Saudi Diabetes Clinical Practice Guidelines (SDCPG)

Saudi National Diabetes Center (SNDC)
(First Edition 2021)
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SDCPG was developed to help healthcare providers in determining the most appropriate treatment options. These guidelines should be used to help healthcare providers apply their clinical judgment for the benefit of patients, based on the most up-to-date data, and to eliminate unwarranted variations in clinical practice. The responsible healthcare provider must make the final choice regarding any clinical procedure or treatment plan for a specific clinical circumstance(s).

**Disclaimer:**

SDCPG was developed to help healthcare providers in determining the most appropriate treatment options. These guidelines should be used to help healthcare providers apply their clinical judgment for the benefit of patients, based on the most up-to-date data, and to eliminate unwarranted variations in clinical practice. The responsible healthcare provider must make the final choice regarding any clinical procedure or treatment plan for a specific clinical circumstance(s).

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For comments, suggestions and any enquiries about the guidelines please email it to SNDC: s.alhosan@shc.gov.sa
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- SNDC Scientific committee for their continued support in reviewing the guidelines and cooperation during workshops. (full names listed in Appendix 1).
- Saudi Scientific Diabetes Society for their valuable contribution to the SDCPG and their support in holding the guidelines workshops.
- Saudi Society of Endocrinology and Metabolism for their comments and recommendations on SDCPG
- SDCPG workshop participants (consultants and specialists in endocrinology and diabetes) from all regions of Kingdom of Saudi Arabia, held in Riyadh and Jeddah for their contribution during workshops. (full names listed in Appendix 2).
Diabetes mellitus (DM) is a major health issue in the Kingdom of Saudi Arabia (KSA), affecting 13.4% of individuals aged 15 years and above. Recently, the Saudi National Diabetes Center (SNDC) was established to tackle the national challenges of DM. SNDC has pioneered a strategic plan for diabetes care in KSA, which aims to substantially improve diabetes care in the Saudi community over the next coming years. Among the SNDC strategy goals is to establish local guidelines in DM and update them periodically.

The SDCPG offers practical guidance for the health care workers (HCW) caring for individuals with DM for several reasons:
1) to ultimately serve as a national reference on diabetes clinical practice. 2) to improve equity in diabetes care between different health organizations and HCW. 3) to lower malpractice that will improve patient’s safety. 4) to improve the quality of diabetes care. 5) to provide local goals and targets of glycemic control and other related conditions.

The work was established by the SNDC task force, composed of local experts in diabetes from different health sectors, and consequently discussed in two workshops involving many endocrinologists, diabetologists and other related specialties nationwide. The SDCPG provide comprehensive and up-to-date management practical guidelines that covers many diabetes-related clinical issues.

Due to the lack of appropriate local and regional studies, the available international guidelines were the primary references in this work. Most of the practical recommendations were quoted from major international guidelines, namely the American Diabetes Association (ADA), the American Association of Clinical Endocrinologists (AACE), the National Institute of Clinical Excellence (NICE), and the International Diabetes Federation (IDF). A pre-specified methodology was applied to involve the latest evidence-based practice from different resources.

A unique feature in the SDCPG is the ketoacidosis and hyperglycemic-hyperosmolar state treatment pathways, which will provide essential and necessary clinical aid to physicians.

This project is a practical guideline in its first edition; therefore, we did not involve a grading system for evidence yet, a step planned for future versions.

This document has 12 sections covering different aspects of diabetes. The recommendations listed should be taken in the context of excellent clinical care and individual preference. Other comorbidities should be taken into account when considering these suggestions.

This project was initiated and financially supported solely by SNDC.
### List of Abbreviations Used

<table>
<thead>
<tr>
<th>Abbreviation</th>
<th>Description</th>
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<tbody>
<tr>
<td>2h PP</td>
<td>2-h Post Prandial</td>
</tr>
<tr>
<td>ABI</td>
<td>Ankle-Brachial Index</td>
</tr>
<tr>
<td>ACE</td>
<td>Angiotensin-Converting Enzyme</td>
</tr>
<tr>
<td>ACR</td>
<td>Albumin-to-Creatinine Ratio</td>
</tr>
<tr>
<td>ADA</td>
<td>American Diabetes Association</td>
</tr>
<tr>
<td>AIDS</td>
<td>Acquired Immune Deficiency Syndrome</td>
</tr>
<tr>
<td>ARB</td>
<td>Angiotensin Receptor Blocker</td>
</tr>
<tr>
<td>BG</td>
<td>Blood Glucose</td>
</tr>
<tr>
<td>BMI</td>
<td>Body Mass Index</td>
</tr>
<tr>
<td>BP</td>
<td>Blood Pressure</td>
</tr>
<tr>
<td>CAD</td>
<td>Coronary Artery Disease</td>
</tr>
<tr>
<td>CGM</td>
<td>Continuous Blood Glucose Monitoring</td>
</tr>
<tr>
<td>CHF</td>
<td>Congestive Heart Failure</td>
</tr>
<tr>
<td>CI</td>
<td>Confidence Interval</td>
</tr>
<tr>
<td>CKD</td>
<td>Chronic Kidney Disease</td>
</tr>
<tr>
<td>CV</td>
<td>Cardiovascular</td>
</tr>
<tr>
<td>CVD</td>
<td>Cardiovascular Disease</td>
</tr>
<tr>
<td>DCCT</td>
<td>Diabetes Control and Complications Trial</td>
</tr>
<tr>
<td>DKA</td>
<td>Diabetic Ketoacidosis</td>
</tr>
<tr>
<td>DKD</td>
<td>Diabetic Kidney Disease</td>
</tr>
<tr>
<td>DM</td>
<td>Diabetes Mellitus</td>
</tr>
<tr>
<td>DPP-4</td>
<td>Dipeptidyl Peptidase 4</td>
</tr>
<tr>
<td>DPP-4i</td>
<td>Dipeptidyl Peptidase 4 Inhibitor</td>
</tr>
<tr>
<td>DR</td>
<td>Diabetic Retinopathy</td>
</tr>
<tr>
<td>DSMES</td>
<td>Diabetes Self-Management Education and Support</td>
</tr>
<tr>
<td>eGFR</td>
<td>Estimated Glomerular Function</td>
</tr>
<tr>
<td>FBG</td>
<td>Fasting Blood Glucose</td>
</tr>
<tr>
<td>GDM</td>
<td>Gestational Diabetes Mellitus</td>
</tr>
<tr>
<td>GLP-1</td>
<td>Glucagon-Like Peptide-1</td>
</tr>
<tr>
<td>GLP-1 RA</td>
<td>GLP-1 Receptor Agonist</td>
</tr>
<tr>
<td>Hba1c</td>
<td>Glycosylated Hemoglobin A1c</td>
</tr>
<tr>
<td>HDL</td>
<td>High Density Lipoprotein Cholesterol</td>
</tr>
<tr>
<td>HDL-C</td>
<td>High Density Lipoprotein Cholesterol</td>
</tr>
<tr>
<td>HF</td>
<td>Heart Failure</td>
</tr>
<tr>
<td>HHS</td>
<td>Hyperosmolar Hyperglycemic State</td>
</tr>
<tr>
<td>HIV</td>
<td>Human Immunodeficiency Virus</td>
</tr>
<tr>
<td>IDF</td>
<td>International Diabetes Federation</td>
</tr>
<tr>
<td>IFG</td>
<td>Impaired Fasting Glucose</td>
</tr>
<tr>
<td>IGT</td>
<td>Impaired Glucose Tolerance</td>
</tr>
<tr>
<td>KSA</td>
<td>Kingdom of Saudi Arabia</td>
</tr>
<tr>
<td>LDL</td>
<td>Low-Density Lipoprotein</td>
</tr>
<tr>
<td>MENA</td>
<td>Middle East and North Africa Region</td>
</tr>
<tr>
<td>mg/dL</td>
<td>milligrams per deciliter</td>
</tr>
<tr>
<td>mmol/L</td>
<td>millimoles per liter</td>
</tr>
<tr>
<td>mmol/mol</td>
<td>millimoles per mole</td>
</tr>
<tr>
<td>Abbreviation</td>
<td>Definition</td>
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<td>--------------</td>
<td>---------------------------------------------------------------------------</td>
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<tr>
<td>MODY</td>
<td>Maturity-Onset Diabetes of the Young</td>
</tr>
<tr>
<td>NAFLD</td>
<td>Non-Alcoholic Fatty Liver Disease</td>
</tr>
<tr>
<td>NASH</td>
<td>Non-Alcoholic Steatohepatitis</td>
</tr>
<tr>
<td>NGSP</td>
<td>National Glycohemoglobin Standardization Program</td>
</tr>
<tr>
<td>OGGT</td>
<td>Oral Glucose Tolerance Test</td>
</tr>
<tr>
<td>OSA</td>
<td>Obstructive Sleep Apnea</td>
</tr>
<tr>
<td>PCOS</td>
<td>Polycystic Ovarian Syndrome</td>
</tr>
<tr>
<td>PDE5</td>
<td>Phosphodiesterase type 5</td>
</tr>
<tr>
<td>RBG</td>
<td>Random Blood Glucose</td>
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</table>
Methodology

Adult and pediatric endocrinologists from different health-care sectors in KSA have been chosen to create a national guideline for the management of DM. With the initiation of the guideline meeting, all members had to disclose any conflicts of interest. The panel had regular meetings in the Saudi Health Council and drafted the outline and road map of implementing SDCPG according to state-of-the-art available literature. Four international guidelines were reviewed, including ADA, The AACE, the NICE, and IDF. Data from available Saudi literature were included. The guideline was divided into sections and was distributed to all members. Each member was assigned to at least one or more sections to draft. Recommendations should be evidence-based. All members scientifically assessed the data in a comprehensive manner and the final recommendation is approved if the majority agrees. Controversial topics were discussed in two workshops done in Jeddah and Riyadh. These workshops were participated by mostly endocrinologists, diabetologists and specialists (pharmacists, health educators and dietitians) whose comments and observations were considered in the final document.
Section 1:
Prevalence, definition and classification:

- Epidemiology
- Definitions
- Risk factors for development of T2DM in Saudi population
- Classification of diabetes
Epidemiology

Diabetes mellitus (DM) is a major health problem worldwide. KSA is among the top ten countries with the highest prevalence of DM, and is expected to be among the top five countries with the highest prevalence of type 2 DM (T2DM) in 2030 [1]. In Al Nozah et al, 2004 alone, the overall prevalence of DM in KSA among Saudis 30 years old and above is 24% [2], a figure that increased 10-folds higher as compared to 2.5% in 1982 (see table 1). [3]

Table 1: Prevalence of DM over three decades [3]

<table>
<thead>
<tr>
<th>Year</th>
<th>Prevalence of DM</th>
<th>Author</th>
</tr>
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<tbody>
<tr>
<td>1982</td>
<td>2.5% (Age &gt; 15)</td>
<td>Bacchus et al. [4]</td>
</tr>
<tr>
<td>1987</td>
<td>4.3%</td>
<td>Fatani et al. [3]</td>
</tr>
<tr>
<td>1992</td>
<td>4.6%</td>
<td>Abu-Zeid et al. [6]</td>
</tr>
<tr>
<td>1996</td>
<td>9.5% (age &gt; 14yrs)</td>
<td>El-Hazmi et al. [7]</td>
</tr>
<tr>
<td>1997</td>
<td>17% (age &gt; 30yrs)</td>
<td>Al-Nuaim et al. [8]</td>
</tr>
<tr>
<td>2004</td>
<td>24% (age &gt; 30yrs)</td>
<td>Al-Nozha [2]</td>
</tr>
<tr>
<td>2014</td>
<td>11.9% (Age 0-100)</td>
<td>Al-Rubeaan et al. [9]</td>
</tr>
<tr>
<td></td>
<td>25.4% (above 30 years)</td>
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</table>

According to IDF Atlas, the worldwide prevalence of DM in adults (20-79 years) was 8.8% (7.2-11.3%) in 2017, and is expected to increase to 9.9% (7.5-12.7%) in 2045. The number of people with DM worldwide in 2017 was 425 million, and is expected to increase by as much as 45% in 2045 (629 million). Analysis by region revealed that the highest increase would be in Africa (156%) and Middle-East and North Africa (MENA) (110%). [1]

In 2014, the crude prevalence of DM in KSA is 13.4% (N=1,745,532) and it increases with the age. This total group is the sum of measured diabetes (N=1,193,075, 68.4%) and those who were on diabetes medication with controlled levels of HbA1c (N=552,457, 31.6%). Among those identified to have DM,
43.6% were undiagnosed. Moreover, 15.2% of Saudis (N=979,953) had prediabetes. This alarming trend of DM in KSA over the last three decades has created a big burden on the healthcare system. Published in International Journal of Public Health by Bacheraoui et al, 2014.

As of 2017, the number of people (20-79 years) with DM in the MENA region was 39 millions, and is expected to become 82 millions by the year 2045. Algeria (N=42,500), KSA (N=35,000), and Morocco (N=31,800) had the highest number of people with type 1 DM (T1DM) in children and adolescents (0-19 years) in 2017.

Definitions

Diabetes is a Greek word that means a siphon, from the word [dia = through + bainein = to go]. It is a general term referring to disorders characterized by excessive urination (polyuria), as in DM and diabetes insipidus. DM is considered a syndrome with a metabolic disorder, and inappropriate hyperglycemia results from impaired secretion of insulin or to a combination of both insulin resistance and inadequate secretion of insulin. Prediabetes is impaired fasting glucose (IFG), impaired glucose tolerance (IGT), or glycated hemoglobin (HbA1c) of 5.7-6.4%. Individuals with such values are at high risk of developing DM.

Risk factors for T2DM in the Saudi population:

These risk factors include non-modifiable risk factors such as genetic or familial predisposition, where a strong family history of DM in first or second-degree relatives is associated with the development of DM. In addition, age is another non-modifiable risk factor where several epidemiological research studies had shown that as the population grows older, susceptibility to DM increases. In Al Nozha et al.’s study, the prevalence of DM after the age of 30 years was almost 24%. However, if the age group of 50 years and above was taken, the prevalence had increased to almost 50%. Moreover, babies of mothers with gestational diabetes mellitus (GDM) are at high risk for DM later in life. In the SEARCH study group had found that intrauterine exposures to maternal DM and obesity are strongly associated with T2DM in youth. The exposure to maternal DM had an odds ratio [OR] 5.7 [95% CI 2.4 –13.4]) while exposure to maternal obesity had an odds ratio of 2.8 [1.5–5.2]). Modifiable risk factors include obesity, sedentary lifestyle, and bad nutritional habit. In one report, the prevalence of obesity ranged from 14% in children
less than six years to about 83% in adults \[15\]. In addition, in a school-based cross-sectional study of lifestyle factors on Saudi adolescents, a very high proportion (84% for males and 91.2% for females) spent more than two hours on screen daily. Almost half of the males and three-quarters of the females did not meet daily physical activity guidelines (participation in moderately vigorous physical activity for 60 minutes daily). \[16\]

### Classification of DM

The following is a simple classification of DM. The main objective of classification is to help in the best management of cases, as each type of DM has its specific plan of management.

<table>
<thead>
<tr>
<th>Diabetes Mellitus (DM)</th>
<th>T1DM</th>
<th>T2DM</th>
<th>GDM</th>
<th>DM due to other causes</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Autoimmune β-cell destruction, usually leading to absolute insulin deficiency</td>
<td>A progressive loss of b-cell insulin secretion frequently on the background of insulin resistance</td>
<td>Diabetes diagnosed in the second or third trimester of pregnancy that was not clearly overt diabetes prior to gestation</td>
<td><strong>Monogenic diabetes syndromes</strong> (such as neonatal diabetes and maturity-onset diabetes of the young [MODY])</td>
</tr>
<tr>
<td></td>
<td><strong>Diseases of the exocrine pancreas</strong> (such as cystic fibrosis and pancreatitis)</td>
<td><strong>Drug- or chemical-induced diabetes</strong> (such as with glucocorticoid use, in the treatment of HIV/AIDS, or after organ transplantation)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Figure 1**: Classification of DM
Section 2:
Screening and Prevention of DM

- Screening for T1DM
- Screening of T2DM in asymptomatic adolescents
- Screening of T2DM in asymptomatic adults
- Prevention or delay of T2DM
- Prevention of cardiovascular diseases in individuals with prediabetes
Due to the increased prevalence of diabetes in KSA, it is crucial to screen for prediabetes and asymptomatic T2DM in both asymptomatic adolescents and adults. [10]

**Screening for T1DM**

Routine screening for T1DM is not recommended, as there is no evidence for any preventive interventions to prevent or delay it. [13]

**Screening of T2DM in asymptomatic adolescents:**

Risk-based screening for prediabetes and/or asymptomatic T2DM should be carried out for children after the age of ten or the onset of puberty, whichever occurs earlier, in those who are overweight (BMI ≥ 85th percentile) or obese (BMI ≥ 95th percentile) and have one more of the following risk factors:

- T2DM in a first- or second-degree relative
- Signs or conditions associated with insulin resistance (e.g., hypertension, dyslipidemia, acanthosis nigricans, polycystic ovary syndrome (PCOS), or small for gestational age birth weight).
- Maternal history of DM or GDM during the child's gestation. [8, 17, 18]

**Recommendation**

Screen adolescents for prediabetes or T2DM, if they are overweight or obese and has at least one risk factor for T2DM.

**Screening of T2DM in asymptomatic adults**

Based on epidemiological data of the high prevalence of T2DM in KSA among 35-year-old adults and above, and due to increase in obesity rates and sedentary life in our community, it is cost-effective to screen all asymptomatic adults for T2DM after the age of 35 year.

**SNDC criteria for T2DM screening in asymptomatic adults**

1. **Age 35 and above**

2. **Overweight Adults with (BMI ≥25 kg/m²), or with abdominal obesity (≥102 for men and ≥88 for women) who have, in addition, at least one of the following risk factors** [13]:
   - Family history of DM: first-degree relative with DM
   - Ladies with history of GDM
   - History of CVD
   - Hypertension (≥140/90 mmHg or on therapy for hypertension)
- HDL cholesterol level <35 mg/dL (0.90 mmol/L)
- Triglycerides level >250 mg/dL (2.82 mmol/L)
- Smoking history
- History of pancreatitis
- Hyperuricemia/gout
- Non-alcoholic steatohepatitis
- Psychiatric disorders (bipolar disorder, depression, schizophrenia)
- HIV infection
- Obstructive sleep apnea
- Cystic fibrosis
- Use of drugs associated with diabetes: glucocorticoids, atypical antipsychotics, statins, highly active antiretroviral therapy or anti-rejection drugs
- Women with PCOS
- Women with a history of delivery of a macrosomic infant or multiparity
- Physical inactivity
- Other conditions known to be associated with insulin resistance: acanthosis nigricans … etc.

If normal, the test should be repeated every three years and every year for high-risk individuals.

### Recommendations

Screen adults who are overweight or obese (even abdominal obesity only) who have, in addition, at least one risk factor for prediabetes or T2DM.

For all other people, testing should begin at age 35 years.

If testing results are normal, it should be repeated at least 3-year intervals.

Patients with prediabetes should be tested yearly.

Women with history of GDM should have lifelong testing at least every 3 years.

More frequent testing should be done depending on the initial results and the risk status.

### Criteria for the screening and diagnosis of DM

**Table 2: Diagnosis of DM and prediabetes**

<table>
<thead>
<tr>
<th></th>
<th>Fasting blood glucose (FBG)</th>
<th>2 hours post glucose (PPBG)</th>
<th>Glycosylated Hemoglobin A1c (HbA1c)</th>
<th>Random blood sugar (RBG)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Prediabetes</strong></td>
<td>≥ 100 mg/dl but &lt; 126 mg/dl (≥ 5.6 but &lt;7 mmol/L)</td>
<td>≥ 140 but &lt;200 mg/dl (≥ 7.8 but &lt;11.1 mmol/L) during 75 gm. Oral Glucose Tolerance Test (OGTT)</td>
<td>≥ 5.7 till 6.4%</td>
<td></td>
</tr>
<tr>
<td><strong>DM</strong></td>
<td>≥ 126 mg/dl (7 mmol/L)</td>
<td>≥ 200 mg/dl (11.1 mmol/L) during OGTT</td>
<td>≥ 6.5%</td>
<td>≥ 200 mg/dl (11.1 mmol/L)</td>
</tr>
</tbody>
</table>
Fasting is defined as no calorie intake for at least 8 hours. HbA1c test should be performed using a method that is certified by the National Glycohemoglobin Standardization Program (NGSP) (www.ngsp.org) and standardized to the DCCT assay. Random blood sugar is only diagnostic in a patient with classic symptoms of hyperglycemia or hyperglycemic crisis. The individual can be diagnosed with DM if he or she has one of the previous criteria in the presence of explicit hyperglycemia; otherwise, the diagnosis requires two abnormal tests. [13, 17, 19-23]

**Prevention or delay of T2DM**

Prevention or delay of T2DM in prediabetes include screening, educational program, lifestyle modifications, nutrition program, pharmacologic intervention and prevention of cardiovascular diseases. [22-24]

**a. Increase Awareness: educational programs**

Development of prediabetes educational program is recommended and should be encouraged by different health care sectors which may include, but not limit to, awareness days, social campaigns, and printed materials. It should target and tailored according to different populations [25-26].

**b. Lifestyle modifications:**

Intensive lifestyle modifications can reduce the incidence of T2DM. Lifestyle modifications include a healthy diet, increase physical activity, and encourage weight loss for overweight or obese individuals. [24, 27-29]

**c. Body weight management and physical activity**

<table>
<thead>
<tr>
<th>Recommendations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Refer Individuals with prediabetes to an intensive behavioral lifestyle intervention program with a target to achieve and maintain a 7% loss of their initial body weight.</td>
</tr>
<tr>
<td>Increase moderate-intensity physical activity (such as brisk walking) to at least 150 min/week.</td>
</tr>
</tbody>
</table>

**d. Nutrition**

For individuals who are overweight or obese, a structured behavioral weight loss therapy is recommended. That includes a low-calorie meal plan and physical activity. The eating patterns that might be helpful for prediabetes include the Mediterranean eating plan (high in vegetables, fruits, whole grains, beans, nuts and seeds, and olive oil.), and the low-calorie plan, and the low-fat eating plan. Overall, encourage healthy, low-calorie eating patterns. [24, 30-39]
Recommendations

Recommend a Mediterranean eating plan, low-calorie plan, and low-fat eating plan. Emphasize whole grains, bread, and cereals, beans, lentils, legumes, nuts, fruits, vegetables, and minimal refined and processed foods.

Increase the consumption of nuts, berries, yogurt, coffee, and tea. Reduce red meats and sugar-sweetened beverages. Use skimmed or semi-skimmed milk and low-fat yogurts. Recommend fish and lean meats instead of fatty meat and processed meat products. Grill or steam food instead of frying. Avoid high-fat food: like mayonnaise, chips, or crisps.

e. Pharmacologic Interventions

Recommendations

Prescribe metformin for prevention of T2DM in individuals with prediabetes, those with high BMI ≥35 kg/m², women with prior GDM, and those aged <60 years.

The initial starting dose is 500 mg once daily and increased as tolerated up to 1500–2000 mg daily. Fasting blood glucose or HbA1c levels should be monitored at 3-6 month intervals and assess the situation with the time. Also, recommend orlistat if BMI is 28.0 kg/m² or more. [24, 40-47]

Prevention of cardiovascular diseases in individuals with prediabetes

Screening for modifiable risk factors for cardiovascular disease (CVD) is suggested. Management of those factors is vital. Treatment goals of hypertension and dyslipidemia for people with prediabetes are the same as for the general population. [24, 46-51]

Recommendations

In individual with prediabetes, screen for CVD modifyable risk factors and manage them.
Section 3:

Assessment: Patient’s Profiling

- Comprehensive medical evaluation
- Assessment of comorbidities
- Assessment of risk factors that can affect DM management
After confirmed DM diagnosis, a comprehensive medical evaluation of the patient is recommended to help categorize patients into subtypes for a better allocation of treatment. This includes assessment of comorbidities and risks for DM complications.

