Management of Type 2 Diabetes Mellitus

Name of Presenter:
What is Diabetes Mellitus?

Diabetes mellitus is a group of metabolic diseases characterized by hyperglycemia resulting from defects in insulin secretion, insulin action, or both.
Number of people with diabetes worldwide and per region in 2017 and 2045 (20-79 years)

Amongst the 425 million people affected with diabetes in 2017, over 200 million come from Asia.
Top Ten Countries/Territories for Number of People with Diabetes (20-79 years)

<table>
<thead>
<tr>
<th>Rank</th>
<th>Country/territory</th>
<th>Number of people with diabetes</th>
<th>Rank</th>
<th>Country/territory</th>
<th>Number of people with diabetes</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>China</td>
<td>114.4 million (104.1-146.3)</td>
<td>1</td>
<td>India</td>
<td>134.3 million (103.4-165.2)</td>
</tr>
<tr>
<td>2</td>
<td>India</td>
<td>72.9 million (55.5-90.2)</td>
<td>2</td>
<td>China</td>
<td>119.8 million (86.3-149.7)</td>
</tr>
<tr>
<td>3</td>
<td>United States</td>
<td>30.2 million (28.8-31.8)</td>
<td>3</td>
<td>United States</td>
<td>35.6 million (33.9-37.9)</td>
</tr>
<tr>
<td>4</td>
<td>Brazil</td>
<td>12.5 million (11.4-13.5)</td>
<td>4</td>
<td>Mexico</td>
<td>21.8 million (11.0-26.2)</td>
</tr>
<tr>
<td>5</td>
<td>Mexico</td>
<td>12.0 million (6.0-14.3)</td>
<td>5</td>
<td>Brazil</td>
<td>20.3 million (18.6-22.1)</td>
</tr>
<tr>
<td>6</td>
<td>Indonesia</td>
<td>10.3 million (8.9-11.1)</td>
<td>6</td>
<td>Egypt</td>
<td>16.7 million (9.0-19.1)</td>
</tr>
<tr>
<td>7</td>
<td>Russian Federation</td>
<td>8.5 million (6.7-11.0)</td>
<td>7</td>
<td>Indonesia</td>
<td>16.7 million (14.6-18.2)</td>
</tr>
<tr>
<td>8</td>
<td>Egypt</td>
<td>8.2 million (4.4-9.4)</td>
<td>8</td>
<td>Pakistan</td>
<td>16.1 million (11.5-23.2)</td>
</tr>
<tr>
<td>9</td>
<td>Germany</td>
<td>7.5 million (6.1-8.3)</td>
<td>9</td>
<td>Bangladesh</td>
<td>13.7 million (11.3-18.6)</td>
</tr>
<tr>
<td>10</td>
<td>Pakistan</td>
<td>7.5 million (5.3-10.9)</td>
<td>10</td>
<td>Turkey</td>
<td>11.2 million (10.1-13.3)</td>
</tr>
</tbody>
</table>

