

# NATIONAL CLINICAL GUIDELINES

THE DIAGNOSIS & MANAGEMENT OF  
TYPE 2 DIABETES MELLITUS IN ADULTS & THE ELDERLY

## Ministry of Public Health

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المبادئ الإرشادية السريرية لدولة قطر  
NATIONAL CLINICAL GUIDELINES FOR QATAR



وزارة الصحة العامة  
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## Version History

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2.0	Final	29 <sup>th</sup> March 2021	Guidelines Team	Updated version for publication.

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## Abbreviations

The abbreviations used in this guideline are as follows:

<b>ACC / AHA</b>	American College of Cardiology / American Heart Association
<b>ACE</b>	Angiotensin converting enzyme
<b>ACR</b>	Albumin-creatinine ratio
<b>ADL</b>	Activities of daily living
<b>AIDS</b>	Acquired Immune Deficiency Syndrome
<b>ALT</b>	Alanine aminotransferase
<b>ARB</b>	Angiotensin receptor blocker
<b>ASCVD</b>	Atherosclerotic cardiovascular disease
<b>BG</b>	Blood glucose
<b>BMI</b>	Body mass index
<b>BP</b>	Blood pressure
<b>CCB</b>	Calcium channel blocker
<b>CGM</b>	Continuous glucose monitoring
<b>CKD</b>	Chronic kidney disease
<b>CSII</b>	Continuous subcutaneous insulin infusion
<b>DESMOND</b>	Diabetes Education and Self-Management for Ongoing and Newly Diagnosed
<b>DKA</b>	Diabetic ketoacidosis
<b>DPP-4</b>	Dipeptidyl peptidase-4
<b>DSME</b>	Diabetes Self-Management Education

<b>DSMS</b>	Diabetes Self-Management Support
<b>eGFR</b>	Estimated glomerular filtration rate
<b>GDM</b>	Gestational diabetes mellitus
<b>HAAF</b>	Hypoglycaemia-associated autonomic failure
<b>HBA<sub>1c</sub></b>	Glycated haemoglobin level
<b>HDL-C</b>	High-density lipoprotein cholesterol
<b>HIV</b>	Human Immunodeficiency Virus
<b>IV</b>	Intravenous route
<b>GLP-1</b>	Glucagon-like peptide-1
<b>LDL-C</b>	Low-density lipoprotein cholesterol
<b>MDT</b>	Multi-disciplinary team
<b>MNT</b>	Medical Nutrition Therapy
<b>MOPH</b>	Ministry of Public Health of Qatar
<b>NAFLD</b>	Non-alcoholic fatty liver disease
<b>NPH</b>	Neutral protamine Hagedorn
<b>OGTT</b>	Oral glucose tolerance test
<b>PCOS</b>	Polycystic ovary syndrome
<b>PCV13</b>	13-valent pneumococcal conjugate vaccine
<b>PHQ-2</b>	2-question Patient Health Questionnaire
<b>PHQ-9</b>	9-question Patient Health Questionnaire
<b>PPSV23</b>	23-valent pneumococcal polysaccharide vaccine
<b>SGLT-2</b>	Sodium glucose cotransporter-2
<b>SMBG</b>	Self-monitoring of blood glucose
<b>SU</b>	Sulfonylurea
<b>T1DM</b>	Type 1 diabetes mellitus
<b>T2DM</b>	Type 2 diabetes mellitus
<b>TZD</b>	Thiazolidinedione

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# 1 Information about this Guideline

## 1.1 Objective and Purpose of the Guideline

The purpose of this guideline is to define the appropriate diagnosis and management of type 2 diabetes mellitus in adults and the elderly. The objective is to improve appropriate investigation, prescribing and referral of patients presenting to provider organisations in Qatar. It is intended that the guideline will be used primarily by physicians, nurses and health educators in primary/generalist care.

## 1.2 Scope of the Guideline

Aspects of care covered in this guideline include the following:

- Assessment and management of type 2 diabetes mellitus in adults and older adults including:
  - Screening for type 2 diabetes and prediabetes.
  - Comprehensive medical evaluation.
  - Lifestyle and non-pharmacological management of confirmed type 2 diabetes.
  - Glycaemic targets and glucose monitoring.
  - Pharmacological treatment for type 2 diabetes.
  - Hypoglycaemia prevention and management.
  - Management considerations in older adults.

Aspects of care not covered in this guideline include the following:

- Management of complications of diabetic foot disease, renal disease, eye disease and atherosclerotic cardiovascular disease risk.
- Diabetes in children and adolescents.
- Diabetes in pregnancy.
- Management of diabetic ketoacidosis (DKA) or hyperosmolar hyperglycaemic state (HHS).

## 1.3 Editorial Approach

This guideline document has been developed and issued by the Ministry of Public Health of Qatar (MOPH), through a process which aligns with international best practice in guideline development and localisation. The guideline will be reviewed on a regular basis and updated to incorporate comments and feedback from stakeholders across Qatar.

The editorial methodology, used to develop this guideline, has involved the following critical steps:

- Extensive literature search for well-reputed published evidence relating to the topic.
- Critical appraisal of the literature.
- Development of a draft summary guideline.
- Review of the summary guideline with a Guideline Development Group, comprised of practising healthcare professionals, subject matter experts and patient representatives, from across Qatar.
- Independent review of the guideline by the National Clinical Guidelines & Pathways Committee, appointed by the MOPH, from amongst stakeholder organisations across Qatar.

Whilst the MOPH has sponsored the development of the guideline, the MOPH has not influenced the specific recommendations made within it.

## 1.4 Sources of Evidence

The professional literature has been systematically queried using specially developed, customised, and tested search strings. Search strategies are developed to allow efficient yet comprehensive analysis of relevant publications for a given topic and to maximise retrieval of articles with certain desired characteristics pertinent to a guideline.

For each guideline, all retrieved publications have been individually reviewed by a member of the Editorial Team and assessed in terms of quality, utility, and relevance. Preference is given to publications that:

1. Are designed with rigorous scientific methodology.
2. Are published in higher-quality journals.
3. Address an aspect of specific importance to the guideline in question.

Further information about the literature search and appraisal process is included in *Appendix B*.

## 1.5 Evidence Grading and Recommendations

Recommendations made within this guideline are supported by evidence from the medical literature and where possible the most authoritative sources have been used in the development of this guideline. In order to provide insight into the evidence basis for each recommendation, the following evidence hierarchy has been used to grade the level of authoritativeness of the evidence used, where recommendations have been made within this guideline.

Where the recommendations of international guidelines have been adopted, the evidence grading is assigned to the underlying evidence used by the international guideline. Where more than one source has been cited, the evidence grading relates to the highest level of evidence cited:

- **Level 1 (L1):**
  - Meta-analyses.
  - Randomised controlled trials with meta-analysis.
  - Randomised controlled trials.
  - Systematic reviews.
- **Level 2 (L2):**
  - Observational studies, examples include:
    - Cohort studies with statistical adjustment for potential confounders.
    - Cohort studies without adjustment.
    - Case series with historical or literature controls.
    - Uncontrolled case series.
  - Statements in published articles or textbooks.
- **Level 3 (L3):**
  - Expert opinion.
  - Unpublished data, examples include:
    - Large database analyses.
    - Written protocols or outcomes reports from large practices.

In order to give additional insight into the reasoning underlying certain recommendations and the strength of recommendation, the following recommendation grading has been used, where recommendations are made:

- **Recommendation Grade A (RGA):** Evidence demonstrates at least moderate certainty of a net benefit from the recommendation.
- **Recommendation Grade B (RGB):** Evidence is insufficient, conflicting, or poor and demonstrates an incomplete assessment of net benefit vs harm; additional research is recommended.
- **Recommendation Grade C (RGC):** Evidence demonstrates potential harm that outweighs benefit; additional research is recommended.
- **Recommendation of the GDG (R-GDG):** Recommended best practice on the basis of the clinical experience of the Guideline Development Group members.

## 1.6 Guideline Development Group Members

The following table lists members of the Guideline Development Group (GDG) nominated by their respective organisations and the National Clinical Guidelines & Pathways Committee. The GDG members have reviewed and provided their feedback and approval of the guideline document. Each member has completed a declaration of conflicts of interest, which has been reviewed and retained by the MOPH.

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<sup>1</sup> Dr Ahmed Babiker attended the MOPH in his capacity as a Clinical Pharmacist and advisor on the availability of medications in Qatar.

## 1.7 National Clinical Guidelines & Pathways Committee Members

The following table lists members of the National Clinical Guidelines & Pathways Committee (NCGPC), appointed by the MOPH. The NCGPC members have reviewed and provided their feedback and approval of the guideline document. Each member has completed a declaration of conflicts of interest, which has been reviewed and retained by the MOPH.

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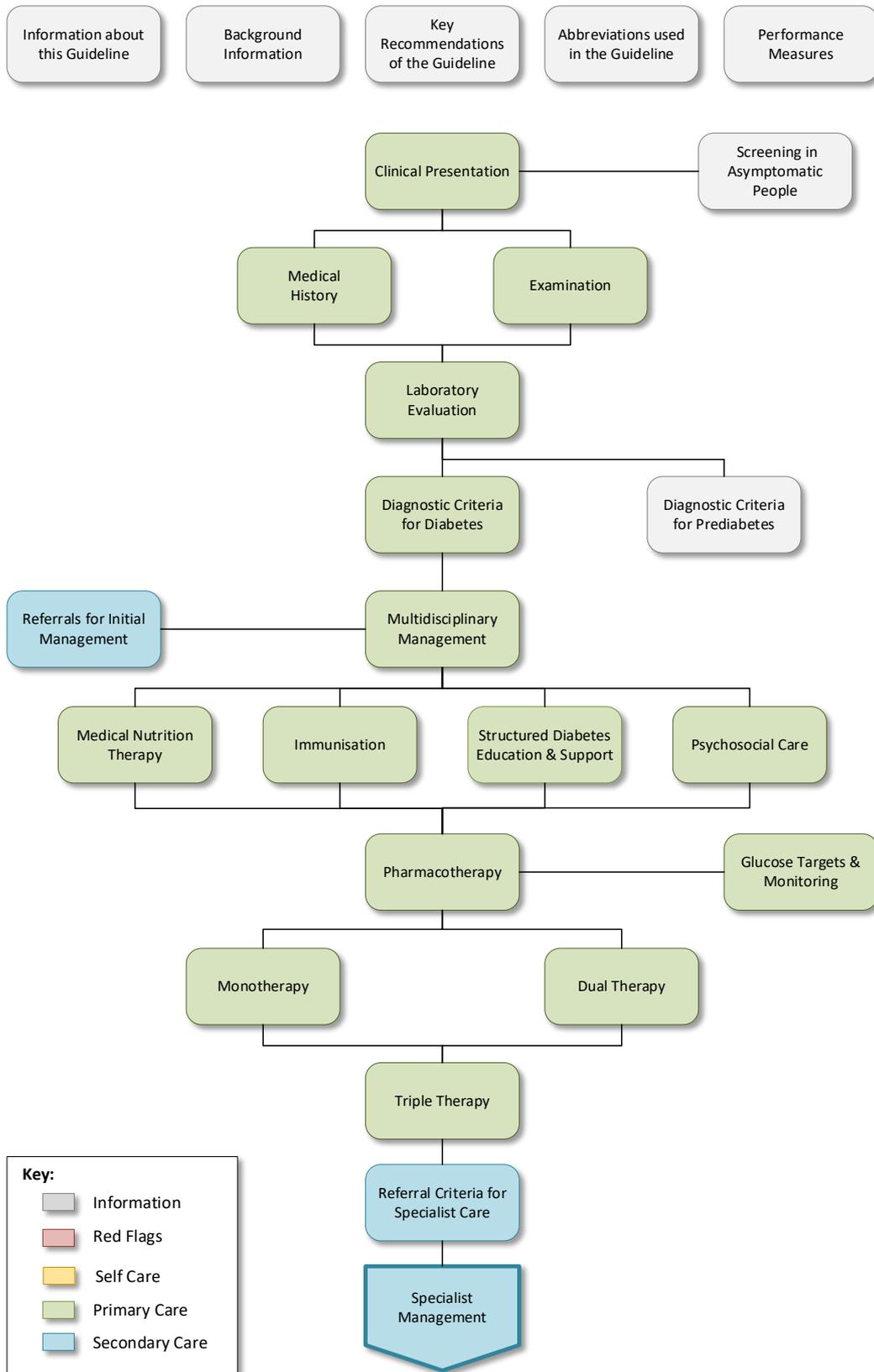
## 1.8 Responsibilities of Healthcare Professionals

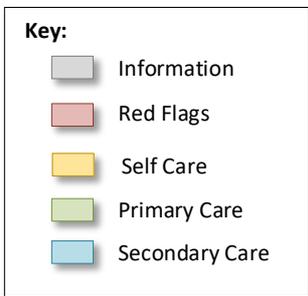
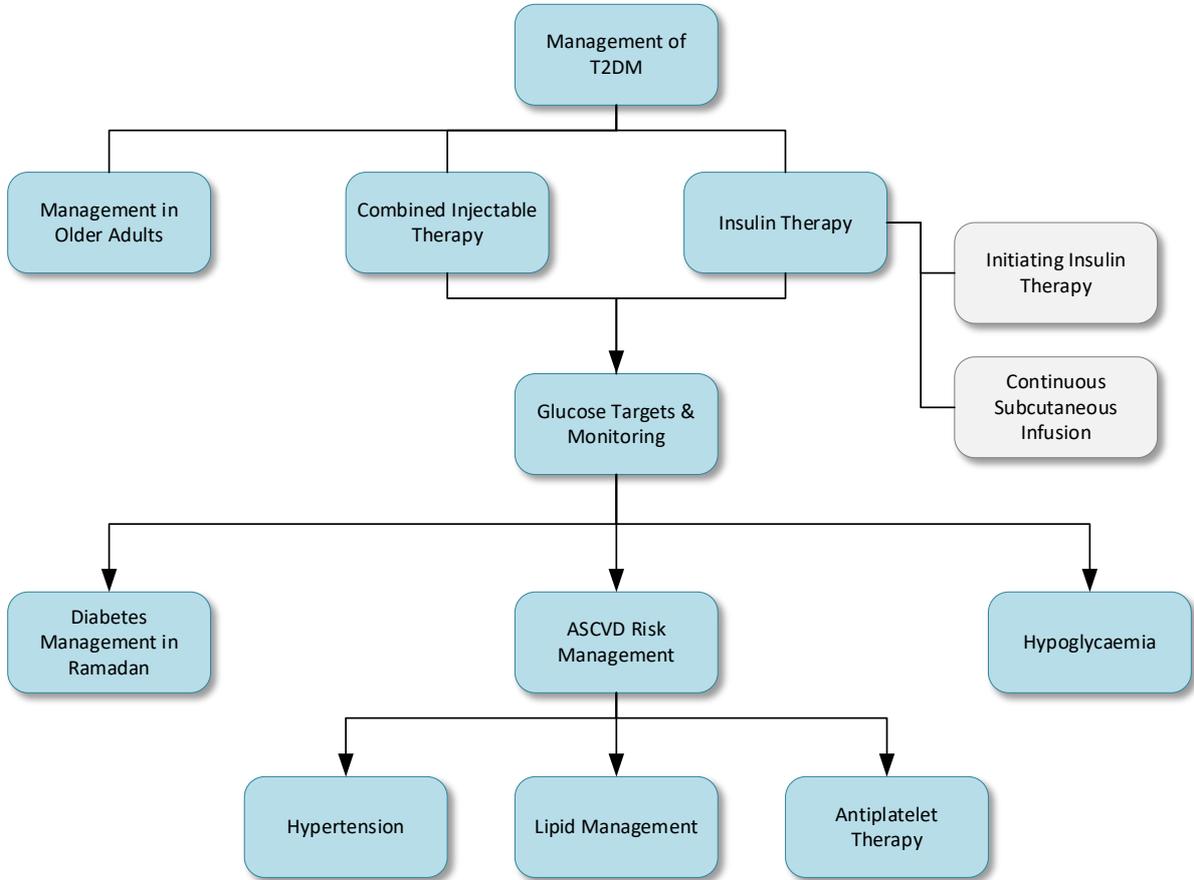
This guideline has been issued by the MOPH to define how care should be provided in Qatar. It is based upon a comprehensive assessment of the evidence as well as its applicability to the national context of Qatar. Healthcare professionals are expected to take this guidance into account when exercising their clinical judgement in the care of patients presenting to them.