**Comprehensive medical evaluation**

Treatment planning and the risk assessment of acute and chronic complications of DM are fundamental components of initial and follow-up visits. [52]

**Table 3: Comprehensive medical evaluation**

<table>
<thead>
<tr>
<th>Visits</th>
<th>Visits</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>In the initial visit:</strong></td>
<td><strong>In follow-up visits</strong></td>
</tr>
<tr>
<td>- Confirm the diagnosis and classify DM</td>
<td>- Assess DM self-management behaviors</td>
</tr>
<tr>
<td>- DM complications and comorbid conditions</td>
<td>- Assess nutrition and the psychosocial health</td>
</tr>
<tr>
<td>- Review previous treatment</td>
<td>- Detect the need for referrals, immunizations, or routine screening</td>
</tr>
<tr>
<td>- Review risk factors control in established DM</td>
<td></td>
</tr>
<tr>
<td>- Formulate a management plan with the patient</td>
<td></td>
</tr>
<tr>
<td>- Past medical and family history</td>
<td></td>
</tr>
<tr>
<td>- Lifestyle assessment</td>
<td></td>
</tr>
<tr>
<td>- Medications and use of self-monitoring of blood glucose (SMBG)</td>
<td></td>
</tr>
<tr>
<td>- Psychosocial conditions</td>
<td></td>
</tr>
<tr>
<td>- DM self-management skills</td>
<td></td>
</tr>
<tr>
<td>- Pregnancy planning</td>
<td></td>
</tr>
<tr>
<td>- Complete physical examination</td>
<td></td>
</tr>
<tr>
<td>- Laboratory evaluations</td>
<td></td>
</tr>
</tbody>
</table>

**Assessment of comorbidities:**

Several comorbidities may complicate DM management; thus, the assessment for these conditions is crucial for better management. [22, 23, 52, 53]
a. **Autoimmune Diseases:** consider screening for autoimmune thyroid disease and celiac disease after confirmed diagnosis of T1DM.

b. **Cancer:** As DM increases the risk for cancers of the following areas (the liver, pancreas, endometrium, colon/rectum, breast, and bladder), it is highly recommended to do routine cancer screening.

c. **Pancreatic adenocarcinoma:** New-onset DM in lean-body-type, negative-family-history adult patient necessitates the attentiveness to pancreatic adenocarcinoma.

d. **Nonalcoholic Fatty Liver Disease:** Evaluate for nonalcoholic steatohepatitis (NASH) and liver fibrosis in patients with T2DM or prediabetes if they have elevated liver enzymes or fatty liver on ultrasound.

e. **Hypogonadism:** If there is decreased sexual desire (libido) or activity, or erectile dysfunction in men with DM, assess the morning serum testosterone level.

f. **HIV:** antiretroviral therapy can lead to increased blood glucose (BG) and affect the management of DM.

g. **Serious mental diseases:** atypical antipsychotic medications can lead to increased BG and affect DM management. Therefore, monitor for weight changes, glycemic control, and cholesterol levels carefully and reassess the treatment accordingly.

h. **Cognitive impairment:** In people with a history of cognitive impairment, treatment should be tailored to avoid hypoglycemia.

i. **Anxiety disorders:** People with hypoglycemia unawareness or fear of hypoglycemia should be treated using BG awareness training to reduce the fear of hypoglycemia.

j. **Depression:** All patients with DM should be screened annually for depression. If positive, refer for further assessment to psychiatric clinic

k. **Disordered eating behavior** can affect DM management; consider reevaluating the treatment regimen for those patients.

l. Hearing impairment, hip fractures, obstructive sleep apnea (OSA), and periodontal disease are common in DM.

**Assessment of risk factors that can affect DM management**

Assessing the risk for atherosclerotic CVD (ASCVD) and heart failure (HF), CKD, and medication-associated hypoglycemia to individualize the glycemia, blood pressure, and lipids targets, and to select specific glucose-lowering medication, antihypertension medication, or statin treatment intensity. [52] Since no local data in KSA is available, several international risk calculators can be used to assess ASCVD risk. One of them is the ASCVD risk calculator (Risk Estimator Plus) of the American College of Cardiology/ American Heart Association that can be used to calculate the 10-year ASCVD risk. It should be assessed at least annually in all individuals with DM. These risk factors include the history of ASCVD or HF, obesity/overweight, smoking, and a family history of premature coronary disease, hypertension, dyslipidemia, CKD, and albuminuria. [54]
Measure blood pressure each visit. To diagnose hypertension (≥140/90 mmHg), patients should have their blood pressure confirmed in multiple readings, including a separate-day measurement. All DM hypertensive patients should monitor blood pressure at home. Investigations for CAD should be considered if unexplained dyspnea or chest discomfort, carotid bruits, transient ischemic attack, stroke, claudication, peripheral arterial disease, or ECG abnormalities (e.g., Q waves) present. Among those < 40 years old and not on statins or other antihyperlipidemic agents, obtain a lipid profile at the time of DM diagnosis, an initial medical evaluation, and every five years after that, or more frequently if indicated. [22, 23, 54]

Assess for CKD. At least annually, assess both urinary albumin (spot urinary albumin-to-creatinine ratio; ACR) and eGFR in patients with more than 5-years T1DM, in all T2DM patients, and all patients with comorbid hypertension [22, 23, 55]. Staging of CKD is essential for better management (table 4). [55]

Table 4: Staging of chronic kidney disease

<table>
<thead>
<tr>
<th>Stage</th>
<th>eGFR (ml/min/1.73 m²)</th>
<th>Evidence of kidney damage</th>
<th>Evaluate and treat risk factors for CKD progression</th>
<th>Evaluate and treat CKD complications</th>
<th>Prepare for renal replacement therapy</th>
</tr>
</thead>
<tbody>
<tr>
<td>No clinical evidence of CKD</td>
<td>≥60</td>
<td>-</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Stage 1</td>
<td>≥90</td>
<td>+</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Stage 2</td>
<td>60–89</td>
<td>+</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Stage 3</td>
<td>30–59</td>
<td>+/-</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Stage 4</td>
<td>15–29</td>
<td>+/-</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Stage 5</td>
<td>&lt;15 or dialysis</td>
<td>+/-</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
</tbody>
</table>

Hypoglycemia risk: assess for factors that increase the risk of treatment-associated hypoglycemia: [22, 23, 55, 56]

Table 5: Risk factors for hypoglycemia

<table>
<thead>
<tr>
<th>Risk factor</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Polypharmacy</td>
<td>Old age or cognitive impairment</td>
</tr>
<tr>
<td>Use of insulin or insulin secretagogues</td>
<td>Physical or intellectual disabilities that impair the proper response to hypoglycemia</td>
</tr>
<tr>
<td>Alcohol use</td>
<td>Impaired counter-regulatory response or hypoglycemia unawareness</td>
</tr>
<tr>
<td>Impaired kidney or hepatic functions</td>
<td>Longer duration of diabetes</td>
</tr>
</tbody>
</table>
Section 4:
Goal setting & treatment plan

- Glycemic targets
- Treatment plan
Glycemic targets

The primary measure that demonstrate the benefits of improved glycemic control is the HbA1c test [22, 27]. It reflects the average BG over three months, and usually, the NGSP-certified assays are accurate enough to guide the management plan [58]. In multiple landmark trials (DCCT and EDIC trials), reduction of microvascular and macrovascular complications were observed among individuals with HbA1c of 7% compared to 9% in patients with T1DM and was associated with long-term 50-60% reduction in microvascular complications (retinopathy, nephropathy, and neuropathy) and 57% less CVD events. Similar findings were also confirmed in patients with T2DM having lower HbA1c in the UKPDS study, where a 25% reduction in microvascular complications and a 15% reduction of macrovascular complications were observed. However, achieving HbA1c lower than 7% is associated with a significantly increased risk of hypoglycemia in T1DM and T2DM and polypharmacy in patients with T2DM. [59-62]

Therefore, an HbA1c of <7% is a reasonable universal target for most patients if achieved safely. Higher and lower HbA1c targets are appropriate in certain patients, depending on their clinical profile (Figure 2). Individualized HbA1c target could change over time and should be reviewed regularly. Generally, HbA1c should be performed routinely in patients with DM at diagnosis and every 3-6 months. The frequency of measuring HbA1c depends largely on the patient’s glycemic control [57]. Recently, the use of point of care HbA1c as a tool can aid in timely management plan changes if available and well standardized. [55, 63, 64]
As HbA1c is the main follow-up parameter in patients with DM, the test's accuracy is essential. Health care providers need to be aware of the pitfalls in HbA1c measurement; in particular, they should be aware of the clinical conditions that may affect the accuracy of HbA1c measurement (Figure 3). This should be considered, especially when there is a discrepancy between the HbA1c result and SMBG and/or CGM readings. In such cases, other indicators of glycaemic control like fructosamine are possible alternatives instead of HbA1c. [22-24, 52, 57]
Figure 3: Clinical conditions that can affect HbA1c levels
The correlation between HbA1c and SMBG is well established. To achieve an HbA1c of 7%, the SMBG has to be consistently within 80-130mg/dl in the fasting state and peak reading after meals less than 180mg/dl [57, 65]. SMBG is an essential tool in patients on intensive insulin therapy (multiple daily insulin injections or pump therapy), especially if the patient is empowered by proper education on how to use the SMBG readings to adjust his insulin doses and modify his lifestyle accordingly [66]. Generally, such patients are advised to self-monitor their BG before meals and at bedtime. Patients on SMBG can add other times like postprandial, before driving, before exercise, when hypoglycemia is suspected, and during the management of hypoglycemia. On the other hand, SMBG use in patients with T2DM on oral hypoglycaemic agents is of limited benefit. However, SMBG use may give them an insight into the glycemic effects of their lifestyle and medications on their glucose levels [67-69]. Moreover, SMBG confirms hypoglycemia if suspected, and it is an essential tool in patients where HbA1c is considered inaccurate. Despite the advances in DM care in general, there is still a gap in achieving HbA1c targets in our population. Studies had shown that less than 50% of Saudi patients have HbA1c at 7% or less, which indicates the need for further studies to identify the gaps in DM care in the country. [70, 71]

**Recommendations**

<table>
<thead>
<tr>
<th>Recommendation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Individualize HbA1c target according to patient’s profile and involve them in decision making.</td>
</tr>
<tr>
<td>The HbA1c target in most adults with DM is &lt;7%. However, the target can be &lt; 6.5% and &lt; 8% in some other cases. It is more or less a spectrum from 6.5-8%, from which the suitable target according to the case is chosen. See Figures 2.</td>
</tr>
<tr>
<td>Encourage people with DM to achieve and maintain the target unless there are adverse effects or if there is impairment in the quality of life.</td>
</tr>
<tr>
<td>Over time, reassess glycemic targets based on the factors mentioned in Figure 2.</td>
</tr>
<tr>
<td>HbA1c is to be tested at least twice a year in controlled patients (meeting targets and who have stable glycemic control) and four times a year in uncontrolled cases or change in treatment.</td>
</tr>
<tr>
<td>Point of care HbA1c could help make timely decisions about patient care if the test is available, and its accuracy is established.</td>
</tr>
<tr>
<td>If HbA1c is invalid because of disturbed RBCs turnover or abnormal HB; use the total glycated HB estimation (if abnormal HB) or use fructosamine estimation.</td>
</tr>
<tr>
<td>Educate people with DM to do SMBG and adjust treatment, especially if on insulin. The frequency of SMBG depends on the patient’s specific needs and goals.</td>
</tr>
</tbody>
</table>

**Treatment plan**

The goals of treatment of DM are to prevent or delay complications, maintain quality of life through lifestyle modifications, achieve glycemic targets, and manage coexisting comorbidities. Treatment planning is an indispensable element of initial and follow-up encounters with the patient. A patient-centred approach
where the patient has an active role based on preferences, values, and goals is vital in improving DM care. The multidisciplinary treatment plan should consider patient profiles like age, cognitive function, social support, literacy level, comorbidities, and education. It should also focus on the patient's empowerment with problem-solving skills in all aspects of DM care. Physicians, nurse practitioners, physician assistants, nurses, dietitians, exercise specialists, pharmacists, dentists, podiatrists, and mental health professionals constitute the health care team that will work together with the patient to achieve treatment goals. The health care provider-patient relationship should address and solve barriers to better DM care without blame. [72-74].

**Recommendations**

Treatment goals and plans should be created collaboratively with individuals with DM as they must assume an active role in their care (Figure 4).
Figure 4: Patient-centered glycemic management plan in T2DM.
Section 5:
Life-style modification

- Diabetes self-management education and support (DSMES)
- Nutritional therapy
- Sleep
- Physical activity
- Smoking cessation
- Refer to a mental health provider
Lifestyle management is a fundamental aspect of care, and it should be developed in collaboration with the patient and modified regularly starting from the patient's first visit. It includes diabetes self-management education and support, nutritional therapy, physical activity, sleep health, smoking & alcohol cessation counseling, and psychosocial care.

**Diabetes self-management education and support (DSMES)**

<table>
<thead>
<tr>
<th><strong>Recommendations</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>Individuals with DM should be encouraged to participate in DM self-management education.</td>
</tr>
</tbody>
</table>

Trained educators should deliver a structured curriculum in the DM education program. The program should be reviewed by trained independent assessors and outcomes should be regularly audited \[25\]. The program has to be patient-centered \[76\]. It can be customized according to patients' needs and delivered with others or via technology. Also, a new application may be used to assist patients in DM self-management \[77,79\]. The program should be re-assessed regularly: at diagnosis, annually if complications emerged or in any transition of care. Evaluation includes assessment of clinical outcomes, health status, and quality of life. \[80\]

**Nutritional therapy**

Diet is a fundamental part of management in all individuals with DM. Treatment cannot be effective unless adequate attention is given to appropriate nutrition \[81\]. Diet treatment should ensure weight control, provide nutritional requirements, allow reasonable glycemic control and correct any associated blood lipid abnormalities \[81–84\]. Weight loss (> 5%) can benefit obese or overweight adults with T2DM and those with prediabetes, which may be achievable through caloric restriction and lifestyle modification. \[85\]

**a. Goals of Nutrition Therapy for Adults with DM**

Maintain the pleasure of eating while individualize goals based on nutrition needs. Provide an educational program about healthy eating patterns rather than focusing on individual macronutrients, micronutrients, or single foods. \[22, 53\]

**b. Eating patterns**

A variety of eating plans can be implemented short term (1–2 years) to achieve weight loss in overweight/obese people with DM \[22, 53\]. They are structured low-calorie meal plans that include meal
replacements, the Mediterranean eating pattern [86, 87], and low-carbohydrate meal plans [84, 85, 89]. There is no evidence indicating an ideal dietary distribution of calories among carbohydrates, fats, and proteins for people with DM; therefore, meal plans should be individualized based on the patient’s requirements, total calorie intake, and metabolic goal. [82, 83, 90]

c. **Carbohydrates, Proteins, Fats and others**

Limit sucrose-containing, high fructose-containing, or other or high-glycemic-index foods, and adjust insulin doses to match carbohydrate intake (e.g., carbohydrate counting with glucose monitoring) [53, 91]. Intake should emphasize nutrient-dense sources that are high in fiber, including vegetables, fruits, legumes, whole grains, and dairy products [56]. Education on how to use carbohydrate counting and how to consider fat and protein content to determine mealtime insulin dosing should be carried out. [92, 93]

For individuals whose daily insulin dosing is fixed, a consistent carbohydrate intake pattern with respect to time and amount is recommended [94]. Avoidance of sugar-sweetened beverages (including fruit juices) is recommended.

Minimization of the consumption of foods with added sugar that can displace healthier, more nutrient-dense food choices is recommended [95-97]. In individuals with T2DM, carbohydrate sources high in protein should be avoided if there is a risk for hypoglycemia as ingested protein appears to increase insulin response without increasing plasma glucose concentrations. [98]

An eating plan emphasizing a Mediterranean-style diet rich in monounsaturated and polyunsaturated fats can improve glucose metabolism and lower CVD risk [86, 87]. Eating foods rich in long-chain omega-3 fatty acids, such as fatty fish and nuts and seeds, is recommended [99, 100]. Dietary supplementation with vitamins, minerals (such as chromium and vitamin D), herbs, or spices (such as cinnamon or aloe vera) is not recommended for glycemic control. [101-103]

d. **Sodium**

Sodium consumption should be limited to 2,300 mg/day for the general population as well as people with DM. [82]
e. **Non-nutritive sweeteners**

A low-calorie or non-nutritive-sweetened beverage may be used to replace sugar-sweetened beverages. Overall, people are encouraged to decrease both alternatives, with an emphasis on water intake. [104]

f. **Alcohol**

Alcohol is prohibited in KSA. It increases the risk of hypoglycemia, and should be addressed as part of a comprehensive medical assessment. [82, 103]

---

### Recommendations

Develop a nutrition therapy plan for each patient to achieve treatment goals, to be provided by a registered nutritionist for all individuals with DM, prediabetes, or GDM.

---

### Sleep

Adequate rest is essential for maintaining energy levels and well-being, and all patients should be advised to sleep approximately 7 hours per-night. Screen for sleep disorders. [22, 23, 91, 98-104]

---

### Physical activity

**Recommendations**

Encourage planned physical activity according to each individual profile (Figure 5).

---

a. **Pre-exercise Evaluation**

In asymptomatic patients, routine CHD screening is not recommended. However, the physician should perform a careful history, assess CVD risk factors, and be aware of the atypical presentation of CAD in patients with DM before planning exercise [105]. Consider investigations for coronary artery disease in the presence of any of the following: atypical cardiac symptoms (e.g., unexplained dyspnea, chest discomfort); signs or symptoms of associated vascular disease including carotid bruits, transient ischemic attack, stroke, claudication, or peripheral arterial disease; or electrocardiogram abnormalities (e.g., Q waves). [52] Patient’s age and level of past physical activity should be considered [52]. High-risk individuals should be advised to initiate a low-intensity exercise at short periods and increase the intensity and time as tolerated [105]. Providers should assess patients for conditions that might contraindicate certain types of exercise or predispose to injuries, such as uncontrolled hypertension, untreated proliferative retinopathy, autonomic neuropathy, peripheral neuropathy, and a history of foot ulcers or Charcot's foot. [106]
In cases with retinopathy

If there is proliferative diabetic retinopathy or serious non-proliferative diabetic retinopathy, vigorous-intensity aerobic or resistance exercise is contraindicated as it increases the possibility of vitreous hemorrhage or retinal detachment [107]. Consultation with an ophthalmologist before engaging in an intense exercise regimen may be appropriate. [52]

c. In cases with peripheral neuropathy

A comprehensive evaluation should ensure that neuropathy does not alter kinesthetic or proprioceptive sensation during physical activity, particularly in individuals with more severe neuropathy [51]. Studies have shown that walking at moderate intensity pose no risk of new foot ulcers or re-ulceration in individuals with peripheral neuropathy using proper footwear [108]. Those with peripheral neuropathy should wear proper footwear and check their feet regularly to detect lesions early [52]. Those with a foot injury or open sore should avoid weight-bearing. [52]

d. In cases with autonomic neuropathy

The risk of exercise-induced injury can be elevated due to autonomic neuropathy. It can lead to a reduction of the cardiac response to exercise, an impairment of thermal regulation, postural hypotension,
impaired night vision, and increased susceptibility to hypoglycemia \cite{109}. Thus, before starting physical exercise, individuals with diabetic autonomic neuropathy should undergo cardiac investigation. \cite{110}

e. \textit{In cases with diabetic kidney disease}

Physical exercise can increase urinary albumin excretion. There is no proof, however that vigorous-intensity exercise raises risk of diabetic kidney disease, and there appears to be no need for specific exercise restrictions for those patients. \cite{107}

f. \textit{In cases with hypoglycemia}

In individuals taking insulin and/or insulin secretagogues, if the dosage of medication or carbohydrate intake is not altered, physical activity can induce hypoglycemia. Individuals on these therapies need to consume some additional carbohydrates if pre-exercise glucose levels are < 90 mg/dL (5.0 mmol/L), depending on whether they are capable of reducing insulin doses during exercise (such as with an insulin pump or decreased pre-exercise insulin dosage), the time-of-day exercise, and the strength and length of the exercise. \cite{106, 111}

**Smoking cessation** \cite{52}

<table>
<thead>
<tr>
<th>Recommendations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Include smoking cessation counseling as a routine DM care component and advise all people with DM not to use cigarettes or other tobacco products.</td>
</tr>
</tbody>
</table>

**Psychosocial issues** \cite{52}

<table>
<thead>
<tr>
<th>Recommendations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Assess all people with DM for symptoms of distress, depression, anxiety, disordered eating, and cognitive capacities using appropriate tools at the initial visit, at periodic intervals, and when there is a change in disease, treatment, or life circumstance.</td>
</tr>
<tr>
<td>Monitor for distress, mainly when treatment targets are not met and/or at the onset of complications.</td>
</tr>
<tr>
<td>Special attention should be paid to screen those aged &gt;65 years with DM for cognitive impairment and depression.</td>
</tr>
</tbody>
</table>

**Refer to a mental health provider** \cite{52}

<table>
<thead>
<tr>
<th>Recommendations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Consider referral to mental health provider in certain circumstances (Figure 6).</td>
</tr>
</tbody>
</table>
Figure 6: Referral to mental health provider

- Depressive symptoms, anxiety or fear of hypoglycemia
- Disordered eating behavior
- Suspected serious mental illness
- Cognitive impairment
- Declining or impaired ability to perform diabetes self-care
- Before and after surgery for obesity
Section 6:

Obesity and overweight management plan

- Effects of Antihyperglycemic drugs on weight
- Treatment options for overweight and obesity in T2DM
- Metabolic Surgery
6. Obesity and overweight management plan

Obesity is a chronic condition with multiple physical and mental comorbidities. Obese individuals are at higher risk of CVD and mortality. The prevalence of obesity has increased in the recent few decades, secondary to many genetic and environmental factors associated with higher rates of DM. According to WHO reports 2016, the prevalence of obesity in KSA is 35.4%, and overweight is 69.7% being among the highest internationally reported prevalence. Reducing weight is a crucial step for proper and sustained plasma glucose control and has to be addressed in the management plan.

---

**Recommendations**

- More than 5% weight reduction should be achieved and maintained in subjects with T2DM.
- BMI should be measured and documented in each visit.
- Weight reduction maintenance is essential and should be encouraged and monitored.
- The dietary plan should be individualized to maintain an energy deficit of 500-750 kcal/day.
- Short-term (3-month) interventions with very-low-calorie diets (<800 kcal/day) and total meal replacements may be used with close medical monitoring. Long-term comprehensive weight-maintenance counseling is needed to maintain weight.
- Pharmacotherapy may be used for weight loss for selected patients with BMI ≥27 kg/m². Consider reassessment of pharmacotherapy after three months according to the effect on body weight.
- The use of anti-diabetes medications that increases weight should be minimized (Figure 9).
- Medications associated with increased weight are insulin, sulfonylurea, TZDs, and metiglinide.
- Weight neutral medications are DPP-4i, metformin and α-glucosidase inhibitors.
- Medications associated with weight reduction are glucagon-like peptide-1 receptor agonist (GLP-1 RA) and sodium-glucose co-transporter-2 inhibitor (SGLT2i).
- Life-style modifications should be applied to all patients.
- Medications that reduce weight could be considered in DM subjects with BMI>27.

**Effects of antihyperglycemic drugs on weight**

Antihyperglycemic drugs may have variable effects on weight. The following figure demonstrate these effects. Weight medications are listed in table 6.
Figure 7: Effects of antihyperglycemic drugs on weight

Treatment options for overweight and obesity in T2DM

Table 6: Medications for the treatment of obesity in T2DM

<table>
<thead>
<tr>
<th>Class</th>
<th>Relative weight loss</th>
<th>Side Effects</th>
<th>Therapeutic Considerations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gastrointestinal lipase inhibitor: (orlistat)</td>
<td>↓</td>
<td>Loose stools, GI upset, rare liver failure</td>
<td>Oral medication, decreases fat absorption, may require vitamin supplementation</td>
</tr>
<tr>
<td>GLP-1 RA: (liraglutide 3.0 mg)</td>
<td>↓↓</td>
<td>Nausea, GI upset, rare gallstones and pancreatitis</td>
<td>Subcutaneous injectable, increases satiety</td>
</tr>
</tbody>
</table>
Metabolic Surgery

The option of metabolic surgery should be advised for subjects with DM and a BMI of 30-34.9 kg/m² (27.5-32.4 kg/m² for Asians) and recommended for those with BMI >35 kg/m² (>32.5 kg/m² for Asians). [22, 23, 113]

Table 7: Treatment options for overweight and obesity in T2DM

<table>
<thead>
<tr>
<th>Intervention</th>
<th>BMI category (kg/m²)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>25.0-26.9</td>
</tr>
<tr>
<td>Diet, physical activity &amp; counseling</td>
<td>+</td>
</tr>
<tr>
<td>Pharmacotherapy</td>
<td>+</td>
</tr>
<tr>
<td>Metabolic surgery</td>
<td>+/-</td>
</tr>
</tbody>
</table>
Section 7:
Pharmacologic approaches to glycemic treatment in T2DM

- Tailoring treatment
- Pharmacologic therapy for T2DM Treatment (initial therapy, combination Therapy and insulin therapy)
The following section presents the current recommendations for the pharmacologic therapy of T2DM according to the most recent medical literature and the clinical practice.