### Top Ten Countries for Number of IGT 2017 (20-79 years)

<table>
<thead>
<tr>
<th>Rank</th>
<th>Country/territory</th>
<th>Number of people with IGT 2017</th>
<th>Rank</th>
<th>Country/territory</th>
<th>Number of people with IGT 2045</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>China</td>
<td>48.6 million (24.9-110.7)</td>
<td>1</td>
<td>China</td>
<td>59.9 million (29.8-136.1)</td>
</tr>
<tr>
<td>2</td>
<td>United States</td>
<td>36.8 million (31.4-42.4)</td>
<td>2</td>
<td>United States</td>
<td>43.2 million (35.6-49.0)</td>
</tr>
<tr>
<td>3</td>
<td>Indonesia</td>
<td>27.7 million (14.7-29.9)</td>
<td>3</td>
<td>India</td>
<td>41.0 million (31.1-78.6)</td>
</tr>
<tr>
<td>4</td>
<td>India</td>
<td>24.0 million (18.3-48.4)</td>
<td>4</td>
<td>Indonesia</td>
<td>35.6 million (22.7-37.6)</td>
</tr>
<tr>
<td>5</td>
<td>Brazil*</td>
<td>14.6 million (10.5-19.4)</td>
<td>5</td>
<td>Brazil*</td>
<td>20.7 million (15.7-27.0)</td>
</tr>
<tr>
<td>6</td>
<td>Mexico*</td>
<td>12.1 million (10.3-13.9)</td>
<td>6</td>
<td>Mexico*</td>
<td>20.6 million (17.0-23.3)</td>
</tr>
<tr>
<td>7</td>
<td>Japan</td>
<td>12.0 million (10.3-15.2)</td>
<td>7</td>
<td>Nigeria*</td>
<td>17.9 million (7.1-42.0)</td>
</tr>
<tr>
<td>8</td>
<td>Pakistan</td>
<td>8.3 million (4.1-11.8)</td>
<td>8</td>
<td>Pakistan</td>
<td>16.7 million (8.7-23.6)</td>
</tr>
<tr>
<td>9</td>
<td>Thailand*</td>
<td>8.2 million (6.8-10.3)</td>
<td>9</td>
<td>Ethiopia*</td>
<td>14.1 million (11.1-30.1)</td>
</tr>
<tr>
<td>10</td>
<td>Nigeria*</td>
<td>7.7 million (2.6-17.4)</td>
<td>10</td>
<td>Japan</td>
<td>10.3 million (8.9-13.0)</td>
</tr>
</tbody>
</table>

*Data was extrapolated from similar countries.

Masalah DM di Indonesia
Tahun 2007 - 2013

Sumber: Riskesdas 2007

Sumber: Riskesdas 2013
Prevalensi Diabetes Melitus
Pada Penduduk Usia ≥ 15 Tahun Menurut Provinsi di Indonesia Tahun 2013

(Sumber: Riskesdas, 2013)
Classification of Diabetes

**Type 1 Diabetes**
- due to autoimmune β-cell destruction, usually leading to absolute insulin deficiency

**Type 2 Diabetes**
- due to progressive loss of β-cell insulin secretion frequently on the background of insulin resistance

**Gestational diabetes mellitus**
- Diabetes diagnosed in the second or third trimester of pregnancy that was not clearly overt diabetes prior to gestation

**Specific types of diabetes due to other causes**
- monogenic diabetes syndromes (such as neonatal diabetes and maturity-onset diabetes of the young), diseases of the exocrine pancreas
Diabetes Symptoms

- Weight loss—event eating more (type 1), Tingling, pain, or numbness in the hands/feet (type 2)
- Urinating often
- Blurry vision
- Feeling very thirsty
- Extreme fatigue
- Cuts/bruises that are slow to heal
- Feeling very hungry

Multiple, Complex Pathophysiologial Abnormalities in T2DM

- Gut carbohydrate delivery & absorption
- Incretin effect
- Hepatic glucose production
- Renal glucose excretion
- Peripheral glucose uptake

Adapted from: Inzucchi SE, Sherwin RS in: Cecil Medicine 2011
Natural History of Type 2 Diabetes

*IGT=impaired glucose tolerance

ARE YOU AT RISK FOR
TYPE 2 DIABETES?

Diabetes Risk Test

1. How old are you?
   - Less than 40 years (0 points)
   - 40—49 years (1 point)
   - 50—59 years (2 points)
   - 60 years or older (3 points)
   Write your score in the box.

2. Are you a man or a woman?
   - Man (1 point)
   - Woman (0 points)

3. If you are a woman, have you ever been diagnosed with gestational diabetes?
   - Yes (1 point) No (0 points)

4. Do you have a mother, father, sister, or brother with diabetes?
   - Yes (1 point) No (0 points)

5. Have you ever been diagnosed with high blood pressure?
   - Yes (1 point) No (0 points)

6. Are you physically active?
   - Yes (0 points)
   - No (1 point)

7. What is your weight status?
   (see chart at right)

If you scored 5 or higher:
You are at increased risk for having type 2 diabetes. However, only your doctor can tell for sure if you
do have type 2 diabetes or prediabetes (a condition that precedes type 2 diabetes in which blood
glucose levels are higher than normal). Talk to your doctor to see if additional testing is needed.

