Clinical Practice Guidelines: 
Management of Type 2 Diabetes Mellitus 
(5th Edition) 2015

Topic 1: 
Overview of CPG 
For the Management of T2DM
Diabetes: The Disease

• T2DM is primarily due to insulin resistance as well as deficiency. The insulin resistance state results in increased hepatic glucose output, reduced utilisation of glucose by various organs, increased renal reabsorption of glucose and reduced incretin hormones production among others.

• In general T2DM is an important risk factor for cardiovascular disease and results in various other complications namely nephropathy, retinopathy, neuropathy and dermatopathy.

• Currently there is no known cure but the disease can be controlled enabling the individual to have an improved quality of life.

• The main aim of management is directed at reducing acute and chronic complications (microvascular and macrovascular).
Diabetes: The Burden

- The National Health and Morbidity Survey (NHMS) 2015 reported diabetes prevalence figures of 17.5% for adults above the age of 18 years.

- Among adults above the age of 18 years old, the prevalence was highest in the Indians (22.1%) followed by Malays (14.6%) and Chinese (12.0%).

- Of concern, 53% of those with diabetes above the age of 18 years old were unaware of their diagnosis. The percentage of undiagnosed diabetes is highest among the Malays (67%) followed by Chinese (64%) and Indians (53%).

- Similarly the proportion of undiagnosed diabetes is also highest in the young.
Diabetes: The Burden

• The prevalence of T2DM is increasing in the young with 5.5% (mostly undiagnosed) of those between ages 18-19 years affected by it.

• In terms of diabetes control, only 23.8% of patients in primary care and 12.7% in tertiary institutions were able to achieve their specified glycaemic targets.

• Up to 25.1% of T2DM patients in the general population were on insulin compared to 65.4% in tertiary institutions.
Burden of Diabetes in Malaysia: (Adults age 18 years & above)

2015 projection

Prediction Made in 2011
## Status of Diabetes Mellitus in Malaysia in the past 20 years

<table>
<thead>
<tr>
<th>Remarks</th>
<th>2006 NHMS III</th>
<th>2011 NHMS IV</th>
<th>2015 NHMS V</th>
<th>2009 MSSM</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prevalence</td>
<td>11.6%</td>
<td>15.2 %</td>
<td>17.5%</td>
<td>22%</td>
</tr>
<tr>
<td>Known diabetes</td>
<td>7.0%</td>
<td>8.2 %</td>
<td>8.3%</td>
<td>11 %</td>
</tr>
<tr>
<td>Undiagnosed diabetes</td>
<td>4.5%</td>
<td>7.0 %</td>
<td>9.2%</td>
<td>11%</td>
</tr>
<tr>
<td>Impaired Glucose Tolerance (IGT) / Fasting Glucose (IFG)</td>
<td>4.2%**</td>
<td>4.9 %</td>
<td>4.7%</td>
<td>20.5%</td>
</tr>
</tbody>
</table>

Use of fasting capillary finger prick BG
# Prevalence of Risk Factors In Malaysia (1996-2015)

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Age Group</td>
<td>≥18 yrs</td>
<td>≥ 18yrs</td>
<td>≥ 18yrs</td>
<td>≥ 18yrs</td>
</tr>
<tr>
<td>Smoking</td>
<td>24.8%</td>
<td>21.5%</td>
<td></td>
<td>22.8%</td>
</tr>
<tr>
<td>Physically inactive</td>
<td>88.4%</td>
<td>43.7%</td>
<td></td>
<td>33.5%</td>
</tr>
<tr>
<td>Unhealthy Diet</td>
<td>N.A.</td>
<td>N.A.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Overweight (BMI ≥ 25 &amp; &lt; 30kg/m²)</td>
<td>16.6%</td>
<td>29.1%</td>
<td></td>
<td>30.0% (WHO) 33.4% (M’sian CPG)</td>
</tr>
<tr>
<td>Obesity (BMI ≥30kg/m²)</td>
<td>4.4%</td>
<td>14.0%</td>
<td></td>
<td>17.7% (WHO) 30.6% (M’sian CPG)</td>
</tr>
</tbody>
</table>
Type 2 diabetes increases CVD risk