The guidance does not override individual professional responsibility to take decisions which are appropriate to the circumstances of the patient concerned. Such decisions should be made in consultation with the patient, their guardians, or caregivers and should consider the individual risks and benefits of any intervention that is contemplated in the patient's care.

## 2 Management of Type 2 Diabetes in Adults Pathway

Click on a box below to see the relevant page of the Pathway.





### 3 Key Recommendations of the Guideline

The key recommendations of this guideline are:

#### Diagnosis:

- The diagnosis of T2DM requires one of the following <sup>1</sup> :
  - Fasting plasma glucose  $\geq 7.0$  mmol/L (126 mg/dL).
  - A plasma glucose of  $>11.1$  mmol/L (200 mg/dL) recorded 2 hours after the administration of 75g of anhydrous glucose dissolved in water as part of an oral glucose tolerance test (OGTT).
  - Patients who have exhibited symptoms of a hyperglycaemia with a random plasma glucose reading of  $>11.1$  mmol/L (200 mg/dL).
  - HBA<sub>1C</sub> of  $\geq 6.5\%$ .
- Pre-diabetes is diagnosed if any of the following criteria are met <sup>1</sup> :
  - Fasting plasma glucose 5.6 - 6.9 mmol/L (100 – 125 mg/dL).
  - 2-hour plasma glucose 7.8 - 11.0 mmol/L (140 – 199 mg/dL) during OGTT performed using a glucose load containing the equivalent of 75g anhydrous glucose dissolved in water.
  - HBA<sub>1C</sub> of 5.7 - 6.4%.

#### Screening:

- Consider screening for T2DM and pre-diabetes:
  - In all adults with a body mass index (BMI)  $\geq 25$  kg/m<sup>2</sup> and one additional risk factor (see *Section 4.3*) for T2DM [R-GDG].
    - Use lower BMI thresholds in South-Asian people [R-GDG].
  - If tests are negative, repeat screening every 3 years, with consideration given to more frequent testing depending on initial results <sup>1</sup> [L3, RGA].

#### Non-Pharmacological Management:

- Patients should receive care within a specialised multidisciplinary team (MDT).
- The management plan should be individualised to the patient <sup>1,2</sup> [L2].
- Diabetes self-management education (DSME) programmes should comprise of <sup>2-4</sup> :
  - Smoking cessation <sup>1,2,5</sup> .
  - Physical activity and exercise <sup>1,6-8</sup> :
    - Patients who take insulin and/or insulin secretagogues are at increased risk of hypoglycaemia as a result of exercise.
    - Intense activities may raise BG levels instead of lowering them.
  - Individualised Medical Nutrition Therapy, preferably delivered by a registered dietitian <sup>1</sup> [L1, RGA].
  - Immunisation <sup>1,9,10</sup> .
  - Psychosocial screening <sup>1</sup> [L2].
  - Weight management <sup>1</sup> .

#### Glucose Monitoring and Treatment Targets <sup>1,2</sup> :

- A reasonable HBA<sub>1C</sub> goal for non-pregnant adults is  $\leq 7.0\%$ .
- Lower HBA<sub>1C</sub> goals (e.g.  $\leq 6.5\%$ , may be considered if it can be achieved without problematic hypoglycaemia.
- A higher HBA<sub>1C</sub> goal e.g.  $\leq 8.0\%$  may be acceptable for patients with:
  - A history of severe hypoglycaemia.
  - Limited life expectancy.
  - Advanced microvascular or macrovascular complications.

- Extensive comorbidities.
- Poor engagement despite multiple attempts to improve glycaemic control.

#### **Self-Monitoring of Blood Glucose (SMBG):**

- SMBG should be used in the following groups <sup>1,2</sup> :
  - Insulin-treated diabetics.
  - Patients with a history or symptoms of hypoglycaemic episodes.
  - Patients taking medication associated with increased risks of hypoglycaemia (e.g. a sulfonylurea).
  - Patients who are pregnant or planning pregnancy.
- Patients who do not require insulin therapy may also benefit from SMBG [R-GDG].

#### **Pharmacotherapy for Type 2 Diabetes:**

- The risks and benefits of drug treatment and the options available should be discussed with the patient <sup>1,2</sup> .

#### **Monotherapy:**

- If tolerated and not contraindicated, metformin monotherapy is the usual initial treatment <sup>1</sup> [L1].
  - Stop metformin if the eGFR is  $\leq 30$  ml/min/1.73m<sup>2</sup> <sup>2,11</sup> .
  - Prescribe metformin with caution in patients at risk of a sudden deterioration in kidney function and those at risk of their eGFR falling below 45 ml/min/1.73m<sup>2</sup> <sup>2</sup> [L2].
  - Patients on metformin should be monitored for vitamin B12 deficiency <sup>5</sup> [L2]:
- If metformin is not tolerated or contraindicated, consider monotherapy with any of the following <sup>1,2</sup> :
  - Sulfonylurea (SU).
  - Thiazolidinedione (TZD).
  - Dipeptidyl peptidase-4 (DPP-4) inhibitor.
  - Sodium glucose cotransporter-2 (SGLT2) inhibitor.
  - Glucagon-like peptide-1 (GLP-1) receptor agonist.
  - Basal insulin.

#### **Dual Therapy:**

- If the patient's HBA<sub>1C</sub> target is not achieved after approximately 3 months of monotherapy or the patient's HBA<sub>1C</sub> is  $\geq 9.0\%$ , commence dual therapy <sup>1</sup> .
- Dual therapy comprises of metformin plus one of <sup>1,11</sup> :
  - SU.
  - TZD.
  - DPP-4 inhibitor.
  - SGLT2 inhibitor.
  - GLP-1 receptor agonist.
  - Basal insulin.
- An SGLT2 inhibitor or GLP-1 receptor agonist is recommended if the patient has ASCVD, established kidney disease, or heart failure <sup>1</sup> [L1, RGA].
- For patients with type 2 diabetes and diabetic kidney disease, consider use of a SGLT2 inhibitor in patients with an estimated glomerular filtration rate of  $\geq 30$  mL/min/1.73 m<sup>2</sup> and urinary albumin. $>300$  mg/g creatinine<sup>1</sup> [L1, RGA].

### Triple Therapy:

- If the HBA<sub>1C</sub> goal has not been achieved after 3 months of dual therapy, then triple therapy should be commenced. The exact regimen should be dependent on patient- and disease-specific factors<sup>1,11</sup>.
- Triple therapy comprises of any combination of the following drugs<sup>1,11</sup>:
  - Metformin plus any two of:
    - SU.
    - TZD.
    - SGLT2 inhibitor.
    - Either a DPP-4 inhibitor or a GLP-1 receptor agonist.
    - Basal insulin.
  - NB: Avoid the use of a DPP-4 inhibitor in combination with a GLP-1 receptor agonist<sup>1</sup>.
- The prescription of a GLP-1 receptor agonist to be taken in conjunction with insulin should only be given after discussion with a specialist and with long-term support from a consultant-led diabetes MDT<sup>2</sup> [**L3, RGA**].

### Combination Injectable Therapy:

- Comprises of<sup>1,11</sup>:
  - Metformin; with
  - Basal insulin; with either
  - Mealtime insulin or a GLP-1 receptor agonist.
- Consider starting combination injectable therapy when HBA<sub>1C</sub> is ≥10%, especially if symptomatic.

### Insulin Therapy:

- Insulin, with or without additional medications, should be considered in newly diagnosed patients<sup>1</sup> [**L2, RGA**]:
  - Who are markedly symptomatic and/or have elevated BG or HBA<sub>1C</sub>.
  - Do not use insulin as a threat’.
  - Do not describe insulin as a failure or punishment.
  - A self-care algorithm using SMBG for titration of insulin doses may benefit patients managed with insulin.
- Consider insulin in patients who are not newly diagnosed<sup>12</sup> [**L1**]:
  - When non-insulin anti-hyperglycaemic therapy fails to attain glycaemic control.
  - When a patient has symptomatic hyperglycaemia.
  - NB: Insulin therapy should not be delayed in patients with T2DM who are not attaining glucose goals<sup>1</sup>.
- See Section 9.5.1 on the initiation of insulin therapy.

### Referral from Primary Care to Specialist Care:

- See Section 10 for specific criteria for appropriate referral.

### Considerations for Elderly Patients:

- Older adults with diabetes should be screened and monitored for cognitive impairment<sup>1</sup> [**L2, RGA**].
- Consider screening and treating depression in older adults (more than or equal to 65 years of age) with diabetes as a high priority<sup>1</sup> [**L2**].

### Treatment Goals in the Elderly:

- In elderly patients, who are cognitively and functionally intact and have significant life expectancy, consider setting treatment targets which are similar to those used in younger adults <sup>1</sup> [L3, RGA].
- Blood glucose targets may be relaxed in elderly adults on an individual basis, e.g. in patients with <sup>1</sup> [L3, RGA]:
  - Advanced diabetes.
  - Life-limiting comorbid illness.
  - Substantial cognitive or functional impairment.

### HBA<sub>1c</sub> Targets <sup>13,14</sup> :

- A target of <7.0% should be set (if it can be achieved without problematic hypoglycaemia) in the following patients:
  - With absent, or very mild, microvascular complications; and
  - Who are free of major concurrent illnesses; and
  - Who have a life expectancy of at least 10-15 years.
- A target of <8.0% should be set in the following patients:
  - A longer duration diabetes (> 10 years).
  - With comorbid conditions.
  - Who need combination medication treatments, including insulin.
- A target of 8.0-9.0% should be set for patients with any of the following:
  - Advanced microvascular complications.
  - Major comorbid conditions.
  - Life expectancy of <5 years.

### Pharmacological Therapy in the Elderly:

- See *Section 14.6*.
- Common comorbidities to consider when managing diabetes include <sup>15</sup> [L2]:
  - Confusion, cognitive dysfunction, delirium.
  - Depression.
  - Physical disability.
  - Skin problems, e.g. infections, ulcers, delayed wound healing.
  - Hearing and vision impairment.
  - Oral health problems, teeth decay, dry mouth.

## 4 Background Information

### 4.1 Classification

The general categories of diabetes are classified as follows <sup>1,16,17</sup> :

- Type 1 diabetes mellitus (T1DM) is caused by damage to the insulin-producing beta-cells within the pancreas. This results in an absolute deficiency of insulin, requiring exogenous replacement.
- Type 2 diabetes mellitus (T2DM) is caused by a progressive reduction in insulin secretion occurring in conjunction with increasing resistance to endogenous insulin.
- Gestational diabetes mellitus (GDM) is carbohydrate intolerance that occurs in pregnant women without known pre-existing diabetes.
- Specific types of diabetes due to other causes, such as <sup>1</sup> :
  - Monogenic diabetes syndromes, e.g.:
    - Neonatal diabetes.
    - Maturity-onset diabetes of the young.
- Secondary diabetes includes:
  - Diseases of the exocrine pancreas, e.g. <sup>1,16</sup> :
    - Any process that extensively injures the pancreas can cause diabetes e.g., cystic fibrosis, haemochromatosis:
      - Pancreatitis.
      - Trauma.
      - Infection.
      - Pancreatectomy.
      - Pancreatic carcinoma.
  - Drug- or chemical-induced diabetes, e.g. <sup>1</sup> :
    - With glucocorticoid use.
    - In HIV/AIDS treatment.
    - After organ transplantation.
  - Endocrinopathies <sup>16</sup> :
    - Acromegaly.
    - Cushing's syndrome or disease.
    - Glucagonoma.
    - Pheochromocytoma.
    - Hyperthyroidism.

### 4.2 Diagnostic Criteria

#### 4.2.1 Type 2 Diabetes

The diagnosis of T2DM requires one of the following <sup>1</sup> :

- Fasting plasma glucose  $\geq 7.0$  mmol/L (126 mg/dL) (where fasting is for at least 8 hours).
  - A plasma glucose of  $>11.1$  mmol/L (200 mg/dL) recorded 2 hours after the administration of 75g of anhydrous glucose dissolved in water as part of an oral glucose tolerance test (OGTT).
  - Patients who have exhibited symptoms of a hyperglycaemia with a random plasma glucose reading of  $>11.1$  mmol/L (200 mg/dL).
- HBA<sub>1c</sub> of  $\geq 6.5\%$ :
  - Does not require the patient to fast.
  - Some haemoglobinopathies and anaemias may make interpretation difficult:

- For patients with abnormal haemoglobin but normal red blood cell turnover, an HBA<sub>1C</sub> assay without interference from abnormal haemoglobins should be used <sup>1</sup> [L2].