Type 2 diabetes is more common in African Americans, Hispanics/ Latinos, American Indians, and Asian Americans and Pacific Islanders.

Higher body weights increase diabetes risk for everyone.
Asian Americans are at increased diabetes risk at lower body weights than the rest of the general public (about 15 pounds lower).

For more information, visit us at diabetes.org or call 1-800-DIABETES (1-800-342-2383)

Lower Your Risk
The good news is that you can manage your risk for type 2 diabetes. Small steps make a big difference and can help you live a longer, healthier life.
If you are at high risk, your first step is to see your doctor to see if additional testing is needed.
Visit diabetes.org or call 1-800-DIABETES (1-800-342-2383) for information, tips on getting started, and ideas for simple, small steps you can take to help lower your risk.
Various Environmental Factors of Diabetes Development in Asian Population

- **Urbanization and modernization**
  - less walking, less biking, and less daily physical activity.

- **Dietary factors**
  - Higher fat and lower carbohydrate intake
  - Unhealthy trans fats and saturated fats

- **White rice consumption**
  - Higher glycemic index (GI) than whole grains

- **Smoking**
  - Associated with higher abdominal fat and a 45% increased risk of developing diabetes

- **Environmental pollutants**
  - Also increase risk of insulin resistance and diabetes.

- **Sleep-disordered breathing and sleep deprivation**
  - Increases risk of diabetes and poor glycemic control

- **Chronic infections**
  - H. Pylori, Hepatitis B virus, etc.
Diagnosis and Goal of Treatment in Type 2 Diabetes
## Kadar Tes Laboratorium Darah untuk Diagnosis Diabetes dan Prediabetes

<table>
<thead>
<tr>
<th></th>
<th>HbA1c (%)</th>
<th>Glukosa darah puasa (mg/dL)</th>
<th>Glukosa plasma 2 jam setelah TTGO (mg/dL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diabetes</td>
<td>≥ 6.5</td>
<td>≥ 126</td>
<td>≥ 200</td>
</tr>
<tr>
<td>Prediabetes</td>
<td>5.7 - 6.4</td>
<td>100-125</td>
<td>140-199</td>
</tr>
<tr>
<td>Normal</td>
<td>&lt; 5.7</td>
<td>100</td>
<td>&lt; 140</td>
</tr>
</tbody>
</table>

Konsensus Perkeni 2015
**Sasaran Pengendalian DM**

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Target</th>
</tr>
</thead>
<tbody>
<tr>
<td>IMT (kg/m2)</td>
<td>18.5 - &lt; 23</td>
</tr>
<tr>
<td>Tekanan darah sistolik (mmHg)</td>
<td>&lt;140</td>
</tr>
<tr>
<td>Tekanan darah diastolic (mmHg)</td>
<td>&lt;90</td>
</tr>
<tr>
<td>Glukosa darah preprandial kapiler (mg/dl)</td>
<td>80-130</td>
</tr>
<tr>
<td>Glukosa darah 1-2 jam PP kapiler (mg/dl)</td>
<td>&lt;180</td>
</tr>
<tr>
<td>HbA1c (%)</td>
<td>&lt; 7 (atau individual)</td>
</tr>
<tr>
<td>Kolesterol LDL (mg/dl)</td>
<td>&lt;100 (&lt;70 bila risiko KV sangat tinggi)</td>
</tr>
<tr>
<td>Kolesterol HDL (mg/dl)</td>
<td>Laki-laki: &gt;40; Perempuan: &gt;50</td>
</tr>
<tr>
<td>Trigliserida (mg/dl)</td>
<td>&lt;150</td>
</tr>
</tbody>
</table>