Tailoring treatment

<table>
<thead>
<tr>
<th>Recommendations</th>
</tr>
</thead>
<tbody>
<tr>
<td>After categorizing patients according to their profile and considering drug efficacy, use the developed overall approach plan (Figure 9 &amp; 10).</td>
</tr>
</tbody>
</table>

The following is non-exhaustive list for factors related to the patient and to therapy: [22, 23, 53, 114]

- Newly diagnosed versus established cases
- Age category: children, young adult, elderly
- Sex: male versus female
- Type of DM
- Important comorbidities such as ASCVD, CKD, HF or liver failure
- Hypoglycemia risk
- Effects on body weight
- Side effects
- Cost
- Patient preferences
- Special categories: pregnancy, children, mental illness, fasting

Pharmacologic therapy for T2DM

Characteristics of pharmacologic therapy for DM are discussed and shown in Table 8. [22, 23, 53, 114]

Initial therapy

The preferred initial treatment for T2DM is metformin unless contraindicated. It can be used as monotherapy or in combination with lifestyle modifications. Metformin is a suitable medication achieving DM targets, safe, low cost, and may reduce CVD risk and death. Many forms of metformin can be used twice daily dosing or once daily. The adverse effects of metformin, such as lactic acidosis, are very rare. Metformin still has some side effects like gastrointestinal intolerance due to bloating, abdominal discomfort, and diarrhea. Metformin is safe in those with reduced estimated glomerular filtration rates (eGFR) > 30 mL/min/1.73 m². Prolonged use of metformin may lead to vitamin B12 deficiency and worsening of neuropathy symptoms, suggesting periodic checking levels of vitamin B12. For use of other oral agents as initial therapy of T2DM, still, there is little systematic data about that. [114] If metformin is contraindicated or not tolerated, other initial therapy from another class should be based on patient factors. Dual combination therapy should be used when HbA1c is >1.5% above glycemic target. [22]
If hyperglycemia is severe, especially when catabolic features are present (weight loss, hypertriglyceridemia, and ketosis), insulin is preferred to overcome glucose toxicity. In addition, insulin should be considered part of any combination regimen even in the early course of treating the disease if the patient has hyperglycemia symptoms like polyuria or polydipsia, which may indicate glucose toxicity. Consider starting insulin/GLP-1 RA therapy if BG is >300 mg/dL or HbA1c is >10%. [22, 23, 53, 114]

**Combination Therapy**

Any new class of non-insulin agents added to initial therapy generally reduces HbA1c by approximately 0.7–1.0% based on a comparative effectiveness meta-analysis. In a patient without ASCVD or CKD, if the HbA1c target is not achieved after approximately three months from initial therapy, consider a combination therapy of metformin and any one of the preferred treatment options. These include a sulfonylurea, TZDs, dipeptidyl peptidase 4 (DPP-4) inhibitor, SGLT2i, GLP-1 RA, or basal insulin. The choice is based on drug-specific effects and patient factors. [22, 23, 53, 114]

For patients with increased risk for ASCVD, HF, or CKD, a GLP-1 RA or SGLT2i (see Figure 9) (with demonstrated CVD risk reduction) is preferred as a second-line therapy, after consideration of drug-specific and patient factors. For those without proven ASCVD or CKD, scientific evidence does not yet direct a second agent's choice to add to metformin. Instead, drug selection is based on avoidance of side effects, particularly hypoglycemia and weight gain, price, and patient preferences. [114]

In patients who need a third agent to achieve glycemic goals, similar considerations are applied. The effectiveness, adverse effects, and patient burden of treatment regimens need to be reviewed constantly in all cases. Patients will require a reduction or discontinuation of medication in certain cases such as ineffectiveness, intolerable side effects, cost, or a change in glycemic goals are common reasons. [22, 23, 53, 114]
Comorbid Conditions

**Type 2 DM plus established ASCVD**
- sodium-glucose co-transporter 2 (SGLT2) inhibitors or glucagon-like peptide 1 (GLP-1) receptor agonists with CVD benefit are recommended

**Type 2 DM and chronic kidney disease (CKD):**
- Use of SGLT2 inhibitor or GLP-1 receptor agonist shown to reduce risk of CKD progression cardiovascular events or both

**In most patients who need the greater glucose-lowering effect of an injectable medication:**
- GLP-1 receptor agonists are preferred to insulin

**In patients with ASCVD at high risk of heart failure or in whom heart failure coexists**
- SGLT2 inhibitors are preferred

**Figure 8: Recommendations in comorbid condition**

**Insulin therapy**

Insulin therapy in T2DM should be considered in the following conditions regardless of the duration of DM: Severe weight loss (catabolic effect) and osmotic symptoms, HbA1c >10%, BG levels are consistently >300mg/dL, if HbA1c is above target with three or more DM treatment agents used for three months or more. Do not delay insulin therapy when needed. When initiating insulin, start with basal insulin at 0.1-0.2 units/kg/day if HbA1c < 8% and 0.2-0.3 unit per kg per day if HbA1c > 8%. The patient should titrate insulin dose by two units every third day to achieve FBG set. \(^{22, 23, 53, 114}\) Add prandial insulin if there is severe postprandial hyperglycemia despite FBG at or close to target or HbA1c above target despite FBG at target. Add one dose of prandial insulin with the largest meal and other meals as needed. The initial prandial dose could be 4-5 units or 10% of basal insulin dose. Titrate prandial insulin dose by 1-2 units or 10% change every 2-3 days until 2hr PPBG is at the target set. \(^{22, 23, 53, 114}\) Premixed insulin could be considered in patients with HbA1c above target and plan to add prandial insulin. Premixed insulin should be used at least twice daily and a maximum of three times daily. Always assess insulin injection techniques and sites to avoid inadequate insulin delivery. On initiating insulin, monitor the patient closely (every two weeks until SMBG) close to the target. The need for insulin could be reassessed over time when glycemic
<table>
<thead>
<tr>
<th>Control improves. [22, 23, 53, 114]</th>
<th>Metformin</th>
<th>SGLT-2i</th>
<th>GLP-1 RAs</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Efficacy</strong></td>
<td>High</td>
<td>Intermediate</td>
<td>High</td>
</tr>
<tr>
<td>Hypoglycemia</td>
<td>No</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td>Weight change</td>
<td>Neutral</td>
<td>Loss</td>
<td>Loss</td>
</tr>
<tr>
<td>CV effects: ASCVD</td>
<td>Potential benefit</td>
<td>Benefit: empagliflozin, canagliflozin</td>
<td>Benefit: liraglutide, semaglutide</td>
</tr>
<tr>
<td>CHF</td>
<td>Neutral</td>
<td>Benefit: empagliflozin, canagliflozin, dapagliflozin</td>
<td>Neutral: Liraglutide, semaglutide</td>
</tr>
<tr>
<td>Oral/SC</td>
<td>Oral</td>
<td>Oral</td>
<td>SC</td>
</tr>
<tr>
<td>Renal effects: progression of CKD</td>
<td>Neutral</td>
<td>Benefit: empagliflozin, canagliflozin, dapagliflozin</td>
<td>Benefit: liraglutide</td>
</tr>
<tr>
<td>Dose/use considerations</td>
<td>• Contraindicated with e GFR &lt; 30</td>
<td>• Renal dose adjustment required (canagliflozin, dapagliflozin, empagliflozin)</td>
<td>• Renal dose adjustment required (exenatide, lixisenatide)</td>
</tr>
<tr>
<td></td>
<td>• Diarrhea</td>
<td>• Risk of amputation (canagliflozin)</td>
<td>• Risk of thyroid C-cell tumors in mice (not proved in humans)</td>
</tr>
<tr>
<td></td>
<td>• Nausea</td>
<td>• Risk of fracture (canagliflozin)</td>
<td>• Nausea, vomiting, diarrhea</td>
</tr>
<tr>
<td></td>
<td>• B12 deficiency</td>
<td>• DKA risk (all agents, rare in T2DM)</td>
<td>• Injection site reactions</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Genitourinary infection</td>
<td>• ? Acute pancreatitis</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Risk of volume depletion, hypotension</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Increase LDL</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Risk of gangrene</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>DPP-4 inhibitors</th>
<th>Thiazolidinediones (2nd generation)</th>
<th>Sulfonylureas</th>
</tr>
</thead>
<tbody>
<tr>
<td>Efficacy</td>
<td>Intermediate</td>
<td>High</td>
</tr>
<tr>
<td>Hypoglycemia</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>Weight change</td>
<td>Neutral</td>
<td>Gain</td>
</tr>
<tr>
<td>CV effects: ASCVD</td>
<td>Neutral</td>
<td>Potential benefit: pioglitazone</td>
</tr>
<tr>
<td>CHF</td>
<td>Potential risk: saxagliptin, alogliptin</td>
<td>Increased risk</td>
</tr>
<tr>
<td>-----</td>
<td>----------------------------------------</td>
<td>---------------</td>
</tr>
<tr>
<td>Oral/SQ</td>
<td>Oral</td>
<td>No dose adjustment</td>
</tr>
<tr>
<td>Renal effects: progression of CKD</td>
<td>Neutral</td>
<td>No dose adjustment in renal impairment (fluid retention)</td>
</tr>
<tr>
<td>Dose/use considerations</td>
<td>Neutral</td>
<td>General considerations</td>
</tr>
<tr>
<td>Additional consideration</td>
<td>Neutral</td>
<td>Potential risk of acute pancreatitis</td>
</tr>
<tr>
<td></td>
<td>Neutral</td>
<td>Joint pain</td>
</tr>
<tr>
<td></td>
<td>Neutral</td>
<td>• Benefit in NASH</td>
</tr>
<tr>
<td></td>
<td>Neutral</td>
<td>• Risk of fractures</td>
</tr>
<tr>
<td></td>
<td>Neutral</td>
<td>• Bladder cancer (pioglitazone)</td>
</tr>
<tr>
<td></td>
<td>Neutral</td>
<td>• Increase LDL (rosiglitazone)</td>
</tr>
</tbody>
</table>

**Table 8:** Characteristics of pharmacologic therapy for DM
Figure 9: Antihyperglycemic medication in T2DM with risk factors for CVS diseases: overall approach
Figure 10: Intensifying injectable therapies
**Recommendations**

<table>
<thead>
<tr>
<th>Recommendation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Metformin is the preferred initial pharmacologic agent for the treatment of T2DM.</td>
</tr>
<tr>
<td>Continue metformin unless not tolerated or contraindicated.</td>
</tr>
<tr>
<td>Consider periodic measurement of vitamin B12 level in patient on long-term therapy with metformin as it may cause vitamin B12 deficiency, especially in those with anemia or peripheral neuropathy.</td>
</tr>
<tr>
<td>Metformin therapy should be temporarily halted on the day of radiocontrast administration and restarted a day or two later after confirmation that renal function has not deteriorated.</td>
</tr>
<tr>
<td>Advise initiating insulin therapy if there is evidence of ongoing catabolism (weight loss), or symptoms of hyperglycemia are present, or when HbA1c levels 10%.</td>
</tr>
<tr>
<td>Dual therapy should be considered in patients with newly diagnosed T2DM if HbA1c &gt; 1.5% above their glycemic target.</td>
</tr>
<tr>
<td>Use a patient-centered approach for the choice of pharmacologic agents. Consider comorbidities such as ASCVD, HF, CKD, hypoglycemia risk, impact on weight, cost, the risk for side effects, and patient preferences.</td>
</tr>
<tr>
<td>Recommend SGLT-2i or GLP1-RA with demonstrated CVD benefit for patients with T2DM and established ASCVD.</td>
</tr>
<tr>
<td>Use SGLT-2i in patients with ASCVD at high risk of HF or in whom HF failure coexists.</td>
</tr>
<tr>
<td>Use SGLT-2i or GLP1-RA, which is shown to reduce the risk of CKD progression, cardiovascular events, or both in patients with T2DM and CKD.</td>
</tr>
<tr>
<td>Use of GLP1-RA in patients who need a greater glucose-lowering effect of an injectable medication.</td>
</tr>
<tr>
<td>Intensification of treatment in T2DM should not be delayed for patients not meeting treatment goals.</td>
</tr>
<tr>
<td>Re-evaluate and adjust medication regimen every 3–6 months.</td>
</tr>
</tbody>
</table>
Section 8:

Blood glucose monitoring and DM technology

- Diabetes technology in KSA
- Self-Monitoring of Blood Glucose (SMBG)
- Continuous Glucose Monitors (CGM)
- CGM and SMBG, which is better?
- CGM versus SMBG
- Flash Glucose Monitoring (FGM)
- Flash Glucose Monitoring; the clinical utility
8. Blood glucose monitoring and DM technology

By definition, DM technology is the hardware, device, and software that people with DM can use to manage their BG levels. They are divided into two classes. The first class includes insulin administration tools like a syringe, pen, or pump. The second class is BG monitoring, as assessed with a meter or CGM system. Currently, it has expanded to include devices that can monitor glucose and deliver insulin, and an extra soft-ware that help provide diabetes self-management support. Applied appropriately, this technology can improve their lives and health. [64, 115]

DM technology in KSA

In KSA, insulin pump therapy and continuous blood glucose monitoring systems (CGMs) are now available and increasing as a modality both for better management of DM and as an educational tool for patients and healthcare providers. New user-friendly generations of CGMs encourage people with DM to use them. CGMs are available in KSA with in all four categories: Real-time CGMs like the Dexcom; intermittently scanned CGMs like the FreeStyle Libre; blinded (professional) CGMs like the Guardian; and the unblinded CGMs, which measure glucose levels and displayed to the patient. Although CGMs became the gold standard in managing patients on intensive insulin therapy, some physicians remain reluctant to use them due to the lack of experience and knowledge with this technology [116-119]. Also, the use of SMBG has increased over the years to help in better glycemic control among people with DM in KSA. [120]

Self-Monitoring of Blood Glucose (SMBG)

In general, SMBG allows people with DM to evaluate their response to treatment and achieve their glycemic targets. That can be a useful tool for the guidance of life-style measurement modifications like nutrition and physical activity. It can also help in the adjustment of medications and prevention of hypoglycemia. [115] Over the years, SMBG has been incorporated in the management plan of people with DM who are insulin-treated, as it is beneficial for glycemic control with its consequence on the DM complications [59]. It can help guide treatment decisions and self-management for those taking less frequent insulin injections. In people with T2DM who do not use insulin, routine glucose monitoring may be of limited additional clinical benefit. For some, it can provide insights into the impact of diet, physical activity, and medications on glucose levels. It may also be useful in assessing hypoglycemia, glucose levels during intercurrent illness, or discrepancies between measured HbA1c and glucose levels when there is concern that an HbA1c result may not be reliable. [64, 115]
Individuals using intensive insulin regimens should assess glucose levels using SMBG or CGM before meals and snacks, at bedtime, occasionally postprandial, before exercise, when they suspect low BG, after treating low BG until they are normoglycemic, and before critical tasks such as driving. [64, 115] People with DM should receive ongoing education and regular evaluation of their ability to use data from SMBG as well as CGM to adjust therapy [115]. The ongoing need for and frequency of SMBG use should be reevaluated at each routine visit to avoid overuse, especially if SMBG is not being used effectively for self-management. [121-124]

**Continuous Glucose Monitors (CGM)**

The two basic types of CGMs only measure the interstitial glucose level. These provide unblinded data to the user and those that are blinded with data available to the physician and the patient. A few require SMBG calibration, and others do not [125, 126]. Sensor-augmented pump therapy should be considered for children, adolescents and adults to improve glycemic regulation to avoid an increase in hypoglycemia or severe hypoglycemia. Adherence to continued use of the system is associated with benefits. Robust DM education, training, and support are required for optimal implementation and ongoing use of CGMs. Benefits of CGMs correlate with adherence to ongoing use of the device. [64, 115]

Real-time CGMs should be considered in children and adolescents with T1DM using multiple daily injections or continuous subcutaneous insulin infusion as an additional tool to improve glucose control and reduce risk of hypoglycemia. It is also a useful tool to lower HbA1c in adults with T1DM who are not meeting glycemic targets. Moreover, it can be used effectively to improve HbA1c levels and neonatal outcomes in pregnant women with T1DM. [127-133]

Sensor-augmented pump therapy with automatic low-glucose may be considered for adults with T1DM at high risk of hypoglycemic episodes and reduce their severity. Intermittently scanned CGM use may be considered a substitute for SMBG in adults requiring frequent glucose testing. It is a useful tool for those with hypoglycemia unawareness and/or frequent hypoglycemic episodes. It should be used as close to daily as possible for maximum benefit. [64, 115]

As a complement to SMBG, CGMs are used to measure glucose concentration in the interstitial fluid (ISF) of the subcutaneous fat tissue, utilizing a sensor, is measured and stored at regular intervals. However, the time required for the analysis in CGMs is high, and the interpretation of the data requires some extensive experience of the DM team, mainly because there is a variety of software for analysis, and no standardized software is currently available. Thus, the need for more technology is crucial. Flash glucose monitoring was developed to provide lower costs technology cheaper than CGMs with no need for calibration, and a more straightforward standardized reporting system. [134, 135]
CGM and SMBG, which is better?

Several large controlled clinical trials (such as DCCT and UKPDS) have demonstrated that intensive therapeutic management, aimed at attaining tight glycemic control, is associated with a significant reduction in serious DM-related complications and improved quality of life, and a decrease in the economic burden of this disorder. The achievement of tight glycemic control with intensive therapy necessitates frequent BG monitoring. [62, 136-139] Regardless of how often SMBG is used, discrete results offer only a static picture at any point and do not provide a sense of the number, intensity, and duration of glycemic excursions. By contrast, CGM provides the opportunity to match intensive therapy demands with a period of equally intensive glucose monitoring. [62, 136-139]

The continuous glucose profiles and summary statistics provided by CGM monitors have been demonstrated to identify periods of undetected nocturnal hypoglycemia and postprandial hyperglycemia that allow the DM team to apply specific changes in the timing and dosage of insulin infusion or injection, dietary and physical activity alterations, and changes in the timing and frequency of BG measurements. Thus, for the same patient, who is considered highly compliant, even when data was obtained from SMBG up to six times a day, important information was still missed. Glucose values vary for numerous reasons, and this results in significant glycemic variability. SMBG and HbA1c do not always provide a complete picture of change in patients’ glucose levels. [62, 136-139]

Time and skills are required to interpret the varying quality of recorded glucose values provided by their patients. Limitations from solo use of HbA1c or SMBG limit comprehensive understanding of changes to therapy. Also, different time points are needed to interpret reports and logbooks to make sense of the next therapy step. CGM is the only option that provides a complete picture of glycemic variability. [62, 136-139]
CGM versus SMBG [140]

<table>
<thead>
<tr>
<th>SMBG</th>
<th>CGM</th>
</tr>
</thead>
</table>
| • The FBG and PPBG are recommended to diagnose DM.  
  − The PPBG can diagnose more people with DM because early deterioration of glucose control is characterized by loss of PPBG control.  
  − Both FBG and PPBG provide a ‘snapshot’ of glucose values.  
  − PPBG helps assess meal-induced glucose excursions and efficacy of DM treatment.  
• The glycemic risk assessment diabetes equation (GRADE), refers to the risk associated with glucose profile. SMBG quantifies both hyper- and hypoglycemia by obtaining the % of time spent (GRADE hypoglycemia, GRADE euglycemia & GRADE hyperglycemia). Values <5 correspond to euglycemia.  
• Average daily risk range (ADRR) is 1 month of SMBG data, ideally three to five readings a day. The BG data needs to be transformed to give their corresponding risk values. The values are stratified into low <20; moderate 20–40; and high >40 | • Target-range and time-in-range can be expressed as ‘% of glucose readings’ or ‘hours per day.’ Target-range of 70–180 mg/dL is acceptable as it was observed that 50% of SMBG readings are in this range, HbA1c would be around 7%.  
• Glucose exposure is the average BG. Mean glucose exposure for specific periods during CGM (e.g., overnight, fasting, and 2–4 h postprandial) evaluate the effects of food, exercise, or insulin and is easy to implement in practice.  
• Indices of glycemic variability (GV) is a strong predictor of hypoglycemia, leading to poor glucose control, which results in poor satisfaction and compliance. Minimizing GV is necessary to achieve glucose stability and decrease risk of hypoglycemia. To standardize measures of glycemia, and ease of use, familiarity and correlation with other factors of glycemic control, three measures of GV were proposed: standard deviation around the mean glucose (SD), coefficient of variation (CV), and interquartile range (IQR).  
• Hypoglycemia is the main barrier in people with DM and preventing euglycemia: Given the significance of reducing hypoglycemia, attempts were made for a consensus to disclose its incidence and severity. CGM users can categorize hypoglycemia according to glucose levels:  
  • Low if glucose is <70 mg/dL  
  • Very low if glucose is <60 mg/dL  
  • Dangerously low if glucose is <50 mg/dL  
• ADA and the EASD proposed the following BG levels as hypoglycemia in clinical trials:  
  − Glucose alert: value at ≤70 mg/dL  
  − A glucose level <54 mg/dL indicate serious and clinically important hypoglycemia  
  − Severe cognitive impairment requiring external assistance for recovery  
• Hyperglycemia – levels of BG:  
  − High >180 mg/dL  
  − Very high >250 mg/dL  
  − Dangerously high >400 mg/dL |
Flash Glucose Monitoring (FGM)

FGM has several advantages over CGM despite having the same mechanism for glucose measurement as it has updated sensors incorporating osmium. The sensor is light, tiny, non-obtrusive, and mostly stays in place for two weeks. The application helps create a consolidated overview of glycemic levels and quantification of measured glucose exposure, variability, and stability. It is also able to report the incidence and duration of hypoglycemia in an easily interpretable manner. 

It measures BG levels without having to prick the fingers. There is only one FGM manufactured at the moment, known as the Freestyle Libre. FGM is a CGM that tests the interstitial fluid glucose. Since 2014, it has been available in Europe, and in 2017, it was approved by the US FDA.

The personal FGM has a receiver that displays real-time glucose values and trend arrows after scanning over the sensor by the individual. Data can be uploaded, and a report can be generated using available programs. The patient does not carry any receiver in the professional version; the data is blinded to the patient, and can be downloaded by the care provider using the provider's receiver and program. The FGM sensor is smaller than those of other systems and is water-resistant. FGM does not need SMBG calibration because it is factory calibrated. Acetaminophen does not affect glucose readings. The manufacturer's absolute relative mean difference (MARD) is 9.4%. It tracks glucose every minute, records measurements every 15 minutes, shows data up to 8 hours. Unlike real-time CGM systems, FGM has no alarms. FGMs are cheaper than real-time CGM systems. Studies indicate that FGMs have acceptable accuracy than SMBG, although the accuracy may be lower at extreme glucose levels.

FGM the clinical utility:

Two pivotal trials highlight the significant contribution FGM systems in DM monitoring. IMPACT (T1DM) and REPLACE (T2DM) show that the FGM systems can safely and successfully replace routine SMBG and deliver important clinical benefits to T1DM and T2DM patients using insulin. The multi-center randomized controlled study on adults with T2DM on intensive insulin therapy (REPLACE study) from 26 European DM centers was conducted to assess the safety and efficacy of new flash glucose-sensing technology to replace SMBG and concluded that its use in T2DM with intensive insulin therapy had no difference in HbA1c change and reduced hypoglycemia, thus offering a safe, adequate replacement for SMBG. Both studies (IMPACT) and (REPLACE) showed that the FGM system significantly reduced all key measures of hypoglycemia without increasing HbA1c (time in range). The key measures of hypoglycemia were time spent in hypoglycemia (<70 mg/dL/<3.9 mmol/L), time spent in nocturnal hypoglycemia (23:00 to 06:00), and time spent in serious
hypoglycemia (<55 mg/dL/<3.1 mmol/L). Hypoglycemia reduction was quick and sustained without an increase in HbA1c vs. SMBG. [142, 143]

The SELFY trial was conducted in UK, Irish, and German children with T1DM aged 4-17. The study showed that children improved glycemic control safely and effectively with short-term FGM than SMBG in a single-arm study. However, the study was one-arm non-comparative. [144]

The FGM improved QOL and patient-reported outcome measures. Two different measurements of QOL (the Diabetes-Treatment-Satisfaction Questionnaire and the Diabetes Quality of Life survey) showed an increased overall satisfaction for FGM vs. taking finger-sticks. These results serve as a reminder of how much hypoglycemia affects T2DM as well. [142, 143]

A cost analysis was conducted by Khan-Mirón et al. (2017) showed that while FGM is a great innovation that simplifies daily DM management and can enhance patient adherence to recommended testing frequency. However, the costs associated with this technology are still a significant barrier to patient access. [145]

**Recommendations**

Although SMBG is helpful, CGM reveals hidden data not seen in SMBG even when the patient is highly compliant. Therefore, treatment-related decisions for the same patient vary accordingly.

FGM is a subtype of CGM recommended to be used in children and adults with T1DM or T2DM using multiple insulin injections, GDM who need further glycemic control, individuals with hypoglycemia unawareness, or at high risk for hypoglycemia. It is also recommended for a short period for those who require intensive BG control or during acute illness or stress.