*p < 0.1; †p < 0.05; ‡p < 0.01; §p < 0.001

Adapted from Kannel WB et al. Am Heart J 1990; 120: 672–6.
Mortality rate is twice as great in patients with diabetes.
Every 1% reduction in HBA$_{1c}$ Reduced Risk

- Deaths from diabetes: -21%
- Heart attacks: -14%
- Microvascular complications: -37%
- Peripheral vascular disorders: -43%


*p<0.0001*
## NDR – Patients registered (Active patients; as of 27 August 2012)

<table>
<thead>
<tr>
<th>States</th>
<th>Returns</th>
<th>Coverage of registration (Active patients)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>NDR</td>
<td>% Coverage</td>
</tr>
<tr>
<td>Johor</td>
<td>81,013</td>
<td>87,001</td>
</tr>
<tr>
<td>Kedah</td>
<td>77,931</td>
<td>37,114</td>
</tr>
<tr>
<td>Kelantan</td>
<td>24,774</td>
<td>26,102</td>
</tr>
<tr>
<td>Melaka</td>
<td>31,427</td>
<td>36,446</td>
</tr>
<tr>
<td>Negeri Sembilan</td>
<td>39,393</td>
<td>40,890</td>
</tr>
<tr>
<td>Pahang</td>
<td>43,871</td>
<td>38,215</td>
</tr>
<tr>
<td>Perak</td>
<td>68,372</td>
<td>65,336</td>
</tr>
<tr>
<td>Perlis</td>
<td>10,338</td>
<td>11,368</td>
</tr>
<tr>
<td>Pulau Pinang</td>
<td>31,895</td>
<td>37,942</td>
</tr>
<tr>
<td>Sabah</td>
<td>9,205</td>
<td>10,956</td>
</tr>
<tr>
<td>Sarawak</td>
<td>64,848</td>
<td>45,902</td>
</tr>
<tr>
<td>Selangor</td>
<td>104,137</td>
<td>91,965</td>
</tr>
<tr>
<td>Terengganu</td>
<td>16,944</td>
<td>18,585</td>
</tr>
<tr>
<td>WP Kuala Lumpur</td>
<td>23,728</td>
<td>28,901</td>
</tr>
<tr>
<td>WP Labuan</td>
<td>535</td>
<td>815</td>
</tr>
<tr>
<td><strong>Malaysia</strong></td>
<td><strong>628,411</strong></td>
<td><strong>577,538</strong></td>
</tr>
</tbody>
</table>
# Diabetes Clinical Audit (2012)

<table>
<thead>
<tr>
<th>Variable</th>
<th>Targets</th>
<th>Total no. of tests</th>
<th>Meeting target (%)</th>
<th>Mean</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>HbA1c</td>
<td>&lt; 6.5 %</td>
<td>99,823</td>
<td>23.7</td>
<td>8.1</td>
<td>8.1 - 8.1</td>
</tr>
<tr>
<td>BP: Systolic</td>
<td>&lt; 130 mmHg</td>
<td>121,751</td>
<td>47.6</td>
<td>135.5</td>
<td>135.4 - 135.6</td>
</tr>
<tr>
<td>BP: Diastolic</td>
<td>&lt; 80 mmHg</td>
<td>121,726</td>
<td>67.2</td>
<td>78.4</td>
<td>78.3 - 78.4</td>
</tr>
<tr>
<td>Blood pressure</td>
<td>&lt; 130 / 80 mmHg</td>
<td>121,698</td>
<td>40.9</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total cholesterol</td>
<td>&lt; 4.5 mmol/l</td>
<td>101,286</td>
<td>28.5</td>
<td>5.2</td>
<td>5.2 - 5.2</td>
</tr>
<tr>
<td>TG</td>
<td>≤ 1.7 mmol/l</td>
<td>101,008</td>
<td>60.6</td>
<td>1.8</td>
<td>1.8 - 1.8</td>
</tr>
<tr>
<td>HDL</td>
<td>≥ 1.1 mmol/l</td>
<td>76,214</td>
<td>65.5</td>
<td>1.3</td>
<td>1.3 - 1.3</td>
</tr>
<tr>
<td>LDL</td>
<td>≤ 2.6 mmol/l</td>
<td>75,734</td>
<td>37.8</td>
<td>3.1</td>
<td>3.1 - 3.1</td>
</tr>
<tr>
<td>BMI</td>
<td>&lt; 23 kg/m2</td>
<td>108,559</td>
<td>16.6</td>
<td>27.4</td>
<td>27.3 - 27.4</td>
</tr>
<tr>
<td>Waist</td>
<td>&lt; 90 cm (Male)</td>
<td>35,520</td>
<td>33.6</td>
<td>94.0</td>
<td>93.9 - 94.1</td>
</tr>
<tr>
<td>circumference</td>
<td>&lt; 80 cm (Female)</td>
<td>55,493</td>
<td>14.4</td>
<td>90.7</td>
<td>90.6 - 90.8</td>
</tr>
</tbody>
</table>