Keterangan: KV = Kardiovaskular, PP = Post prandial
Depicted are patient and disease factors used to determine optimal A1C targets (ADA, 2018)

### Approach to the Management of Hyperglycemia

<table>
<thead>
<tr>
<th>Patient / Disease Features</th>
<th>More stringent</th>
<th>A1C 7%</th>
<th>Less stringent</th>
</tr>
</thead>
<tbody>
<tr>
<td>Risks potentially associated with hypoglycemia and other drug adverse effects</td>
<td>low</td>
<td>high</td>
<td></td>
</tr>
<tr>
<td>Disease duration</td>
<td>newly diagnosed</td>
<td>long-standing</td>
<td></td>
</tr>
<tr>
<td>Life expectancy</td>
<td>long</td>
<td>short</td>
<td></td>
</tr>
<tr>
<td>Relevant comorbidities</td>
<td>absent</td>
<td>few / mild</td>
<td>severe</td>
</tr>
<tr>
<td>Established vascular complications</td>
<td>absent</td>
<td>few / mild</td>
<td>severe</td>
</tr>
<tr>
<td>Patient attitude and expected treatment efforts</td>
<td>highly motivated, adherent, excellent self-care capabilities</td>
<td>less motivated, nonadherent, poor self-care capabilities</td>
<td></td>
</tr>
<tr>
<td>Resources and support system</td>
<td>readily available</td>
<td>limited</td>
<td></td>
</tr>
</tbody>
</table>
Major microvascular and macrovascular complications of diabetes

**Microvascular**
- Cognitive impairment
- Diabetic retinopathy
- Diabetic nephropathy
- Diabetic neuropathy
  - Cardiac autonomic neuropathy
- Skin infection
- Gastro-intestinal and bladder dysfunction
- Sexual dysfunction
- Peripheral sensory dysfunction
- Diabetic foot

**Macrovascular**
- Cerebrovascular disease
- Coronary disease
  - Coronary heart disease
- Atherosclerosis
- Peripheral vascular disease

UKPDS 35: Impact of increasing A1c on Cardiovascular Disease in T2DM

- Fatal and non-fatal MI: 14% rise in rise per 1% ↑ in A1c
- Fatal and non-fatal stroke: 12% rise in rise per 1% ↑ in A1c
- Amputasi/death from PVD: 43% rise in rise per 1% ↑ in A1c
- Heart failure: 16% rise in rise per 1% ↑ in A1c

Stratton et al. UKPDS 35. BMJ 2000;321:405-412
Aim of treatment: to prevent the complications of diabetes

- Diabetic retinopathy
- Diabetic nephropathy
- Diabetic neuropathy
- Limb amputation

Non-vascular complications:
- Cancer
- Infections
- Degenerative diseases
- Depression
- Cognitive disorders
- ...

* The most common cause of death in patients with diabetes

Diabetes is a vascular disease

Guidelines of the Management of Type 2 Diabetes
Penatalaksanaan Diabetes Melitus

1. Edukasi
2. Terapi gizi medik
3. Latihan Jasmani
4. Intervensi Farmakologis

Langkah-langkah penatalaksanaan DM

Algorithm of type 2 diabetes management in Indonesia

Healthy Life Style Modification

- **HbA1C <7.5%**
  - In 3 months, HbA1C > 7%
    - Monotherapy* with one of below
      - Metformin
      - GLP1 R-agonist
      - DPP4-I
      - AGI
      - SGLT2-I*
      - Thiazolidindione
      - Sulfonylurea
      - Glinide

- **HbA1C ≥7.5%**
  - + Monotherapy in 3 months, HbA1C > 7%
    - Combination 2 drugs* with different mechanism
      - GLP1 R-agonist
      - DPP4-I
      - Thiazolidindione
      - SGLT2-I*
      - Basal Insulin
      - SU / Glinide
      - Cholesevelam**
      - Bromocriptin QR**
      - AGI

