentary lifestyle, age ≥ 35 years and plan to begin a vigorous exercise program
- Those with two or more of the risk factors:
  - 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
  - BP > 130/85 mmHg
  - Smoking
  - Family history of premature CHD
  - Positive micro / macro-albuminuria test

Slide 17

Aspirin for Primary Prevention

- Primary prevention of CVD with low dose aspirin (75-100 mg) is NOT recommended in people with diabetes unless they are at high risk based on Framingham Risk Assessment Score.

Slide 18

Diabetic Foot: Introduction

- Foot ulcerations and amputations are major causes of morbidity and mortality in patients with diabetes.
- Peripheral neuropathy predisposes to ulcerations and vasculopathy retards the healing process.
Slide 19

Prevention of Foot Ulcers

- Prevention starts with examination of the feet and identifying those at high risk of ulceration.
- Those patients at risk are then given foot care 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.

Slide 20

Risk Factors for Foot Ulcers

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

Slide 21

Diabetic Foot: Assessment

- Neuropathy assessed with 10 g monofilament and one other modality i.e. pin prick, vibration sense using 128 Hz tuning fork, ankle reflexes or vibration perception threshold testing using biothesiometer.
- Loss of protective sensation (LOPS) would be considered present if one or more of the tests abnormal.
- Vasculopathy assessed by asking for symptoms of claudication and examining dorsalis pedis and posterior tibial pulses.
Slide 22

Foot Care Advice

Relevant education for patients:
- In reduced sensation, look at feet daily using mirror to detect early ulcerations
- Wear flat, soft and well fitted shoes to avoid callosities
- Ensure no foreign objects in shoes before putting feet in
- Have one pair of shoes for indoor use as well

Slide 23

Diabetic Foot: Management

- Ulcers in patient with any of the above risk factors warrant early referral to specialist for future shared care.
- Ulcers with cellulitis require antibiotics.
- Trauma induced ulcers with no other risk factors require standard wound care and close follow-up until full recovery.

Slide 24

Erectile Dysfunction: Introduction

- Erectile Dysfunction (ED) defined as consistent or recurrent inability to attain and/or maintain penile erection sufficient for sexual performance.
- ED affects about 34-45% 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.

Slide 25

ED: Screening

- All adult males over the age of 40 should be asked about ED.
- Preservation of early morning erection suggests psychological cause.
- Screening can be done using the 5-item version of the International Index of Erectile Function (IIEF) questionnaire.
Slide 26

ED: Treatment

- Avoid medications (if possible) that may cause ED:
  - Anti-hypertensives (thiazides, beta blockers, methyldopa, spironolactone)
  - Anti-depressants and tranquilisers
  - NSAIDS
  - H2 antagonists (cimetidine)
  - Narcotics
  - Miscellaneous drugs (ketoconazole, anti-cancer agents)
- Psychosexual counselling recommended in functional ED.

Slide 27

ED: Treatment (cont.)

- Phosphodiesterase-5 (PDE-5) inhibitors e.g. sildenafil, tadalafil and vardenafil can be used to treat ED.
- PDE-5 inhibitors 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, e.g. intraurethral alprostadil, vacuum devices with constricting band and surgery.
Case Study: Management of Chronic Complications

Management of Type 2 Diabetes Mellitus
(4th Edition)

Training Module For Health care Providers

Slide 1

Introduction

- Mr. R.S., 48 y.o. male teacher
- Diabetic since 1992 at age 32 years.
- Treated with OHA
- Since 2003, insulin added to OHA
- Family history – both parents had DM
- In 2003, noted to have mild non-proliferative retinopathy both eyes.

Slide 2

On Examination...

- Weight 74 kg
- Height 169 cm
- WC 94 cm
- BP 130/80 mmHg
- Both eyes: dot and blot haemorrhages, hard exudates
- Both feet: reduced sensation
Slide 3

Investigations

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Slide 4

Current Treatment

- S/C Actrapid pre-meals 14 units TDS
- S/C Lantus 20 units ON
- Metformin 850 mg TDS
- Amlodipine 5 mg OD
- Losartan 100 mg OD
- Metoprolol 100 mg BD
- Atorvastatin 40 mg ON
- Fenofibrate 160 mg OD
- Aspirin 150 mg OD

Slide 5

Question

What are his problems?