Total: 130,340 Patients
### Diabetes Clinical Audit (2009-2012)

<table>
<thead>
<tr>
<th>Anti-Diabetics</th>
<th>2009</th>
<th>2010</th>
<th>2011</th>
<th>2012</th>
</tr>
</thead>
<tbody>
<tr>
<td>Metformin</td>
<td>81.7%</td>
<td>85.7%</td>
<td>82.3%</td>
<td>82.2%</td>
</tr>
<tr>
<td>Sulphonylureas</td>
<td>65.2%</td>
<td>62.9%</td>
<td>59.5%</td>
<td>56.6%</td>
</tr>
<tr>
<td>Alpha-glucosidase inhibitors</td>
<td>4.7%</td>
<td>5.9%</td>
<td>6.5%</td>
<td>4.8%</td>
</tr>
<tr>
<td>Insulin</td>
<td>12.0%</td>
<td>11.9%</td>
<td>17.1%</td>
<td>21.3%</td>
</tr>
<tr>
<td><strong>Monotherapy (OHA)</strong></td>
<td>33.6%</td>
<td>34.1%</td>
<td>27.8%</td>
<td>27.3%</td>
</tr>
<tr>
<td>&gt;= 2 OHA</td>
<td>51.1%</td>
<td>51.7%</td>
<td>48.7%</td>
<td>45.5%</td>
</tr>
<tr>
<td><strong>OHA + insulin</strong></td>
<td>8.8%</td>
<td>8.9%</td>
<td>13.2%</td>
<td>16.2%</td>
</tr>
<tr>
<td>Diet only</td>
<td>3.4%</td>
<td>2.3%</td>
<td>6.4%</td>
<td>5.9%</td>
</tr>
</tbody>
</table>
DiabCare Malaysia 2008 vs 2013: Blood glucose values

<table>
<thead>
<tr>
<th></th>
<th>ADA</th>
<th>AACE, IDF</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>2008</td>
<td>2013</td>
</tr>
<tr>
<td>HbA1c &gt;7% (%)</td>
<td>71.9</td>
<td>76.3</td>
</tr>
<tr>
<td>FPG &gt;7.2 mmol/L (%)</td>
<td>39.6</td>
<td>48.6</td>
</tr>
</tbody>
</table>

~ ¾ of patients were above ADA targets for HbA1c
DiabCare Malaysia 2008 vs 2013: Blood glucose values

Blood Glucose values, 2008 vs 2013

<table>
<thead>
<tr>
<th></th>
<th>2008</th>
<th>2013</th>
</tr>
</thead>
<tbody>
<tr>
<td>HbA1c</td>
<td>8.66</td>
<td>8.52</td>
</tr>
<tr>
<td>FPG</td>
<td>7.98</td>
<td>8.68</td>
</tr>
<tr>
<td>PPG</td>
<td>12.96</td>
<td>10.86</td>
</tr>
</tbody>
</table>

Similar HbA1c and FPG but slightly lower PPG values in 2013 vs 2008
Asian Countries Diabetes Complications
Coronary Heart Disease & Strokes
2008