- **HbA1C >9.0%**
  - Clinical features (-)
    - Combination 2 drugs
    - Insulin ± other drugs
  - Clinical features (+)
    - Combination 3 drugs
    - Starts or intensification insulin therapy

Notes:
* Registered drugs, its selection and usage is considered based on benefit, adverse, and availability
** Cholesevelam is not yet available in Indonesia, and Bromocriptin QR is generally used in pituitary tumor

Indonesian Endocrine Society (Perkeni) Consensus 2015
Sulfonylurea – Focus on Glimepiride

• For decades, sulfonylureas (SUs) have been important drugs in the antidiabetic therapeutic.

• They have been used as monotherapy as well as combination therapy.

• Modern SUs, such as glimepiride are associated with better safety profiles.
Sulfonilurea – mekanisme kerja

[Diagram]

1. Sulfonilurea berikatan pada reseptor sel beta
2. Kanal kalium menutup
3. Hal ini menyebabkan kanal kalsium sel beta membuka, meningkatkan aliran kalsium ke dalam sel
4. Peningkatan kadar kalsium intraseluler memicu lepasnya insulin
5. Insulin disekresi dalam darah

Adapted from Porte et al, 2003

Sulfonilurea menstimulasi sekresi insulin oleh sel β pankreas
Glimepiride: Unique Dual Mode of Action

<table>
<thead>
<tr>
<th></th>
<th>Action on insulin secretion</th>
<th>Action on insulin resistance</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Glimepiride</strong></td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Conventional Sulfonylureas</td>
<td>+</td>
<td>-</td>
</tr>
<tr>
<td>Glinides</td>
<td>+</td>
<td>-</td>
</tr>
<tr>
<td>Biguanides</td>
<td>-</td>
<td>+</td>
</tr>
<tr>
<td>Glitazones</td>
<td>-</td>
<td>+</td>
</tr>
<tr>
<td>α-Glucosidase Inhibitors</td>
<td>-</td>
<td>+</td>
</tr>
</tbody>
</table>

References:
Changes in A1c Observe with Oral Antihyperglycemic Therapy in subject with DM2

<table>
<thead>
<tr>
<th>Drug</th>
<th>Maximum daily dose (mg/day)</th>
<th>Monthly average cost†</th>
<th>Percent reduction in HbA$_1^c$ from baseline‡</th>
</tr>
</thead>
<tbody>
<tr>
<td>Glipizide GITS</td>
<td>20</td>
<td>45</td>
<td>10–25</td>
</tr>
<tr>
<td>Glimepiride</td>
<td>8</td>
<td>52</td>
<td>15–40</td>
</tr>
<tr>
<td>Metformin</td>
<td>2550</td>
<td>105</td>
<td>10–25</td>
</tr>
<tr>
<td>Rosiglitazone</td>
<td>8</td>
<td>154</td>
<td>6–20</td>
</tr>
<tr>
<td>Pioglitazone</td>
<td>45</td>
<td>160</td>
<td>6–20</td>
</tr>
<tr>
<td>α-Glucosidase inhibitors</td>
<td>300</td>
<td>70</td>
<td>7–14</td>
</tr>
<tr>
<td>Repaglinide</td>
<td>12</td>
<td>167</td>
<td>7–16</td>
</tr>
<tr>
<td>Nateglinide</td>
<td>360</td>
<td>90</td>
<td>7–12</td>
</tr>
</tbody>
</table>

Kabadi UM et al. Manage Care 2004
Insulin Secretion of Glimepiride

Glimepiride: Treat fasting AND postprandial hyperglycemia

**First and second phase insulin secretion before and after treatment with Glimepiride**

Incremental plasma insulin (pmol/L)

- **First Phase**
  - Before treatment
  - After treatment
  - $p=0.04$

- **Second Phase**
  - Before treatment
  - After treatment
  - $p=0.02$

Euglycemic and hyperglycemic clamp studies in 11 obese patients with T2DM with good glycemic control before and after 4 months treatment with glimepiride to assess effect of glimepiride on insulin secretion.