Slide 5 - Notes

Key Points
- Long standing poorly controlled diabetes
- Hypertension on treatment
- Dyslipidaemia (LDL 3.8, TC 5.8, TG normal)
- Presence of diabetes complications (retinopathy, peripheral neuropathy)
Slide 6

Question

- How would you manage him?

Slide 6 - Notes

Key Points
- Teach patient self titration insulin adjustments
- Check on monitoring on blood sugar
- Check insulin injection techniques
- Optimise dyslipidaemia therapy
- If confirmed nephropathy, target BP is 125/70.
- Aspirin appropriate as patient have multiple risk factors
- Refer to eye specialist
- Foot care (as having neuropathy)
- Review dietary practices
- Weight reduction.
- Physical activity

Slide 7

Case 2: Madam Z.M.

Introduction

- 42 y.o. lady, Para 1
- T2DM diagnosed in 2000 - Presented with left foot infection and severe hyperglycaemia – required I & D
- Started on Metformin
- Usual follow-up in Hospital Kajang

Slide 8

In Mac 2005...

- Mac 2005 – amputation of left big toe for complicated infection in Hospital Kajang
- Mac 2005 – also diagnosed with Hypertension
- Urine protein 3+
- Symptomatic peripheral neuropathy
- Referred to diabetes clinic, HPJ
Slide 9

At Hosp. Putrajaya...

- Seen in HPJ April 2005
- BP 170/100 mmHg
- Wt. 65 kg; BMI 26 kg/m²; WC 88 cm
- Bilateral leg oedema
- Proliferative retinopathy
- Peripheral neuropathy
- Foot deformity and chronic foot ulcer
- Proteinuria

Slide 10

Laboratory Results

- HbA1c 8.1%
- Haemoglobin 9.3 g% - normocytic normochromic
- Lipids: TC 7.2; LDL 4.3; HDL 2.2; TG 1.4; 24 h urine protein 2.2 g 24h
- Creatinine 155 µmol/L

Slide 11

Questions

- Comment on her status?
- What complications does she have?
- What would you do to improve the glycaemic control?
- How would you manage her other problems?

Slide 11 - Notes

Key Points

- Poor glycaemic control
- Already have hypertension & dyslipidaemia
- Complications: Neuropathy, diabetic foot, retinopathy, nephropathy
- Requires multidisciplinary management
- For glycaemic control: add on Bedtime Insulin, stop Metformin
- Add statins + of anti HPT
- Regular or 3 monthly follow-up
- Referral to Diabetes Nurse Educator
- Referred to Dietician (if available)
- Self Blood Glucose Monitoring
- Correct anemia - haematinics
- Early referral to Nephrologist
- Referral to Ophthalmologist

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TEMPLATES FOR TRAINING PROGRAM / SCHEDULE
MANAGEMENT OF TYPE 2 DIABETES MELLITUS
(4th Edition)
Training Module For Health Care Providers
Training Program
Implementation Of The Clinical Practice Guideline In The Management Of Type 2 Diabetes Mellitus (4th Edition), 2009

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<td>1130-1230 Insulin Therapy</td>
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APPENDIX

2

PRE-TEST & POST-TEST QUESTIONNAIRE

MANAGEMENT OF TYPE 2 DIABETES MELLITUS

(4th Edition)

Training Module For Health Care Providers
Pre-test & Post-test Questionnaire

Implementation Of The Clinical Practice Guideline In The Management Of Type 2 Diabetes Mellitus (4th Edition), 2009

SELECT the best answer for each question on the given answer sheet.