<table>
<thead>
<tr>
<th>Country</th>
<th>Indonesia (%)</th>
<th>Bangladesh (%)</th>
<th>Singapore (%)</th>
<th>Malaysia (%)</th>
<th>Taiwan (%)</th>
<th>Thailand (%)</th>
<th>Philippines (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Angina</td>
<td>10.1</td>
<td>6.6</td>
<td>6.3</td>
<td>19.3</td>
<td>4.7</td>
<td>5.1</td>
<td>10.1</td>
</tr>
<tr>
<td>Heart attacks</td>
<td>5.7</td>
<td>5.3</td>
<td>3.2</td>
<td>12.4</td>
<td>3</td>
<td>2.7</td>
<td>2.6</td>
</tr>
<tr>
<td>Coronary revascularization</td>
<td>1.7</td>
<td>1.4</td>
<td>6.3</td>
<td>13.1</td>
<td>4.6</td>
<td>1.8</td>
<td>0.9</td>
</tr>
<tr>
<td>Stroke</td>
<td>5.8</td>
<td>2.2</td>
<td>4.6</td>
<td>7.2</td>
<td>4.5</td>
<td>4.3</td>
<td>4.6</td>
</tr>
</tbody>
</table>

What are the main changes in 2015?
What are the (10) main changes in 2015?

1. Addition of 8 new sections
   a) New oral agent
   b) Algorithms for FU & Specific Patient Profiles
   c) Table of efficacy, AE of Anti Diabetic Agents
   d) Acute diabetic emergencies ie Hypo, DKA, HHS
   e) Mx of elderly, adolescents, obese, Ramadan
   f) Male & Female Sexual Dysfunction
   g) Mental Health
   h) Unproven therapies incl TCM

2. A1c as a diagnostic tool for T2DM
3. A1c above 6.3% diagnostic of T2DM
4. A1c target of 6.5% consolidated with ADVANCE Trial
5. BP target of 135/75 based on ADVANCE-BP arm
6. 3 or 4 OADs before insulin if A1c < 10.0%
7. Second line for LDL-lowering (IMPROVE-IT)
8. CVD risk estimate for target intensification NOT for cardiological work-up (DAID Study)
9. Primary prevention with aspirin only in those above 65 years old (JPAD Study).
10. Hyperglycaemia in Pregnancy (GDM & T2DM)

For the first time CPG was revised without involvement of pharmaceutical companies.
Algorithm 5: Treatment Algorithm for Newly Diagnosed T2DM

### Diagnosis of Type 2 Diabetes
#### Lifestyle Modification

<table>
<thead>
<tr>
<th>A1c &lt;6.5% AND FPG &lt;6 mmol/L</th>
<th>A1c 6.5% - &lt;7.5% OR FPG 6 - &lt;8 mmol/L</th>
<th>A1c 7.5% - &lt;8.5% OR FPG 8 - &lt;10 mmol/L</th>
<th>A1c 8.5% - 10% OR FPG 10 - 13 mmol/L</th>
<th>A1c &gt;10.0% OR FPG &gt;13 mmol/L</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>LIFESTYLE APPROACH</strong></td>
<td><strong>OAD MONOTHERAPY</strong></td>
<td><strong>DUAL COMBINATION THERAPY</strong></td>
<td><strong>TRIPLE COMBINATION THERAPY</strong></td>
<td><strong>COMBINATION THERAPY</strong></td>
</tr>
<tr>
<td>If postprandial is &gt;11.0 mmol/L, consider one of the following:</td>
<td>Metformin OR SU</td>
<td>Any two combination of: Metformin SU AGI</td>
<td>Any three combination of: Metformin SU AGI</td>
<td>+ BASAL / PREMIXED INSULIN THERAPY</td>
</tr>
<tr>
<td>Metformin</td>
<td>Meglitinide</td>
<td>DPP-4i</td>
<td>DPP-4i</td>
<td>or</td>
</tr>
<tr>
<td>Meglitinide</td>
<td>GLP-1 RA</td>
<td>GLP-1 RA</td>
<td>GLP-1 RA</td>
<td>INTENSIVE INSULIN THERAPY</td>
</tr>
<tr>
<td>AGI</td>
<td>SGLT2i</td>
<td>SGLT2i</td>
<td>SGLT2i</td>
<td>+ OAD</td>
</tr>
<tr>
<td>DPP-4i</td>
<td>Follow-up with A1c after 3 months</td>
<td>Follow-up with A1c after 3 months</td>
<td>Follow-up with A1c after 3 months</td>
<td></td>
</tr>
<tr>
<td>SGLT2i</td>
<td>If A1c ≤6.5%, continue with Lifestyle Approach. If A1c &gt;6.5%, refer Table 21.</td>
<td>If A1c ≤6.5%, continue with Therapy. If A1c &gt;6.5%, refer Table 21.</td>
<td>If A1c ≤6.5%, continue with Therapy. If A1c &gt;6.5%, refer Table 21.</td>
<td></td>
</tr>
</tbody>
</table>