Comparison of Extrapancreatic Action of Glimepiride and Other Sulfonylureas

Glimepiride has better extrapancreatic activity among sulfonylureas

Mean increase in plasma insulin (PI) and mean % decrease in blood glucose (BG) over 6 hours after single dose

- **Glimepiride®**: PI/BG ratio = 0.03 (n=16)
- **Glibenclamide**: PI/BG ratio = 0.16 (n=16)
- **Gliclazide**: PI/BG ratio = 0.07 (n=14)
- **Glipizide**: PI/BG ratio = 0.11 (n=13)

Sulfonylureas tested in fasted male beagle dogs to determine ratios of mean plasma insulin release/blood glucose decrease.
Significantly lower incidence of severe hypoglycemic events with Glimepiride vs glibenclamide (0.86 vs 5.6/1000 person-years)
Safety: Weight

Treatment with Glimepiride has a stable weight neutral or even weight reducing effect in most patients with Type 2 diabetes.

Mean intra-individual weight change relative to baseline

- Months of treatment:
  - 4 months: -1.9 kg ($p<0.0001^*$)
  - 12 months: -2.9 kg ($p<0.05^*$)
  - 18 months: -3.0 kg ($p<0.005^*$)

*vs. baseline

Open, uncontrolled, observational study. 1770 T2DM patients were enrolled and 284 were followed-up for 1.5 years. Patients received 0.5 to > 4 mg glimepiride once daily.

Kejadian Hipoglikemia dan HbA1c sebelum, selama, dan setelah Ramadan

HbA1c (%)

Pre-Ramadan

During Ramadan

Post Ramadan Period

Hypoglycemic events : 25 (in 13 patients)

Hypoglycemic events : 15 (in 11 patients)

Hypoglycemic events : 8 (in 8 patients)

Newly diagnosed (n=100)

Already Treated (n=232)

Glimepiride tidak meningkatkan kejadian Hipoglikemia
Use of Glimepiride during Ramadan

<table>
<thead>
<tr>
<th>Sebelum Ramadan</th>
<th>Selama Ramadan</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pasien dengan diet dan aktivitas jasmani.</td>
<td>Pertimbangkan memodifikasi waktu dan intensitas aktivitas jasmani.</td>
</tr>
<tr>
<td>Pasien dengan obat hipoglikemi oral Metformin 500 mg 3x/hari.</td>
<td>Pastikan asupan cairan yang cukup.</td>
</tr>
<tr>
<td>Sulfonilurea 1x/hari.</td>
<td>Pastikan asupan cairan yang cukup.</td>
</tr>
<tr>
<td>Sulfonilurea 2x/hari.</td>
<td>Berikan 1000 mg waktu buka dan 500 mg waktu sahur.</td>
</tr>
<tr>
<td>Insulin premixed atau insulin intermediate 2x/hari.</td>
<td>Berikan sebelum berbuka puasa, sesuaikan dosis berdasar hasil pemeriksaan glikemi dan risiko hipoglikemi.</td>
</tr>
<tr>
<td></td>
<td>Berikan dosis biasa sebelum buka dan ½ dosis sebelum sahur.</td>
</tr>
<tr>
<td></td>
<td>Pastikan asupan cairan yang cukup.</td>
</tr>
<tr>
<td></td>
<td>Pertimbangkan untuk mengubah menjadi insulin kerja panjang atau insulin kerja menengah di petang hari dan insulin kerja cepat (rapid-acting) atau kerja pendek (short-acting) di waktu makan. Dosis biasa waktu buka dan dosis ½ waktu sahur.</td>
</tr>
</tbody>
</table>

Glimepiride bekerja selama 24 jam mengontrol gula darah harian, cukup dikonsumsi 1x sehari