NB <sup>1,18</sup> :

- A second diagnostic test is required to confirm the diagnosis, unless <sup>1</sup> [L2]:
  - Patient is in hyperglycaemic crisis.
  - Patient has classic symptoms of hyperglycaemia and a random plasma glucose  $\geq 11.1$  mmol/L (200 mg/dL).
  - The results are unequivocal [R-GDG].
- If a second blood test is needed to confirm the diagnosis, the same diagnostic test should be used as previously but on a new blood sample.
- If two different diagnostic tests produce inconsistent results, the test that is above the diagnostic threshold should be repeated as soon as possible.
- If a repeat test is below the diagnostic threshold, the test should be repeated again after 3-6 months.
- Only blood glucose (BG) criteria should be used to diagnose diabetes in conditions associated with increased red blood cell turnover, e.g.:
  - Erythropoietin therapy.
  - Pregnancy (second and third trimesters).
  - Recent blood loss or transfusion.
  - Haemolysis.

#### 4.2.2 Prediabetes

Pre-diabetes is diagnosed if any of the following criteria are met <sup>1</sup> :

- Impaired fasting glucose (IFG):
  - Fasting plasma glucose 5.6 - 6.9 mmol/L (100 – 125 mg/dL)
  - Where fasting is for at least 8 hours.
- Impaired glucose tolerance (IGT):
  - 2-hour plasma glucose 7.8 - 11.0 mmol/L (140 – 199 mg/dL) during OGTT performed using a glucose load containing the equivalent of 75g anhydrous glucose dissolved in water.
- HBA<sub>1C</sub> of 5.7 - 6.4%.

#### 4.3 Risk Factors

Modifiable risk factors for T2DM include <sup>1,12,19</sup> :

- Overweight or obesity.
- Smoking.
- Physical inactivity/sedentary lifestyle.
- Sleep apnoea.
- Hypertension, dyslipidaemia or atherosclerotic cardiovascular disease (ASCVD).
- Prediabetes and/or metabolic syndrome.
- Polycystic ovary syndrome (PCOS), acanthosis nigricans, non-alcoholic fatty liver disease (NAFLD).
- Certain medications, e.g.:
  - Glucocorticoids.
  - Thiazide diuretics.
  - Antipsychotics.

Non-modifiable risk factors for T2DM include <sup>1,12</sup> :

- Age  $\geq$ 40 years.
- Family history of T2DM.
- Previous history of GDM or previous delivery of a baby weighing  $\geq$ 4 kg (9 lb).
- Member of an at-risk racial or ethnic subgroup.

#### 4.4 Epidemiology

The *International Diabetes Federation* estimates the prevalence of T2DM in Qatar (all nationalities) to be 13.5% <sup>20</sup> .

The 2012 Qatar STEPwise survey conducted with Qatari adults aged 18-64 years showed the following results amongst all the respondents <sup>21</sup> :

- 12.7% had been diagnosed with diabetes in the previous 12 months:
  - The rate was slightly higher in women at 13.3%, when compared to men at 12%.
  - There was an increase in rates with increasing age.
  - Of those diagnosed:
    - 29.3% received insulin.
    - 61.7% received oral anti-diabetic medicines.
- 16.7% had a raised BG ( $\geq$ 6.11 mmol/L (110 mg/dL)).
- 5.8% were found to have IFG.
- 66% of all respondents had a positive family history of diabetes (in parents, children, brothers and sisters).

## 5 Diabetes and Prediabetes Screening

### 5.1 Screening for Type 2 Diabetes and Pre-Diabetes in Asymptomatic People

Any of the following tests are appropriate for screening asymptomatic people for T2DM and pre-diabetes<sup>1</sup>:

- Fasting plasma glucose.
- 2-hour post-glucose level on a 75g OGTT.
- HBA<sub>1c</sub>.

Consider screening for T2DM and pre-diabetes:

- In all adults with a body mass index (BMI)  $\geq 25$  kg/m<sup>2</sup> and one additional risk factor (see *Section 4.3*) for T2DM [**R-GDG**]:
  - Use lower BMI thresholds in South-Asian people [**R-GDG**].
- If tests are negative, repeat screening every 3 years, with consideration given to more frequent testing depending on initial results <sup>1</sup> [**L3, RGA**].

## 6 Clinical Assessment

In patients diagnosed with T2DM, a comprehensive evaluation should be carried out at the initial visit and includes <sup>1</sup> :

- Diagnosis and diabetes classification confirmation.
- A full history, examination and appropriate investigations to review all co-morbidities. A review of prior treatments and risk factor control in patients with established diabetes.
- The full involvement of the fully-informed patient to prepare an appropriate care plan.

### 6.1 Medical History

A comprehensive medical history should be taken, including <sup>1</sup> [L2]:

- Confirmation of the diagnosis.
- Age and features of onset of diabetes, e.g.:
  - Asymptomatic laboratory finding; or
  - Symptomatic presentation.
- Review of previous treatment regimens, if any; and response to therapy.
- Results of glucose monitoring.
- Diet and physical activity assessment.
- History of smoking, alcohol consumption, substance use.
- History of acute complications e.g.:
  - Diabetic ketoacidosis (DKA):
  - Hypoglycaemia.
  - Hyperglycaemic hyperosmolar state.
- History of microvascular complications:
  - Retinopathy.
  - Nephropathy.
  - Neuropathy
  - Diabetic foot problems.
  - Erectile dysfunction.
  - Gastroparesis.
- History of macrovascular complications:
  - Coronary artery disease.
  - Cerebrovascular disease.
  - Peripheral vascular disease.
- Diabetes education, self-management, and support history and needs.

Comorbidities for assessment and consideration in T2DM include <sup>1</sup> [L2]:

- Hypertension.
- Dyslipidaemia.
- Obesity.
- Fatty liver disease.
- Heart failure.
- Obstructive sleep apnoea.
- Low testosterone in men.
- Depression.

## 6.2 Examination

A full general physical examination should be performed at the first visit, addressing the following in particular <sup>1</sup> [L2]:

- BMI.
- Blood pressure (BP).
- Skin examination, e.g.:
  - Acanthosis nigricans.
  - Injection sites, if any.
- Comprehensive foot examination:
  - Inspection (particularly for deformities, ulcers, pre-ulcerative signs, inadequate footwear and poor hygiene).
  - Palpation of dorsalis pedis and posterior tibialis pulses.
  - Patellar and Achilles tendon reflexes.
  - Determination of proprioception, vibration, pinprick and monofilament sensation.

## 6.3 Laboratory Evaluation

Laboratory evaluation comprises of <sup>1</sup> :

- HBA<sub>1C</sub>, if there are no results available from the past 3 months <sup>1</sup> [L2].
- If not performed or available within the past year perform the following <sup>1</sup> [L2]:
  - Fasting lipid profile.
  - Liver function tests.
  - Spot urinary albumin-creatinine ratio (ACR).
  - Serum creatinine and estimated glomerular filtration rate (eGFR).
  - Thyroid stimulating hormone in patients with dyslipidaemia or in women aged over 50 years.
  - Vitamin B12 level for patients taking metformin.

## 7 Management of Confirmed Type 2 Diabetes

### 7.1 Multidisciplinary Team Approach

Patients should receive care within a specialised multidisciplinary team (MDT), which includes the following [R-GDG]:

- Physicians.
- Nurses.
- Diabetes educator.
- Dietitians.
- Podiatrists.
- Clinical pharmacists, if available.
- Other professionals which may form part of the team may include:
  - Exercise therapists.
  - Mental health professionals (psychologists).
  - Ophthalmologists.

The management plan should be individualised to the patient <sup>1,2</sup> [L2]:

- Taking patient and family's needs, circumstances and preferences into account.
- People with diabetes must also take an active role in their care.
- Health care providers must take into account:
  - The patient's age.
  - Comorbidities and diabetes-related complications.
  - Life expectancy.
  - Working conditions.
  - Lifestyle choices.
  - Social situation.
  - Cultural factors.
  - Risks of polypharmacy.

### 7.2 Referrals for Initial Care Management

If unavailable within the MDT, consider referral for the following speciality services, after initial diagnosis <sup>1</sup> [L2]:

- Ophthalmologist for dilated eye exam and annual review thereafter.
- Diabetes educator for structured education and support (see *Section 7.3*)
- Registered dietitian for Medical Nutrition Therapy (MNT) (see *Section 7.4*).
- Mental health professional, if indicated (see *Section 7.6*).

### 7.3 Structured Diabetes Education and Support

All patients with T2DM should be provided with a structured education programme to enable them to fully understand how to manage their condition and sustain the skills and behaviours needed.

Diabetes self-management education (DSME) programmes for adults with T2DM should <sup>2-4</sup> [L2]:

- Involve care plans, which are created in conjunction with the patient and offered at time of diagnosis with a formal annual review and reinforcement.
- Be discussed with all members of a specialist diabetes MDT who are familiar with the locally available patient education programmes.

- Involve carers and family as needed.
- Include the following:
  - Quality assurance:
    - Any DSME programme should be reviewed by independent assessors with training to do so and should be measured against standardised criteria that ensure consistency (e.g. *Diabetes Education and Self-Management for Ongoing and Newly Diagnosed* (DESMOND))<sup>3,4</sup>.
  - A structured curriculum.
  - Specific aims and learning objectives.
  - Written education materials.
  - Outcomes that are audited regularly.
  - Group education as the preferred option:
    - An alternative of an equal standard should be provided where the patient is unwilling or unable to participate in group education

### 7.3.1 Smoking Cessation

All patients should be encouraged not to use tobacco products, including cigarettes and shisha<sup>1,2,5</sup> [**L1, RGA**]:

- Include smoking cessation counselling as well as other methods of treatment routinely during diabetes care<sup>1</sup> [**L1, RGA**].

### 7.3.2 Physical Activity and Exercise

Advise patients on physical activity levels<sup>1,6,7</sup> [**L2**]:

- The exercise programme should be individualised to the patient.
- Encourage patients to set short and long-term goals.
- Adults with diabetes should be advised to<sup>7</sup>:
  - Reduce sedentary time, and break up long periods (i.e. >90 mins) spent sitting.
  - Undertake basic activity for >30 mins every day.
    - Basic activity is defined as exercise that raises the heart and respiratory rates but the patient is still able to talk.
  - Undertake aerobic fitness exercise for 20-60 mins over a 24 hour period, 3-5 times per week.
    - Aerobic fitness is defined as exercise that raises the heart and respiratory rates until the patient is out of breath and unable to talk.
  - Undertake strength exercises, 2-3 times per week, until near muscle exhaustion is reached.

#### 7.3.2.1 Contraindications to Physical Activity

Contraindications to certain types of exercise should be assessed for, including<sup>1</sup> [**L2**]:

- Hypertension.
- Coronary artery disease.
- Autonomic neuropathy.
- Peripheral neuropathy.
- Foot lesions.
- Untreated proliferative retinopathy.
- Albuminuria and nephropathy.

### 7.3.2.2 Hypoglycaemia Risk

Risk of hypoglycaemia <sup>1,6-8</sup> :

- Patients who take insulin and/or insulin secretagogues are at increased risk of hypoglycaemia as a result of exercise.
- Medication dose or carbohydrate intake must be altered in line with the amount of physical exercise if pre-exercise glucose levels are <5.6 mmol/L (100 mg/dL).
- Intense activities may raise BG levels instead of lowering them.
- Further risk factors for exertional hypoglycaemia include:
  - Prolonged exercise time.
  - Exercise intensity the patient is not used to.
  - Inadequate supply of energy in relation to blood insulin levels.
- Close blood sugar monitoring pre- and post-exercise can minimise the risk of post exertional hypoglycaemia:
  - Snacks should be consumed prior to exercise if BG levels are falling.
- Patients should carry a readily absorbable source of carbohydrates when exercising, including sporadic housework or outdoor work.
- It may be useful to alter the insulin dose on days with planned exercise, especially in patients with a history of exercise-induced hypoglycaemia and well-controlled diabetes.

## 7.4 Medical Nutrition Therapy

Each member of the healthcare team should be knowledgeable about the principles of MNT and encourage their implementation <sup>1</sup> .

All patients with diabetes should receive individualised MNT, preferably delivered by a registered dietitian <sup>1</sup> [**L1, RGA**]. This should include the following <sup>1</sup> :

- Effectiveness of nutrition therapy.
- Energy balance.
- Eating patterns and both micronutrient and macronutrient distribution.
- If alcohol is consumed, discourage excessive intake.

## 7.5 Immunisation

All adults with T2DM should receive the routine vaccinations in line with general recommendations for the adult population <sup>1</sup> . In addition, the MOPH Public Health department recommends the following <sup>9,10</sup> :

- Annual influenza vaccination prior to the start of the influenza season.
- Pneumococcal vaccination:
  - 1 dose of PCV13.
  - Up to 3 doses of PPSV23, with the final dose given after the age of 65 years.

## 7.6 Psychosocial Care

Consider the patient's psychosocial circumstances while managing patients with T2DM <sup>1</sup> :

- Psychosocial screening, includes consideration of <sup>1</sup> [**L2**]:
  - Attitude about the illness.
  - Expectations surrounding medical management and outcomes.

- Mood.
- Quality of life.
- Resources:
  - Financial.
  - Social.
  - Emotional.
- Psychiatric history.
- Routinely screen for psychosocial problems, using the PHQ-2 questions <sup>1</sup> :
  - If positive, assess for depression using the PHQ-9 scoring system.

Referral to an appropriate mental health specialist should be considered if <sup>1</sup> :

- Self-harm or suicidal ideation.
- Gross disregard for the medical regimen.
- Depression.
- Debilitating anxiety (alone or with depression).
- Indications of an eating disorder.
- Cognitive function that significantly impairs judgement.

Encourage patients to join the *Qatar Diabetes Association* to promote a healthy lifestyle, emotional support and improve motivation [**R-GDG**].

## 7.7 Weight Management

Assess BMI <sup>1,12</sup> :

- Overweight and obesity should be diagnosed using BMI:
  - Overweight: 25 -30 kg/m<sup>2</sup>.
  - Obese: ≥30 kg/m<sup>2</sup>.
- Assess on yearly basis and document the result in the medical record <sup>1</sup> [**L2**].

Consider measuring waist circumference <sup>12</sup> [**L3, RGA**]:

- In patients with a BMI of 25-35 kg/m<sup>2</sup>.
- Patients with values of >102 cm (40 in) for males; and >88 cm (35 in) for females are at increased risk of metabolic disease.