*The agents above are based on historical order*

**Footnote:**
- Metformin: Efficacious, low risk of hypoglycaemia and weight neutral
- SU, Glinides, Insulin: Efficacious, risk of hypoglycaemia and weight gain
- DPP-4i: Moderate efficacy, low risk of hypoglycaemia and weight neutral
- GLP-1 RA, SGLT2i: Moderate efficacy, low risk of hypoglycaemia and weight loss
- TZD: Moderate efficacy, low risk of hypoglycaemia and weight gain
- AGI: Modest efficacy, low risk of hypoglycaemia and weight neutral
### Table 21: Treatment Recommendations for Patients on Clinic Follow-up

<table>
<thead>
<tr>
<th>Glycaemic Control</th>
<th>A1c 6.5–&lt; 7.5% or FPG 6–&lt;8 mmol/L</th>
<th>A1c 7.5–&lt;8.5% or FPG 8–&lt;10 mmol/L</th>
<th>A1c 8.5–10.0% or FPG 10–13 mmol/L</th>
<th>A1c &gt;10.0% or FPG &gt;13 mmol/L</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Lifestyle Treatment</strong></td>
<td>Start metformin (if metformin not tolerated, use an agent from Box 1)</td>
<td>Start metformin and another agent from Box 1 (dual therapy)</td>
<td>Start metformin and 2 other agents from Box 1 (triple therapy)</td>
<td>Start metformin &amp; another agent + insulin (basal or premixed od)</td>
</tr>
<tr>
<td><strong>Monotherapy</strong> (Metformin preferred)</td>
<td>Add 1 agent from Box 1 (dual therapy)</td>
<td>Add 2 agents from Box 1 (triple therapy)</td>
<td>Add 2 agents from Box 1 + insulin (basal or premixed od)</td>
<td>Initiate &amp; intensify insulin (MDI) and continue metformin</td>
</tr>
<tr>
<td><strong>Dual Therapy</strong></td>
<td>Add 1 agent from Box 1 (triple therapy)</td>
<td>Add 1 agent from Box 1 or insulin (basal or premixed od)</td>
<td>Add 1 agent from Box 1 + insulin (basal or premixed od)</td>
<td>Initiate &amp; intensify insulin (MDI) and continue dual therapy (except SU/glulides)</td>
</tr>
<tr>
<td><strong>Triple Therapy</strong></td>
<td>Add 1 agent from Box 1 (quadraple therapy)</td>
<td>Add 1 agent from Box 1 or insulin (basal or premixed od)</td>
<td>Add insulin (basal or premixed od) and continue triple therapy</td>
<td>Initiate &amp; intensify insulin (MDI) and continue triple therapy (except SU/glulides)</td>
</tr>
</tbody>
</table>

MDI = Multiple daily injections; ^5 Intensify involve changing the regimen; SU = sulphonylureas

**Box 1: Selection of Anti-diabetic Agents**

- SU
- Meglitinide
- AGI
- TZD
- DPP-4i
- GLP-1 RA
- SGLT2i

**Footnote:**
1. If symptomatic (weight loss, polyuria, etc) at any A1c and FPG level, consider insulin therapy.
2. Glycaemic target should be individualised, however try to achieve as near normal glycaemia as possible without causing hypoglycaemia.
Recommendations based on 5 priorities:

1. Safety
2. Convenience to aid compliance
3. CVD Global Risk Reduction (eg obesity)
4. Glycaemic Efficacy
5. Cost

Answers the question: What would you give yourself if you were a patient?