Panduan Penatalaksanaan DM Tipe 2 Pada Individu Dewasa di Bulan Ramadan, PERKENI 2015
Renal Impairment

Dose Adjustment for insulin Compounds and oral medicines for Diabetes in CKD

<table>
<thead>
<tr>
<th>Medication Class and Agents</th>
<th>CKD stages 3, 4, and 5 ND</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Insulin</strong></td>
<td></td>
</tr>
<tr>
<td>Glargine</td>
<td>No advised dose adjustment*</td>
</tr>
<tr>
<td>Detemir</td>
<td>No advised dose adjustment*</td>
</tr>
<tr>
<td>Neutral Protamine Hagedom (NPH)</td>
<td>No advised dose adjustment*</td>
</tr>
<tr>
<td>Regular</td>
<td>No advised dose adjustment*</td>
</tr>
<tr>
<td>Aspart</td>
<td>No advised dose adjustment*</td>
</tr>
<tr>
<td>Lispro</td>
<td>No advised dose adjustment*</td>
</tr>
<tr>
<td>Glulisine</td>
<td>No advised dose adjustment*</td>
</tr>
<tr>
<td><strong>First-generation sulfonylureas</strong></td>
<td></td>
</tr>
<tr>
<td>Acetohexamide**</td>
<td>Avoid use</td>
</tr>
<tr>
<td>Chlorpropamide</td>
<td>GFR 50-80 mL/min/1.73 m²: reduce dose 50%, GFR &lt;50 mL/min/1.73 m²: avoid use</td>
</tr>
<tr>
<td>Tolazamide</td>
<td>Avoid use</td>
</tr>
<tr>
<td>Tolbutamide</td>
<td>Avoid use</td>
</tr>
<tr>
<td><strong>Second-generation sulfonylureas</strong></td>
<td></td>
</tr>
<tr>
<td>Glipizide</td>
<td>No dose adjustment</td>
</tr>
<tr>
<td>Glimepiride</td>
<td>Start conservatively at 1 mg daily</td>
</tr>
<tr>
<td>Glybunde</td>
<td>Avoid use</td>
</tr>
<tr>
<td>Gliclazide**</td>
<td>No dose adjustment</td>
</tr>
<tr>
<td><strong>Meglitinides</strong></td>
<td></td>
</tr>
<tr>
<td>Repaglinide</td>
<td>If GFR &lt;30 mL/min/1.73 m² start conservatively at 0.5 mg with meals</td>
</tr>
<tr>
<td>Nateglinide</td>
<td>If GFR &lt;30 mL/min/1.73 m² start conservatively at 60 mg with meals</td>
</tr>
<tr>
<td><strong>Biguanides</strong></td>
<td></td>
</tr>
<tr>
<td>Metformin***</td>
<td>United States FDA label states, &quot;do not use if Scr ≥1.5 mg/dL in men, ≥1.4 mg/dL in women&quot; British National Formulary and the Japanese Society of Nephrology recommend cessation if eGFR &lt;30 mL/min/1.73 m²</td>
</tr>
</tbody>
</table>
• SUs are associated with a significantly lower cost per QALYs and result in the longest time to insulin dependent\(^1\)

• The cost comparison indicates that SUs would be the preferred as an add-on to metformin\(^2\)

• Lower cost without compromising the glycemic efficacy and tolerability will make SUs the prime choice\(^2\)

SUs incurs lower cost per QALY

- Use of SU was associated with significantly lower cost per quality-adjusted lifeyears (QALY) and resulted in the longest time to insulin dependent

Take Home Message…….

• Diabetes can be managed by healthy lifestyle in combination with medical treatment

• Choosing the medication for patients should refer to doctor’s recommendation

• **Early detection** and treatment of diabetes can decrease the risk of developing the **complications of diabetes**

• Based on PERKENDI guideline **Glimepiride** as an oral antidiabetic, can be initiated as monotherapy or combination with oral antidiabetics/insulin/GLP-1 agonist in treating patients with newly diagnosed T2DM