*Finally, FGM could be used as an educational tool for any individuals with DM to study the impact of some aspects of life-style modifications on their immediate BG level.*

According to the MOH scientific committee, the following are indications for FGM and CGMs:

First: Provide the devices continuously:

1- All individuals with type 1 diabetes children and adults
2- T2DM on multiple daily injections and one of the following conditions:
   a. Hypoglycemia un-awareness
   b. Chronic renal failure on dialysis or with transplant
   c. Suffering from gastroparesis

Second: Provide the devices temporarily to individuals with T2DM on insulin injections and has poor diabetes control at least 3 times per year, 14 days each time to adjust the therapy plan
Section 9:
Managing CV risks in individuals with DM

- Introduction
- Hypertension and blood pressure control in DM
- Lipid management
- Antiplatelet therapy
9. Managing CV risks in individuals with DM

Introduction

CV complications are the leading cause of mortalities in individuals with DM [146]. Chronic higher glucose levels, dyslipidemia, hypertension, and smoking exert a harmful effect on the intimal arterial wall resulting in atherosclerosis. In T1DM, DCCT/EDIC showed a reduction in CV mortalities with tight glucose control, whereas this has not been approved in large prospective trials as in ADVANCE and ACCORD in T2DM despite a trend being noticed on pooled data [147-149]. Furthermore, SGLT2i and GLP-1 RA have shown benefits in reducing CV adverse outcomes in T2DM subjects. In particular, Empagliflozin, Semaglutide, and Liraglutide have shown CV mortality benefits [150-152]. In KSA and according to the Saudi project for assessment of coronary events (SPACE) registry, 58.1% of those presented with ACS have DM, 55.3% with hypertension, 41.1% with hyperlipidemia, and 32.8% were smokers. Patients in this registry were about 10-years younger (mean age 58 years) than registries in other countries, indicating ACS occurs at a younger age group in the Saudi population [153]. A holistic approach is needed to manage CV risk in DM that should address all modifiable CVS risk factors.

Hypertension and blood pressure control in DM

BP control to less than 140/90 has shown benefits in lowering both macro and microvascular complications. Further reduction of BP to less than 130/80 was associated with better outcomes in some studies and preferable if it can be achieved safely [154-156]. Individualize BP targets according to CVD risk, adverse effects of antihypertensive drugs, and patient’s preferences and use the appropriate treatment strategy [24, 53]. If blood pressure is greater than 160/100 mmHg, use lifestyle therapy, initiate, and titrate two drugs or a single-pill combination of drugs known to decrease CVD events. [22, 23, 53, 156]

Use drug classes known to reduce CV events in DM individuals: ACEIs, ARBs, thiazide-like diuretics, and dihydropyridine calcium channel blockers. Avoid the use of combinations of ACEIs with ARBs and ACEIs or ARBs with direct renin inhibitors. An ACEI or ARB is the recommended first-line management of hypertension in DM subjects who have urinary ACR ≥300 mg/g creatinine or 30–299 mg/g creatinine. Serum creatinine/eGFR and serum potassium need to be checked annually for those on ACEI, ARB, or diuretic. Use mineralocorticoid receptor antagonist if patients are uncontrolled on three classes of antihypertensive drugs (including a diuretic). [22, 23, 53, 156] Also, use ACEI or ARB in adults with T1DM or T2DM with: Clinical CVD, age >55 years with an additional CV risk factor or end-organ damage (albuminuria, retinopathy, left ventricular hypertrophy) or microvascular complications. [22, 23, 53, 156]
**Recommendations**

High-risk subjects with 10-years ASCVD >15%，BP of <130/80 is an appropriate target if can be achieved safely.

Lower-risk subjects with 10-years ASCVD<15%，BP of <140/90 mmHg is an appropriate target if can be achieved safely.

**Lipid management:**

DM subjects often present with abnormalities in lipid metabolism. Using statins was associated with lower ASCVD events when used for both primary and secondary prevention. [157, 158] In 1270 Saudis with T2DM, the LDL goal was achieved only in 48% while on statins. [159]

**Recommendations**

A lipid profile should be obtained at the start of lipid-lowering therapy, after 2-3 months or at the change in dose, and annually after that.

For those aged 40 years or older who are not using lipid lowering agents, request lipid profile at diagnosis, at medical evaluation and every five years thereafter or more frequent if indicated.

Use the statin treatment schema provided (Figure 12 & 13) and treat other lipoprotein fractions (Table 10).

Intensify lifestyle therapy and optimize glycemic control for those with elevated triglyceride levels (≥150 mg/dL [1.7 mmol/L]) and/or low HDL cholesterol (<40 mg/dL [1.0 mmol/L] for men, <50 mg/dL [1.3 mmol/L] for women).

Recommend lifestyle modification focusing on weight loss (if indicated), apply Mediterranean eating plan or Dietary Approaches to Stop Hypertension (DASH) dietary pattern (lower sodium and rich in potassium, magnesium and calcium foods), reduce saturated fat and trans-fat, increase dietary omega-3 fatty acids, viscous fiber, and plant intake, and increase physical activity. [156]

**Figure 11:** ASCVD risk factors in DM
**Figure 12:** Statin therapy for primary prevention

- **Age 40-75 years, No ASCVD**
  - Moderate intensity
- **Age 20-39 with additional ASCVD**
  - Start statins
- **Age 50-70 with multiple ASCVD**
  - Use high intensity statins
- **ASCVD risk >20%**
  - Add maximum tolerated statins plus ezetimibe to reach >50% reduction

ASCVD risk estimation using the American College of Cardiology Score System

**Figure 13:** Statin therapy for secondary prevention

- **All ages and ASCVD**
  - High intensity statins
  - Lie style modification
- **High risk ASCVD with LDL >70 mg/dl**
  - Maximum dose high intensity
  - Add Ezetimibe or PCSK9 inhibitor if affordable
- **Age >75**
  - Continue statins if already used
  - Initiate after evaluating risk/benefits

ASCVD risk estimation using the American College of Cardiology Score System
Table 9: Statin therapy intensity

<table>
<thead>
<tr>
<th>High intensity statins</th>
<th>Moderate intensity statins</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lowers LDL &gt;50%</td>
<td>Lowers LDL by 30-50%</td>
</tr>
<tr>
<td>Atorvastatin 40-80 mg</td>
<td>Atorvastatin 10-20 mg</td>
</tr>
<tr>
<td>Rosuvastatin 20-40 mg</td>
<td>Rosuvastatin 5-10 mg</td>
</tr>
<tr>
<td>Simvastatin 20-40 mg</td>
<td>Simvastatin 10-40 mg</td>
</tr>
<tr>
<td>Pravastatin 40-80 mg</td>
<td>Pravastatin 10-40 mg</td>
</tr>
<tr>
<td>Lovastatin 40 mg</td>
<td>Lovastatin 10-20 mg</td>
</tr>
<tr>
<td>Pitavastatin 2-4 mg</td>
<td>Pitavastatin 1-2 mg</td>
</tr>
</tbody>
</table>

Table 10: Treatment of Hypertriglyceridemia

<table>
<thead>
<tr>
<th>Fasting triglyceride levels ≥500 mg/dL (5.7 mmol/L)</th>
<th>Adults with moderate hypertriglyceridemia (fasting or non-fasting triglycerides 175–499 mg/dL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>□ Search for 2yr causes of hypertriglyceridemia.</td>
<td>□ Mange modifiable lifestyle risk factors (obesity and metabolic syndrome)</td>
</tr>
<tr>
<td>□ Start treatment to reduce the risk of pancreatitis.</td>
<td>□ Treat secondary factors (DM, chronic liver or kidney disease and/or nephrotic syndrome, hypothyroidism)</td>
</tr>
<tr>
<td></td>
<td>□ Avoid drugs that raise triglycerides</td>
</tr>
<tr>
<td></td>
<td>□ Recently Icosapent ethyl (a form of omega 3 not available in KSA) was shown to reduce CV events including deaths in subjects with higher TG.</td>
</tr>
</tbody>
</table>

Antiplatelet therapy

Aspirin use for primary prevention in subjects with T2DM has been a controversial issue. While several trials have shown no benefits in preventing ASCVD, but the relatively most recent randomized controlled ASCEND study has shown benefits, however, with increased bleeding tendency. Therefore, aspirin use in T2DM should be individualized and used for high-risk subjects. For secondary prevention, aspirin is recommended for prevention for further protection against ASCVD. If ASA is not tolerated, recommend clopidogrel 75 mg.
Section 10:
DM complications

- Acute complications of DM
  a. Hypoglycemia
  b. Diabetic ketoacidosis (DKA) for patients older than 14 years old
  c. Hyperglycemic Hyperosmolar State (HHS) /Hyperglycemic hyperosmolar non ketotic state/coma (HONK)

- Chronic complications of DM
  a. Diabetic Retinopathy
  b. Diabetic Neuropathy
  c. Diabetic Foot
  d. Chronic Kidney Disease
  e. Sexual Dysfunction
Complications of DM are classified to acute and chronic complications. [163]

<table>
<thead>
<tr>
<th>Acute complications of DM</th>
<th>Chronic complications of DM</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hypoglycemia</td>
<td>Eyes</td>
</tr>
<tr>
<td>Diabetic ketoacidosis (DKA)</td>
<td>Diabetic retinopathy</td>
</tr>
<tr>
<td>Hyperosmolar hyperglycemic state (HHS)</td>
<td>Non-proliferative (background)</td>
</tr>
<tr>
<td>Lactic Acidosis</td>
<td>Proliferative</td>
</tr>
<tr>
<td></td>
<td>Cataracts</td>
</tr>
<tr>
<td>Kidneys</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Intercapillary glomerulosclerosis</td>
</tr>
<tr>
<td></td>
<td>Diffuse</td>
</tr>
<tr>
<td></td>
<td>Nodular</td>
</tr>
<tr>
<td>Infection</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Pyelonephritis</td>
</tr>
<tr>
<td></td>
<td>Perinephric abscess</td>
</tr>
<tr>
<td></td>
<td>Renal papillary necrosis</td>
</tr>
<tr>
<td></td>
<td>Renal tubular necrosis</td>
</tr>
<tr>
<td></td>
<td>Following dye studies</td>
</tr>
<tr>
<td>Nervous System</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Peripheral neuropathy</td>
</tr>
<tr>
<td></td>
<td>Distal, symmetric sensory loss</td>
</tr>
<tr>
<td>Motor neuropathy</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Foot drop, wrist drop</td>
</tr>
<tr>
<td></td>
<td>Cranial nerves III, IV, VI, VII</td>
</tr>
<tr>
<td></td>
<td>Diabetic amyotrophy</td>
</tr>
<tr>
<td>Autonomic neuropathy</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Postural hypotension</td>
</tr>
<tr>
<td></td>
<td>Resting tachycardia</td>
</tr>
<tr>
<td></td>
<td>Loss of sweating</td>
</tr>
<tr>
<td></td>
<td>Gastroparesis</td>
</tr>
<tr>
<td></td>
<td>Diabetic diarrhoea</td>
</tr>
<tr>
<td></td>
<td>Urinary bladder atony</td>
</tr>
<tr>
<td></td>
<td>Impotence (may also be secondary to pelvic vascular disease)</td>
</tr>
<tr>
<td>Skin</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Diabetic dermopathy (shin spots)</td>
</tr>
<tr>
<td></td>
<td>Necrobiosis lipoidica diabeticorum</td>
</tr>
<tr>
<td></td>
<td>Candidiasis</td>
</tr>
<tr>
<td></td>
<td>Foot and leg ulcers</td>
</tr>
<tr>
<td></td>
<td>Neurotropic</td>
</tr>
<tr>
<td></td>
<td>Ischemic</td>
</tr>
<tr>
<td>Cardiovascular System</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Heart disease</td>
</tr>
<tr>
<td></td>
<td>Myocardial infarction</td>
</tr>
<tr>
<td></td>
<td>Cardiomyopathy</td>
</tr>
</tbody>
</table>

67
Acute complications of DM

a. Hypoglycemia

Hypoglycemia is the most frequent acute complication in DM patients treated with insulin, and it can occur in a patient taking oral medications that stimulates pancreatic β cells (e.g., sulfonylureas). It is defined as low BG levels, with or without the typical symptoms of hypoglycemia. (22, 23, 164)

The risk factors for hypoglycemia in DM: (22, 23, 164)
- Insulin secretagogues or insulin
- Decreased inputs of glucose as after missed meals and during fasting.
- Increased glucose utilization as in physical exercise.
- Increased insulin sensitivity as after weight loss and in physical exercise
- Decreased insulin clearance (renal failure)
- Prior event of severe hypoglycemia
- Current low HbA1c (<6.0%)
- Hypoglycemia unawareness
- Long duration of insulin therapy
- Autonomic neuropathy
- Low economic status, food insecurity or low health literacy
- Preschool-aged children or adolescence
- Pregnancy
- Elderly
- Cognitive impairment

Table 11: Symptoms and Signs of Hypoglycemia: (22)

<table>
<thead>
<tr>
<th>Adrenergic symptoms</th>
<th>Neuroglycopenic</th>
</tr>
</thead>
<tbody>
<tr>
<td>Occur first and caused by autonomic nervous system activity</td>
<td>Occur later and caused by decreased activity of CNS</td>
</tr>
</tbody>
</table>
Hypoglycemia is categorized into the following classes:  [22, 23, 164]

Table 12: Categories of hypoglycemia

<table>
<thead>
<tr>
<th>Level 1</th>
<th>Level 2</th>
<th>Level 3</th>
</tr>
</thead>
<tbody>
<tr>
<td>BG &lt;70 mg/dL</td>
<td>BG &lt;54 Neuroglycopenic symptoms.</td>
<td>Severe event</td>
</tr>
<tr>
<td></td>
<td>Requires immediate action</td>
<td>Requires assistance from another person for</td>
</tr>
<tr>
<td></td>
<td></td>
<td>recovery (associated with increase mortality)</td>
</tr>
</tbody>
</table>

Asymptomatic hypoglycemia (Hypoglycemia unawareness)

Hypoglycemia unawareness is hypoglycemia in the absence of symptoms and is associated with a six-fold increased risk for severe hypoglycemia. It results from recurrent untreated hypoglycemia. The diminished adrenergic response is the mechanism as it leads to loss or impairment of the warning symptoms.  [22, 23, 164]

Management of hypoglycemia

Use the developed algorithm (Figure 14).

Prevention of further hypoglycemia events

The most crucial step is to identify causes to prevent future events. Thus, the patient and his family's education about precipitating factors, signs, symptoms, and hypoglycemia management are essential. Drugs associated with a high risk of recurrent or severe hypoglycemia should be avoided, and the frequency of SMBG should be increased. For a patient with hypoglycemia unawareness, less stringent glycemic targets up to 3 months is recommended. In addition, the medications/insulin can be modified if neither dietary factors nor lifestyle changes were beneficial. While driving, an emergency supply of glucose or sweets should be kept in the vehicle, considering unexpected delays or breakdowns. On a long journey, the BG should be monitored periodically, and snacks should be taken regularly.  [165]

Recommendations

Ask each patient about hypoglycemia (symptomatic or asymptomatic) at each visit especially those at risk for hypoglycemia.

In case of hypoglycemia unawareness or level-2 hypoglycemia in patients treated with insulin, raise the glycemic target for at least one month to reverse the hypoglycemia unawareness and reduce the risk of subsequent events.

For patients with cognitive impairment, regular assessment is advised with better attentiveness for hypoglycemia.

Advise the patients to wear medical identification that tells others he has DM (bracelet or necklace). Then, if he does become hypoglycemic, people may be better able to help him.
Management of Hypoglycemia

**STEP 1:** Assess ABC, level of consciousness and the ability to drink.

Send blood sample to the laboratory for verification (but do not wait for the result)

**STEP 2**

**Conscious AND able to drink**

- Give 15 gram of glucose (sugar) orally (1/2 cup apple or orange juice or one tablespoonful sugar dissolved in water or one tablespoon of honey)
- Repeat BG test after 15 minutes
- If BG is still ≤ 4.0 mmol/L repeat the process x 3 till BG is > 4.0 mmol/L.
- Then give a snack of 15-20 gram of complex carbohydrate such as one toast

**Unconscious OR unable to drink**

**INTRAVENOUS ACCESS IS SECURED:**

- MILD (2.5 – 4.0 mmol/L):
  - Administer 25 mL 50 % dextrose IV over 1-3 minutes
  - Repeat BG test in 5 minutes
  - If BG is still ≤ 4.0 mmol/L, re-administer the dose and check BG using finger stick in 5 minutes; repeat the process until BG level exceeds 4.0 mmol/L

- SEVERE (< 2.5 mmol/L):
  - Administer 50 mL of 50 % dextrose IV over 1-3 minutes
  - Repeat BG test in 5 minutes
  - If BG is still ≤ 4.0 mmol/L, re-administer the dose (50 mL of 50 % dextrose IV over 1-3 minutes) and check BG using finger stick in 5 minutes; repeat the process until BG level exceed 4.0 mmol/L

**NO SECURED INTRAVENOUS ACCESS:**

- Administer 1 mg glucagon SC or IM
- Repeat BG test in 15 minutes
- If BG is still ≤ 4.0 mmol/L, re-administer the dose and check BG using finger stick in 15 minutes; repeat the process until BG level exceeds 4.0 mmol/L

When the patient is conscious and able to eat, give him a meal of 30 gram of complex carbohydrate such as 2-3 toasts.

**Step 3:** Assess and manage the precipitating factors

**Step 4:** Adjust dose of insulin and other hypoglycemic agents.

---

**Figure 14:** Management of hypoglycemia

For patients with hypoglycemia secondary to long-acting SUs (e.g., glibenclamide), prolonged observation is needed (24-48 hours). Also, prescribe glucagon for all patients on insulin at increased
risk of hypoglycemia to be available when needed. Its place should be known for family members or relatives of these patients and they should know how to use it and when. [165]

b. Diabetic ketoacidosis (DKA) for patients above 14 years old of age

DKA is diagnosed by the biochemical triad of hyperglycemia, ketonemia / ketonuria, and high anion-gap metabolic acidosis. It is a fatal condition and should be suspected and treated quickly. T1DM subjects are at risk of developing DKA if they acquire an infection, secondary to frequently missed insulin doses or due to marked stress. Newly diagnosed T1DM often present with DKA. Subjects with T2DM may present with DKA if they have persistent hyperglycemia for a long time or become under the effect of a stressor. Ketone bodies should be checked if BG ≥ 14 mmol/l in T1DM or when DKA is suspected. All DM patients with positive ketones or when the DKA is suspected must be directed to the ER for further workup and management. [166]

Clinical presentation of DKA

DKA can present by polyuria, polydipsia, weight loss, weakness. There are also physical signs of dehydration: dry buccal mucosa, sunken eyeballs, poor skin turgor, tachycardia, hypotension, and shock in severe cases. Kussmaul respiration, acetone breath, nausea, vomiting, and abdominal pain may also occur primarily in DKA. Abdominal pain correlates with the severity of acidosis. [166]

Diagnostic Criteria for DKA

The following biochemical criteria are required for the diagnosis: BG ≥ 200 mg/dl (11.1 mmol/L) or known DM; positive serum ketones or significant ketonuria (≥2+ urine ketone) and; venous or arterial HCO3 < 15 mmol/L and/ or pH < 7.3. [166]

Investigations

Investigations should be towards finding the precipitating factors and should be ordered by the treating physician whenever appropriate. They include CBC, glucose, electrolytes, BUN/creatinine, Ca, Mg2, phosphate, urine glucose, and ketones. Also, ABG and ECG (MI possible precipitant; and electrolyte disturbances may predispose to dysrhythmia). [166]

Markers of severity (Manage in HDU/ICU) [166]

- GCS < 12
- pH < 7.1
- Serum ketones > 6 mmol/L
- HCO3 < 5 mmol/L
- K+ < 3.3 or > 6.0 mmol/L
- SBP < 90 mmHg
- SpO2 < 92% in room air and pulse rate > 100 or < 60 bpm
- Urine output < 0.5 ml/kg/hr. or evidence of acute kidney injury
Management of DKA:

DKA's main treatment is rehydration, insulin administration, and electrolytes balance, mainly potassium, together with identification and treatment of the precipitating factor. Treatment of DKA mandates good monitoring of fluid status, electrolytes, acidosis, and BG. [22, 23, 53, 166]

**Rehydration:** Start with a normal saline bolus followed by a high-rate normal saline infusion (beware of overhydration and cerebral edema). Beware of pseudo hyponatremia due to hyperglycemia (add 3 Na+ per 10 glucose over 5.5 mmol/L). The initial fluid is isotonic saline at the rate of 15–20 ml/kg body weight per hour or 1–1.5 L during the first hour. The choice of fluid for further repletion depends on the hydration status, serum electrolyte levels, and urinary output. In hypernatremic patients, 0.45% Na Cl infused at 4–14 ml/kg/hour is appropriate, and 0.9% Na Cl at a similar rate is preferred in patients with eunatremia or hyponatremia. The target is to replace 50% of the estimated water deficit over 12-24 hours. The protocol is not designed for hemodynamically unstable subjects, and those will require management by the ICU team. In patients with hypotension, aggressive fluid therapy with isotonic saline should continue until BP is stabilized. [22, 23, 53, 166]

**Potassium:** Supplementation should be started for plasma potassium <5.0 to 5.2 mmol/L after establishing diuresis, usually with the second liter of saline. Replacement should be started when the level falls below the upper limit of normal to prevent hypokalemia. In the case of presentation with normal or low potassium levels, potassium should be started at once, at concentrations in the IV fluid between 10 to 40 mmol/L, at a maximum rate of 40 mmol/h. Insulin, correction of acidosis, and rehydration decrease the serum potassium level. In the case of serum potassium <3.3 mmol/L, no insulin and/or bicarbonate until the restoration of potassium level to ≥3.3 mmol/L by replacement at 40 mmol/h. Also, treat the potassium deficit of HHS in the same manner. [22, 23, 53, 166]

Patients with DKA who had severe vomiting or had been on diuretics may present with significant hypokalemia. In such cases, potassium replacement should begin with fluid therapy, and insulin treatment should be postponed until potassium concentration becomes > 3.3 mEq/L to prevent arrhythmias and respiratory muscle weakness. Adequate monitoring of potassium level is crucial during the management of DKA. [22, 23, 53, 166]

**Insulin:** Do not give insulin if potassium is less than 3.3 mmol/L. An initial bolus of 5-10 U short-acting/regular insulin (or 0.2 U/kg) IV in adults (controversial – may start with infusion). They are to be followed by continuous infusion at 5-10 U (or 0.1 U/kg) per hour. Add 5% dextrose to IV fluids when BG <15 mM to prevent hypoglycemia. Bicarbonate is not given unless the patient is at risk of death or shock (typically pH <7.0). Treatment with IV insulin should be established once the serum potassium level is >3.3 mEq/l and should be continued until the patient is out of DKA and can be shifted to subcutaneous insulin. [22, 23, 53, 166]
Switch to SC insulin when venous HCO3 ≥ 18 mmol/L and/or pH ≥ 7.3, closed anion gap, and the patient is able to take orally. Overlap the first dose of rapid-acting insulin for one hour with the insulin infusion before stopping. [22, 23, 53, 166]

Bicarbonate is considered if pH is less than 6.9: NaHCO3 (50 mmol) dilute in 200 ml H2O infuse at 200 ml/hr., hold if K is below 3.3 mmol/l. Repeat HCO3 infusion every 2 hours until pH is more than 6.9. Monitor K+ level every 2 hours while on bicarbonate infusion. [22, 23, 53, 166]
Order Sheet for the Management of Adult Patients (> 14 years old) with DKA

**Patient:**

**MRN:**

Please admit to □ General Ward □ ICU, as a case of ____________, secondary to ______________ under the care of Dr. ______________ ____________.

**Vital Signs:** □ STAT □ Then every ___________ □ GCS □ STAT □ Then every ___________

**Diet:** □ Diabetic Diet □ NPO Urinary Catheter: □ Yes □ No Nasogastric Tube needed: □ Yes □ No

**Investigations:**
- VBG: □ STAT □ Then every ___________
- Urea / Electrolytes: □ STAT □ Then every ___________
- CBC □ Urine Analysis □ Urine Ketones □ Urine culture/sensitivity □ Blood Culture □ Random Blood sugar □ S. Ketones □ Phosphorus □ Ca □ Mg □ CR □ ECG □ Troponin/CK-MB □ Others ___________

**Monitoring:**
- Check BG, by glucometer (if hourly readings are between 5-10 mmol/L for 3 consecutive hours, then the frequency of BG checking can be reduced to 2 hourly). □ Input/output Chart □ Daily Weight

**Fluids:** (If the patient is hemodynamically unstable, DON’T use this protocol)
- If Systolic BP is more than or equal to 90 mmHg, please use the algorithm below: Be cautious with elderly patients, very young patients, and patients with compromised cardiac status due to risk of fluid overload.