1) The primary problem of diabetes is that:
   a. The body cannot digest sugar and carbohydrates
   b. Insulin is not moving enough glucose into the cells or there is a lack of insulin
   c. The liver produces too much sugar and it builds up in the blood stream
   d. There is a defect in the kind of insulin that is made and the body does not recognise it
   e. The kidney excretes glucose leading to compensatory increased glucose production

2) Fatimah is 52 years of age. She first had high blood sugar when she was pregnant but she was fine after delivery. About 10 years ago at a routine check up, her doctor said she had diabetes and started her on oral diabetes pills. She had maintained blood sugars in target range until recently and she just started on Insulin. What kind of diabetes do you think she most likely has?
   a. Gestational Diabetes
   b. Type 1 Diabetes
   c. Type 2 Diabetes
   d. Stable or borderline diabetes.
   e. Secondary Diabetes.

3) Diabetic retinopathy, all are true except:
   a. Microaneurysms is the first ophthalmologic sign
   b. Hard exudates are characteristic
   c. Prominent soft exudates indicates an advanced retinopathy state or an associated
   d. IRMAs (intra-retinal vascular abnormalities) mainly indicate a pre-proliferative stage
   e. Venous loops and beadings are seen mainly in proliferative stage

4) Which lunch meal probably contains the most carbohydrates?
   a. Chicken and Vegetable soup with a few crackers
   b. Rice and Samosa
   c. Rice and Dhal Curry
   d. Grilled beef patty, cottage cheese and slice tomatoes
   e. Yong Tau Fu
5) Which is considered one serving or one carbohydrate ‘choice’ and contains about 15 grams of carbohydrate?
   a. Half (1/2) cup of fruit juice
   b. 1 cup of milk
   c. 3 teaspoons of sugar
   d. One third (1/3) of a cup rice
   e. All of the above

6) To lower your risk of heart and blood vessel diseases and to lower cholesterol, the single most important type of fat to reduce is:
   a. Saturated fat (meat, whole milk dairy products)
   b. Monounsaturated fats (olive oil, avocado)
   c. Polyunsaturated fat (corn oil, safflower oil)
   d. Trans-fatty acids (margarines)
   e. Cholesterol (eggs, liver)

7) Diabetic ketoacidosis, all are true except:
   a. Caused by severe and absolute insulin deficiency
   b. Average fluid loss is 6 liters and potassium loss is 330 meq/L
   c. Any sudden impairment in consciousness during treatment should alert you to possibility of brain edema
   d. Sudden gastric dilatation may occur
   e. Leukocytosis indicates infection

8) Supposed that you are taking a medication that can lower the blood sugar. If you begin to feel a little shaky and weak and a blood sugar check shows the level at 3.4 mmol/L, what is the recommended action?
   a. Lie down and rest for about 30 minutes; avoid strenuous exercise
   b. Drink a tall glass of orange juice with several spoons of sugar stirred in
   c. Have a few peanut butter crackers or a small chocolate bar
   d. Eat 3 to 4 glucose tablets or drink a half (1/2) can of regular soda/coke
   e. Call 911 or 999 for help

9) The recommended action to take if you are sick and do not feel like eating is to:
   a. Stop taking insulin or pills to avoid risk of low blood sugar
   b. Take half (1/2) the dose of your diabetes medication
   c. Take the usual dose of your diabetes medication and must have a light meal
   d. Double the dose of your diabetes medication
   e. Take a high protein diet without medication

10) The target range for blood glucose before meals is:
    a. 2.8 to 3.9 mmol/L
    b. 3.9 to 6.9 mmol/L
    c. 6.9 to 8.9 mmol/L
    d. 8.9 to 11.1 mmol/L
    e. 12.0 to 15.9 mmol/L
11) Patients with diabetes have no control over the development of complications.
   a. True
   b. False
   c. True for chronic complications
   d. True for acute complications
   e. True in Type 1 Diabetes

12) “Tight” control of diabetes means:
   a. Keeping blood glucose as close to normal as possible
   b. Frequent self-monitoring
   c. Reduced complications
   d. Adequate knowledge of diabetes
   e. All of the above

13) What is the maximum dose per day for metformin in order to achieve diabetes control?
   a. 1 gm
   b. 2 gm
   c. 3 gm
   d. 1.5 gm
   e. 750 mg