Weight management:

- Clinicians should determine each patient's willingness to achieve weight loss <sup>1</sup> [**L2**].
- Strategies include <sup>1</sup> [**L2**]:
  - Diet.
  - Physical activity.
  - Behavioural therapy.
  - Pharmacological therapy:
    - May be used in combination to diet, physical activity, and behavioural therapy for carefully selected patients.
  - Bariatric surgery.
    - May be used in combination to diet, physical activity, and behavioural therapy for carefully selected patients.

## 8 Glucose Monitoring and Treatment Targets

### 8.1 HBA<sub>1C</sub> Testing and Goals

HBA<sub>1C</sub> testing<sup>1</sup> :

- Should be carried out routinely at initial assessment and as part of ongoing management.
- At least twice a year <sup>1,2</sup> :
  - In patients who are achieving their treatment goals; and
  - Who have stable glycaemic control.
  - Every 3-6 months until HBA<sub>1C</sub> is stable on stable treatment, tailored to individual needs.
  - Every 6 months once both HBA<sub>1C</sub> measurements and BG lowering therapy are stable.
- Quarterly in patients who <sup>1</sup> :
  - Have undergone a change in therapy; or
  - Who are not meeting their glycaemic targets.
- Consider point of care testing, if available, in order to provide quicker treatment changes <sup>1</sup> [**L3, RGA**].

Consider seeking advice from a specialist diabetologist or the clinical biochemistry team, if <sup>2</sup> :

- HBA<sub>1C</sub> monitoring is invalid, e.g. due to disturbed erythrocyte turnover or abnormal haemoglobin type; or
- There are unexplained discrepancies between HBA<sub>1C</sub> and other glucose measurements.

HBA<sub>1C</sub> targets<sup>1,2</sup> :

- Involve patients in decisions and individualise HBA<sub>1C</sub> targets.
- Patients should be encouraged to achieve their individual target unless the pursuit of this target adversely affects their quality of life.
- A reasonable HBA<sub>1C</sub> goal for non-pregnant adults is ≤7.0%.
- Lower HBA<sub>1C</sub> goals (e.g. ≤6.5%, may be considered if it can be achieved without problematic hypoglycaemia.
- A higher HBA<sub>1C</sub> goal e.g. ≤8.0% may be acceptable for patients with:
  - A history of severe hypoglycaemia.
  - Limited life expectancy.
  - Advanced microvascular or macrovascular complications.
  - Extensive comorbidities.
  - Poor engagement despite multiple attempts to improve glycaemic control.
- Clinicians should be aware that there are other causes of low HBA<sub>1C</sub> level, such as:
  - Deteriorating renal function.
  - Sudden weight loss.

### 8.2 Self-Monitoring of Blood Glucose

Self-monitoring of blood glucose (SMBG) <sup>12</sup> :

- SMBG may provide feedback about the effects of their lifestyle and pharmacologic therapy.
- Patients who do not require insulin therapy may also benefit from SMBG [**R-GDG**].
- Frequency of testing should be individualised to the patient.
- SMBG should be used in the following groups <sup>1,2</sup> :
  - Insulin-treated diabetics.
  - Patients with a history or symptoms of hypoglycaemic episodes.
  - Patients taking medication associated with increased risks of hypoglycaemia (e.g. a sulfonylurea).
  - Patients who are pregnant or planning pregnancy.

- Consider short-term SMBG <sup>2</sup> [**L3, RGA**]:
  - When starting treatment with oral or intravenous corticosteroids; or
  - To confirm suspected hypoglycaemia.

SMBG in patients using insulin <sup>12</sup> :

- SMBG should be used by patients on insulin <sup>12</sup> [**L2**]:
  - Minimum twice a day, and
  - Ideally before insulin injections.
  - More frequent monitoring after meals, or in the middle of the night, may be needed in patients:
    - With frequent hypoglycaemia.
    - Suspected hypoglycaemia unawareness.
    - Those not yet achieving their HBA<sub>1C</sub> target.
- Should be used in all patients on intensive insulin regimens <sup>1,12</sup> [**L2**]:
  - Before meals and snacks.
  - Occasionally post-prandially if hypoglycaemia is frequent.
  - At bedtime.
  - Before exercise.
  - When the patient suspects low BG.
  - After treating low BG until they are normoglycaemic.
  - Before critical tasks such as driving.

Assessment of SMBG in all patients who are testing their BG <sup>2</sup> [**L2**]:

- Should be carried out at least annually as part of the annual review of the patient.
- Should include an assessment of:
  - The patient's self-monitoring skills.
  - The quality and frequency of testing.
  - Checking that the patient knows how to interpret the BG results and what action to take.
  - The impact on the patient's quality of life.
  - The continued benefit to the patient.
  - The equipment used.

### 8.3 Continuous Glucose Monitoring

Continuous glucose monitoring (CGM) <sup>1,2,12,18</sup> :

- Is not routinely used for people with T2DM.
- May be used in addition to SMBG in patients with hypoglycaemia unawareness or frequent hypoglycaemic episodes.
- Should be considered in patients using basal-bolus therapy <sup>12</sup> [**L2**].
- Before prescribing CGM <sup>1</sup> [**L3, RGA**]:
  - Assess the patient's readiness for continuing to use CGM.
  - Educate and support the patient in order to optimise CGM implementation and ongoing use.

## 9 Pharmacotherapy for Type 2 Diabetes

The risks and benefits of all drug treatment should be discussed with patients to allow them to make an informed decision<sup>1,2</sup>. The choice of drug should be based on the following<sup>1,2</sup> [L2, RGA]:

- Safety and tolerability of the drug.
- The patient's individual clinical circumstances, e.g.:
  - Comorbidities.
  - Risk of polypharmacy.
- The patient's individual employment circumstances, e.g. whether:
  - Driving for work.
  - Working at heights.
  - Operating heavy machinery.
- Relative cost:
  - If two drugs in the same class are appropriate, choose the option with the lowest cost.

The table on the next page outlines the main points of comparison between the principal drugs used in the pharmacological management of T2DM.

Prescribers should ensure they refer to the *Qatar National Formulary* for the most up-to-date information [R-GDG].

Class	Compound	Physiological action	Advantages	Disadvantages	Safety and monitoring
<b>Biguanides</b>	<ul style="list-style-type: none"> <li>Metformin.</li> </ul>	<ul style="list-style-type: none"> <li>Decreases hepatic glucose production.</li> <li>Decreases intestinal absorption of glucose.</li> <li>Potentiates insulin action.</li> </ul>	<ul style="list-style-type: none"> <li>Low risk of hypoglycaemia.</li> <li>Reduced cardiovascular events.</li> <li>Weight-neutral.</li> </ul>	<ul style="list-style-type: none"> <li>Gastrointestinal side effects (diarrhea, abdominal cramping).</li> <li>Lactic acidosis.</li> <li>Vitamin B12 deficiency.</li> <li>Multiple contraindications: <ul style="list-style-type: none"> <li>Chronic kidney disease.</li> <li>Dehydration etc.</li> </ul> </li> </ul>	<ul style="list-style-type: none"> <li>Monitor creatinine at least annually.</li> <li>Check vitamin B12 and folate levels in anaemic patients.</li> <li>Stop metformin if eGFR is <math>\leq 30</math> ml/min/1.73m<sup>2</sup>.</li> <li>Hold at least 24 hours before and 48 hours after IV iodinated contrast media.</li> <li>Use cautiously in patients with: <ul style="list-style-type: none"> <li>Liver dysfunction.</li> <li>Heart failure.</li> <li>Alcohol abuse,</li> <li>Severe pulmonary disease.</li> <li>Age &gt; 80 years.</li> </ul> </li> </ul>
<b>Sulfonylureas</b>	2 <sup>nd</sup> Generation: <ul style="list-style-type: none"> <li>Glyburide/glibenclamide.</li> <li>Glipizide.</li> <li>Glicazide.</li> <li>Glimepiride.</li> </ul>	<ul style="list-style-type: none"> <li>Increased insulin secretion.</li> </ul>	<ul style="list-style-type: none"> <li>Reduced microvascular risk.</li> </ul>	<ul style="list-style-type: none"> <li>Increased risk of hypoglycemia.</li> <li>Weight gain.</li> <li>Frequent dosing schedule.</li> </ul>	<ul style="list-style-type: none"> <li>Use cautiously in the following: <ul style="list-style-type: none"> <li>Renal or hepatic impairment.</li> <li>Known hypersensitivity.</li> </ul> </li> <li>Glyburide/glibenclamide is not recommended in the elderly.</li> </ul>
<b>Meglitinides (glinides)</b>	<ul style="list-style-type: none"> <li>Repaglinide.</li> <li>Nateglinide.</li> </ul>	<ul style="list-style-type: none"> <li>Increased insulin secretion.</li> </ul>	<ul style="list-style-type: none"> <li>Reduces postprandial glycaemic excursions.</li> <li>Flexible dosing.</li> </ul>	<ul style="list-style-type: none"> <li>Weight gain.</li> <li>Frequent dosing schedule</li> </ul>	<ul style="list-style-type: none"> <li>Use cautiously in renal or hepatic impairment.</li> </ul>
<b>Thiazolidinedione (TZD)</b>	<ul style="list-style-type: none"> <li>Pioglitazone.</li> </ul>	<ul style="list-style-type: none"> <li>Increases peripheral insulin sensitivity.</li> </ul>	<ul style="list-style-type: none"> <li>Low risk of hypoglycemia.</li> <li>Increases HDL-C.</li> <li>Reduces triglycerides.</li> <li>Once daily dosing.</li> </ul>	<ul style="list-style-type: none"> <li>Weight gain.</li> <li>Associated with: <ul style="list-style-type: none"> <li>Oedema.</li> <li>Heart failure.</li> <li>Fractures.</li> <li>Diabetic macular oedema.</li> <li>Bladder cancer.</li> </ul> </li> </ul>	<ul style="list-style-type: none"> <li>Contraindicated in patients with heart failure or history fo bladder cancer.</li> <li>Monitor for signs and symptoms of fluid retention.</li> <li>Periodic ALT and eye examination required.</li> </ul>
<b>DPP-4 inhibitors</b>	<ul style="list-style-type: none"> <li>Sitagliptin.</li> <li>Vildagliptin.</li> <li>Saxagliptin.</li> <li>Linagliptin.</li> </ul>	<ul style="list-style-type: none"> <li>Increases insulin secretion.</li> <li>Decreases glucagon secretion.</li> </ul>	<ul style="list-style-type: none"> <li>Low risk of hypoglycemia.</li> <li>Well tolerated.</li> <li>Not associated with weight gain.</li> </ul>	<ul style="list-style-type: none"> <li>Angioedema/urticaria and other immune-mediated dermatological effects.</li> </ul>	<ul style="list-style-type: none"> <li>Adjustments are needed for renal dysfunction (sitagliptin and saxagliptin).</li> <li>Monitor serum creatinine prior to and after initiation of therapy and then periodically thereafter.</li> <li>Saxagliptin dose adjustment is required with the use of strong CYP450 3A4/5 inhibitors.</li> <li>Long term safety is unknown.</li> </ul>

Class	Compound	Physiological action	Advantages	Disadvantages	Safety and monitoring
<b>SGLT2 inhibitors</b>	<ul style="list-style-type: none"> <li>• Canagliflozin.</li> <li>• Dapagliflozin.</li> </ul>	<ul style="list-style-type: none"> <li>• Blocks glucose reabsorption by the kidney, increasing glycosuria.</li> </ul>	<ul style="list-style-type: none"> <li>• Low risk of hypoglycemia</li> <li>• Weight loss.</li> <li>• Reduces BP.</li> <li>• Effective at all stages of T2DM.</li> </ul>	<ul style="list-style-type: none"> <li>• Polyuria</li> <li>• Volume depletion/ hypotension /dizziness.</li> <li>• Increases LDL-C.</li> <li>• Increases creatinine (transient).</li> </ul>	<ul style="list-style-type: none"> <li>• Increased risk of genital mycotic infections.</li> <li>• Increased risk of hypoglycaemia when used with insulin and insulin secretagogues.</li> <li>• Hypersensitivity has been documented.</li> <li>• Not recommended for treatment of patients with: <ul style="list-style-type: none"> <li>○ eGFR <math>\leq</math>30 ml/min/1.73m<sup>2</sup> or End stage renal failure.</li> </ul> </li> </ul>
<b>GLP-1 receptors agonist</b>	<ul style="list-style-type: none"> <li>• Exenatide.</li> <li>• Liraglutide.</li> <li>• Lixisenatide.</li> <li>• Dulaglutide.</li> </ul>	<ul style="list-style-type: none"> <li>• Increases insulin secretion.</li> <li>• Decreased glucagon secretion.</li> <li>• Slow gastric emptying</li> <li>• Increased satiety</li> </ul>	<ul style="list-style-type: none"> <li>• Low risk of hypoglycemia.</li> <li>• Weight loss.</li> <li>• Reduces postprandial glucose excursions.</li> <li>• Reduces some Cardiovascular risk factors.</li> </ul>	<ul style="list-style-type: none"> <li>• Gastrointestinal side effects: e.g. nausea/vomiting/diarrhea.</li> <li>• Increased heart rate.</li> <li>• Injectable.</li> </ul>	<ul style="list-style-type: none"> <li>• Contraindicated in patients with gastroparesis or severe gastrointestinal disease.</li> <li>• Liraglutide contraindicated in patients with a personal or family history of medullary thyroid carcinoma or Multiple Endocrine Neoplasia Type 2.</li> <li>• Use with caution in patients with moderate-severe renal impairment.</li> </ul>
<b>Insulin</b>	See Table 9.5	<ul style="list-style-type: none"> <li>• Increases glucose disposal.</li> <li>• Reduces hepatic glucose production.</li> </ul>	<ul style="list-style-type: none"> <li>• Nearly universal response.</li> <li>• Theoretically unlimited efficacy.</li> <li>• Reduces microvascular risk.</li> </ul>	<ul style="list-style-type: none"> <li>• Risk of hypoglycemia.</li> <li>• Weight gain.</li> <li>• Injectable.</li> </ul>	<ul style="list-style-type: none"> <li>• Regular SMBG is advised especially those at risk of hypoglycaemia.</li> </ul>

**Table A1:** Comparison of Drugs Used for Glycaemic Control in T2DM [Adapted from <sup>1,11,22</sup>].

## 9.1 Monotherapy

If tolerated and not contraindicated, metformin monotherapy is the usual initial treatment <sup>1</sup> [L1]:

- The dose of metformin (standard-release formulation) should be increased slowly over several weeks to reduce possible gastrointestinal side effects <sup>2</sup> [L2]:
  - Modified-release metformin should be considered in patients who experience gastrointestinal side effects <sup>2</sup> [L2, RGA].
- Review the dose of metformin if the eGFR is  $<45 \text{ mL/min/1.73m}^2$  <sup>2</sup> [L2].
- Stop metformin if the eGFR is  $\leq 30 \text{ mL/min/1.73m}^2$  <sup>2,11</sup>.
- Prescribe metformin with caution in patients at risk of sudden deterioration in kidney function and those at risk of eGFR falling  $<45 \text{ mL/min/1.73m}^2$  <sup>2</sup> [L2].
- Patients on metformin should be monitored for vitamin B12 deficiency <sup>5</sup> [L2]:
  - Vitamin B12 supplements should be given to patients with deficiency.