<table>
<thead>
<tr>
<th>Weight at presentation more than 50 kg</th>
<th>Weight at presentation less than or equal to 50 kg</th>
</tr>
</thead>
<tbody>
<tr>
<td>□ 0.9% Na CI 1L over 1st hour (no added KCI)</td>
<td>□ Do not use this protocol.</td>
</tr>
<tr>
<td>□ 0.9% Na CI 1L over 2nd hour (no added KCI)</td>
<td></td>
</tr>
<tr>
<td>□ 0.9% Na CI 1L over 4th hour (KCI as per K replacement algorithm)</td>
<td></td>
</tr>
</tbody>
</table>

- Continue NS fluid at a rate of (100 – 250 ml/hr.) ……………………ml/hour with potassium as in potassium algorithm.
- When blood sugar is less than 13 mmol/L, change to D5 NS at a rate (100 – 250 ml/hr.) ……………………ml/hour.
- If blood sugar is less than 4.0 mmol/L, give a bolus of 25 ml of Dextrose 50%.

**Insulin:** (Don’t start insulin till K level is available)
- Mix 50 units of human regular insulin with 50 ml with 0.9% Na CI solution.
- Infuse insulin at a fixed rate (0.1 unit/kg/hr.) __________ units/hour. (No bolus)
- Check blood sugar hourly by glucometer.
- When the blood sugar is less than 6 mmol/L, decrease insulin infusion to (0.05 unit/kg/hr.) __________ units/hour.
- If the patient is using Levemir/ Glargine continue same dose at the same time __________ units at __________ daily (optional)

- If the patient is using Levemir/ Glargine continue same dose at the same time _______ units at _______ daily (optional)

- When the blood sugar is less than 6 mmol/L, decrease insulin infusion to (0.05 unit/kg/hr.) __________ units/hour.

- Perform ECG
- Apply cardiac monitor to patient
- Increase the rate of KCI infusion but do not exceed the maximum rate of 10 mEq/KCI per hour.
- Request a higher KCl concentration infusion from pharmacy.
- Once ready, give 40 mEq of KCI in 500 ml 0.9% normal saline to run over 4 hours.
- Resume insulin infusion when serum K is ≥ to 3.3 mmol/L.

- Potassium drip concentration should be changed whenever the serum potassium level is checked as per potassium chloride replacement algorithm. Insulin infusion should be resumed after correction of potassium level.

**Physician’s Name and Stamp:** ___________________________ Date: _____________

**Signature:** ___________________________ Time: _____________

**Nurse’s Name:** ___________________________ Date: _____________

**Signature:** ___________________________ Time: _____________

The main treatment of DKA is rehydration, insulin administration and electrolytes balance, mainly potassium, together with identification and treatment of the precipitating factor.
c. **Hyperglycemic Hyperosmolar State (HHS) /Hyperglycemic hyperosmolar non ketotic state/coma (HONK)**

It is identified by severe hyperglycemia, hyperosmolality, and dehydration without ketoacidosis. It accounts for <1% of hospital admissions in patients with DM, with most cases seen in elderly patients with T2DM and some also been reported in children and young adults. It has an overall mortality rate ten times higher than that in patients with DKA. The advanced age, severity of dehydration, and the presence of comorbidities determine the prognosis. The metabolic derangement in HHS results from synergistic factors, including insulin deficiency and increased levels of counter-regulatory hormones (glucagon, catecholamines, cortisol, and growth hormone). [22, 23, 53, 166]

**Clinical presentation of HHS:**

Suspect HHS if there are signs and symptoms of severe hyperglycemia: BG 30 mmol/l or more, drowsiness, confusion, coma, seizures, vomiting, features of the precipitating factor, severe dehydration, and negative or mild positive test for ketones. [22, 23, 53, 166]

<table>
<thead>
<tr>
<th>Diagnostic criteria</th>
</tr>
</thead>
</table>
| • **Marked Hyperglycemia** (> plasma glucose > 30 mmol/L, **without significant hyperketonemia** (negative urine ketones or trace) or **acidosis** (PH > 7.3, serum Bicarbonate > 15))

Plus

• **Serum Osmolality > 320 mOsmol/kg)** 

Formula for calculating serum Osmolality = 2X [Na + Glucose] + Urea (mmol/L)

Precipitating factors for HHS include new onset T2DM, infection, high dose steroids, MI, vomiting, stroke, VTE, poor treatment compliance, and impaired sense of thirst.

**Investigations:**

- BG
- Urea & electrolytes
- Venous blood gas (VBG) to rule out DKA (unless hypoxic, then do ABG)
- Urine analysis
- Serum osmolality (if difficult to obtain, and then use calculated osmolality).
- Chest X Ray
- ECG, CBC, CRP, Troponin, CK-MB, Amylase
- Consider CT Brain if obtunded.
Management:

The treatment goals of HHS are to treat the underlying cause and to normalize the plasma osmolality gradually and safely. Replace fluid and electrolyte losses. Normalize BG. Other goals include prevention of arterial or venous thrombosis, cerebral edema, central pontine myelinolysis and foot ulceration. [166]

Immediate Management: Ensure the patient has intact airway, breathing and circulation as indicated. Put in cardiac monitor. Apply urinary catheter (if indicated). Consider central venous pressure and nasogastric tube if there is a necessity. [166]

Intravenous fluid: If the patient is hemodynamically unstable, aggressive resuscitation should be done initially to stabilize the patient first until SBP is > 90, and then follow this fluid replacement policy. Be cautious with elderly patients and patients with compromised cardiac and renal status due to the risk of fluid overload. Patients with HHS often have a fluid deficit of over 8 liters (10-22 ml/kg). Fluid resuscitation is the mainstay of treatment together with a small dose of insulin. It is important not to correct the fluid and electrolytes abnormalities abruptly as this could precipitate cerebral edema and heart failure. Aim to replace 4 liters of the fluid losses in the first 12 hours starting with 0.9 % NS. Start a liter of 0.9 % NS over one hour with no added potassium while waiting for serum potassium's lab result. Give three more liters of 0.9 % NS over the next 11 hours with added potassium as detailed in the potassium section. If the BG is < 13 mmol/L, change to D5 0.9% NS at the same rate. Monitor therapy by measuring/calculating serum osmolality at time 0 hours, 3 hours, 6 hours, 12 hours, and then every 12 hours until resolution of metabolic abnormalities. If serum osmolality is falling too quickly (i.e., > 5 mOsmol/kg/hr.), reduce IV fluids' rate. Aim to reduce serum osmolality by about five mOsmol/kg per hour. Expect an initial rise in serum sodium after treatment initiation; however, as far as serum osmolality is falling, continue with 0.9 % N.S. However, if serum osmolality is not declining by > 5 mOsmol/kg per hour despite adequate positive fluid balance and /or serum Na > 150), then change the fluid to 0.45 % NS. The rate of fall in serum sodium should not exceed ten mmol/L over 24 hours. [166]

Potassium (K): Aim to keep serum K levels within the normal range. Make sure the patient has good urine output and has normal renal function. Be cautious as most patients with HHS may have a degree of renal impairment due to severe dehydration. Typical recommendations suggest that potassium supplementation should be started for plasma K <5.0 to 5.2 mmol/L once diuresis has been established, usually with the second liter of saline. If normo- or hypokalemic, potassium should be given immediately, at concentrations in the intravenous fluid between 10 to 40 mmol/L, at a maximum rate of 40 mmol/h. In the case of frank hypokalemia (serum potassium <3.3 mmol/L), insulin should be
withheld until potassium replacement at 40 mmol/h has restored plasma K to ≥3.3 mmol/L. It is reasonable to treat the potassium deficit of HHS in the same way. [166]

<table>
<thead>
<tr>
<th>K more than 5.2 mmol/L</th>
<th>K = 3.3 to 5.2 mmol/L</th>
<th>K less than 3.3 mmol/L</th>
</tr>
</thead>
<tbody>
<tr>
<td>NIL</td>
<td>40 mmol/L</td>
<td>Hold insulin for 2 hours or until K ≥ 3.3 mmol/L.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Increase the rate of the fluid replacement not ≥ 10 mEq/ KCl per hour or Give KCl 40 mEq in 500 ml normal saline to run over 4 hours</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Apply cardiac monitor to patient</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Perform ECG</td>
</tr>
</tbody>
</table>

**Insulin:** Mix 50 units of regular insulin in 50 ml of 0.9 % NS in a syringe. Use intravenous route for insulin infusion as per the following sliding scale. Patients with HHS need half the dose of insulin that is used to treat DKA. Make sure the patient has received reasonable amount of fluid (at least 1 liter of IV fluid) before insulin is started due to the risk of circulatory collapse in case of sudden reduction of plasma glucose without enough intravascular volume repletion. Please do not exceed a maximum of 0.05 units/kg/hour (e.g., 4 units in an 80 kg patient). [166]

<table>
<thead>
<tr>
<th>Capillary BG mmol/L</th>
<th>IV insulin infusion rate (ml/hr.)</th>
</tr>
</thead>
<tbody>
<tr>
<td>If BG ≥ 13</td>
<td>IV insulin (0.05/kg/hr.) .......... Units/hr.</td>
</tr>
<tr>
<td>If BG &lt;13</td>
<td>IV insulin 0.025/kg/hr. ............ Units/hr.</td>
</tr>
<tr>
<td>If BG &lt; 5</td>
<td>Start D10 as in the fluid algorithm</td>
</tr>
</tbody>
</table>

**Timeline for interventions:**

First Hour: Start one liter of 0.9% NS over one hour. Only commence IV insulin infusion (0.05 units/kg/hour) if there is significant ketonemia or ketonuria 2+ (Mixed DKA and HHS). Remember, IV fluid alone can result in a significant drop in plasma glucose in patients with HHS. The earliest start of IV insulin infusion should be after the patient has received at least one liter of IV fluid. Clinical assessment includes foot exam. Investigations: (VBG, U&E, Lactate, CBC, CRP, Measured/calculated plasma osmolality, ECG, CXR, urine analysis and culture, blood cultures). Monitor hourly BG, serum osmolality, serum sodium, serum potassium at time zero and then every 3 hours (or more frequent if needed), hourly urine output, and pulse oximetry and cardiac monitor (if available). Use prophylactic low molecular weight heparin. Decide about antibiotic need. [166]
Sixty minutes-6 hours: Aim to achieve a gradual decline in osmolality (by ~ 5 mOsmol/kg/hour). Use 0.9 % NS and target 2-3 liters positive fluid balance by 6 hours (caution with cardiac patients). Observe goals regarding osmolality, and glucose fall. Aim for target plasma glucose between 10-15 mmol/L, if the glucose is not falling <5 mmol/L, or if the fluid balance is inadequate, increase fluid rate, or if already in positive fluid balance, commence low dose IV insulin (0.05 units/kg/hour). Aim to maintain potassium in the normal reference rate. [166]

Six hours -12 hours: Aim to achieve a fluid balance of 3-6 liters by 12 hours. Make sure clinical and biochemical parameters are met. Assess for occurrence of complications. Continue to treat the precipitating factor. Avoid hypoglycemia (change fluid to D5 0.9 % NS if glucose falls below 13 mmol/L). [166]

Twelve-24 hours: Ensure continuous improvement in clinical and biochemical parameters. Continue IV fluid to replace the remaining balance of fluid loss within the next 12 hours. Continue insulin as per sliding scale in the insulin algorithm. Assess for complications. [166]

Further management: Consider full anticoagulation with low molecular weight heparin and TED stockings in all patients unless contraindicated. Start broad-spectrum antibiotics if there is evidence of an infection. Treat precipitating factor as appropriate. [166]

Foot protection: These patients are at very high risk of developing foot ulceration; so an initial foot examination and assessment must be done, together with the application of heel protectors for those at risk of ulceration, such as patients with neuropathic feet, foot deformities, and peripheral vascular disease. [166]

Anti-infective agents: An infective source should be sought on the clinical history, and physical examination and CRP may be helpful. Antibiotics should be given when there are clinical signs or imaging and/or laboratory evidence of their presence. [166]

Recovery phase: Complete correction of electrolytes and osmolality abnormalities may take more than 24 hours (unlike DKA). Aggressive correction could prove harmful. Recovery in most of these patients, who are usually elderly, will be determined by their previous functional status. IV insulin can be discontinued once they are eating and drinking normally, but IV fluids may be required for longer if oral intake is inadequate. Most patients should be transferred to SC insulin (the regime should be individualized). Newly diagnosed DM patients or well-controlled patients on oral agents could be considered after their condition becomes stable. All patients need to be seen by DM educators. [166]
Order Sheet for the Management of Adults with Hyperosmolar Hyperglycemic State

<table>
<thead>
<tr>
<th>Patient:</th>
<th>MRN:</th>
</tr>
</thead>
</table>

Please admit the patient to: □ General Ward □ ICU, as a case of ___________________________ secondary to ______________________ under the care of Dr. __________________________.

Vital signs: □ Stat □ Then every ____________________________

Investigations: VBG (to rule out DKA): □ STAT □ Serial □ Random □ Urine Culture & Microscopy □ CBC □ ECG □ Troponin/CK-MB □ Amylase □ Lactate Check BG, by glucometer, every hour (if hourly readings are between 5-10 mmol/L for 3 consecutive hours, then the frequency of BG checking can be reduced to 2 hourly).

Diet: □ Diabetic □ NPO □ Input/output Chart □ Daily Weight

Dietary: (If patient is hemodynamically unstable, DON’T use this protocol)

□ If Systolic BP is more than or equal to 90 mmHg, please use the algorithm below: Be cautious with elderly patients, and patients with compromised cardiac and renal status due to risk of fluid overload.

Order

<table>
<thead>
<tr>
<th>Instruction</th>
<th>Order</th>
</tr>
</thead>
<tbody>
<tr>
<td>Always refer to corrected Na when calculating the osmolality.</td>
<td>□ Over the 1st hour, Start a liter of 0.9 % N.S (without KCl). Then,</td>
</tr>
<tr>
<td>Monitor therapy by measuring/calculating serum osmolality at time: 0 hours, 3 hours, 6 hours, 12 hours and then 12 hourly until resolution of metabolic abnormalities.</td>
<td>□ Over the next 12 hours, give 0.9%NS at a rate of 250 ml/hour (with KCl as in the K algorithm). Then,</td>
</tr>
<tr>
<td>Aim to reduce serum osmolality by 5 mOsmol/kg per hour. If serum osmolality is falling by &gt; 5 mOsmol/kg/hour, reduce the rate of intravenous fluids by 50%.</td>
<td>□ Decrease IVF to 0.9%NS at a rate of (100-250 ml/hour) as per the K algorithm.</td>
</tr>
<tr>
<td>If serum osmolality is not declining by &gt; 5 mOsmol/kg/hour despite adequate positive fluid balance and/or corrected serum Na &gt; 150, then change fluid to 0.45 % N.S at the same rate.</td>
<td>□ If BG is ≤ 3 mmol/L add D10% W to run at a rate of (50-100 ml/hr.) till BG reaches 10 mmol/L</td>
</tr>
<tr>
<td>The rate of fall in corrected serum sodium should not exceed 10 mmol/L over 24 hours.</td>
<td></td>
</tr>
<tr>
<td>Fluid infusion rate not to exceed 250 ml/hr. at any time.</td>
<td>□ If BG is between 3.3 and 5.2 mmol/L</td>
</tr>
<tr>
<td>□ 20 mmol/L</td>
<td>• Hold insulin infusion for 2 hours or until serum K is ≥ 3.3 mEq/L</td>
</tr>
<tr>
<td>□ 30 mmol/L</td>
<td>• Perform ECG and apply cardiac monitor</td>
</tr>
<tr>
<td>□ 40 mmol/L</td>
<td>• Increase the rate of KCl infusion but don’t exceed the maximum rate of 10 mEq/KCl per hour.</td>
</tr>
<tr>
<td>□ NIL</td>
<td>• Request a higher KCl concentration infusion from pharmacy.</td>
</tr>
<tr>
<td>□ 0 mmol/L</td>
<td>• Once ready, give 40 mEq of KCl in 500 ml 0.9 % normal saline to run over 4 hours.</td>
</tr>
<tr>
<td>□ 3.3 mmol/L</td>
<td>• Resume insulin infusion when serum K is ≥ 3.3 mmol/L.</td>
</tr>
<tr>
<td>□ &gt; 5.2 mmol/L</td>
<td>□ &lt; 3.3 mmol/L</td>
</tr>
</tbody>
</table>

Potassium: Aim to keep serum potassium levels in the normal range. Make sure the patient has good urine output and has normal renal function. Be cautious as most patients with HHS may have a degree of renal impairment due to severe dehydration.

Insulin
Mix 50 units of regular insulin in 50 ml of 0.9 % NS (1 ml=1 unit). Use intravenous route for insulin infusion as per the following sliding scale

Make sure the patient has received reasonable amount of fluid before insulin is started due to risk of circulatory collapse and cerebral edema.

Capillary BG mmol/L | Intravenous Insulin Infusion Rate (Unit/hr.)
<table>
<thead>
<tr>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>If BG ≥ 13</td>
<td>IV insulin (0.05/kg/hr.)………………..Units/hr.</td>
</tr>
<tr>
<td>If BG &lt;13</td>
<td>IV insulin 0.025/kg/hr………………..Units/hr.</td>
</tr>
<tr>
<td>If BG &lt; 5</td>
<td>Add D10% W as in the fluid algorithm ( Do not stop insulin)</td>
</tr>
</tbody>
</table>

Physician’s Name and Stamp: ____________________________ Date: ____________________________

Signature: __________________________________________ Date: ____________________________

Nurse’s Name: __________________________________________ Date: ____________________________

Signature: __________________________________________ Time: ____________________________

Osmolality = [2X (Na) + Glucose (mmol/L) + Urea (mmol/L)]
Chronic complications of DM

a. Diabetic Retinopathy

Diabetic retinopathy (DR) is the most common cause of incident blindness (legal) in working-age people \[167\]. The global prevalence of DR in 2015-2019 was 27.0%. The lowest prevalence was in South East Asia at 12.5% and highest in Africa at 33.8%, MENA at 33.8%, and the Western Pacific region at 36.2% \[167\]. Previous data showed the prevalence rate of proliferative retinopathy in people with T1DM to be 23%, in T2DM on insulin therapy is 14%, and in T2DM not on insulin therapy is 3. Macular edema occurs in 11%, 15% and 4% of these groups, respectively \[168, 169\]. Higher prevalence of DR has been observed in KSA. \[170-175\]

In order to decrease DR risk or slow its progression, you should optimize glycemic, blood pressure, and serum lipid control. \[164\] Adults with T1DM and those with T2DM should have an initial comprehensive eye examination by an ophthalmologist within five years after the onset of T1DM and at the time of T2DM diagnosis. It should be done annually or more frequently if there was evidence of retinopathy; else, it should be every three years. Pregnant women or those planning pregnancy with T1DM or T2DM should be counseled on the risk of DR, and should have eye examinations every trimester, then 1-year postpartum according to the degree of DR. Results of the eye examinations should be communicated to the primary care physician. \[22, 164\] During each visit, the physician should ask about changes in eyesight, blurred vision, pain in the eye, redness, enquire about the last eye examination by the ophthalmologist, and history of diabetic nephropathy or neuropathy. If any of these symptoms are present, refer to an ophthalmologist. If the last eye assessment was more than one year, refer the patient to an ophthalmologist. \[22, 164\]

<table>
<thead>
<tr>
<th>Recommendations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Immediately refer DM patients with any level of macular edema, severe non-proliferative DR, or any proliferative DR to experienced ophthalmologist.</td>
</tr>
<tr>
<td>Patients with high-risk proliferative DR or severe non-proliferative DR should have laser photoagulation to reduce vision loss.</td>
</tr>
<tr>
<td>Intra-vitreous injections of anti-vascular endothelial growth factor ranibizumab are not inferior to traditional panretinal laser photoagulation, and are indicated to reduce the risk of vision loss in patients with proliferative DR.</td>
</tr>
<tr>
<td>Intra-vitreous injections of anti-vascular endothelial growth factor are indicated for central involved macular edema. Lowering BP has been shown to decrease retinopathy progression. ACE inhibitors and ARBs are both effective treatments in DR. Progression of DR can be delayed by the addition of fenofibrate in patients with dyslipidemia, especially with very mild baseline nonproliferative DR.</td>
</tr>
<tr>
<td>The presence of DR is not a contraindication to prescribe aspirin for cardio-protection.</td>
</tr>
</tbody>
</table>

b. Diabetic Neuropathy

Neuropathy in DM can affect the sensory, motor, and autonomic nervous systems and can be disabling. Neuropathic pain can be severe, can affect the quality of life and contribute to depression in
DM patients. Elevated BG levels, elevated TG, high BMI, smoking, and hypertension are among the risk factors for neuropathy. The effective primary prevention or secondary intervention of neuropathy in people with T1DM is intensive glycemic control. Lower BG levels are associated with a reduced frequency of neuropathy in T2DM. Simple physical examination screening tests, such as the 10 g monofilament (on the dorsal aspect of the great toe bilaterally) and vibration perception (with 128 Hz tuning fork), perform reasonably well in the identification of neuropathy and prediction of its future onset. \[22, 164, 167-180\]

### Recommendations

<table>
<thead>
<tr>
<th>Adults with T1DM and those with T2DM should be assessed for peripheral neuropathy within five years after the onset of T1DM and at the time of T2DM diagnosis. It should be done annually.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Assess for distal symmetric polyneuropathy by a careful history, and temperature or pinprick sensation, or vibration sensation (with 128 Hz tuning fork) Annual 10-g monofilament testing (identify feet at risk for ulcer).</td>
</tr>
<tr>
<td>Assess for symptoms and signs of autonomic neuropathy. It can have a wide spectrum of symptoms by affecting different systems, like the CVS, GIT, and genitourinary systems. This results in postural hypotension, erectile dysfunction, gastroparesis (heartburn, nausea, and vomiting), unexplained diarrhea that happens particularly at night, and neurogenic bladder.</td>
</tr>
<tr>
<td>Intensified glycemic control is recommended to prevent the onset and progression of neuropathy.</td>
</tr>
<tr>
<td>Optimize glucose control to prevent or delay the development of neuropathy in those with T1DM and to slow its progression in those with T2DM.</td>
</tr>
<tr>
<td>Improve the QOL of the patient by reduction of pain related to diabetic neuropathy and other symptoms of autonomic neuropathy.</td>
</tr>
<tr>
<td>The following drugs can be used alone or in combination for painful peripheral neuropathy: pregabalin, valproate, gabapentin, duloxetine, venlafaxine, or amitriptyline. Then, topical nitrate spray. If failed, opioid analgesics: tramadol (take care of abuse, tolerance, and dependency).</td>
</tr>
</tbody>
</table>

c. **Diabetic Foot**

Lower extremity complications are a significant cause of morbidity and mortality in people with DM. The frequency of amputation is much higher in people with DM than people without. The treatment of foot ulcers requires an interprofessional approach that addresses glycemic control, infection, off-loading of high-pressure areas, lower-extremity vascular status, and local wound care. \[181-184\]

### Recommendations

<table>
<thead>
<tr>
<th>A detailed history is critical: Ask about previous ulceration, amputation, Charcot foot, vascular surgery, smoking, retinopathy, and renal disease.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Assess for present symptoms of neuropathy (pain, numbness, burning) and peripheral vascular disease (claudication or leg fatigue).</td>
</tr>
<tr>
<td>Health-care providers should perform foot examinations to identify people with DM at risk for ulcers and lower-extremity amputation at least annually and at more frequent intervals in high-risk people.</td>
</tr>
</tbody>
</table>
The examination:

- Gait
- Foot morphology (Charcot arthropathy, bony prominences)
- Toe morphology (claw-toe, hammertoe, number of toes)
- Skin: blisters, abrasions, calluses, subkeratotic hematomas or hemorrhage, ulcers, absence of hair, toe nail problems, edema, abnormal color
- Status of nails
- Foot hygiene (cleanliness, tinea pedis)
- Pedal pulses
- Temperature (increased or decreased warmth)
- Sensation to 10 g monofilament

If there is claudication or diminished pedal pulses, refer for ABI (ankle-brachial index) and specialist. A foot ulcer or infection should be treated promptly by an inter-professional health-care team. Specialized therapeutic footwear is recommended for high-risk patients. Educate all DM patients about preventive foot self-care.

### Recommendations

Foot care instruction (including consultation to prevent foot trauma) and properly tailored footwear should be provided to people with DM who are at high risk of developing foot ulcers. Early referral to a health-care provider specialized in foot care is advised when foot complications start. An interprofessional health care team with experience in the management of foot ulcers should immediately treat people with DM who develop a foot ulcer or display symptoms of infection to avoid repeated foot ulcers and amputations. There is inadequate evidence to suggest any particular form of dressing. Debridement of the nonviable tissue in addition to the general principles of wound care should be offered. Routine use of wound-healing treatments (e.g., granulocyte colony-stimulating factors or topical growth factors) for typical DM foot ulcers have not sufficient evidence. If all other modifiable factors (e.g., pressure off-loading, infection, foot deformity) have been dealt with and healing is not achieved, those adjunctive wound-healing therapies can be considered.

### d. Chronic Kidney Disease

In KSA, DM is the leading cause of chronic kidney disease (CKD). Kidney disease can be a devastating complication, as it is associated with significant reductions in both length and QOL. A variety of CKD forms in DM can include diabetic nephropathy, ischemic nephropathy related to vascular disease, and hypertensive nephrosclerosis.