2nd Gen SU = selected 2nd generation sulphonylurea; SGLT2i = sodium-glucose cotransporter 2 inhibitor; GLP-1 RA = glucagon-like peptide-1 receptor agonist; TZD = thiazolidinedione; SU = sulphonylurea.
### 3.7.4 Table 22: Efficacy of Various Anti-diabetic Agents

<table>
<thead>
<tr>
<th></th>
<th>MET</th>
<th>SU</th>
<th>GLN</th>
<th>AGI</th>
<th>TZD</th>
<th>DPP4-i</th>
<th>SGLT2-i</th>
<th>GLP-1 RA</th>
<th>Insulin</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>A1c reduction, %</strong></td>
<td>1.0-1.5</td>
<td>1.5</td>
<td>1.0-1.2</td>
<td>0.5-0.8</td>
<td>0.5-1.4</td>
<td>0.5-0.8</td>
<td>0.7</td>
<td>0.5-1.4</td>
<td>&gt;1.5</td>
</tr>
<tr>
<td><strong>FPG vs PPG</strong></td>
<td>FPG</td>
<td>FPG</td>
<td>Both</td>
<td>PPG</td>
<td>FPG</td>
<td>Both</td>
<td>Both</td>
<td>Both</td>
<td>Both</td>
</tr>
<tr>
<td><strong>Hypoglycaemia</strong></td>
<td>←→</td>
<td>↑↑</td>
<td>▲</td>
<td>←→</td>
<td>←→</td>
<td>←→</td>
<td>←→</td>
<td>←→</td>
<td>↑↑</td>
</tr>
<tr>
<td><strong>Weight change</strong></td>
<td>↓</td>
<td>↑↑</td>
<td>▲</td>
<td>↑↑</td>
<td>↑↑</td>
<td>↑↑</td>
<td>↑↑</td>
<td>↑↑</td>
<td>↑↑</td>
</tr>
<tr>
<td><strong>GI symptoms</strong></td>
<td>↑↑</td>
<td>←→</td>
<td>←→</td>
<td>←→</td>
<td>←→</td>
<td>←→</td>
<td>↑</td>
<td>←→</td>
<td>←→</td>
</tr>
<tr>
<td><strong>Congestive heart failure</strong></td>
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<td><strong>Cardiovascular disease</strong></td>
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<td><strong>Bone loss</strong></td>
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<td><strong>CKD</strong></td>
<td>Avoid GFR&lt;30</td>
<td>Hypoglycaemia</td>
<td>Hypoglycaemia</td>
<td>←→</td>
<td>Fluid retention</td>
<td>Dose adjustment</td>
<td>Avoid GFR&lt;60</td>
<td>Avoid GFR&lt;30</td>
<td>Hypoglycaemia</td>
</tr>
<tr>
<td><strong>References</strong></td>
<td>75 (Level I)</td>
<td>159 (Level I)</td>
<td>82 (Level I)</td>
<td>160 (Level I)</td>
<td>85-89 (Level I)</td>
<td>142-144 (Level I)</td>
<td>108-111 (Level I)</td>
<td>112 (Level I)</td>
<td>151,152,161,162 (Level I)</td>
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</table>

**MET** = metformin; **SU** = sulphonylureas; **GLN** = glinides; **GLP-1 RA** = glucagon-like peptide-1 receptor agonists; **DPP4-i** = dipeptidyl peptidase-4 inhibitors; **SGLT2-i** = sodium-glucose co-transporter 2 inhibitors; **AGI** = α-glucosidase inhibitor; **TZD** = thiazolidinediones

The efficacy data for the above anti-diabetic agents were established with baseline A1c level below 10%. Efficacy of all OADs is dependent on the baseline A1c levels. The higher the A1c level, the more efficacious is the agent.

- Beneficial
- Possible benefit
- Neutral
- Minimal risk
- Increased risk

**Taking into account most recent clinical trials**

**Colour coded based on risk vs benefit**
**Algorithm 7: Principles of Management**

**1st Hour: Immediate Management**

**Step 1.** Commence 0.9% saline drip using large bore cannula. (See box below for rate of fluid replacement)

**Step 2.** Commence a fixed rate intravenous insulin infusion (VII) (0.1 unit/kg/hr based on estimate of weight).

50 units short-acting human insulin made up to 50 mL with 0.9% saline solution.