If metformin is not tolerated or contraindicated <sup>1,2</sup> :

- Consider monotherapy with any of the following:
  - Sulfonylurea (SU).
  - Thiazolidinedione (TZD).
  - Dipeptidyl peptidase-4 (DPP-4) inhibitor.
  - Sodium glucose cotransporter-2 (SGLT2) inhibitor.
  - Glucagon-like peptide-1 (GLP-1) receptor agonist.
  - Basal insulin.

## 9.2 Dual Therapy

If the patient's HBA<sub>1C</sub> target is not achieved after approximately 3 months of monotherapy or the patient's HBA<sub>1C</sub> is  $\geq 9.0\%$ , commence dual therapy <sup>1</sup>. The choice of drugs dependent on variety of patient- and disease-specific factors <sup>1,2,11</sup>.

Dual therapy comprises of <sup>1,11</sup> :

- Metformin plus one of:
  - SU.
  - TZD.
  - DPP-4 inhibitor.
  - SGLT2 inhibitor.
  - GLP-1 receptor agonist.
  - Basal insulin.

An SGLT2 inhibitor or GLP-1 receptor agonist is recommended if the patient has ASCVD, established kidney disease, or heart failure <sup>1</sup> [L1, RGA].

For patients with type 2 diabetes and diabetic kidney disease, consider use of a SGLT2 inhibitor in patients with an estimated glomerular filtration rate of  $\geq 30 \text{ mL/min/1.73 m}^2$  and urinary albumin  $>300 \text{ mg/g creatinine}$  <sup>1</sup> [L1, RGA].

## 9.3 Triple Therapy

If the HBA<sub>1C</sub> goal has not been achieved after 3 months of dual therapy, then triple therapy should be commenced. The exact regimen should be dependent on patient and disease-specific factors <sup>1,11</sup>.

Triple therapy comprises of any combination of the following drugs <sup>1,11</sup> :

- Metformin plus any two of:
  - SU.
  - TZD.
  - SGLT2 inhibitor.
  - Either a DPP-4 inhibitor or a GLP-1 receptor agonist.
  - Basal insulin.
- NB: Do not use a DPP-4 inhibitor in combination with a GLP-1 receptor agonist <sup>1</sup>.
- The prescription of a GLP-1 receptor agonist to be taken in conjunction with insulin should only be given after discussion with a specialist and with long-term support from a consultant-led diabetes MDT <sup>2</sup> [**L3, RGA**].

Other medications <sup>1</sup> :

- Fast-acting secretagogues (meglitinides) may be an alternative to sulfonylureas in patients:
  - With irregular meal schedules; or
  - Who develop late post-prandial hypoglycaemia with sulfonylureas.
- An alternative may be alpha-glucosidase inhibitors; however, these are generally not preferred due to side effects, modest efficacy, and/or frequency of administration [**R-GDG**].

#### 9.4 Combination Injectable Therapy

Combination injectable therapy <sup>1,11</sup> :

- Comprises of:
  - Metformin; with
  - Basal insulin; with either
  - Mealtime insulin or a GLP-1 receptor agonist.
- Consider starting combination injectable therapy when HBA<sub>1c</sub> is ≥10%, especially if symptomatic.

#### 9.5 Insulin Therapy

Insulin, with or without additional medications, should be considered in newly diagnosed patients<sup>1</sup>[**L2, RGA**]:

- Who are markedly symptomatic and/or have elevated BG or HBA<sub>1c</sub>.
- Do not use insulin as a threat'
- Do not describe insulin as a failure or punishment
- A self-care algorithm using SMBG for titration of insulin doses may benefit patients managed with insulin.

Consider insulin in patients who are not newly diagnosed <sup>12</sup> [**L1**]:

- When non-insulin anti-hyperglycaemic therapy fails to attain glycaemic control.
- When a patient has symptomatic hyperglycaemia.
- NB: Insulin therapy should not be delayed in patients with T2DM who are not attaining glucose goals <sup>1</sup>.

Use a structured programme when starting insulin treatment, including <sup>2</sup>:

- Injecting site training, including rotation of site to avoid repeated injections at the same point within a site.
- Dose titration to target levels.
- SMBG.
- Dietary understanding.

- Guidance on driving.
- Management of hypoglycaemia.
- Management of acute changes in plasma glucose control.
- Continuing telephone support.
- Support and advice from appropriate healthcare professionals trained and experienced in diabetes management.

Insulin Type	Trade Name	Onset of Action	Duration of Action
<b>Rapid-Acting Analogues</b>			
Lispro	<i>Humalog</i>	5-15 minutes	2-4 hours
Aspart	<i>Novorapid</i>		
Glulisine	<i>Apidra</i>		
<b>Short-Acting</b>			
Human Regular	<i>Actrapid</i>	30 minutes	5-8 hours
<b>Intermediate- Acting</b>			
Human NPH	<i>Isophane</i>	1-3 hours	12-18 hours
<b>Basal Insulin Analogues</b>			
Glargine	<i>Lantus</i>	1-2 hours	20-24 hours
Glargine U300	<i>Toujeo</i>	1-2 hours	Up to 36 hours
Detemir	<i>Levemir</i>	1-3 hours	6-24 hours
Degludec	<i>Tresiba</i>	1-2 hours	up to 42 hours
<b>Premixed (Several Types)</b>			
Human regular/NPH	<i>Human Mixtard 30/70</i>	Variable	Variable
Lispro/lispro protamine	<i>Humalog Mix 25/75</i>	Variable	Variable
Lispro/lispro protamine	<i>Humalog Mix 50/50</i>	Variable	Variable
Aspart/aspart protamine	<i>NovoMix 30/70</i>	Variable	Variable
Aspart/aspart protamine	<i>NovoMix 50/50</i>	Variable	Variable

NPH: Neutral protamine Hagedorn

**Table 9.5:** Common Insulin Options Available [R-GDG].

See *Appendix A* for a list of all insulin aspart preparations currently registered in Qatar.

### 9.5.1 Initiating Insulin Therapy

#### Step 1: Basal insulin<sup>1</sup>:

- Initially prescribe 10 Units/day (or 0.1-0.2 Units/kg/day).
- Adjust by 2-4 Units (or 10-15%), once or twice weekly to reach the fasting blood glucose (FBG) target.
  - The cause of a hypoglycaemic episode should be determined and the corresponding insulin dose should be reduced by 2-4 Units (or 10-20%).

### **Step 2: Consider additional insulin injections or GLP-1 trial <sup>1</sup> :**

If SMBG is not controlled after FBG target has been reached (or if the dose is >0.5 Units/kg/day):

- Treat post-prandial glucose excursions with mealtime insulin with one of the following:
  - Option 1: Step-wise introduction of bolus insulin with:
    - Addition of a rapid-insulin injection before the main meal, then prior to breakfast and then prior to other meals.
  - Option 2: Consider changing to a premixed insulin twice a day.
  - Move to Step 3 (see below).
- Use of a GLP-1 receptor agonist with insulin, should only be offered on specialist advice and with the ongoing support from a consultant-led MDT <sup>2</sup> [L3, RGA].

#### **Option 1: Step-wise introduction of bolus insulin:**

Add a rapid-insulin injection before the largest main meal of the day, followed by an injection prior to breakfast and then an injection before any other meal of the day <sup>1</sup> :

- For each injection, start with 4 Units, (or 0.1 Units/kg), or 10% of the basal dose:
  - If HBA<sub>1C</sub> is <8.0%, consider decreasing the basal dose by the same amount.
- Increase the dose by 1-2 Units (or 10-15%) once to twice weekly until the BG target is reached.
  - If hypoglycaemia occurs, determine and address the cause, and decrease the corresponding dose by 2-4 Units (or 10-20%).
- If not controlled, move to Step 3.

#### **Option 2: Change to a premixed insulin twice daily <sup>1</sup> :**

- Divide the current basal dose into either:
  - 2/3 in the morning, 1/3 in the evening; or
  - 1/2 in the morning, 1/2 in the evening.
- Increase the dose by 1-2 Units (or 10-15%), once to twice weekly until the BG target is reached.
  - If hypoglycaemia occurs, determine and address the cause, and decrease the corresponding dose by 2-4 Units (or 10-20%).
- If not controlled, move to Step 3.

### **Step 3: Changing to a basal-bolus regimen <sup>1</sup> :**

- Add ≥2 rapid insulin injections before meals.
- Administer 4 Units, (or 0.1 Units/kg), or 10% of the basal dose per meal:
  - If HBA<sub>1C</sub> is <8.0%, consider decreasing basal insulin by the same amount.
- Increase the dose by 1-2 Units (or 10-15%) once to twice weekly until the BG target is reached.
  - If hypoglycaemia occurs, determine and address the cause, and decrease the corresponding dose by 2-4 Units (or 10-20%).

## **9.5.2 Continuous Subcutaneous Insulin Infusion**

Continuous subcutaneous insulin infusion (CSII) <sup>12</sup> [L1]:

- Patients with T2DM who are insulin-treated, are candidates for CSII, if all other measures have failed to adequately improve glycaemic control.
- CSII should only be used in patients who are knowledgeable and motivated in self-care, including insulin adjustment.
- Patients using CSII must receive DSME and be periodically re-evaluated.
- For patients who are at risk of hypoglycaemia, consider sensor-augmented CSII including those with a threshold-suspend function.

- Prescribing physicians must have expertise in CSII therapy, which should be started in a specialist centre [R-GDG]:

### 9.5.3 Additional Considerations

Additional considerations when prescribing insulin <sup>2,5</sup> :

- A GLP-1 mimetic should only be given in addition to insulin after specialist input and with ongoing support from a consultant-led MDT <sup>2</sup> [L3, RGA].
- Metformin should be continued when commencing insulin therapy, contraindications or intolerance:
  - Review the continued need for other BG lowering therapies.
- Patients receiving insulin therapy typically gain around 1-3 kg of weight in comparison to those receiving other agents.

## 9.6 Medication Adjustment

Medication adjustments <sup>8</sup> :

- A thorough review of BG patterns throughout the day may indicate vulnerable periods that warrant medication adjustments.
- Adjustments include <sup>8</sup> :
  - Substitution of regular insulin by rapid-acting insulin analogues.
  - Substitution of intermediate-acting insulin by basal insulin analogues.
  - CSII offers flexibility for adjusting the dose and dosing pattern in order to counteract iatrogenic hypoglycaemia.
- Sulfonylureas have a greater risk of hypoglycaemia than any other currently available oral medication <sup>21</sup> :
  - In cases of troublesome hypoglycaemia, a medication change should be considered, e.g. alternative oral agents or GLP-1 analogues.

## 9.7 Pharmacotherapy in Obese Patients

Pharmacotherapy in obese patients <sup>1,12</sup> :

- May be considered if lifestyle modifications have failed to result in weight loss goals being achieved.
- When prescribing glucose lowering agents in overweight or obese patients, consider their effect on weight:
  - Insulin secretagogues, TZD and insulin have been linked to weight gain.
  - SGLT2 and GLP-1 agonist use is associated with weight reduction.
  - DPP-4 inhibitors are weight-neutral.
- Minimise the prescribing of medications for comorbidities that are associated with weight gain <sup>1</sup> [L3, RGA], such as:
  - Atypical antipsychotics.
  - Antidepressants.
  - Glucocorticoids.
  - Oral contraceptives that contain progestins.
  - Anticonvulsants.

**Weight loss medication:**

Consider the pharmacological treatment of obesity only within a multi-disciplinary weight loss service [R-GDG].

## 10 Referral from Primary Care to Specialist Care

Consider referring the following groups of patients from primary care to specialist care [R-GDG]:

- HBA<sub>1c</sub> >8.0% after 3 months of treatment with triple oral therapy.
- Patients requiring more intensive treatment than basal insulin alone.
- Any pregnant woman who is a known diabetic or is diagnosed with T2DM during pregnancy screening.
- Patients suspected or confirmed to have monogenic diabetes.
- Patients with suspected or confirmed secondary diabetes that requires specialist treatment (e.g. post-pancreatectomy).
- Patients with diabetic foot disease that cannot be managed in primary care.
- All patients with cystic fibrosis.
- Patients with T2DM and evidence for end organ damage should be referred for shared care with endocrinology e.g. post-MII, neuropathy, retinopathy or nephropathy.
- Transplant patients with pre-diabetes or confirmed T2DM.

## 11 Hypoglycaemia

### 11.1 Definition and Treatment

Hypoglycaemia is defined as <sup>1</sup> :

- Plasma glucose concentration of <3.9 mmol/L (70 mg/dL).

Mild to moderate hypoglycaemia is defined as [derived from <sup>1</sup>]:

- Plasma glucose concentration of 3.0 - 3.9 mmol/L (54 - 70 mg/dL).
- Which does not require assistance from another person.

Severe hypoglycaemia is defined as <sup>1</sup> :

- Plasma glucose concentration of <3.0 mmol/L (54 mg/dL).
- Hypoglycaemia requiring assistance from another person.
- Cognitive impairment that may lead to neurological symptoms, including loss of consciousness, seizures, coma, or death.

Patients at risk for hypoglycaemia should be asked about symptomatic and asymptomatic hypoglycaemia at each encounter <sup>1</sup> . Patients should also be aware of situations in which they have an increased risk of hypoglycaemia, including [**R-GDG**]:

- Fasting.
  - For medical tests or procedures.
  - During Ramadan or for other religious purposes.
- During or after intense exercise.
- During sleep.

Treatment <sup>1</sup> :

- Oral glucose (15-20 g) is the recommended treatment and route of choice to treat hypoglycaemia if the individual is conscious, although any form of carbohydrate that contains glucose may be used
- This should be repeated after 15 minutes if hypoglycaemia remains, as indicated by SMBG.
- When SMBG returns to a normal level, a meal or snack should be eaten to prevent hypoglycaemia recurrence.
- Prescribe glucagon to all patients at risk of severe hypoglycaemia.
- As glucagon administration is not limited to health care professionals, all caregivers, school personnel and family should be taught on how to administer it.