### Recommendations

At least annually, assess both urinary albumin (spot urinary ACR) and eGFR (The Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) equation) is generally preferred in patients with more than 5-years T1DM, in all T2DM patients, and in all diabetic patients with comorbid hypertension. The random spot urine test for urine ACR is indicated at diagnosis of T2DM, after 3 to 5 years of T1DM, and in cases with retinopathy. Staging of diabetic nephropathy can be carried out according to the urine ACR (Table 13).
CKD is diagnosed as eGFR <60 mL/min/1.73m² and/or random urine ACR ≥2.0 mg/mmol on at least two of three samples over a three-month period. Active urinary sediment (containing red or white blood cells or cellular casts), rapidly increasing albuminuria or nephrotic syndrome, rapidly decreasing eGFR, or the absence of retinopathy (in T1DM) suggests alternative or additional causes of kidney disease. For patients with these features, referral to a nephrologist for further diagnosis, including the possibility of kidney biopsy, should be considered. [164]

Optimize control of BG and blood pressure to reduce CKD risk or slow its progression.

Avoid nephrotoxic drugs (like aminoglycosides, NSAID and contrast media).

For patients with T2DM and CKD with eGFR >30 mL/min/1.73m², and urinary albumin>30 mg/g creatinine, particularly in those with urinary albumin >300 mg/g creatinine, the use of SGLT2i proved to reduce the risk of CKD progression, CV events, or both.

If SGLT2i is not tolerated or contraindicated or if the eGFR is less than 30 mL/min/1.73m² add GLP-1 RA with proven CVD benefit.

The daily protein intake should be 0.8 g/kg body weight for non-dialysis patients with CKD. It should be higher for those on dialysis. [164]

In non-pregnant patients with DM and hypertension or albuminuria, ACE inhibitors or ARBs are recommended for those with modestly elevated urinary ACR (30–299 mg/g creatinine) and is strongly recommended if urinary ACR ≥300 mg/g creatinine and/or eGFR <60 mL/min/1.73 m². [164]

Those on ACE inhibitors, ARBs, or diuretics should have their serum creatinine, and potassium levels monitored starting from baseline. ACE inhibitors or ARBs are not recommended for the primary prevention of CKD in DM normotensive patients with normal urinary ACR (<30 mg/g creatinine) and normal eGFR. [164]

Assess and manage potential complications of CKD if eGFR <60 mL/min/1.73 m². Refer patients to nephrologist for evaluation for renal replacement treatment if eGFR <30 mL/min/1.73 m². [164]

Referral to a Nephrologist [164]

[1] You are uncertain about the etiology of CKD
[3] Unable to achieve target BP.
[4] Difficult management issues (anemia, secondary hyperparathyroidism, metabolic bone disease, or electrolyte disturbances)

[5] Urine ACR persistently >60 mg/mmol

[6] Unable to remain on ACE inhibitor or ARB due to adverse effects (hyperkalemia or a >30% increase in serum creatinine) within 3 months of starting these drugs.

[7] Stage 4 CKD (eGFR <30 mL/min/1.73 m2) requiring discussion of renal replacement therapy for end-stage renal disease.

- Metformin use in patient with CKD:
  [1] It is contraindicated in patients with an eGFR <30 mL/min/1.73 m2
  [2] eGFR should be monitored while taking metformin
  [3] Should not be initiated for patients with an eGFR <45 mL/min/1.73 m2 and the benefits and risk of continuing it should be reassess at this level of eGFR.
  [4] Should be temporarily discontinued at the time of or before iodinated contrast imaging procedures in patients with eGFR 30–60 mL/min/1.73 m2.

Table 14: Management of CKD in DM [194]

<table>
<thead>
<tr>
<th>eGFR</th>
<th>Recommendation</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>All patients</strong></td>
<td>Measure creatinine, ACR, potassium annually</td>
</tr>
<tr>
<td>eGFR=45–60 (ml/min/1.73m2)</td>
<td>Refer to the nephrologist if there is heavy proteinuria, rapid fall in eGFR, resistant hypertension, active urinary sediments Adjust drugs dose Test eGFR biannually Test electrolytes, bicarbonate, HB, Ca, Ph, PTH annually Exclude osteomalacia and vitamin D deficiency Test bone density Refer for nutritional specialist</td>
</tr>
<tr>
<td>eGFR=30–44</td>
<td>Test eGFR every 3 months Test electrolytes, bicarbonate, HB, Ca, Ph, PTH, HB, albumin, weight every 3–6 months Adjust drugs dose</td>
</tr>
<tr>
<td>eGFR ≤30</td>
<td>Refer to a nephrologist</td>
</tr>
</tbody>
</table>

e. **Erectile Dysfunction**

Erectile dysfunction (ED) affects approximately adult men with DM. It has been demonstrated to negatively affect the QOL and may be an early clinical indication of CVD. All adult men with DM should be regularly screened for ED with a sexual function history. Phosphodiesterase type 5 (PDE5) inhibitors are the backbone of therapy for ED. They have been shown to have major impacts on erectile function and QOL, with a low reported side effect profile, and should be offered as first-line therapy to men with DM wishing treatment for ED. [195-198]
All men with diabetes should be regularly screened for ED with a sexual function history. It should begin at diagnosis of DM.

Validated questionnaires (e.g. International Index of Erectile Function or Sexual Health Inventory for Men) can be used in determining the presence of ED and assessing response to treatment.

Men with DM and ED should be further investigated for hypogonadism. [195-198]

BG level control decreases the incidence and progression of ED, the DCCT and UKPDS proved that intensive control is effective for the primary prevention of and the secondary intervention for neuropathy, which impair sensory feedback, leading to ED [59, 61]. One meta-analysis suggested a benefit from statin treatment of ED as dyslipidemia and hypertension are also risk factors for it. [199] The PDE5 inhibitors are the current backbone of treatment for ED in men with DM. Contraindications include unstable angina or untreated cardiac ischemia and concomitant use of nitrates [200-177]. Those who are not responding to PDE5 inhibitors should be referred to a specialist in ED to consider other therapy. [205-208]
Section 11:

Management of DM in special populations

- Introduction
- Older Adults
- Children and Adolescents with T2DM
- In-Hospital Management of DM
- Diabetes in Ramadan
11. Management of DM in special populations

Introduction

Adopting a patient-centered approach to choose appropriate pharmacologic treatment of DM is essential. Thus, the evaluation of the patient’s profile is critical to categorize patients for better treatment. Drug efficacy and key patient factors should be considered. The following is a non-comprehensive list of factors related to the patient and to therapy: newly diagnosed versus established cases, age category (children, young adult, elderly), and gender, type of diabetes, comorbidities, hypoglycemia risk, effects on body weight, adverse effects, and special categories such as pregnancy, children, and in-hospital patients. [79, 209]

Older Adults

DM and prediabetes are highly prevalent among people above 65 years. Older people with DM have a high risk of impaired cognition, falls, and urinary incontinence. They also have a high rate of functional disability and comorbid illnesses, like hypertension, coronary heart disease, and stroke. Therefore, they need special consideration when it comes to diabetes management. [210, 211] Elderly people with DM needs special considerations via fair assessment of their medical, psychological, functional (self-management abilities), and social domains. Also, those with limitations in their necessary daily activities should be screened for geriatric syndromes. [211-214]

Recommendations

They should be screened for cognitive impairment, dementia and depression in the initial visit and annually. Screening for DM complications with special attention to those leading to functional impairment. [22, 23, 215]

Those who are functionally independent with a life expectancy > 10 years, same glycemic, BP, and lipid targets as younger people should be used. In functionally independent older with few coexisting chronic illnesses and intact cognitive function, lower goals HbA1c < 7.5% (58 mmol/mol) can be used. [22, 23, 215]

For those who are functionally dependent with multiple coexisting chronic illnesses, cognitive impairment: Glycemic goals HbA1c 8.0–8.5% (64–69 mmol/mol), BP goals should be relaxed. Finally, in the end-of-life people, avoid symptomatic hyperglycemia and any hypoglycemia without measurement of HbA1c. Hypoglycemia should be avoided by adjusting glycemic targets and pharmacologic interventions. Drugs that increase risk of hypoglycemia should be avoided. Lipid-lowering therapy and aspirin therapy are beneficial for primary or secondary prevention. [22, 23, 215]

Optimal nutrition and protein intake are recommended as well as regular exercise, aerobic activity, and resistance training when it is safe to engage in them. Besides, the clock-drawing test can be used to detect those with difficulty learning about insulin injection. They should receive DM education with stress on tailored care and psychological support. [22, 23, 215]

To avoid the risk of hypoglycemia, medication classes with a low risk of hypoglycemia should be used. Also, avoid overtreatment of DM. Simplify complex regimens to reduce the risk of hypoglycemia via the decreased frequency of administration, fewer finger stick testing, decreasing the need for any calculations. SU increases the risk of hypoglycemia, use DPP-4 inhibitors as second-line therapy to
metformin. If SU is to be used, start by half the dose for younger patients and increase slowly. Gliclazide and glimepiride should be used instead of glibenclamide. [22, 23, 215]

Meglitinides can be used instead of glibenclamide to reduce hypoglycemia risk, principally in patients with irregular eating habits. [22, 23, 215]

SGLT2i and GLP-1 RA with CV benefits can be used in those with CVD and uncontrolled glycemia with existing medications if they have an eGFR >30 mL/min/1.73m2. Basal insulin analogues can be used instead of NPH or human 30/70 insulin. Premixed insulins and prefilled pens can be used to reduce dosage errors and to improve glycemic control. [22, 23, 215]

**Children and Adolescents with T2DM**

T2DM in youth has been increased over the past three decades worldwide and in KSA. The Centers for Disease Control and Prevention published projections for the prevalence of T2DM; assuming an annual increase of 2.3%, the prevalence in those < 20 years will increase 400% in the next four decades. [1, 216-219] In youth, T2DM is different not only from T1DM but also from T2DM in adults. It is a more rapidly progressive decline in the function of β-cell and acceleration of DM complications. However, there is a significant overlap between T1DM and T2DM in children. [216, 220]

### Recommendations

The family and friends of a child with DM should be included and educated. Structured educational programs can be used. Lifestyle counseling and modifications should be done for the whole family. [22, 23, 220, 221]

Long-term safety is vital in children with T2DM. Aim for HbA1c targets in the normal range without hypoglycemia. [22, 23, 220, 221]

For screening & prevention, all children should be encouraged to follow healthy eating, limit sugar-sweetened beverage intake, limit screen time, improve sleep quantity and quality, decrease sedentary lifestyle, and increase light and vigorous physical exercise. Besides, obese children and their families should be educated by counseling and behavior therapy. [22, 23, 220, 221]

Children and adolescents should be screened every two years (by HbA1c and FBG or RBG) if they have obesity, first-degree relative with T2DM and/or exposure to hyperglycemia in utero, or signs/symptoms of insulin resistance with ≥two risk factors: PCOS, IFG and/or IGT, or the use of atypical antipsychotic medications. If there is a discrepancy between the HbA1c and FPG or random plasma glucose, testing may be repeated, or a 2-hour OGTT (1.75 g/kg; maximum 75 g) may be performed. [22, 23, 220, 221]

For better glycemic control, home SMBG should be encouraged, and HbA1c should be done every three months. HbA1c target (most children and adolescents) on oral agents alone is < 7%. HbA1c targets < 6.5% are optimal for those with a short period of DM with a reduced degree of β-cell impairment, and for those treated with lifestyle or metformin with a substantial improvement in weight. HbA1c targets (patients on insulin) should be individualized, considering the relatively low hypoglycemia rates in youth-onset T2DM. [22, 23, 220, 221]

All youth with T2DM and their families should have comprehensive DM self-management education and support. Also, youth with overweight/obesity and T2DM and their families should be educated with appropriate comprehensive lifestyle programs to achieve a 7–10% decrease in excess weight. They should be encouraged to participate in at least 30–60 min of moderate to vigorous physical activity at least five days per week (and strength training on at least three days/week) and they should be advised to decrease sedentary behavior. [22, 23, 220, 221]

Nutrition should focus on healthy eating patterns: high-quality foods and decreased calorie-dense, nutrient-poor foods, particularly sugar-added beverages. [22, 23, 220, 221]

The pharmacologic therapy options available are metformin and basal insulin. They should be initiated, in addition to lifestyle therapy, at diagnosis of T2DM. Metformin is the initial treatment (if renal function
is normal) in newly diagnosed or metabolically stable patients (HbA1c < 8.5% [69 mmol/mol] and asymptomatic). Basal insulin should be initiated while metformin is started and titrated for those with marked hyperglycemia (BG ≥ 250 mg/dL, HbA1c ≥ 8.5% [69 mmol/mol]) without acidosis at diagnosis who are symptomatic with polyuria, polydipsia, nocturia, and/or weight loss. [22, 23, 220, 221]

In ketosis/ketoacidosis, treat with SC or IV insulin. Once acidosis is resolved, metformin should be started while SC insulin is continued. In individuals presenting with severe hyperglycemia (BG ≥ 600 mg/dL [33.3 mmol/L]), consider assessment for the hyperglycemic hyperosmolar nonketotic syndrome. [22, 23, 220, 221]

If uncontrolled on metformin monotherapy (or contraindications or intolerable side effects of metformin develop,) initiate basal insulin. Switch to basal insulin and premeal bolus insulins if the patient was on basal insulin (1.5 units/kg/day) and uncontrolled. If controlled on initial insulin and metformin based on SMBG, insulin can be tapered over 2–6 weeks by decreasing the dose by 10–30% every week. [22, 23, 220, 221]

Screen for neuropathy at diagnosis. Screen for retinopathy at diagnosis and annually after that. Screen for CKD with a first-morning urine ACR or a random ACR. Confirm abnormal results one month later with a first morning ACR. Albuminuria (ACR >2.5 mg/mmol) should not be diagnosed unless it is persistent, as demonstrated by two consecutive first morning ACR obtained at 3- to 4-month intervals over a 6- to 12-month period. If persistent albuminuria, refer to a pediatric nephrologist. [22, 23, 220, 221]

Measure fasting lipid profile at diagnosis of DM and annually after that. Screen for hypertension beginning at diagnosis of DM and every clinical encounter after that (at least biannually). Screen at diagnosis for comorbid conditions associated with insulin resistance, including NAFLD, OSA, and PCOS in pubertal females, and annually after that. Screen at diagnosis for depression and disordered eating (particularly binge eating) and every clinical encounter after that (at least biannually). [22, 23, 220, 221]

**In-Hospital Management of DM**

On admission, an HbA1c should be done on all patients with DM admitted to the hospital if not performed in the last three months. The type of DM should be stated. Insulin should be used on a written protocol. [22, 23, 222]

<table>
<thead>
<tr>
<th>Recommendations</th>
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<tbody>
<tr>
<td>Initiate insulin if BG ≥180 mg/dL (10.0 mmol/L). The target BG: 140–180 mg/dL (7.8–10.0 mmol/L). More strict targets: 110–140 mg/dL (6.1–7.8 mmol/L) for selected cases. (Take care to avoid significant hypoglycemia). Hyperglycemia in the hospitalized is BG &gt;140 mg/dL (7.8 mmol/L). Bedside BG monitoring should be started. Monitor BG before meals (if the patient is eating). Else, monitor it every 4–6 h. Test every 30-120 min if IV insulin infusion. [22, 23, 222]</td>
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</table>

In most cases, insulin is the preferred treatment. Basal insulin or a basal plus bolus correction insulin regimen is preferred for non-critically ill patients with poor or no oral intake. Basal, prandial, and correction components insulin regimen is preferred for non-critically ill patients with good nutritional intake. In the critical care units, continuous IV insulin infusion is the best method. [22, 23, 222]

Hypoglycemia should be documented and tracked in the patient medical record. Review the treatment regimen and change as needed when a BG is <70 mg/dL (3.9 mmol/L). [22, 23, 222]

**Diabetes in Ramadan**

Fasting in Ramadan (the holy month) is one of the five foundations of the Muslim religion; it is mandatory for all adult Muslims. [221] While the disease is a fasting exemption, the vast majority of diabetes Muslims do not consider themselves unwell and continue to fast. This should be appreciated,
and assistance should be provided to such patients to help them quickly. In KSA, Ramadan is a month of nocturnal life. Ramadan fasting in KSA has profound changes in sleeping and eating habits, with an almost complete reversal of the rest/sleep versus wake cycle and restriction of nighttime food consumption only. For individuals to relax before and after Suhoor and Iftaar, operating hours for school and offices are shortened to 6 hours on working days. According to a new report, Saudis stay up at night and sleep for most of the day during Ramadan fasting, mimicking the habits of shift workers. In a cross-sectional analysis in Riyadh, most DM patients (76%) were able to fast during Ramadan. Hypoglycemic episodes were registered in 60% of people with T1DM and in 8% of people with T2DM. It was concluded that without medical advice, over half of the patients with DM who fast during Ramadan will change their medication schedule.

The recent IDF and Diabetes and Ramadan (DAR) International Alliance guidelines (2017) proposed three categories of risk for Muslim patients during Ramadan fasting.

**Recommendations**

<table>
<thead>
<tr>
<th>Risk Category</th>
<th>Guidelines</th>
</tr>
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<tbody>
<tr>
<td>Very High</td>
<td>Patients taking SU's or insulin will need to adjust the dose and/or timings to reduce the risk of hypoglycemia, and SMBG is recommended.</td>
</tr>
<tr>
<td>High</td>
<td>Fasting should be interrupted if BG values are &lt;70 mg/dl (3.9 mmol/L) or above 300 mg/dl (16.7 mmol/L). Newer antihyperglycemic drugs, including basal insulin analogues, are associated with a lower risk of hypoglycemia and may be preferable for use during Ramadan.</td>
</tr>
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</table>

The guidelines for DM treatment by the ADA/EASD consensus stress the need to consider patient variables, including comorbidities, when deciding on drug choices. Considering the prevalence of comorbidities such as ASCVD, HF, and CKD, the risk of hypoglycemia, weight disorders, and cost-effectiveness are the basic criteria used in the decision loop in the ADA/EASD consensus relate to Ramadan. With joint decision sharing between the provider and the patient, treatment should be individualized. For patients during Ramadan, formal curriculum and pre-Ramadan therapy are central components of effective DM management. These should include all essential issues such as Ramadan glycemic targets, SMBG, food, physical exercise like Taraweeh prayers, changes in dosage of glucose-lowering medicine, side effects and determination when to break the fast. A decision cycle for patient-centered glycemic management in Muslim patients during Ramadan is presented elsewhere, and it can be used to provide an aid for the assessment in the specific situation of Ramadan. It is recommended that people with T1DM and T2DM should be advised not to fast because of high risk of complications. Because of the potential unfavorable maternal and fetal effects, pregnant women with DM or GDM are also advised to skip fasting. During Ramadan, new technology and CGM could maximize the result, although the cost is a major barrier…Continuous monitoring and control are an essential part of a good result, and it needs a proper management strategy. In the light of recent emerging evidence and technology, Ramadan guidelines for patients with diabetes should be regularly revised.
Section 12:

T1DM in Children and Adolescents

- Introduction
- Management of T1DM
- T1DM in the School Setting
- Transition Care in DM
- Guidelines for Diagnosis & Management of Diabetic Ketoacidosis (DKA) in Children under 14 years of Age and/or < 50kg weight
12. T1DM in Children and Adolescents

Introduction

T1DM develops secondary to autoimmune pancreatic β-cell destruction in genetically susceptible children. This process begins before clinical presentation, with symptomatic hyperglycemia or the more severe DKA presentation. KSA is amongst the top ten countries with the highest incidence rates of T1DM in children. A new diagnosis of T1DM has an incidence rate of 33.5 cases per 100,000 population per year. It is estimated that there are 35,000 children with T1DM in KSA with 3900 new cases per year, with DKA as a typical presentation. [1, 230]

Recommendations

The diagnosis of DM should be made if one of the following criteria are met:

a. RBG of 11.1 mmol/L (200 mg/dL) or greater with classic symptoms of hyperglycemia; OR
b. FBG of 7 mmol/L (126 mg/dL) or greater (no intake for a minimum of 8 hours); OR
c. 2-hour PPBG of 11.1 mmol/L (200 mg/dL) or greater at the time of an OGGT test (glucose load of 1.75 g/kg to a maximum of 75 g)

If hyperglycemia symptoms are absent, repeat testing is required to confirm the diagnosis.

Monogenic DM should be suspected if there is a strong family history of diabetes with an autosomal dominant pattern, in infants (mostly less than six months of age), in those with mild non-progressive fasting hyperglycemia or if there is an extended honeymoon period for over one year with low insulin requirements.

A multi-disciplinary team following children and adolescents with T1DM includes physicians, diabetes educators, dieticians, social workers, and/or mental health specialists.

The treatment for children and adolescents with T1DM should be with intensive insulin therapy, either by multiple-dose injection regimen (MDI) or continuous SC insulin infusion (insulin pump therapy) if available.

The starting total daily dose of insulin in newly diagnosed T1DM ranges from 0.3 to 0.8 U/kg/day, depending on the age and clinical presentation. Insulin requirements will vary according to age, pubertal status, weight, duration and stage of diabetes, daily routine, and activity levels.

The BG levels should be monitored multiple times per day in youth with T1DM, with a minimum of 4 times (pre-meals and bedtime) up to 6-10 times.

An HbA1c target of 7.5% or less should be considered across all age groups.

Diabetes education should be provided for all pediatric patients, their families, and regular caregivers at the time of diagnosis with ongoing education regularly.

A registered dietician should be part of the DM team.

In mild hypoglycemia cases, where the individual is still conscious and responsive, oral glucose should be administered as fast-acting sugar (e.g., juice, table sugar, or honey). The recommended dose is 0.3 g/kg of glucose or 5 g for children weighing < 15 kg, 10 g for a 15-30 kg child, and 15 g for a child who weighs 30 kg or more.

Families should receive education regarding the prevention of DKA, including monitoring BG levels and ketones, the importance of insulin administration, appropriate sick-day management, and when to present to medical care.

Physical activity should be encouraged.

Mental health specialists (social workers, psychologists) are essential members of the DM team. A psychosocial assessment should be carried out every year.

Children and adolescents who are newly diagnosed with T1DM require close follow up, 2-3 weeks after discharge, then regular follow up should occur every three months for youth with T1DM with a multidisciplinary diabetes team.
HbA1c should be measured every three months.

Screen for autoimmune thyroid disease by measuring TSH levels and thyroid autoantibodies (thyroid peroxidase antibodies and thyroglobulin antibodies) at the time of diagnosis and every other year after that.

Screen for celiac disease at diagnosis. Repeat the screening at two years and five years after diagnosis.

Youth with T1DM should be screened regularly for hypertension, at least once yearly.

Youth with T1DM should be screened for dyslipidemia at age 12 years and again at age 17 years.

Albuminuria should be screened for on an annual basis starting at age 12 years in those with a DM duration > 5 years.

Youth with T1DM duration of > 5 years should be screened yearly starting at the age of 10 years of age for retinopathy.

Adequate education and training of school personnel is essential and should be guided by the diabetes team caring for the student.

Between the ages of 13-14 years, the youth with T1DM should be referred to a diabetes transition clinic. That clinic should be run by both adult and pediatric endocrinologists.