**Step 3. Assess patient**
- BP
- Pulse
- Temperature
- Respiratory rate
- Oxygen saturation
- Glasgow Coma Scale
- Hydration status
- Full clinical examination

**Step 4. Investigations**
- Capillary and venous blood glucose
- Arterial blood gases
- Blood or urinary ketones
- BUN
- FBC
- Blood cultures
- MSU
- ECG (if indicated)
- CXR (if indicated)

**Step 5. Outline monitoring regimen**
- Hourly capillary blood glucose
- Vital signs and input-output charting hourly
- Venous bicarbonate and potassium at 80 minutes, 4 hours and 6-hourly thereafter
- 6-hourly BUSE and urine ketone
- Continuous pulse oximetry (if indicated)
- Continuous cardiac monitoring (if indicated)

**Step 6. Look for precipitating causes and treat accordingly**
Start broad-spectrum antibiotics if infection suspected

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**Initial Fluid & Potassium Replacement**

**Potassium replacement:**

- Give 50 mL 10% potassium over 2 hours
- Most patients require further potassium
- Consider i.v. replacement of electrolyte deficit (see q 

**Systolic BP on admission ≥90 mmHg**

- Give 1000 mL of 0.9% saline for first 60 minutes

- Withhold potassium replacement if no urine output

**Intravenous bicarbonate:**

The use of intravenous bicarbonate is not indicated to correct acidosis

- Rise in pCO2 in CSF which may lead to a paradoxical increase in CSF acidosis
- Delay in the fall of blood lactate and ketone level
- Risk of cerebral oedema especially in younger age groups

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**Time-based protocol ensures patients are constantly monitored**

**In first 24 hrs patients are reviewed at least 4X (1hr, 2-6hr, 6-12hr, 12-24hr)**

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**2nd-4th Hour**

**Aims of treatment:**
- Keep the blood ketones at least 0.5 mmol/L or
- Bicarbonate-base rate 3 mmol/L/hr and
- Blood glucose fall 3 mmol/L/hr
- Maintain serum potassium in normal range
- Avoid hypoglycaemia

**Step 7.** Removes patient, monitor vital signs
- Hourly blood glucose (lab blood glucose if meter reading >140)
- 4-hourly blood or urine ketone
- Venous blood gas for pH, bicarbonate and potassium at 60 minutes, followed by 4-hourly (depending on the severity of acidosis)
- If potassium is outside normal range, assesses potassium replacement and check 1-hourly depending on the severity

**Step 8. Continue fluid replacement via infusion pump as follows:**
- 1000 mL of 0.9% saline with potassium chloride over next 2 hours
- 1000 mL of 0.9% saline with potassium chloride over next 4 hours
- Once blood glucose falls below 14 mmol/L:
  - Switch to 5% dextrose at 25 mL/h and reduce insulin infusion rate to 0.65 units/kg/h or
  - Switch to 10% dextrose at 125 mL/h and no change in insulin infusion rate

**More cautious fluid replacement in young people aged under 18 years, elderly, pregnant, have heart or renal failure.**

(Monitor HR and CVP and renal tests)

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**6th-12th Hour**

**Aims:**
- Ensure clinical and biochemical parameters improving
- Continue IV fluid replacement
- Avoid hypoglycaemia
- Assess for complications of treatment e.g. fluid overload, cerebral oedema

**12-24 hours**

By 24 hours the ketonemia and acidosis should have resolved.

**Aims:**
- Ensure that clinical and biochemical parameters are continuing to improve or are normal
- Continue IV fluid replacement if not eating and drinking
- If ketonemia cleared and patient is not eating and drinking, titrates insulin infusion rate accordingly
- Reassess for complications of treatment e.g. fluid overload, cerebral oedema
- Continue to treat precipitating factors
- Change to subcutaneous insulin if patient is eating and drinking normally

**Step 12.** Reassess patient, monitor vital signs, review biochemical and metabolic parameters
- At 12 hours check venous pH, bicarbonate, potassium, capillary ketones and glucose
- Resolution is defined as ketones <0.3 mmol/L, venous pH >7.35
- If not resolved reassess Step 9 and Step 10

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**Reassesses cardiovascular status at 12 hours; further fluid may be required**

**Check for fluid overload**

**Step 11. Review biochemical and metabolic parameters**

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**Step 5. Assess response to treatment**

- Insulin infusion rate may need review if:
  - Blood ketones not falling by at least 0.5 mmol/L/hr
  - Venous bicarbonate not falling by at least 3 mmol/L/hr
  - Plasma glucose not falling by at least 3 mmol/L/hr
  - Continue fluid into 4th hour, if ketones less than 0.3 mmol/L and venous pH over 7.38, and/or bicarbonate over 16 mmol/L

If ketone and glucose are not falling as expected always check the insulin infusion pump is working and connected and that the correct insulin dose is being administered.