14) Which two from the following list are contraindications to the use of TZDs?
   i) BP > 170/95
   ii) Concurrent use of insulin
   iii) TG > 5 mmol/L
   iv) BG > 24 mmol/L
   v) ALT greater than 2.5 times limit of normal
   a. i and ii
   b. ii and v
   c. iv and ii
   d. iv and v
   e. i and v

15) Which two of the following list are long acting insulin analogues?
   i) Detemir
   ii) Ultralente
   iii) Glargine
   iv) Exubera
   v) Mixtard 30
   a. i and iv
   b. i and ii
   c. iii and iv
   d. i and iii
   e. iii and v
16) For OAD to work, the body must be able to make some insulin.
   a. Possible
   b. True
   c. False
   d. Sometimes
   e. None of the above

17) The insulin cartridge in your pen that's being used should be stored in:
   a. A cool, dry place
   b. The freezer
   c. The medicine cabinet
   d. The refrigerator
   e. The oven

18) Which exercise is best for patients with “insensitive” feet?
   a. Swimming
   b. Jogging
   c. Running
   d. Tap dancing
   e. Skipping

19) If blood glucose is more that 16.7 mmol/L, insulin should be adjusted or exercise should be delayed.
   a. False
   b. True
   c. Maybe
   d. Possible
   e. Not necessary

20) Carbohydrates should make up what percent of your total daily calories?
   a. 5% to 10%
   b. 15%
   c. 40%
   d. 55% to 60%
   e. 70% to 80%

21) Oral glucose tolerance test, all are true except:
   a. Is not used in the routine diagnosis of diabetes mellitus
   b. There should be unrestricted carbohydrate diet 3 days before test
   c. The patient may be allowed to smoke during the test
   d. The patient should fast overnight
   e. If the 2 hours plasma glucose is between 7.8-11.1mmol/L it is called impaired glucose tolerance test
22) Diagnosis of diabetes mellitus, all are true except:

- a. Glycated hemoglobin is not used for the diagnosis
- b. The presence of glycosuria should warrant further investigation and should not used a diagnostic per se
- c. Ketonuria is not pathognomonic for diabetes and may found in normal people after prolonged fasting or exercise
- d. The fasting blood glucose is always preferred over the random one in the diagnosis
- e. The random blood glucose of more than 11.1 mmol/L on 2 or more occasion is diagnostic for diabetes mellitus

23) Diabetic peripheral neuropathy; all are true except:

- a. Variable combination of axonopathy and demyelination and thickening Shwann cell basal lamina
- b. Overall seen in 50% of cases and usually not that symptomatic
- c. May be associated with Charcot joints
- d. Mainly motor and is irreversible
- e. May cause tropic ulceration in the feet

24) A 54 years old man with Type 2 Diabetes is now on full replacement insulin therapy. He experienced a hypoglycemia episode at 4.00 p.m. His current insulin therapy is Insulatard 30 units & Actrapid 12 units (before breakfast), Insulatard 16 units & Actrapid 8 units (before dinner). BGMS/SMBG on that day showed blood glucose of 6.0 mmol/L before breakfast & 5.8 mmol/L before lunch. The following factors can lead to the hypoglycemia except:

- a. Inadequate carbohydrate intake at lunch time.
- b. Excessive dose of Insulatard in the morning
- c. Mowing the lawn and heavy lifting at 3.00 p.m.
- d. Inadequate carbohydrate intake at breakfast time
- e. Episode of nausea and vomiting after eating lunch

25) In the absence of other factors; appropriate change in therapy is needed. Which of the following would be the sensible action?

- a. Stopping insulin and re-starting oral anti-diabetic agent
- b. Reducing the next day morning dose of Actrapid
- c. Reducing the next day morning dose of Insulatard
- d. Reducing the evening dose of Actrapid
- e. Increasing the evening dose of Insulatard
Name: ______________________________

**ANSWER SHEET: PRE-TEST & POST-TEST QUESTIONNAIRE**


CIRCLE the best answer for each question.

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PRE-TEST & POST-TEST QUESTIONNAIRE


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