The role of HbA1c in diagnosing T1DM in children is unclear and should not be used as the only diagnostic test for the diagnosis of DM in children. Additionally, HbA1c results may be affected by many medical conditions, such as iron deficiency anemia, hemoglobinopathies, hemolytic anemias, liver and kidney disease. Therefore, an HbA1c of less than 6.5% does not rule out DM, but an elevated HbA1c would support the diagnosis in the proper clinical context and other laboratory values. T1DM, the autoimmune-mediated type, is the most common type of DM in children and adolescents. [231, 232]

Depending on the presentation, other types of DM may be considered. That is important as the type of DM influences the management plan. T2DM or concomitant insulin resistance may be suspected in the presence of features such as obesity, history of intrauterine growth retardation of gestational diabetes in the mother, family history of T2DM, high-risk ethnicity, and acanthosis nigricans. [232] Monogenic DM should be suspected if there is a strong family history of DM with an autosomal dominant pattern, in infants (< six months of age), in those with mild non-progressive fasting hyperglycemia or if there is an extended honeymoon period for over one year with low insulin requirements. The presence of deafness, optic atrophy, or syndromic features should raise the concern for mitochondrial diseases. [233, 234]

If the diagnosis of T1DM is in question, diabetes autoantibodies should be measured (glutamic acid decarboxylase 65 autoantibodies (GAD), insulin autoantibodies (IAA), tyrosine phosphatase-like insulinoma antigen 2 (IA2), specific zinc transporter eight autoantibodies (ZnT8)). In cases where monogenic DM is suspected, genetic testing should be undertaken. [235, 236, 237]

Management of T1DM

The management goals for children with T1DM presenting with hyperglycemia are adequate hydration, nutrition, and insulin. It should be in a manner that prevents symptomatic hyperglycemia and ketosis while avoiding hypoglycemia and permitting average growth and development with the long-term goals of preventing diabetic complications. [224]
**Insulin**

The DCCT, which include adolescents, demonstrated that intensive insulin therapy gave better control of BG level and reduced the risk of complications related to T1DM [25]. A basal-bolus regimen using multiple daily injections (MDI) with 1–2 injections of long-acting insulin daily and rapid-acting insulin for meals and snacks is now the standard of care. Alternatively, continuous SC insulin infusion or an insulin pump can be used. [239-245]

**Newly diagnosed**

Once the child is rehydrated and clinically stable, insulin therapy should be initiated. The starting total daily dose of insulin ranges from 0.3 to 0.8 U/kg/day, depending on the patient’s age and clinical presentation [208]. Please see below for the distribution of insulin doses. The insulin dose is titrated over the following few weeks to achieve a blood sugar reading within the desired target range. Frequent communication and advice from the diabetes team are required during this period. Additionally, we strongly advocate that carbohydrate counting be taught as part of diabetes education around the time of diagnosis. [246, 247]

**Insulin dosage and regimens**

Insulin requirements will vary depending on the patient’s age, pubertal status, weight, duration and stage of diabetes, daily routine, and activity levels. The total daily dose may range from less than 0.5 unit/kg/day during the honeymoon period to greater than 1 unit/kg/day during puberty. Prepubertal children typically require between 0.7-1 unit/kg/day. [247, 248] The role of basal insulin is to control blood sugar during sleep and in between meals. The role of bolus insulin is to cover carbohydrate intake at meals and snacks in addition to correcting elevated blood sugars at that time. The insulin sensitivity factor can be calculated by dividing 1500-1800 by the total daily insulin dose. Typically, 40-50% of the total daily dose of insulin is given as basal insulin when rapid-acting insulin is used. If regular insulin is being used, the proportion of basal insulin is usually closer to 30%, as regular insulin also provided some basal action. [247, 248]

The insulin regimen chosen should be tailored to each patient depending on their age, glycemic targets, duration of DM, daily routines, and parent/patient preferences. Insulin regimens usually include rapid-acting or regular insulin as prandial insulin. These should be given ideally 15-20 minutes pre-meals when using rapid-acting insulin and 20-30 minutes before meals for regular insulin. In addition to prandial insulin, intermediate-acting insulin is given twice a day, or long-acting basal insulin is given once to twice a day. Biosimilar insulin cannot be automatically switched as recommended by international guidelines such as NICE [249, 250], IDF [251] & Canadian Diabetes Association [252]. SFDA guidelines state that close monitoring of the patients’ responses should be performed when
interchangeability or substitution is warranted, perhaps daily, until results are satisfactory and stable \(^{221}\). Pharmacists cannot substitute biosimilars without such consultations with treating physicians.

**Follow up**

Insulin doses should be reviewed at each clinic visit, including total daily dose, the proportion of basal and bolus insulin, insulin to carbohydrate ratio, insulin sensitivity factors, and adherence to an insulin regimen. Doses should be adjusted based on trends identified from self-monitored BG readings; CGM or FGM in conjunction with HbA1c and the clinical picture. Insulin injection sites should be examined at each visit for lipohypertrophy. \(^{244}\)

**Continuous Subcutaneous Insulin Infusion (CSII) or insulin pump therapy**

CSII is safe and effective in managing pediatric patients with T1DM; it has been used in Saudi children with T1DM with good results \(^{85}\). CSII can help achieve better glycemic control, reduce hypoglycemic events, provide greater flexibility and improved quality of life when compared to MDI. It should be considered as a treatment option for patients with T1DM (table 15). Ideal candidates are those who are motivated, with a good understanding of basic diabetes management. Individuals who started on an insulin pump should receive thorough and comprehensive education regarding insulin pump therapy, including recognizing and treating infusion site failures to avoid DKA. Regular follow up is recommended, with more communications that are frequent and follow up with the diabetes team around the time of pump starts and as needed thereafter. \(^{241, 242}\)

Table 15: Indications of insulin pumps. \(^{240}\)

<table>
<thead>
<tr>
<th>Conditions under which insulin pumps should be considered</th>
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<tbody>
<tr>
<td>• Recurrent severe hypoglycemia</td>
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<tr>
<td>• Wide fluctuations in BG levels regardless of HbA1c</td>
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<tr>
<td>• Suboptimal diabetes control (i.e., HbA1c exceeds target range for age)</td>
</tr>
<tr>
<td>• Microvascular complications and/or risk factors for macrovascular complications</td>
</tr>
<tr>
<td>• Good metabolic control but insulin regimen that compromises lifestyle</td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>Circumstances in which insulin pumps may be beneficial</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Young children and especially infants and neonates</td>
</tr>
<tr>
<td>• Children and adolescents with pronounced dawn phenomenon</td>
</tr>
<tr>
<td>• Children with needle phobia</td>
</tr>
<tr>
<td>• Pregnant adolescents, ideally preconception</td>
</tr>
<tr>
<td>• Ketosis prone individual</td>
</tr>
</tbody>
</table>

According to Saudi MOH diabetes scientific committee, the following are the agreed upon indications for insulin pump use:

**Insulin pump indications:**

- Children and adults of type 1 diabetes.
- Pregnant women with diabetes.
- Special cases of type 2 patients dependent on multiple daily injections of insulin and have one of the followings:
- Severe glucose variability with elevated glycated hemoglobin (HbA1c) despite regular daily treatment with required insulin doses and adherence to the specified diet.
- Insulin resistance syndrome such as lipodystrophy syndrome.
- Repeated severe hypoglycemia at night, with insensitivity to hypoglycemia.
- Chronic kidney patients who have a kidney transplant.
- Short bowel syndrome.

Indications for the use of sensor augmented pumps: Sensors connected to the pump or sensor augmented pump indicated only for type 1 diabetes patients as follows:

<table>
<thead>
<tr>
<th>Indications</th>
<th>Frequency of the sensor/year</th>
</tr>
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<tbody>
<tr>
<td>Children below 14 years of age with type 1 diabetes</td>
<td>Continuously</td>
</tr>
<tr>
<td>Adolescents and young adults 14 to 20 years with frequent hypoglycemia or hypoglycemia unawareness</td>
<td>Continuously</td>
</tr>
<tr>
<td>Adults beyond 20 years of age with frequent hypoglycemia or hypoglycemia unawareness</td>
<td>Intermittent sensors 2 per month</td>
</tr>
<tr>
<td>Adults with poor control with great variability</td>
<td>At least twice per year for dose adjustment</td>
</tr>
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</table>

**Blood Glucose Monitoring**

Blood sugar levels should be monitored multiple times per day in youth with T1DM, with a minimum of four times (pre-meals and bedtime) up to 6-10 times. Monitoring frequency increases in specific circumstances such as exercise, driving, hypoglycemia, intercurrent illness, and following insulin dose adjustments. [248] Studies have shown a positive relationship between the frequency of blood sugar tests per day or CGM and glycemic control if the child is on MDI or an insulin pump [121]. Insulin pumps with CGM devices demonstrate significant glycemic control in pediatric patients with suboptimal BG control at baseline. [243] BG levels can be monitored using standard glucometers, CGM, or FGM. CGM has been shown (for both injectors and pumpers) to decrease HbA1c levels, decrease hypoglycemic events and time spent in hypoglycemia, and decrease BG variability. The benefits of CGM are positively correlated with the amount of sensor use [244]. CGM should be offered to all children and adolescents with T1DM, whether on an MDI regimen or an insulin pump therapy, to improve glycemic control. More importantly, it should be offered to children with high BG variability, with a history of severe hypoglycemia, those with hypoglycemia unawareness, and those unable to express symptoms of hypoglycemia. Individuals should be encouraged to use sensors as frequently as possible to maximize benefit. Additionally, CGM data should be reviewed regularly to identify blood sugar patterns and adjust insulin doses accordingly. [244]

As an alternative, FGM can be offered. FGM is safe in the pediatric population and has been shown to reduce hypoglycemia in adults with T1DM [254]. It should be used as an adjunct to
glucometers and not as a complete replacement. It is important to note that, as both CGM and FGM utilize sensors that measure glucose levels in the interstitial fluid, not in the blood, there is an expected lag time of 15 minutes between the sensor glucose reading and actual BG levels. That is very important in situations with rapidly changing blood sugar levels.

**Glycemic Control**

An HbA1c target of 7.5% or less should be considered in pediatric patients with T1DM across all age groups. However, this target should be personalized depending on the circumstances of the patient and their family. A lower target can be considered (< 7%) if the patient can achieve it without undue hypoglycemia. BG targets should be 90-130 mg/dL during the day (pre-meals) with slightly higher targets overnight (up to 150 mg/dL). [216, 255]

**The Diabetes Team**

A multi-disciplinary team should follow children and adolescents with T1DM. This includes physicians, diabetes educators, dieticians, social workers and/or mental health specialists. [255]

**Diabetes education**

All pediatric patients, their families, and regular caregivers should receive diabetes education at the time of diagnosis with ongoing education regularly. That should include but is not limited to daily tasks such as BG monitoring, counting carbohydrates, calculating insulin doses and administering insulin, proper storing of insulin, recognizing and managing low blood sugars [210]. Additionally, at the time of diagnosis, care should be given to the sense of grief and loss felt by the patient and their family; any guilt or blame should be explored and addressed. Other areas of diabetes education include insulin dose adjustment, ketone monitoring, sick day management, diabetes and exercise, diabetes, and driving. Children and adolescents should receive developmentally appropriate education; and be encouraged to be involved in their diabetes care to the degree that is appropriate for their age, developmental stage, and capabilities while ensuring adequate supervision by parents or other family members. [255]

**Nutrition**

Nutritional education is integral to managing those with T1DM, and a registered dietician should be part of the diabetes team. The nutritional plan should be tailored to each family, depending on their circumstances. Carbohydrate counting should be taught at diagnosis and regularly reviewed after that. Healthy eating habits should be emphasized, and annual reviews with the dietician are essential. Regular monitoring of height, weight, and BMI should occur at each clinic visit to ensure adequate growth. Poor growth should alert the physician to an underlying condition such as poor glycemic control, insulin omission, underlying celiac disease or adrenal insufficiency, disordered
eating. The team should also monitor for excessive weight gain obesity to prevent obesity in this population. [255]

**Hypoglycemia**

Individuals with T1DM and their caregivers should be educated on how to identify hypoglycemia and its symptoms. If hypoglycemia is suspected, this should be confirmed with a BG check (BG < 70 mg/dL or 3.9 mmol/L). [256, 257] Education should also include the management of hypoglycemia. In mild hypoglycemia cases, where the individual is still conscious and responsive, oral glucose should be administered as fast-acting sugar (e.g., juice, table sugar, or honey). The recommended dose is 0.3 g/kg of glucose or 5 g for children weighing < 15 kg, 10 g for a 15-30 kg child, and 15 g for a child who weighs 30 kg or more. [257]

The BG level should be checked within 15 minutes to confirm the resolution of hypoglycemia [257]. Individuals using CGM should be aware of the lag time between CGM readings and BG and consider that when confirming that BG has recovered to avoid overtreatment and rebound hyperglycemia. A snack containing complex carbohydrates and protein should be considered if the next meal is more than an hour away. [257] Glucagon should be prescribed to all individuals with T1DM, and caregivers should receive education on when and how to administer it. In a situation of severe hypoglycemia (low BG associated with severe cognitive impairment), glucagon should be administered either IM or SC. The recommended dose is 1 mg for children > 25 kg and 0.5 mg for children < 25 kg. [257]

**Sick-day management**

DKA is considered a life-threatening but preventable complication of T1DM. All families should receive education regarding the prevention of DKA, which includes monitoring BG levels and monitoring ketones, the importance of insulin administration, appropriate sick-day management, and when to present to medical care. The DM care team should provide T1DM patients and their families a clear guidance on how to manage DM during intercurrent illnesses and how to contact emergency medical facilities. The International Society for Pediatric and Adolescent Diabetes (ISPAD) guideline (2018) stated five general sick-day DM management principles. Sick-day guidelines, including insulin adjustments, should be taught after diagnosis and reviewed at least annually with patients and family members to reduce the risk for DKA and severe hypoglycemia (with GI illnesses). More frequent BG and ketone (blood or urine) monitoring. Never stop insulin. Hydration with adequate water and salt should be maintained. Also, treat any underlying, precipitating illness. Education should be repeated annually, at the time of annual flu shot administration, to avoid uncontrolled or symptomatic hyperglycemia, dehydration, DKA, and severe hypoglycemia. [258]

**Physical activity and exercise**
Physical activity should be promoted in individuals with T1DM. Positive effects of exercise include increased insulin sensitivity, physical fitness, and cardiovascular benefits. However, individuals with T1DM are at higher risk of exercise-induced hypoglycemia from increased insulin sensitivity and depletion of muscle glycogen stores. Additionally, hyperglycemia may be encountered with exercise due to elevated adrenaline levels. Families should be educated about strategies to maintain blood sugars during exercise. Frequent BG monitoring is essential before, during, and after exercise. A BG of 7-13 mmol/L should be targeted pre-exercise with the aim to maintain that target during exercise. Strategies to prevent exercise-induced hypoglycemia include reducing bolus insulin dose for the preceding meal, reducing basal insulin, increasing carbohydrate intake, and eating a bedtime snack to reduce the risk of nocturnal hypoglycemia.

**Recommendations**

Children and adolescents with T1DM should engage in 60 min/day or more of moderate-or vigorous-intensity aerobic activity, with vigorous muscle-strengthening and bone-strengthening activities at least three days/week.

**Psychosocial assessment**

Mental health specialists (social workers, psychologists) are important members of the diabetes team. A psychosocial assessment should be performed on a yearly basis. Based on the child’s age and developmental stage, this should include screening the youth and, or their family for social adjustment, school performance, diabetes burn-out, depression, anxiety, and eating disorders. Appropriate referrals should be initiated if concerns are identified.

**Follow up**

Individuals who are newly diagnosed with T1DM require close follow up 2-3 weeks after discharge. In the meantime, they should have access to frequent communications with the team to adjust insulin doses and address any concerns. Regular follow up should occur every three months for youth with T1DM with a multidisciplinary diabetes team. This should include at least an annual nutrition review and psychosocial assessment. More frequent follow up may be required with different team members for certain individuals, such as situations where gaps in education are identified, concerns with compliance arise, or in those using insulin pumps. HbA1c should be measured every three months, around the time of each regular follow up. Please see the section on Screening for co-morbidities and complications for additional laboratory investigations required.

**Screening for co-morbidities and complications: Autoimmune conditions**

Given the fact that T1DM is an autoimmune process, individuals with T1DM are at an increased risk of other autoimmune conditions, most commonly autoimmune thyroid disease and celiac disease.
Children and adolescents with T1DM should be screened for autoimmune thyroid disease by measuring TSH levels and thyroid autoantibodies (thyroid peroxidase antibodies and thyroglobulin antibodies) at the time of diagnosis and every other year thereafter. These should be rechecked sooner if clinical concerns arise.

Additionally, they should be screened for celiac disease at diagnosis by measuring IgA tissue transglutaminase antibodies and total IgA levels. The measurement of IgG specific antibodies such as deaminated gliadin antibodies can be used if the patient is IgA deficient. Repeat screening should occur at two years and five years after diagnosis, with more frequent screening if the patient is symptomatic or has a positive family history of celiac disease. Individuals who screen positive should be referred to a pediatric gastroenterologist to confirm the diagnosis.

Cardiovascular risk factors

Hypertension

Youth with T1DM should be screened regularly for hypertension, as it is a risk factor for cardiovascular disease. Additionally, elevated blood pressures can worsen diabetic nephropathy and retinopathy. Criteria for diagnosing hypertension in children with T1DM are similar to those for regular children. If pharmacotherapy is warranted, ACE inhibitors should be considered as first-line therapy.

Dyslipidemia

Youth with T1DM should be screened for dyslipidemia at age 12 years and again at age 17 years. Screening should be delayed until glycemic control is achieved. If there is a family history of hypercholesterolemia or premature cardiovascular disease, screening should be initiated sooner, as early as two years of age. A non-fasting lipid profile can be used as the first line. If results show elevated triglyceride levels, a fasting sample should be obtained. LDL cholesterol target should be < 2.6 mmol/L. If LDL cholesterol levels remain > 3.4 mmol/L despite lifestyle and dietary modification, statins should be considered in children more than ten years of age.

Smoking

It is important to avoid cardiovascular risk factors in those with T1DM. Children and adolescents should be screened for smoking, including e-cigarettes, and should be strongly discouraged from smoking. Additional support should be granted for those who are interested in stopping smoking.

Microvascular complications

Youth with T1DM are at increased risk of long-term microvascular complications, including retinopathy, neuropathy, microalbuminuria, and nephropathy. The occurrence of these complications is
affected by various factors, such as diabetes duration, pubertal status, metabolic control, lipid abnormalities, and elevated blood pressure. Please see the table for screening recommendations. [216]

**Nephropathy**

Albuminuria should be screened for annually starting at age 12 years in those with a DM duration > 5 years. Screening should be by either random or early morning urine sample for urine ACR. If random ACR is positive, a repeat first morning should be tested, with repeat sampling to confirm the microalbuminuria. Other causes of albuminuria should be ruled out, such as exercise, fever, urinary tract infections, hyperglycemia, and renal disease. Patients with persistent albuminuria should be referred to a pediatric nephrologist if possible. Persistent albuminuria should be treated with ACEIs. [216, 265]

**Retinopathy**

Youth with T1DM duration of > 5 years should be screened yearly, starting at 15 years of age for retinopathy. If retinopathy is detected, a referral should be made to a specialist with experience in managing diabetic retinopathy. [216, 265]

**Neuropathy**

Screening should start at age 15 years in those with T1DM duration > 5 years. They should be screened clinically, including a comprehensive foot exam [265]. If neuropathy symptoms are present, it is crucial to review glycemic control and ensure that appropriate targets are met.

Table 16: Screening for T1DM complications and comorbidities [216]

<table>
<thead>
<tr>
<th>Complication/comorbidity</th>
<th>Indication and intervals for screening</th>
<th>Screening method</th>
</tr>
</thead>
</table>
| **Nephropathy** | • Yearly screening commencing at 12 years of age in those with a duration of T1DM > 5 years | • The first morning (preferred) or random urine ACR  
• Abnormal ACR requires confirmation at least one month later with a first morning ACR. If abnormal, it should be followed by timed overnight or 24-hour split urine collection for albumin excretion rate.  
• Repeat sampling every 3-4 months over a 6-to 12-month period of demonstrating persistence. |
| **Retinopathy** | • Yearly screening commencing at 15 years of age with a duration of T1DM >5 years  
• Screening interval can increase to 2 years if good glycemic control, duration of diabetes <10 years, and no retinopathy at initial assessment. | • Do a seven-standard field, stereoscopic-color fundus photography with interpretation by a trained reader (gold standard): or  
• Digital fundus photography |
| Neuropathy | Children ≥ 15 years with poor metabolic control should be screened yearly after five years of T1DM. | Question and examine for symptoms of numbness, pain, cramps, and paresthesia, as well as skin sensation, vibration sense, light touch, and ankle reflexes. |
| Dyslipidemia | Delay screening post-diabetes diagnosis until metabolic control has stabilized.  
- Screen at 12 and 17 years of age.  
- In those less than 12 years of age, screen only those with BMI>97th percentile, family history of hyperlipidemia, or premature CVD. | Fasting or non-fasting TC, HDL-C, TG, calculated LDL-C, measurement of non-fasting lipids may be considered if TG are not elevated. |
| Hypertension | Screen all children with T1DM at least twice a year. | Use appropriate cuff size. |

**T1DM in the School Setting**

Children spend a significant number of hours at school each week. Youth with T1DM should be provided with adequate support and supervision in the school setting to participate in school activities (including physical activities and sports) in a manner that is equal to their peers [266-268]. The school's responsibility is to make reasonable exceptions or allowances for children with T1DM to support them adequately. That includes a safe, clean, and private place to administer insulin and check BG levels [266-268]. Additionally, children should have access to their glucose monitoring devices, fast-acting glucose-containing foods, and snacks to detect and treat hypoglycemia [266-268]. A free access to water and bathroom facilities should also be allowed as they may develop polydipsia and polyuria due to hyperglycemia. Adequate school personnel training and education is essential and should be guided by the diabetes team caring for the student [266-268]. It is reasonable to expect that school personnel should identify hypoglycemia symptoms, check BG, and manage hypoglycemia appropriately present. A hypoglycemia kit containing fast-acting sugars and snacks should be available in any school with a child with T1DM. Whether a child can effectively perform diabetes tasks independently is not determined by their age but rather by their developmental stage and capabilities [221-223]. Therefore, school personnel are expected to be adequately trained to either administer insulin or supervise insulin administration based on the treating team's recommendations as documented in a personalized diabetes plan [266-268]. School personnel has to be knowledgeable of the mental health challenges that youth with T1DM face.

Youth with T1DM may need additional allowances during specific activities such as recess, physical activity, and examinations. Effective communication between the school, the family, and the diabetes team is essential. The school should be provided with a personalized diabetes plan for each
child agreed upon by the family and diabetes team and updated regularly [266-268]. It should include, but is not limited to; frequency of blood sugar monitoring, insulin doses, meal plan, instructions on managing low or elevated BG, instructions regarding physical activity, and details on when and how to contact the parent.

**Transition Care in DM**

It is a purposeful, planned transition of those from the young ages with chronic medical conditions from the child-centered to the adult-oriented health care. For some adolescents with T1DM, this can be a high-risk period, with worsening compliance and glycemic control, inadequate clinic follow-ups/visits, risk-taking behavior, mental health concerns, and eating disorders [268]. Therefore, the diabetes team should be sensitive to the unique needs of this population.