**If equipment is working but responses to treatment inadequate, increase insulin infusion rate by 1 units increments hourly until targets achieved.**

**Additional measures**
- Accurate fluid balance chart, minimum urine output 0.5 ml/kg/h
- Consider urinary catheterisation if inpavement or urina (does not pass urine by 60 minutes)
- Nasogastric tube with airway protection if patient obtunded or persistently vomiting
- Measure arterial blood gases and repeat CVP or oxygen saturation less than 95%
- SVF prophylaxis with low molecular weight heparin
- Consider EOS monitoring if ketosis abnormal or concerns about central venous catheter
Algorithm 8: Management of T2DM with Hyperglycaemic Hyperosmolar State

**PROTOCOL FOR MANAGEMENT OF ADULTS PATIENTS WITH HYPERGLYCAEMIC HYPEROSMOLAR STATE (HHS)**

**Initial evaluation:** After history and physical examination, obtain arterial or venous blood gases, full blood count, urinalysis, plasma glucose, renal profile, liver profile STAT as well as an ECG. Chest X-ray and cultures as needed. Start IV fluid: 1000 mL of 0.9% saline per hour initially.

**Diagnostic Criteria:** Blood glucose >33.3 mmol/L, blood pH <7.3, bicarbonate <15 mmol/L, mild ketonuria or ketonaemia and effective serum osmolality >320 mOsm/kg H2O.

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**3 prong approach to the management of Hyperglycaemic Hyperosmolar State**

1. **IV Fluids**
   - **Hypovolemic shock**
     - Administer 0.9% NaCl (1000 mL/hr) and/or plasma expanders
   - **Mild hypotension**
   - **Cardiogenic shock**
     - Haemodynamic Monitoring
     - Evaluate Corrected Serum Na
       - **Serum Na high**
         - 0.45% saline (4-14 mL/kg/hr) depending on state of hydration, 0.9% saline (4-14 mL/kg/hr) depending on state of hydration
       - **Serum Na normal**
       - 0.9% saline (4-14 mL/kg/hr) depending on state of hydration
       - **Serum Na low**
         - 0.45% saline (4-14 mL/kg/hr) depending on state of hydration, 0.9% saline (4-14 mL/kg/hr) depending on state of hydration
   - When serum glucose reaches 14.0 mmol/L
     - Change to 5% dextrose and decrease insulin to 0.05 U/kg/hr or 10% dextrose with insulin rate of 0.1 U/kg/hr to maintain serum glucose between 8-12 mmol/L
     - Check BUSE every 2-4 hours until stable. After resolution of HHS, if the patient is nil by mouth, continue IV insulin and supplement with sc insulin as needed. When the patient can eat, initiate sc insulin or previous treatment regimen and assess metabolic control. Continue IV insulin 1-2 hours to ensure control after initiating daily regimen. Continue to look for precipitating cause(s).

2. **Insulin**
   - 0.05 U/kg/hr IV insulin infusion
   - Check serum glucose hourly. If
     - If serum K is <3.5 mmol/L, give 40 mEq K/hr until K ≥ 3.3 mmol/L
     - If serum K ≥ 5.0 mmol/L, do not give K but check potassium q 2 h.
     - If serum K ≥ 3.3 mmol/L but <5.0 mmol/L, give 20-30 mmol K in each litre of IV fluid to keep serum K at 4-5 mmol/L.

3. **Potassium**

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**Effective serum osmolality calculation:** SI units: $2Na^+ + 2K^+ + \text{Glucose} + \text{Urea} \text{ (all in mmol/L)}$

**Serum Na^+ should be corrected for hyperglycaemia** (SI units: Corrected serum sodium = Measured serum sodium + $[((\text{Glucose measured} - 5.6)/5.6) \times 2.4; \text{all in mmol/L}].$
Clinical practice guidelines aim to help physicians and patients reach the best healthcare decisions.

Steinbrook R. NEJM 2007

Thank you