### 11.2 Hypoglycaemia Unawareness

Hypoglycaemia unawareness is <sup>8</sup> :

- Caused by an attenuated increase in sympatho-adrenal activity.
- The first sign of hypoglycaemia in these patients is confusion.
- Patients will heavily rely on others to recognise and treat hypoglycaemia.

#### 11.2.1 Hypoglycaemia-Associated Autonomic Failure

Hypoglycaemia-associated autonomic failure (HAAF) <sup>8</sup> :

- Is the combination of defective glucose counter-regulation and hypoglycaemia unawareness.
- Often caused by recent iatrogenic hypoglycaemia.
- Is partially reversible by avoiding hypoglycaemia.
- Is associated with a significantly increased risk (≥25 fold) of severe hypoglycaemia.

- Differentiate HAAF from other causes of autonomic dysfunction, such as classical diabetes-related autonomic neuropathy.

Restore recognition of hypoglycaemia in patients with HAAF <sup>8</sup> [L2]:

- Monitoring and goal setting:
  - Encourage SMBG before meals, at bedtime, and when symptoms occur.
  - Encourage SMBG between 02:00 and 05:00, at least three times a week.
  - Set a pre-prandial glucose target of 100-150 mg/dL (5.6-8.3 mmol/L).
- Patient education:
  - Explain to the patient the symptoms of hypoglycaemia and the role of repeated hypoglycaemia in the development of hypoglycaemia unawareness.
  - Ensure that the patient understands that hypoglycaemia unawareness is reversible through avoidance of hypoglycaemia.
- Dietary intervention:
  - Ensure adequate calorie intake.
  - Recommend the consumption of interprandial and bedtime snacks.
  - Ensure that the patient has access to readily absorbable carbohydrates at all times.
  - Consider moderate amounts of xanthine beverages, if tolerated.
- Exercise counselling:
  - Encourage SMBG before, during, and after exercise.
  - If BG is <140 mg/dL (7.8mmol/L), advise:
    - That the patient consumes additional calories before, during, and after exercise.
- Medication adjustment:
  - Consider adjusting the insulin regimen to attain target glucose levels.
  - To reduce the risk of inter-prandial hypoglycaemia:
    - Use rapid-acting insulin analogues.
  - To reduce the risk of nocturnal hypoglycaemia:
    - Use basal insulin analogues.
  - Consider using a CSII pump.
  - Consider a CGM device.

## 12 ASCVD Risk Management

### 12.1 Management of Hypertension

For patients with T2DM without known hypertension, review BP at every visit and at least annually <sup>1,23</sup> . Provide and emphasise lifestyle advice to all diabetic patients <sup>1,23</sup> .

Aim to achieve a clinic BP of <sup>1</sup> :

- <140/90 mmHg; or
- <130/80 mmHg in:
  - Younger patients.
  - Those with albuminuria.
  - Those with hypertension and one or more additional ASCVD risk factors, if the target can be achieved without undue treatment burden.

If BP remains above target levels following lifestyle improvement, add medication to reduce BP to target levels<sup>23</sup>.

#### 12.1.1 First-Line Medication

First-line BP-lowering therapy for patients with T2DM should be <sup>1,23</sup> :

- A once daily angiotensin converting enzyme (ACE) inhibitor; or
- For people of African or Afro-Caribbean descent use an ACE inhibitor plus either a diuretic or calcium channel blocker (CCB).
- For women who may become pregnant, start with a CCB:
  - Avoid the use of ACE inhibitors and angiotensin II-receptor antagonists.
- If there is ongoing intolerance to an ACE inhibitor, other than renal deterioration or hyperkalaemia, an angiotensin receptor blocker ARB may be used instead.
- NB: Unless contraindicated, for diabetic patients with hypertension and renal impairment, an ACE inhibitor or ARB must be the first line drug <sup>1,23</sup> .

BP should be monitored every 1-2 months and therapy intensified until it is in the target range. Continue to reinforce lifestyle advice <sup>23</sup> . If BP is consistently attained at the target level, continue to monitor the patient's BP at every clinic visits and check for adverse effects including risks of hypotension <sup>1,23</sup> .

NB: Antihypertensive medications can increase the likelihood of side effects, e.g. orthostatic hypotension in a patient with autonomic neuropathy <sup>24</sup> .

#### 12.1.2 Inadequate Control with First-Line Medication

If BP is not adequately controlled to the agreed target level <sup>2</sup> :

- Second line treatment:
  - With first-line therapy, add a CCB or a diuretic (usually thiazide or thiazide-like diuretic)<sup>24</sup>.
- Third-line treatment:
  - With dual therapy, add the other drug, i.e. either a CCB; or a diuretic <sup>23</sup>.
- Fourth-line treatment:
  - With triple therapy, add either an alpha-blocker; or a beta-blocker; or a potassium-sparing diuretic <sup>23</sup>.

Note the following key points <sup>2,23</sup> :

- Potassium sparing diuretics should be used with caution if patients are taking an ACE inhibitor or an ARB.
- An ACE inhibitor should not be prescribed in conjunction with an ARB.
- Refer to secondary/specialist care if BP remains above target levels following triple therapy including a diuretic [R-GDG].

## 12.2 Lipid Management

A moderate intensity statin should be started in the following <sup>25</sup> :

- Patients aged 40-75 years with T2DM with a 10-year risk of ASCVD using the ACC/AHA Pooled Cohort Equations of <7.5%.

A high-intensity statin should be started in the following <sup>25</sup> :

- All patients with an LDL-C level of  $\geq 4.9$  mmol/L.
- Patients aged 40-75 years with type 2 diabetes mellitus who have a 10-year risk of ASCVD using the ACC/AHA Pooled Cohort Equations of  $\geq 7.5\%$ .
- All patients with a positive history of an ASCVD event (e.g. myocardial infarction, TIA, stroke).
- As a secondary prevention in all patients with Diabetes and ASCVD <sup>1</sup> .

Ezetimibe is a recommended option for hypercholesterolaemia in adults, under the following conditions <sup>26</sup> [L1, RGA]:

- In conjunction with initial statin treatment when:
  - Serum total cholesterol or LDL-C levels are not appropriately controlled after titration of the statin treatment; or dosing is limited by intolerance to the statin.
- In conjunction with the highest tolerated statin treatment when <sup>1</sup> :
  - ASCVD risk is  $\geq 20\%$ , to reduce the LDL -C levels by 50% or more.
- As monotherapy if there is:
  - A contraindication to initial statin treatment.
  - Intolerance to statin treatment.

To reduce the cardiovascular risk in patients with ASCVD with controlled LDL cholesterol but elevated triglycerides (135–499 mg/dL), icosapent ethyl can be added to the statin treatment <sup>1</sup> .

## 12.3 Antiplatelet Therapy

Aspirin and other antiplatelets are not routinely recommended for patients with T2DM in the absence of established ASCVD <sup>1,25,27,28</sup> .

However, the American Diabetes Association recommends initiating low-dose aspirin use for the primary prevention of ASCVD in adults aged  $\geq 50$  years, who have a 10-year ASCVD risk of a  $\geq 10\%$ , using the ACC/AHA Pooled Cohort Equations. Patients must not be at increased risk for bleeding, have a life expectancy of at least 10 years and be willing to take low-dose aspirin daily for at least 10 years <sup>1</sup> .

## 13 Managing Diabetes During Ramadan

### 13.1 Risk Stratification for Fasting During Ramadan

During fasting, insulin resistance/deficiency may result in <sup>29-32</sup>:

- Excessive glycogen breakdown.
- Increased gluconeogenesis.
- Ketogenesis.
- Increased risk of:
  - Hypoglycaemia.
  - Hyperglycaemia.
  - Diabetic ketoacidosis.
  - Dehydration.
  - Thrombosis <sup>30</sup>:
    - Hyperglycaemia and hypovolaemia contribute towards hypercoagulability, which increases the risk of thrombosis.

A pre-Ramadan assessment should occur 8-12 weeks prior to the start of Ramadan [**R-GDG**] to allow for risk stratification of the patient, determine whether the patient intends to fast, and develop an individualised management plan <sup>29,30</sup> [**L1, RGA**].

Pre-Ramadan risk stratification assessment should incorporate <sup>29,30</sup>:

- A review of the patient's diabetic and general medical history.
- Assessment of the risk of hypoglycaemia and degree of hypoglycaemia unawareness.
- Determination of self-management capabilities.
- Assessment of any diabetic complications or associated comorbidities.

The following risk stratification classifies patients with diabetes into 3 different risk groups <sup>29,31,32</sup>:

- Very high and high risk groups are strongly advised against fasting.
- In moderate/low risk patients, fasting may be possible, where insisted upon by the patient.

Moderate/Low Risk	High Risk	Very High Risk
May be Allowed to Fast	Should NOT Fast	MUST NOT Fast
Well-controlled T2DM in a patient treated with one or more of the following: <ul style="list-style-type: none"> <li>• Lifestyle therapy.</li> <li>• Metformin.</li> <li>• Thiazolidinediones.</li> <li>• Second-generation sulfonylureas (SUs).</li> <li>• Incretin-based therapy.</li> <li>• SGLT-2 inhibitors.</li> <li>• Basal insulin.</li> </ul>	Patient has one or more of the following: <ul style="list-style-type: none"> <li>• T2DM with sustained poor glycaemic control*.</li> <li>• Well-controlled T2DM on multi-dose injections or mixed insulin.</li> <li>• Pregnant T2DM or GDM controlled by diet only or metformin.</li> <li>• Chronic kidney disease (CKD) Stage 3.</li> <li>• Stable macrovascular complications.</li> <li>• Patients with comorbid conditions that present additional risk factors.</li> <li>• People with T2DM performing intense physical labour.</li> <li>• Treatment with drugs that may affect cognitive function.</li> </ul>	Patient has one or more of the following: <ul style="list-style-type: none"> <li>• Severe hypoglycaemia within the 3 months prior to Ramadan.</li> <li>• DKA within the 3 months prior to Ramadan.</li> <li>• Hyperosmolar hyperglycaemic coma within the 3 months prior to Ramadan.</li> <li>• History of recurrent hypoglycaemia.</li> <li>• History of hypoglycaemia unawareness.</li> <li>• Acute co-existing illness.</li> <li>• Pregnancy in pre-existing diabetes, or GDM treated with insulin or SUs.</li> <li>• Chronic dialysis or CKD stage 4 or 5.</li> <li>• Advanced macrovascular complications.</li> <li>• Old age with ill health.</li> </ul>

\*The level of glycaemia control should be agreed between the patient and their physician.

**Table 8.2:** Risk Stratification of Patients with Diabetes Who Wish to Fast During Ramadan <sup>29</sup>.

If patients insist on fasting during Ramadan, then they should <sup>29</sup>:

- Have a pre-Ramadan medical assessment – 2-3 months prior to Ramadan [R-GDG].
- Receive structured pre-Ramadan education (see Section 8.3).
- Be given a robust assessment of hypoglycaemia awareness.
- Be followed by a qualified diabetes team.
- Perform self-monitoring of blood glucose (SMBG) regularly.
- Adjust medication dose according to the recommendations outlined below.
- Be prepared to break a fast if hypoglycaemia or hyperglycaemia develops.
- Be prepared to stop fasting altogether, if frequent hypoglycaemia or hyperglycaemia events occur, or there is worsening of other related medical conditions.

### 13.2 Structured Pre-Ramadan Education

Ramadan-focused education should raise the awareness of the risks of diabetes and fasting, allowing the patient to make informed decisions regarding their diabetes management. Such education should aim to reduce the risks of fasting with a simplified delivery from trained professionals <sup>29</sup> [L2, RGA].

Pre-Ramadan education should comprise of the following components <sup>29,33</sup>:

- SMBG or Continuous Glucose Monitoring:
  - Measuring glucose levels does not invalidate or break the fast.

- All patients should measure their glucose levels after iftar and if experiencing symptoms of either hypoglycaemia, hyperglycaemia or feeling unwell.
- Patients at moderate-low risk of complications:
  - Measure at least 1-2 times/day.
- Patients at high-very high risk (or those taking insulin or sulfonylureas):
  - Measure several times each day.
- Patients should always check their glucose level before driving, especially while fasting.
- Provide education on when patients should break their fast:
  - Glucose level <3.9 mmol/L (70 mg/dL). Recheck within 1 hour if their glucose level is 3.9-5.0 mmol/L (70-90 mg/dL).
  - Glucose level is >16.6 mmol/L (>300 mg/dL).
  - Symptoms of hypoglycaemia, hyperglycaemia, dehydration, or acute illness occur.
- Dietary advice <sup>29</sup>:
  - Divide daily calories between iftar and suhoor, plus 1-2 snacks are permitted if necessary.
  - Ensure meals are well balanced:
    - 45-50% carbohydrate.
    - 20-30% protein.
    - <35% fat (preferably mono- and polyunsaturated).
  - Include low glycaemic index, high fibre foods that release energy slowly before and after fasting, e.g. granary bread, beans, rice.
  - Include some fruits, and plenty of non-starchy vegetables and salads.
  - Minimise foods that are high in saturated fats, e.g. ghee, samosas, pakoras, etc.
  - Avoid sugary desserts.
  - Use small amounts of oil when cooking, e.g. olive oil, rapeseed oil.
  - Keep hydrated between sunset and sunrise by drinking water or other non-sweetened beverages.
  - Minimise caffeinated drinks and avoid sweetened drinks.
- Exercise <sup>29</sup>:
  - Avoid vigorous exercise whilst fasting.
  - Take light-to-moderate exercise during Ramadan (including Tarawih prayers).

### 13.3 Pharmacological Management During Ramadan

The following guidance outlines how patients should adjust their medication when fasting <sup>29</sup>:

#### **Metformin** <sup>29</sup>:

- Daily dose remains unchanged.
- Immediate-release preparations:
  - If taking once/day:
    - Take usual dose at iftar.
  - If taking twice/day:
    - Take usual doses at iftar and suhoor.
  - If taking 3 times/day:
    - Take the morning dose before suhoor.
    - Take afternoon and evening doses together at iftar.
- Modified-release preparation:
  - Take usual dose at iftar.

#### **Thiazolidinediones:**

- No adjustment to thiazolidinedione (TZD) medication is needed during Ramadan and doses can be taken with iftar or suhoor <sup>29</sup>.

**Sulfonylureas:**

Use of older sulfonylureas (SUs), e.g. glyburide/glibenclamide, should be avoided. Second-generation SUs should be used instead (e.g. glicazide, glimepiride) <sup>29</sup>:

- If taking once/day:
  - Take at iftar.
  - Dosing may be reduced if glucose levels are well-controlled.
- If taking twice/day:
  - Take the usual evening dose at iftar.
  - Reduce the suhoor dose if glucose levels are well controlled.