Transition care should start in early adolescence and be tailored to each patient depending on their developmental stage and maturity [216]. Consider a gradual transfer of DM responsibilities to the adolescent while maintaining parental support and supervision. The transition of DM tasks should be in keeping with the youth's developmental capabilities [216]. A more formal transition should occur by mid to late adolescence. [266-268]

Between the ages of 13-14 years, the patient should be referred to a diabetes transition clinic, run by both adult and pediatric endocrinologists [216]. It should include other diabetes team members, specifically mental health specialists [189, 224]. The clinic's purpose is to introduce individuals to the adult health care model and teach them how to navigate the system. Additionally, it should focus on the specific needs of this age group. Adolescents should be seen between 2-4 times in the transition clinic before they are entirely transferred to adult care (around 15-16 years). Until the transfer process is complete, they should continue to follow regularly with their pediatric endocrinologist in addition to the transition clinic. [266-268]

**Guidelines for Diagnosis & Management of Diabetic Ketoacidosis (DKA) in Children under 14 years of Age and/or < 50kg weight**

A committee from three subspecialties (pediatric endocrinology, pediatric critical care, and pediatric intensive care) developed the following recommendations for the diagnosis and treatment of DKA in those under the age of 14 years. It is based on most recent international research and recommendations and is designed to be as clear and as secure as possible in the light of evidence-based practice. However, no recommendations may, however, be deemed absolutely safe, and there could still be risks since the pathophysiology of cerebral edema is still poorly understood. Any patients will require a somewhat changed strategy based on individualized and justified needs. [269]
When to suspect DKA:

You should suspect DKA when having a constellation of the following history and clinical signs:

<table>
<thead>
<tr>
<th>History</th>
<th>Clinical Features</th>
</tr>
</thead>
<tbody>
<tr>
<td>Polyuria</td>
<td>Dehydration</td>
</tr>
<tr>
<td>Polydipsia</td>
<td>Tachypnea; deep (Kussmaul) respiration</td>
</tr>
<tr>
<td>Weight loss</td>
<td>Breath that smells like acetone (ketone)</td>
</tr>
<tr>
<td>Tiredness</td>
<td>Nausea, vomiting, and abdominal pain</td>
</tr>
<tr>
<td></td>
<td>Confusion, lethargy, drowsiness</td>
</tr>
</tbody>
</table>

Definition of DKA:

DKA occurs when hyperglycemia, glycosuria, metabolic acidosis and ketonuria are found in type I (or occasionally type II) diabetic patients. Please confirm the below criteria:

<table>
<thead>
<tr>
<th>The biochemical criteria</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hyperglycemia (BG &gt;11mmol/L ≈ 200mg/dL)</td>
<td>Exclude HHS &amp; HONK</td>
</tr>
<tr>
<td>Venous pH &lt;7.3 or bicarbonate &lt;15mmol/L</td>
<td>Consider other differential</td>
</tr>
<tr>
<td>Ketonemia and/or ketonuria</td>
<td>diagnoses</td>
</tr>
</tbody>
</table>

Caveat 1: Children and adolescents with known DM may rarely develop DKA with normal BG levels

Management in emergency room or urgent care area:

Maintaining the delicate balance between stabilizing the patient and adhering to conservative fluid replacement is the most important part of 1st-hour management. Here is the summarized plan:

For all DKA patients:
- Connect to cardiorespiratory monitor & pulse oximeter.
- Analyze ECG to evaluate for signs of hyper or hypokalemia.
- ABC as needed (as per PALS recommendations).
- Airway support (no elective intubation for significant tachypnea, consult expert).
- Give 100% O2 by face mask.
- Insert two IV cannulas.
- Insert nasogastric tube if indicated (avoid in obtunded if the airway not protected—? aspiration).
- Measure body weight (BW) and estimate for unstable patient (Broselow tape or growth chart).
- Send urgent labs: BG, blood gases (capillary or venous), urea & creatinine, electrolytes, serum osmolality, calcium, magnesium, phosphorus, albumin, CBCs with differential.
- Serum β-hydroxy butyrate concentrate, urine analysis and urine ketones.
- Blood culture, urine culture, throat swab, CXR for suspected infection (as indicated).
- Start fluid replacement as follow:
  Patient could present in shock or only dehydrated but with stable hemodynamics.
  Table below summarize the management of both scenarios.
Fluid Management in 1st hour

<table>
<thead>
<tr>
<th>Dehydrated, not in shock: Estimate the severity of DKA</th>
<th>In clinical shock: (weak peripheral pulses, prolonged capillary refill ≥ 3 seconds, reduced conscious level)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mild: venous pH&lt;7.3 or bicarbonate &lt;15mmol/L</td>
<td>Shock with hypotension (late sign): 10 ml/kg 0.9 Saline bolus over 5-10 minutes. Repeat x3 till normal BP (consult expert)</td>
</tr>
<tr>
<td>Moderate: pH&lt;7.2 or bicarbonate &lt;10mmol/L</td>
<td>Shock, not hypotensive (compensated): 10 ml/kg 0.9 Saline over 1 hour</td>
</tr>
<tr>
<td>Severe: pH&lt;7.1 or bicarbonate &lt;5mmol/L</td>
<td></td>
</tr>
<tr>
<td>Start IV 0.9% Saline at:</td>
<td></td>
</tr>
<tr>
<td>5 ml/kg/h for mild/moderate DKA</td>
<td></td>
</tr>
<tr>
<td>7 ml/kg/h for severe DKA</td>
<td></td>
</tr>
</tbody>
</table>

Caveat 2:
Always discuss the management with the most senior physician in your area. Careful with severe cases that can present in an obtunded state and consider signs & management of Cerebral Edema upon initial presentation. [260]

Management plan after the 1-2 hours

Rehydration, insulin and electrolyte replacement, and close clinical and laboratory control for possible risks, are essential components of DKA treatment, and they are outlined as follows: [260]

<table>
<thead>
<tr>
<th>Fluid calculation principles</th>
<th>Insulin</th>
<th>Monitoring (&amp; record)</th>
</tr>
</thead>
<tbody>
<tr>
<td>IV maintenance + deficit</td>
<td>Mix 50 unit of soluble insulin (e.g. Regular) in 50 ml 0.9% saline bag (1 ml = 1 unit) (50 units in 500 ml second option, 10 ml = 1 unit)</td>
<td>Hourly: Vital Signs Capillary BG (bed side), Neurological status (pupils &amp; GCS), Fluid intake &amp; output</td>
</tr>
<tr>
<td>Maintenance calculation:</td>
<td>Starting dose: 0.05-0.1 unit/kg/hr 0.05 dose for kids: -Younger than 5 years -Newly diagnosed -rapid drop of BG&gt;100mg/dl/hr</td>
<td>Every 2-4 hours: Blood gases (venous or capillary)</td>
</tr>
<tr>
<td>100 ml/kg for the first 10 kg</td>
<td></td>
<td>Every 4 hours: BG, electrolytes, urea, creatinine, phosphorus, calcium, magnesium</td>
</tr>
<tr>
<td>+ 50 ml/kg for the next 10 kg</td>
<td></td>
<td></td>
</tr>
<tr>
<td>+ 20 ml/kg for the rest BW</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Deficit calculation:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>5% for mild/moderate DKA</td>
<td></td>
<td></td>
</tr>
<tr>
<td>10% for severe DKA</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Correct slowly over 48 hours</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Start 0.9% Saline (with KCl)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Potassium: 40 mEq/L KCl (after 1st void &amp; if K level &lt; 5.5)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Caveat 3:

The amount of fluid from the insulin bag is to be counted in the overall rehydration fluid (when using a 500 ml bag for mixing). Drop fluid boluses that are > 20 ml/kg from the overall rehydration fluid with no substitution for the ongoing losses. Consider, only, if the fluid balance stays negative (check Q 4 hrs). Often call for fluid early (expect 1 hr delay).

To minimize calculation burden, errors, and confusion we recommend the following simplified and slightly more conservative total fluid calculation for first 48 hrs after DKA presentation:

<table>
<thead>
<tr>
<th>Simplified calculated rate by weight</th>
<th>≤15 kg</th>
<th>16 to 40 kg</th>
<th>&gt;40</th>
</tr>
</thead>
<tbody>
<tr>
<td>Maintenance + deficit</td>
<td>5 ml/kg/hr</td>
<td>4 ml/kg/hr</td>
<td>3 ml/kg/hr</td>
</tr>
</tbody>
</table>

NB. All fluids given during resuscitation should be documented carefully, particularly in ER.

**Special laboratory consideration in newly diagnosed DM:** HbA1C, insulin antibodies, glutamic acid decarboxylase antibodies, thyroid function and thyroid antibodies (if available). 

---

**Goals of Therapy**

- Correct dehydration slowly (over 48 hrs)
- Correct acidosis and reverse ketosis (don’t interrupt insulin if acidosis is not resolving)
- Restoring blood glucose (BG) to near normal
- Monitor for DKA complications:
  - Manage the patient in advance care unit (PICU, High Dependency Unit, ER)
  - Keep the nurse to patient ratio 1:1 for severe DKA (assign nurse with advanced care skills)
  - Admission to the ward is not recommended as it carry with it a significant risk of inadequate monitoring and possible life threatening errors (potassium errors, hypoglycemia ...etc)
- Identify and treat any precipitating event:
  - Fever could be due to presence of infection, please send cultures and start antibiotics.
  - Psychosocial assessment is crucial to identify correctable causes and prevent recurrences

**Higher risk patient who need rigorous monitoring even when managed in PICU are kids with:**

- Severe DKA with pH<7.1
- Severe dehydration with shock
- Depressed level of consciousness
- Those who are at increased risk for cerebral edema
  - <5 years of age (and more risk in <2 years of age)
  - Lower than expected pCO2 for the degree of metabolic acidosis
  - High urea nitrogen upon presentation
Resolution and shifting to an SC insulin

Introduction of oral fluid and transition to SC insulin:

Oral fluids should be introduced when substantial clinical improvement has occurred (mild acidosis/ketosis may still be present) and the patient indicates a desire to eat. [269]

The indication to start an SC insulin: [269]
- Patient is fully conscious and willing to eat with no nausea or vomiting
- Ketoacidosis has almost resolved (serum bicarbonate >15 mEq/l twice)
- Venous pH >7.3
- Ketone in urine may still be positive

Fluid management:

When oral fluid is tolerated, the IV fluid should be reduced, and oral fluid intake should be included in total rehydration fluid calculation. Start a special diabetic diet after stopping insulin infusion (at least 30 minutes after an SC insulin injection). [269]

Insulin management:

The most convenient time to change to an SC insulin is just before mealtime. The first SC injection should be given 15–30 min with rapid-acting insulin (insulin aspart) or 1–2 h with regular insulin before discontinuing infusion to prevent rebound hyperglycemia. [269]

Insulin dose:

If a patient is a known T1DM on appropriate treatment, then resume the previous doses. If new T1DM with DKA, start 0.75 unit/Kg /day, divided to 30-40 % long-acting (e.g., levemir or glargine)
and 60-70% as rapid-acting insulin before or after meals. Use glargine as long-acting insulin for age > 3 years, and levemir as a basal insulin if < 3 yrs of age. Rapid-acting insulin analogues like aspart, lispro, humalog can be given 15-30 mins before stopping insulin infusion. Monitor BG by gluco-check four times daily (before meals and at bedtime) and adjust the dose of insulin according to BG results. Consult pediatric endocrinologist if available. Diabetic educators and dietitians should be involved early to educate patients and caregivers. If insulin analogues are not available, use a two-dose insulin regimen as shown in the next table:

| Two-doses insulin regimens for newly diagnosed T1DM after resolution of DKA |
|-----------------------------|-----------------|-----------------|
| **Total daily dose**        | Pre-pubertal: 0.5-1.0 unit/kg | Pubertal: 1.0-1.2 unit/kg |
| **Before breakfast**        | Two-thirds of total daily dose (TDD) | One-third rapid-acting insulin |
|                             |                               | Two third intermediate-acting insulin (e.g. NPH) |
| **Before dinner**           | One third of TDD | One-third rapid-acting & two third intermediate-acting insulin OR |
|                             |                               | One-half rapid-acting & one-half intermediate-acting insulin (e.g. NPH) |
**Effective Osmolality = 2 Na + Glucose (glucose value in mmol/L)**

**Corrected Na = measured Na + 2 [(plasma glucose-100/100)] mg/dL**

<table>
<thead>
<tr>
<th>Differential Diagnosis of DKA (hyperglycemia, acidosis, and ketosis)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Diagnosis</strong></td>
</tr>
<tr>
<td>Salicylate Intoxication</td>
</tr>
<tr>
<td>Metabolic Diseases (Inborn Error of Metabolism)</td>
</tr>
<tr>
<td>Severe stress with starvation (?) Sepsis</td>
</tr>
</tbody>
</table>
**Airway considerations** Secure the airway in:
- Comatose patient (GCS <8)
- Abnormal breathing
- By expert physician
- Hyperventilate (same patient CO2 & correct slowly)

**NG insertion:**
Do not induce vomiting if patient can’t protect airway

---

**Order Sheet for Pediatric DKA Patients (< 14 years and/or < 50 kg body weight)**

<table>
<thead>
<tr>
<th>Date:</th>
<th>Time:</th>
<th>Patient Weight:</th>
<th>Length/Height:</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Admit the patient to:**
- [ ] PICU
- [ ] HDU

**Obtain Patient Weight:**
- [ ]

**Connect to cardiorespiratory monitor:**
- [ ]

**Connect to pulse oximeter:**
- [ ]

**Record vital signs hourly:**
- [ ]

**Record neurology assessment hourly:**
- [ ] (pupils size, reactivity, GCS)

**Nothing by mouth (NPO):**
- [ ]

**Insert two IV canulas:**
- [ ]

**Strict intake and output and record hourly:**
- [ ]

**Insert Foley’s catheter (only if indicated):**
- [ ]

**Check Urine for ketones (bedside check):**
- [ ]

**Additional Investigations:**
- [ ] HbA1C
- [ ] Other

**Shock & hypotensive patient:**
- [ ] Start ______ ml (10 ml/kg) 0.9% Saline IV bolus over 5-10 minutes.
- [ ] Still hypotensive: Repeat bolus ______ ml IV (10 ml/kg) over 5-10 minutes
- [ ] Not in shock: Start ______ ml IV infusion 0.9% saline over 1 hour

**Calculation formula:**
- [ ] Start IV 0.9% saline at ______ ml/hour
- [ ] Potassium Chloride Add 40 mmol/L (20 mmol to 500 normal saline bag)
- [ ] Add only if patient is passing urine and K level is < 5.5 mmol/L
- [ ] Add Dextrose 5% to 0.9% saline fluid when blood glucose drops to < 250 mg/dl (14 mmol/L)
- [ ] Add Dextrose 10% to 0.9% Saline fluid when blood glucose drop to < 140-150 mg/dl (8 mmol/L)

**Insulin Infusion:**
- [ ] DO NOT GIVE BOLUS
- [ ] And start after 1-2 hour from fluid initiation

**Antimicrobials (consider for fever, sepsis):**
- [ ]

---

**Patient:**
- [ ]

**MRN:**
- [ ]

**Noted by:**
- [ ]

**Laboratory monitoring:**
- [ ]

**Capillary blood glucose:**
- [ ]

**Serum electrolytes:**
- [ ]

**Blood culture, Urineculture:**
- [ ]

**CBC-differential:**
- [ ]

**Urine analysis:**
- [ ]

**Chest Xray:**
- [ ]

**Physician Name & Signature:**
- [ ]

**Nurse Name & signature:**
- [ ]

---

**Note:**
- [ ]
Algorithm for the Management of DKA in Children

**Confirm DKA Diagnosis**

| Hypoglycemia (BG > 11mmol/L = 200mg/dL) | Venous pH < 7.3 and/or bicarbonate < 15mmol/L | Ketonuria |

**1st Hour Management**

<table>
<thead>
<tr>
<th>DKA in Shock</th>
<th>DKA not in Shock</th>
</tr>
</thead>
<tbody>
<tr>
<td>Notify PICU, Alert senior primary physician</td>
<td>Assess Severity</td>
</tr>
<tr>
<td>Airway: No elective intubation/call expert</td>
<td>Mild: pH &lt; 7.3 or bicarbonate &lt; 15mmol/L</td>
</tr>
<tr>
<td>Breathing: 100% O2 by Face Mask, Check 20 Sat</td>
<td>Moderate: pH &lt; 7.3 or bicarbonate &lt; 10mmol/L</td>
</tr>
<tr>
<td>Circulation: 2 IV canulae, cardiac monitor</td>
<td>Severe: pH &lt; 7.1 or bicarbonate &lt; 5mmol/L</td>
</tr>
<tr>
<td>Hypotensive: 10 ml/kg NS bolus over 5-10 min</td>
<td><strong>1st hour fluid: 0.9% saline</strong></td>
</tr>
<tr>
<td>Repeat if hypotensive (x 3) - consider inotropes</td>
<td>7 ml/kg/h for severe DKA</td>
</tr>
<tr>
<td>Shock with normal BP: 10 ml/kg NS over 1 hr</td>
<td>5 ml/kg/h for mild/moderate DKA</td>
</tr>
</tbody>
</table>

**Always admit high risk patients (e.g., severe DKA, young < 2 years old, newly diagnosed diabetes) to highly monitored area (like PICU, high dependency unit) with nurse to patient ratio of 1:1**

**Post 1st Hour Management**

<table>
<thead>
<tr>
<th>Insulin (DO NOT GIVE BOLUS)</th>
<th>Simplified calculated rate by weight</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mix 50 unit of soluble insulin (Regular) in 50 ml 0.9% saline</td>
<td><strong>&lt;15 kg</strong> 5 ml/kg/hr</td>
</tr>
<tr>
<td>(Alternatively, mix 50 unit in 500 ml 0.5% saline bag, Insulin fluid volume to be included in the total rehydration calculation when using 500 ml bag)</td>
<td><strong>16 to 40</strong> 4 ml/kg/hr</td>
</tr>
<tr>
<td>Starting dose: 0.05-0.1 unit/kg/hr</td>
<td><strong>&gt;60 kg</strong> 3 ml/kg/hr</td>
</tr>
<tr>
<td>0.05 dose for kids:</td>
<td><strong>Remove fluid boluses of &gt; 20 ml/kg from the total replacement</strong></td>
</tr>
<tr>
<td>- Younger than 5 years</td>
<td><strong>Fluid calculation principles</strong></td>
</tr>
<tr>
<td>- Newly diagnosed</td>
<td>IV Maintenance + deficit</td>
</tr>
<tr>
<td>- Rapid drop of BG (&gt; 100mg/dl/hr)</td>
<td>Correct deficit slowly over 48 hours</td>
</tr>
<tr>
<td>- Recently received insulin injection</td>
<td>Deficit calculation: 10% for severe DKA</td>
</tr>
<tr>
<td>- Start after 1-2 hour from starting rehydration fluid</td>
<td>5% for mild to moderate DKA</td>
</tr>
<tr>
<td></td>
<td>Start 0.9% Saline (with KCl)</td>
</tr>
<tr>
<td></td>
<td>Potassium: 40 mEq/L KCl</td>
</tr>
<tr>
<td></td>
<td>(add after 1st void &amp; only if K level &lt; 5.5)</td>
</tr>
<tr>
<td></td>
<td>No routine replacement of ongoing losses but avoid negative balance (reassess every 4 hrs)</td>
</tr>
</tbody>
</table>

**Adjustment & Trouble Shooting**

- BG < 14-17 mmol/l (250-300 mg/dl) = Add Dextrose 5% to 0.9% Saline
- BG < 8 mmol/l (140-150 mg/dl) = Change 0.5% to 0.9% Saline
- Rapid fall of glucose (> 100 mg/dl per hour): May drop insulin to 0.05 u/kg/hr
  - Or change 0.5% to 0.1% if acidosis is not improving
  - Try not to wean insulin dose to < 0.05 u/kg/hr if acidosis still present
- Hypoglycemic attack (< 4 mmol/l = 2-5 ml/kg D10% bolus,
  - Hold insulin temporarily (30-60 min, repeat BG and restart)
- Potassium > 5.6 mmol/l (not hammered) = Hold Potassium
- Potassium > 3.5 mmol/l = Increase KCl to 60 mmol/l (need good IV)
- Phosphorus < 0.5 mmol/l (1.5 mg/dl) = Replace 1% of KCl with K Phos
- Acidosis not improving = trouble shooting (See attached guidelines)
- Always prepare next fluid to be used in advance (expect 1 hour delay)

**Monitoring**

- **Hourly Vital Signs**
- Blood glucose, Neurological status (pupils & GCS)
- Fluid intake & output

**Every 2-4 hours**

- Blood gases (venous or capillary)

**Every 4 hours**

- Electrolytes, urea & creatinine, phosphorus, calcium, magnesium
- Other labs
- CBC & differential, Blood culture, urine culture (with fever)
- For new onset diabetes: see guidelines

**Monitor for Complications**

- Cerebral edema: Neuro exam/hourly
- Hypokalemia: EKG, electrolytes
- Aspiration pneumonia: avoid NS if airway protection is questionable

**Early Signs of Cerebral Edema**

- Severe headache
- Agitation or irritability
- Unexpected fall in heart rate
- Increased blood pressure
- Decreased level of consciousness
- Mannitol or 3% Saline standby

(see attached guidelines for details)
References
References:


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229. International Diabetes Federation. Clinical Practice Recommendations for managing Type 2 DM in Primary Care (IDF 2017)


250. NICE Guidelines on insulin biosimilar; http://nice.org.uk/guidance/esnm64


253. Saudi FDA Guidelines on Biosimilars version 1.1


Appendix 1:

SNDC Scientific Committee Members:

- Dr. Mohammed Alharbi, Consultant Pediatric Endocrinologist and Diabetes, Deputyship for therapeutic Services, MOH
- Dr. Sulieman Alshehri, General Director of SNDC, SHC
- Dr. Saud Alsifri, Consultant Endocrinology and Diabetes, General Directorate of Medical Services of the Armed Forces
- Dr. Saad Alzahrani, Consultant Endocrinology and Diabetes, KFMC
- Dr. Anwar Jammah, Consultant Endocrinology and Diabetes, KSU and KSU medical city
- Dr. Ali Alzahrani, Consultant Endocrinology and Diabetes, King Faisal Specialist Hospital and Research Center
- Dr. Adel Alharf, pharmacists, Vice President for Drug Sector, Saudi Food and Drug Authority
- Dr. Fahad Alsabaan, Consultant Endocrinology and Diabetes, General Directorate of Medical Services, Ministry of Interior
- Dr. Raad Aldahash, Consultant Endocrinology and Diabetes, Health Affairs of Ministry of National Guard
- Dr. Saleh Aljasser, Consultant Endocrinology and Diabetes, Council of Saudi Chambers
- Dr. Mohammed Altouki, pharmacists, Council of Cooperative Health Insurance
- Mr. Abdulaziz Alhumedi, Saudi Diabetes Association
- Saja Alhosan, MPH, SNDC, SHC
Appendix 2:

**Saudi DM Clinical Practice Guidelines workshops participants (consultants and specialists in endocrinology and diabetes) from all regions of KSA, held in Riyadh and Jeddah:**

- Dr. Njoud Alkhaldi, , King Fahad Specialist Hospital – Dammam
- Ms. Bushra AlQarni, General Directorate of Medical Services, Riyadh
- Dr. Aishah Ekhzaimy, King Khalid University Hospital Medical City, Riyadh
- Dr. Fatima Alslail, MOH
- Dr. Mohammed Koshm, General Directorate of Medical Services, Riyadh
- Dr. Hamad Alshbrmei, King Fahd Specialist Hospital, Qassim
- Dr. Bader Alzahrani, Security Forces Hospital, Riyadh
- Dr. Turki Almogbel, King Fahd Specialist Hospital, Qassim
- Dr. Awad Alshahrani, King Abdulaziz Medical City, National Guard Health Affairs Riyadh
- Dr. Hosam Alahmdei, Qassim Health Cluster
- Dr. Waled Hashem, King Saud Medical City, Riyadh
- Dr. Ebtessam Baessa, Dammam Medical Complex
- Dr. Naji Aljohani, KFMC, Riyadh
- Dr. Ibrahim Alkathem, Almana General Hospital Hofuf, AlAhsa
- Dr. Abdulrahman Almaghamsi, KFMC, Riyadh
- Dr. Ali Alqareni, Ministry of National Guard Health Affairs, Eastern Region
- Dr. Abdulraof Almahfouz, King Faisal Specialist Hospital & Research Centre, Riyadh
- Dr. Abduallah Alqarenei, Johns Hopkins Aramco Healthcare, Chair, Women and Children's Health Institute, Eastern Region
- Dr. Eman Shesa, King Salman Hospital, Riyadh
- Dr. Abdulmohsan Alelq, Imam Abdulrahman Bin Faisal University, Eastern Region
- Dr. Mohamed Almaatouq, KSU, Riyadh
- Dr. Moshaeil Alnaeis, MOH, Hail
- Dr. Ahmad Alobedollah, KFMC, Riyadh
- Dr. Mohammed Alsofiani, KSU, Riyadh
- Dr. Muhammad Mujammami, King Khalid University Hospital Medical City
- Dr. Fahad Alsabaan, General Directorate of Medical Services, Riyadh
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Dr. Eman Alshail, Security Forces Hospital, Riyadh
Dr. Ahlam Alotaibi, King Abdullah University Hospital
Dr. Haifa Alfaraidi, King Abdullah Specialist Children Hospital, National Guard Health Affairs Riyadh
Dr. Khaled Aldossari, Prince Sattam Bin Abdulaziz University, Riyadh
Dr. Mohammed Altoukhi, Council Of Cooperative Health Insurance
Dr. Amani Alhozali, King Abdulaziz University, Jeddah
Prof. Siraj Mira
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Dr. Khaled Tayeb, Al Noor Specialist Hospital, Mecca
Dr. Homaid Alsahafi, Diabetes Center, Heraa General Hospital, Mecca
Dr. Mastour Alzayed
Dr. Abdullah Alzahrani
Dr. Samyah Bukhari, Diabetes Center, King Fahd Hospital, Medina
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Dr. Reem Almutairi, Dhurma General Hospital
Ms. Nawal Alshehri, Saudi Charitable Association of Diabetes
Ms. Salma Alhamzah, Saudi Charitable Association of Diabetes
Prof. Abdulrahman Alsheikh, King Abdulaziz University, Saudi Scientific Diabetes Society, Jeddah
Prof. Tarif Zawawl
Dr. Hawazen Zarif, National Guard Health Affairs, King Abdulaziz Medical City, Jeddah
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Dr. Khalid Alghamdi, General Directorate of Medical Services of the Armed Forces, Taif
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Prof. Mohamad Alhadraamy
Dr. Naweed Alzaman, Taibah University, Medina
Dr. Rahmah alshamrani, East Jeddah General Hospital, Jeddah
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<tr>
<th>Name</th>
<th>Institution</th>
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<tbody>
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<td>Dr. Daifallah Almalki, Diabetes Center, Prince Mansour Military Hospital, Taif</td>
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<tr>
<td>Dr. Abdullah Karawagh, King Abdullah Medical Complex, Jeddah</td>
<td>Dr. Abdulkareem Almalki</td>
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<tr>
<td>Dr. Basim Almalki</td>
<td>Prof. Mohammed Alhumaidi, King Khalid University</td>
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<tr>
<td>Dr. Abdulaziz Alsaedi</td>
<td>Dr. Ahmed Alghamdi</td>
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<td>Dr. Mohammad Alqahtani</td>
<td>Dr. Faisal Banah</td>
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<td>Dr. Mohammed Albalawi</td>
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<td>Dr. Ayman Baker</td>
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<td>Dr. Ali Alghadi</td>
<td>Dr. Abdullah Alshahrani, University of Bisha</td>
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<td>Dr. Hossain Hakami, King Fahad Central Hospital, Jizan</td>
<td>Dr. Hussain Badwai</td>
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<td>Dr. Abdullah Othman, Diabetes Center, Asir Central Hospital, Asir</td>
<td>Dr. Khaled Alswaat, Taif University</td>
</tr>
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<td>Dr. Ebaa Samaan</td>
<td>Dr. Matar Almalki, Obstetrics and Gynecology Hospital, Taif</td>
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