**SGLT2 inhibitors** <sup>29</sup>:

- No dose modifications.
- Take the usual dose at iftar.
- Use with caution and consume additional clear fluids during the evening after a fast to reduce the risk of dehydration.
- Should not be used in:
  - The elderly.
  - Patients with renal impairments, hypotension or those taking diuretics.

**DPP-4 inhibitors:**

- No treatment modification is required during Ramadan <sup>29</sup>.

**GLP-1 receptor agonists:**

- No treatment modification is required during Ramadan, as long as the dose has been adequately titrated at least 6 weeks prior to Ramadan beginning <sup>29</sup>.
- Ensure adequate fluid intake throughout Ramadan <sup>33</sup>.

**Insulin:**

The use of insulin analogues is preferred over regular human insulin during Ramadan fasting <sup>31,32</sup> [**L2, RGA**]. Gla-300 <sup>32</sup> and IDegAsp <sup>31</sup> are recommended in patients with T2DM [**L2, RGA**]. IDegAsp should be preferred over BIAsp 30 <sup>31</sup>.

Insulin treatment must be appropriately individualised:

- Long-acting (basal insulin) and short-acting insulin regimens <sup>29</sup>:
  - Basal insulin:
    - If using NPH/detemir/glargine/degludec once daily:
      - Reduce dose by 15-30% and take at iftar.
    - If using NPH/detemir/glargine twice daily:
      - Take the usual morning dose at iftar.
      - Reduce the usual second dose by 50% and take at suhoor.
  - Short-acting insulin:
    - Take the normal dose at iftar.
    - Omit the lunchtime dose.
    - Reduce the suhoor dose by 25-50%.
- Pre-mixed insulin dosing regimen <sup>29</sup>:
  - Once-daily dosing:
    - Take the normal dosing at iftar.
  - Twice-daily dosing:

- Take the larger dose at iftar.
- Take the smaller dose at suhoor and reduce dose by 25-50%.
- 3 times/day dosing:
  - Omit the afternoon dose.
  - Adjust iftar and suhoor doses as for twice daily dosing.
  - Titrate doses every 3 days (see below).

NB: Treatment with an insulin pump system (continuous subcutaneous insulin infusion (CSII)) may benefit those patients with T2DM and poor glycaemic control already being treated with multiple daily injections of insulin, as this can be used safely in patients who fast <sup>29</sup>.

The following table outlines recommended dose adjustments according to SMBG in patients prescribed long and short acting insulin regimens and appropriate dose titration in patients taking pre-mixed insulin.

Fasting, Pre-Iftar or Pre-Suhoor Glucose Results	Pre-iftar	Post-Iftar or Post-Suhoor	Dose Titration
	Basal insulin	Short-acting insulin	Pre-mixed insulin
<b>&lt;3.9 mmol/L (70 mg/dL) or Symptoms</b>	Reduce by 4 units	Reduce by 4 units	Reduce by 4 units
<b>3.9–5.0 mmol/L (70–90 mg/dL)</b>	Reduce by 2 units	Reduce by 2 units	Reduce by 2 units
<b>5.0–7.2 mmol/L (90–130 mg/dL)</b>	No change required	No change required	No change required
<b>7.2–11.1 mmol/L (130–200 mg/dL)</b>	Increase by 2 units	Increase by 2 units	Increase by 2 units
<b>&gt;11.1 mmol/L (200 mg/dL)</b>	Increase by 4 units	Increase by 4 units	Increase by 4 units

**Table 8.4:** Dose Adjustment and Titration in Insulin Regimens <sup>29</sup>.

## 14 Management Considerations in Older Adults

### 14.1 Overview

Older adults<sup>1</sup> :

- Older adults with diabetes experience increased rates of:
  - Premature death.
  - Functional disability.
  - Comorbidities.
- Older adults with diabetes are also at increased risk of:
  - Polypharmacy.
  - Cognitive impairment.
  - Urinary incontinence.
  - Injurious falls.
  - Persistent pain.
- A full evaluation of co-morbidities and general health is required before individual goals and treatment strategies are developed<sup>15</sup> [**L3, RGA**].

### 14.2 Neurocognitive Function

Older adults with T2DM are at increased risk of cognitive decline and institutionalisation<sup>1</sup> :

Screening<sup>1</sup>:

- Older patients should be screened and monitored for cognitive impairment<sup>1</sup> [**L2, RGA**].
- May be considered in older adults with difficulties with their activities of daily living<sup>1</sup> [**L3, RGA**].
- Consider screening and treating depression in older adults (more than or equal to 65 years of age) with diabetes as a high priority<sup>1</sup> [**L2**].

### 14.3 Diabetes Self-Management Education and Support

DSME and Diabetes Self-Management Support (DSMS) in older adults<sup>13,14</sup> [**L2**]:

- Involve care partners (family, friends, or other caregivers) in DSME.
- Educators should be aware that:
  - Patients may have low health literacy and numeracy skills.
  - Patients may be overwhelmed by the presence of multiple comorbidities.

### 14.4 Nutrition

Nutrition considerations<sup>1,15</sup> :

- Older adults may have:
  - Irregular meal consumption.
  - Undernutrition.
  - Anorexia.
  - Impaired swallowing.
- Therapeutic diets may lead to decreased food intake, resulting in poor nutrition and weight loss.
- Diets that take into account the patient's culture and personal preferences and goals may improve their quality of life, nutrition, and meal satisfaction.

- Improvements in food and beverage intake have been demonstrated when using liberal diet plans in this population:
  - Restrictive therapeutic diets should be avoided, as they may cause unintentional weight loss and dehydration<sup>15</sup> [L3].

## 14.5 Treatment Goals

In elderly patients who are cognitively and functionally intact and have significant life expectancy, consider setting treatment targets which are similar to those used in younger adults<sup>1</sup> [L3, RGA].

### 14.5.1 Blood Glucose Targets

Blood glucose targets:

- May be relaxed in elderly adults on an individual basis, e.g. in patients with<sup>1</sup> [L3, RGA]:
  - Advanced diabetes.
  - Life-limiting comorbid illness.
  - Substantial cognitive or functional impairment.
- Hyperglycaemia that results in risk or symptoms of acute hyperglycaemic complications should be avoided<sup>1</sup> [L3, RGA].
- Glycaemic goals and targets, at a minimum, should aim to avoid acute complications, such as<sup>1</sup> [L2]:
  - Dehydration.
  - Poor wound healing.
  - Hyperglycaemic hyperosmolar coma.

Glucose targets<sup>13,14</sup> [L2]:

- Fasting/pre-prandial BG target: 5.0-7.2 mmol/L (90-130 mg/dL).
- Bedtime BG target: 5.0-8.3 mmol/L (90-150 mg/dL).
  - Appropriate in patients with both of the following:
    - Few coexisting chronic illnesses.
    - Intact cognitive and functional status.
- Fasting/pre-prandial BG target: 5.0-8.3 mmol/L (90-150 mg/dL).
- Bedtime BG target: 5.6-10.0 mmol/L (100-180 mg/dL).
  - Appropriate in patients with any of the following:
    - Multiple coexisting chronic illnesses.
    - ≥2 instrumental impairments of activities of daily living (ADL).
    - Mild to moderate cognitive impairment.
- Fasting/pre-prandial BG target: 5.6-10.0 mmol/L (100-180 mg/dL).
- Bedtime BG target: 6.1-11.1 mmol/L (110-200 mg/dL).
  - Appropriate in patients with any of the following:
    - ≥2 ADL dependencies.
    - Long-term care needs.
    - End-stage chronic illnesses.
    - Moderate to severe cognitive impairment.

### 14.5.2 HBA<sub>1c</sub> Targets

HBA<sub>1c</sub> targets<sup>13,14</sup> :

- A target of <7.0% should be set (if it can be achieved without problematic hypoglycaemia) in the following patients:
  - With absent, or very mild, microvascular complications; and
  - Who are free of major concurrent illnesses; and
  - Who have a life expectancy of at least 10-15 years.
- A target of <8.0% should be set in the following patients:
  - A longer duration diabetes (> 10 years).
  - With comorbid conditions.
  - Who need combination medication treatments, including insulin.
- A target of 8.0-9.0% should be set for patients with any of the following:
  - Advanced microvascular complications.
  - Major comorbid conditions.
  - Life expectancy of <5 years.

### 14.6 Pharmacological Therapy

The following should be considered<sup>1</sup> :

- Care plans should be individualised and made in conjunction with the patient and their care-givers.
- Any social issues may cause an impact on the patient's quality of life.
- When offering management and support, consider the patient's circumstances:
  - Patients in care homes may need to rely fully on nursing input and their care plan.
  - Patients receiving palliative care may need treatment focussed on quality of life.

#### Metformin:

- The first-line agent in older adults<sup>1,13-15</sup> [L2]:
  - Contraindicated in patients with:
    - Renal insufficiency.
    - eGFR <30 ml/min/1.73m<sup>2</sup>.
      - Reduce dose if eGFR is 30-60 ml/min/1.73m<sup>2</sup>.
    - Significant heart failure.
  - Gastrointestinal intolerance and weight loss may have a bigger impact in frail patients.
  - May be stopped temporarily prior to procedures, when acute illnesses compromise liver or renal function, and during hospitalisations.
- A timed urine collection to assess creatinine clearance is recommended in patients aged ≥80 years<sup>1</sup> [L2].

#### Thiazolidinediones<sup>1,15</sup> [L2]:

- Low hypoglycaemia risk, low cost, can be used in renal impairment.
- Should be used with caution in people with or at risk of congestive heart failure.
- Have been associated with fractures.

### **Insulin Secretagogues:**

- Sulfonylureas and other secretagogues <sup>1,15</sup> :
  - Are associated with increased risk of hypoglycaemia:
  - Should be used with caution in older patients, especially if eating patterns are inconsistent.
  - Glyburide/glibenclamide is contraindicated in older adults.
- Meglitinides <sup>15</sup> :
  - Have a short duration of action.
  - May be used prior to meals to control post-prandial hyperglycaemia <sup>3,4</sup> .

### **Incretin-Based Therapies <sup>1,15</sup> :**

- GLP-1 receptor agonists and DPP-4 inhibitors:
  - Have few side effects and carry a low risk of hypoglycaemia.
  - Cost may be a barrier to some older patients.
- Incretin-based therapies do not increase the risk of major cardiovascular events.
- GLP-1 receptor agonist use requires:
  - Visual skills.
  - Motor skills.
  - Cognitive skills.

### **SGLT-2 Inhibitors <sup>1,15</sup> :**

- Are more convenient for oral dosing.
- Long-term experience of their use however is limited.
- Monitor for increased urinary frequency, incontinence, lower BP, genital infections, and dehydration.

### **Insulin:**

- High risk of hypoglycaemia <sup>1,13,14</sup> :
  - The risk of hypoglycaemia must be weighed against the benefits of insulin use.
- Matching carbohydrate content with prandial insulin if variable appetite may be difficult.
- Basal insulin combined with oral agents may lower postprandial glucose while reducing hypoglycaemia risk and regimen complexity.
- Continue basal-bolus regimen in patients with T2DM who are insulin-deficient.
- The use of sliding scale insulin alone for chronic glycaemic management is not recommended in inpatient settings and long term care facilities <sup>13,14</sup> [L2].
- Patients or their caregivers should have good visual skills, motor skills, and cognitive ability <sup>1</sup> [L2].

## **14.7 Transitions of Care**

### **Management during transitions of care <sup>15</sup> :**

- Care transitions are important times to revisit diabetes management targets.
- Consider the following <sup>15</sup> [L3, RGA]:
  - Perform a medication reconciliation.
  - Provide education.
  - Re-evaluate the patient's ability to perform diabetes self-care behaviours
  - Have effective communication between transferring and receiving care teams to maintain patient safety and keep readmission rates to a minimum.

- Important documentation as part of the transfer plan should include the following: <sup>15</sup> [L3, RGA]:
  - The current meal plan.
  - Activity levels.
  - Prior treatment regimen.
  - Prior self-care education.
  - Laboratory tests, including:
    - HBA<sub>1C</sub>.
    - Lipid profile results.
    - Renal function.
  - Hydration status.
  - Previous episodes of hypoglycaemia (including symptoms and patient's ability to recognise and self-treat).

## 14.8 Comorbidity Management

Common comorbidities and corresponding treatment approaches include <sup>15</sup> [L2]:

- Confusion, cognitive dysfunction, delirium:
  - Offer a regular diet and preferred food options.
  - Offer food substitutions if food intake is <75% of normal intake.
  - Administer insulin immediately after meals to match carbohydrate intake.
- Block testing:
  - Monitor the patient at different times of the day.
  - Check fasting glucose on some days, pre-lunch or pre-dinner on other days.
  - Glucose monitoring frequency should increase in times of acute mental status or behavioural changes.
  - A long-acting once-daily form of oral medication, or one that can be given crushed or as a liquid, can be considered.
  - Mixed insulin regimens can be considered in order to reduce the number of daily injections, although hypoglycaemia risk will remain high.
- Depression:
  - Assess and treat depression.
  - Encourage physical activity.
  - Encourage socialising, especially during meals (if living in a long-term care facility).
- Physical disability:
  - Encourage activity within the patient's abilities.
  - Assess for pressure ulcers.
  - Encourage independence for ADLs.
- Skin problems, e.g. infections, ulcers, delayed wound healing:
  - Consider a nutrition consult.
  - Consider more frequent glucose monitoring and temporary regimen intensification.
  - Consider non-weight bearing exercises.
  - Regular skin checks and foot assessments by nursing staff.
- Hearing and vision problems:
  - Screen for hearing and vision problems and implement preventive strategies if possible.
- Oral health problems, teeth decay, dry mouth:
  - Regular oral health evaluations and cleaning.
  - Ensure appropriate daily oral care.

## 14.9 End of Life Care

### 14.9.1 Goals

The primary goals for management of T2DM at the end of life are <sup>1,15</sup> [L3, RGA]:

- Overall comfort.
- Prevention of distressing symptoms.
- Preservation of quality of life.
- Preservation of dignity.

At the end of life <sup>1</sup> [L2]:

- Treatment goals should focus on avoiding symptoms and complications from glycaemic management.
- When organ failure develops, several agents will need to be titrated or discontinued:
  - For the dying patient, most agents used in T2DM may be removed.

### 14.9.2 Key Considerations

Key considerations <sup>1</sup> :

- The patient has the right to refuse treatment and testing.
- Healthcare providers may consider limiting testing, such as finger stick testing frequency, and withdrawing treatment if appropriate <sup>1,16</sup> [L3, RGA].
- Any glycaemic targets should aim to prevent hypoglycaemia and hyperglycaemia.
- Bear in mind quality of life when considering treatment interventions.
- Carefully monitor oral intake.
- There may need to be involvement by the patient, their family, and other caregivers as part of the decision process.
- A care plan should be developed that is both convenient and effective for the goals of care.

### 14.9.3 Pharmacological Therapy

Pharmacological therapy <sup>1</sup> [L2]:

- May include oral agents as a first line, followed by a simplified insulin regimen.
- Basal insulin may be used in conjunction with oral agents, without rapid-acting insulin.
- Drugs that cause gastrointestinal symptoms or weight loss may need to be avoided in this setting.

### 14.9.4 Advanced Disease Management

Management of patients with advanced disease <sup>1</sup> [L2]:

- Stable patients:
  - Continue with the patient's current regimen.
  - Focus on:
    - The prevention of hypoglycaemia.
    - The management of hyperglycaemia.
    - Keeping glucose levels below the renal threshold for glucose.
  - There is little need for HBA<sub>1c</sub> monitoring and lowering.
- Patients with organ failure:
  - Preventing hypoglycaemia is of greater significance:
    - Aim for glucose levels in the upper level of the desired target range.
  - Prevent dehydration and manage accordingly.

- Agents that may cause hypoglycaemia may be titrated.
- Dying patients:
  - All medications may be discontinued as they are unlikely to have any oral intake.

## 15 Key Considerations for Patient Preferences

Patient preferences refer to patient perspectives, beliefs, expectations, and goals for health and life, and to the steps employed by individuals in assessing the potential benefits, harms, costs, and limitations of the management options in relation to one another. Patients may have preferences when it comes to defining their problems, identifying the range of management options and selecting or ranking the outcomes used to compare these options.

It is important for healthcare professionals to develop an understanding of the patient as an individual and the unique way in which each person experiences a condition and its impact on their life.

The following recommendations are therefore made for physicians and other healthcare professionals regarding general principles of patient care in Qatar:

- **Respect Patients:** Treat patients with respect, kindness, dignity, courtesy and honesty. Ensure that the environment is conducive to discussion and that the patient's privacy is respected, particularly when discussing sensitive, personal issues. Ask the patient how they wish to be addressed and ensure that their choice is respected and used.
- **Maintain Confidentiality:** Respect the patient's right to confidentiality and avoid disclosing or sharing patients' information without their informed consent. In this context, students and anyone not directly involved in the delivery of care should first be introduced to the patient before starting consultations or meetings, and let the patient decide if they want them to stay.
- **Clarify Third-Party Involvement:** Clarify with the patient at the first point of contact whether and how they like their partner, family members or carers to be involved in key decisions about their care or management and review this regularly. If the patient agrees, share information with their partner, family members or carers.
- **Obtain Informed Consent:** Obtain and document informed consent from patients, in accordance with MOPH policy and guidance.
- **Encourage Shared Decision Making:** Ensure that patients are involved in decision making about their own care, or their dependent's care, and that factors that could impact the patient's participation in their own consultation and care including physical or learning disabilities, sight, speech or hearing impairments and problems with understanding, reading or speaking English are addressed.
- **Disclose Medical Errors:** Disclose errors when they occur and show empathy to patients.
- **Ensure Effective Communication:** Explore ways to improve communication including using pictures, symbols or involving an interpreter or family members. Avoid using medical jargon. Use words the patient will understand and confirm understanding by asking questions.
- **Ensure Continuity of Care:** Provide clear and timely sharing of patient information between healthcare professionals especially at the point of any transitions in care.

## 16 Performance Measures

A list of performance measures is given in the table below. Healthcare organisations are encouraged to monitor service performance using the indicator definitions below <sup>34</sup>.

Number	Numerator	Denominator
T2D01	Number of adult type 2 diabetes patients in whom the most recent HBA <sub>1C</sub> is less than or equal to 9.0%.	Total number of adult type 2 diabetes patients seen more than twice in clinic in the last 12 months.
T2D02	Number of adult type 2 diabetes patients in whom the most recent HBA <sub>1C</sub> is less than or equal to 8.0%.	Total number of adult type 2 diabetes patients seen more than twice in clinic in the last 12 months.
T2D03	Number of adult type 2 diabetes patients in whom the most recent HBA <sub>1C</sub> is less than or equal to 7.0%.	Total number of adult type 2 diabetes patients seen more than twice in clinic in the last 12 months.
T2D04	Number of adult patients with type 2 diabetes who are referred for a structured education programme within 6 months of initial diagnosis.	Total number of adult type 2 diabetes patients seen more than twice in clinic in the last 12 months.
T2D05	Number of adult patients with type 2 diabetes who are a foot or lower limb amputation in the last 12 months.	Total number of adult type 2 diabetes patients seen more than twice in clinic in the last 12 months.

**Table 16.1:** Performance Measures<sup>34</sup>.

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## Appendix A: Insulins Registered in Qatar

The table below provides a list of all insulin aspart preparations currently registered in Qatar.

Trade name	Generic name & Strength	Dosage Form	Package type	Shelf-life	Marketing Company
<b>NovoRapid FlexPen</b>	Insulin Aspart 100 U/ml 100 U/ml	Solution for injection	Pre-filled Pen	30 months	Novo Nordisk A/S
<b>NovoRapid Penfill</b>	Insulin Aspart 100 U/ml	Solution for injection	Cartridge	30 months	Novo Nordisk A/S
<b>NOVO RAPID FLEX TOUCH</b>	INSULIN ASPART 305 mg/ 1ml , 100 U/ML	PFP	PRE-FILLED PEN	30 months	Novo Nordisk A/S
<b>NOVOMIX 50 FLEXPEN</b>	INSULIN ASPART (SOLUBLE) /PROTAMINE-CRYSTALLISED INSULIN ASPART 100U / ML IN THE RATIO OF 50/50	Suspension for injection in a pre-filled pen	Device + Cartridge (Pre-filled Pen)	24 months	Novo Nordisk A/S
<b>NOVOMIX 50 PENFILL</b>	INSULIN ASPART (SOLUBLE) /PROTAMINE-CRYSTALLISED INSULIN ASPART 100U / ML IN THE RATIO OF 50/50	Suspension for injection in a Cartridge	Cartridge	24 months	Novo Nordisk A/S
<b>NOVOMIX 70 FLEXPEN</b>	INSULIN ASPART (SOLUBLE) /PROTAMINE-CRYSTALLISED INSULIN ASPART 100U / ML IN THE RATIO OF 70/30	Suspension for injection in a pre-filled pen	Device + Cartridge (Pre-filled Pen)	24 months	Novo Nordisk A/S
<b>NOVOMIX 70 PENFILL</b>	INSULIN ASPART (SOLUBLE) /PROTAMINE-CRYSTALLISED INSULIN ASPART 100U / ML IN THE RATIO OF 70/30	Suspension for injection in a Cartridge	Cartridge	24 months	Novo Nordisk A/S
<b>NovoMix 30 FlexPen</b>	Biphasic Insulin Aspart 100 U/ml 100 U/ml	Suspension for injection	Pre-filled Pen	24 months	Novo Nordisk A/S
<b>NovoMix 30 Penfill</b>	Biphasic Insulin Aspart 100 U/ml	Suspension for injection	Cartridge	24 months	Novo Nordisk A/S
<b>Ryzodeg 100 IU/ml flex touch</b>	Each 1 ml solution contains (Insulin Degludec 420 nmol 70% +	Solution for injection in pre-filled pen	Carton box containing 5 pre-filled pens each of 3 ml (each PFP contain type I glass cartridge)	30 Months	Novo Nordisk A/S

Trade name	Generic name & Strength	Dosage Form	Package type	Shelf-life	Marketing Company
	Insulin aspart 180 nmol 30%) 100 IU				
<b>Ryzodeg 100 IU/ml flex touch</b>	Each 1 ml solution contains (Insulin Degludec 420 nmol 70% + Insulin aspart 180 nmol 30%) 100 IU	Solution for injection in cartridges	3 ml solution in a cartridge (type I glass) with a plunger (halobutyl) and a stopper (halobutyl/polyisoprene) in a carton	30 months	Novo Nordisk A/S
<b>Fiasp 100 U/ml Vial</b>	Insulin aspart 100 U/ml	Solution for S.C. Injection in vial	Vial Glass	30 months	Novo Nordisk A/S
<b>Fiasp Penfill</b>	Insulin aspart 100 U/ml	Solution for S.C. Injection in cartridges	Cartridges	30 months	Novo Nordisk A/S
<b>Fiasp FlexTouch</b>	Insulin aspart 100 U/ml	Solution for S.C. Injection in Pre-Filled Pen	Pre-filled pen	30 months	Novo Nordisk A/S

**Table A1:** Insulin aspart preparations currently registered in Qatar. {R-GDG}.

## Appendix B: Detailed Description of the Literature Search

A systematic search for existing literature on type 2 diabetes in adults and the elderly was performed in the period July 8<sup>th</sup> – July 20<sup>th</sup>, 2020.

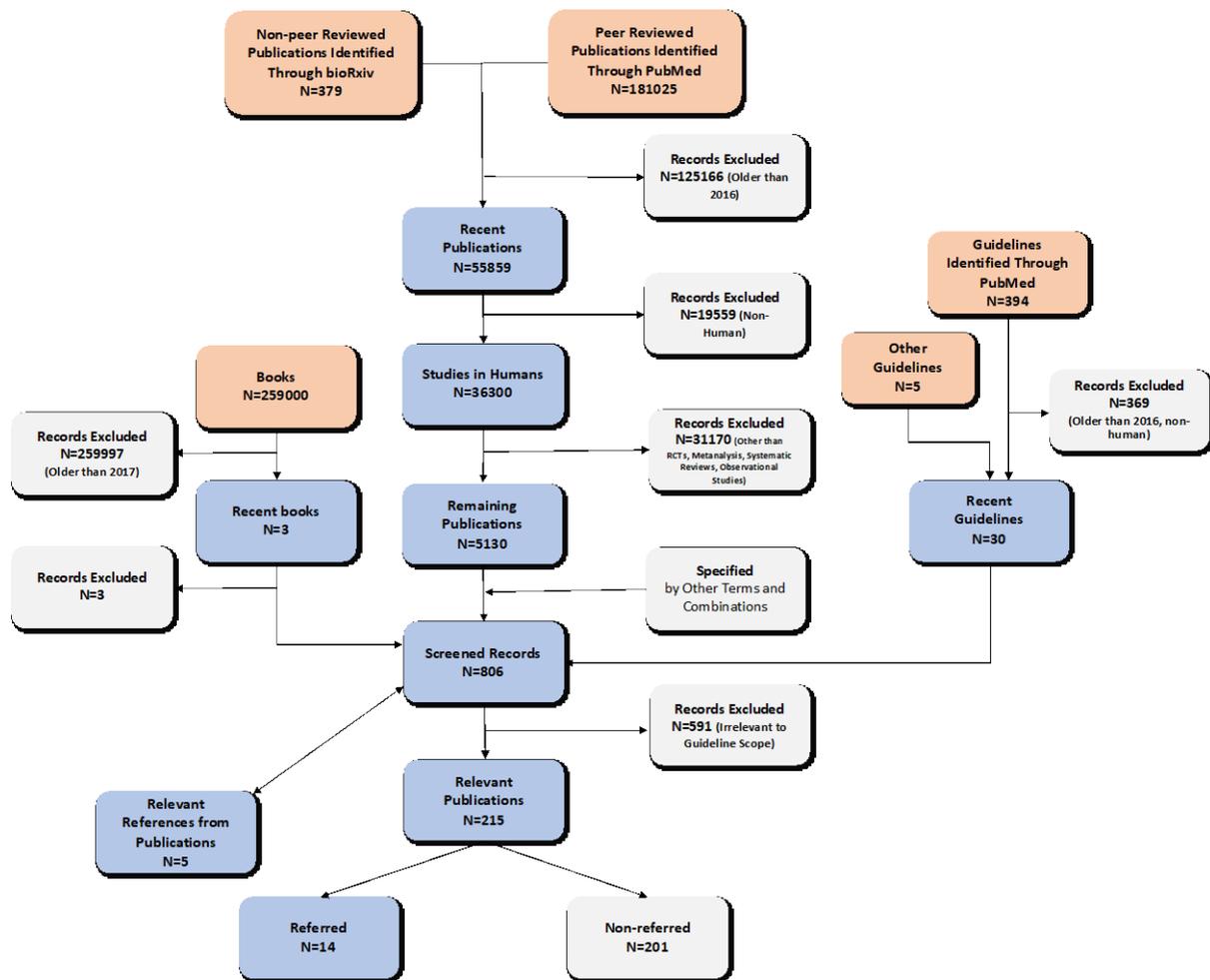
All existing references were evaluated and where necessary and applicable, the latest version of the specific manuscript was used to update the guideline and replace the older reference. The search for clinical practice guidelines on the management of type 2 diabetes in adults was performed in the *PubMed* database and websites of relevant organisations and societies including the *UK NICE*, the *American Association of Clinical Endocrinologists*, the *Scottish Intercollegiate Guidelines Network* and the *American College of Cardiology/American Heart Association*. The present guideline is primarily based on *UK NICE* and the *American Diabetes Association* guidelines and is supplemented with other relevant studies.

Peer-reviewed scientific publications were found in PubMed and via *Google Scholar* Internet search engine. Non-peer reviewed studies were identified in *bioRxiv*. Books were checked on *Amazon* and via *Google* and *Google Scholar* search engines.

The included publications were identified using the terms “*type 2 diabetes*” and specified with the following terms in combinations:

*Guideline, adult, elderly, glucose, diabetes mellitus, prediabetes, classification, prevalence, epidemiology, risk, presentation, screening, history, examination, complication, investigation, diagnosis, multidisciplinary, referral, specialist, self-management, nutrition, weight, smoking, exercise, contraindication, immunization, psychology, HbA<sub>1c</sub>, therapy, pharmacological, monotherapy, dual therapy, triple therapy, combination, regimens, administration, insulin, metformin, ASCVD, hypertension, lipid, antiplatelet, hypoglycaemia, autoimmune failure, fasting, neurocognitive, comorbidity, end of life.*

*Figure A.1* on the next page demonstrates graphically the results of the search and application of exclusion criteria.



**Key:**

- Type of Publication
- Process
- Notes

**Fig A.1:** Literature search results and application of exclusion criteria.

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