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Approach to a Newly Diagnosed Adult with Type 2 Diabetes in the Indian Context: Recommendations by Association of Clinical Endocrinologists Consensus Group

The Association of Clinical Endocrinologists is a non-profit, non-commercial body registered in India, that serves as a platform for like-minded Endocrinologists who aspire to work for the cause of the science of Diabetes and Endocrinology, its utility and application for the betterment of the health of the people and the country. The authors request the readers to please do not confuse this Association of Clinical Endocrinologists with ACE/AACE of USA.

Grading system used for recommendations:

Grading system uses A, B, C, or E to show the evidence level that supports each recommendation.

- **A** — Clear evidence from well-conducted, generalizable randomized controlled trials that are adequately powered.
- **B** — Supportive evidence from well-conducted cohort studies.
- **C** — Supportive evidence from poorly controlled or uncontrolled studies.
- **E** — Expert consensus or clinical experience.

Introduction

Introduction and prevalence

Type 2 diabetes mellitus (T2DM) accounts for about 90% of all diabetes cases worldwide. China, India, and the United States of America are the countries with major number of adults with diabetes aged 20–79 years in 2019 and it is anticipated that it would remain so in 2030 [1]. India ranks second after China in the global diabetes epidemic with 77 million people with diabetes, in 2019, which is predicted to rise to 101 million by 2030 and 134 million by 2045 [2, 3].

Burden

The major risks for the burden of diabetes are metabolic, environmental, and behavioural factors, [2] and the most important modifiable risk factors for the

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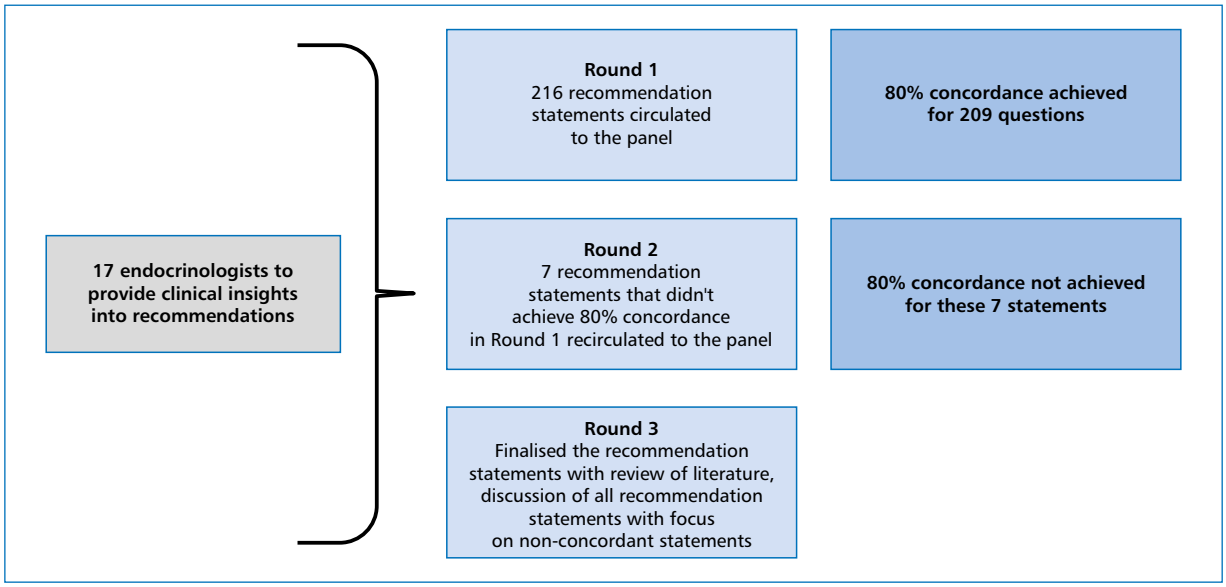


Figure 1. The Modified Delphi Methodology Followed

development of T2DM are overweight and obesity due to an unhealthy diet and physical inactivity [3]. T2DM is a progressive disorder which leads to serious complications and is associated with increased costs to the family, community, and healthcare system. It is a leading threat to public health globally, more so in the low and middle income countries like India, where the burden has risen significantly in the recent decades and will continue to rise in the coming decades [2].

There has been an exponential increase in T2DM prevalence in India in the recent years that has contributed to the increased burden of diabetes in the young [3]. According to the Indian council of medical research, which was carried out in 15 states, the prevalence of diabetes and prediabetes was 10.3% and 7.3%, respectively [4].

Rationale

Vast majority of these people with T2DM are managed by general practitioners and family physicians, most of them practising in areas with less-than-ideal health care facilities in India. Whilst there are guidelines and consensus statements from reputed institutions and medical bodies pertaining to T2DM, there is not a dedicated guideline or consensus statement that deals exclusively with the "Approach to the management of a newly diagnosed adult with T2DM in the Indian context", guiding general physicians and general practitioners. Hence this consensus statement using the modified Delphi method.

Methodology

The Delphi method is a technique that is employed to obtain concordance among multiple experts via repeated questionnaires along with feedback [5]. The Delphi technique is a series of sequential questionnaires or "rounds", interspersed by controlled feedback, which seek to gain the most reliable consensus of opinion of a group of experts. It is useful for situations where individual judgements must be tapped and combined in order to address a lack of agreement or incomplete state of knowledge and is valued for its ability to structure and organize group communication [6].

Types of Delphi and Modified Delphi Method

There are many forms of Delphi such as the modified Delphi, policy Delphi, and the real-time Delphi [7]. The modified Delphi technique, which involves gathering information initially using questionnaires (consensus measurement) and then conducting a formal in-person meeting, maximises the advantages of both consensus procedures (consensus development) [8].

The insights or expert opinions for the current analysis were sought using a 3-step modified Delphi method to enable members of the Association of Clinical Endocrinologists to pool their knowledge and develop recommendations that would facilitate a general physician or general practitioner to address the various challenges and barriers in the diagnosis and management of a newly diagnosed adult (≥ 18 years) with T2DM in India.

The modified Delphi method comprised 2 email-based questionnaire rounds followed by a consensus physical meet to allow direct interaction between the experts in the final round, which allowed panel members to clarify their points from the previous rounds and also present arguments to justify their point of view (Fig. 1).

The initial stage was development of recommendation statements following a comprehensive literature review using PubMed and other online resources for clinical studies, existing guidelines, review articles, consensus statements, and national and international standards on the diagnosis and management of T2DM. The relevant data was retrieved and reviewed, recommendation statements were developed and compiled into a Microsoft excel sheet.

The process of developing the recommendations

Consensus statements by the American Diabetes Association (ADA) have the highest regard amongst health care professionals across the world, including India. But some of those recommendations may not suit the Indian milieu due to a variety of reasons, including practicality, affordability and the healthcare ecosystem being completely different in India compared to the western world. While taking ADA and other peer reviewed evidence-based guidelines and consensus statements into consideration, the expert panel comprising of 17 practising endocrinologists from the Association of Clinical Endocrinologists has drafted new recommendations; amended and adopted existing recommendations from ADA and other reputed medical bodies across the world, subject to their relevance in the Indian context.

The recommendations have been drafted keeping in mind that they are meant for a general physician or a general practitioner who has a newly diagnosed adult with T2DM to deal with. The recommendations are meant to be a framework and template guiding the general physician or general practitioner in diagnosing and managing an adult with newly diagnosed T2DM, right from diagnosis to the later years of life, in a holistic manner.

Round 1

The 216 recommendation statements were circulated to the panel members through email, along with an explanation of the analysis, objectives, and instructions. The questionnaire was presented in a tabular format with columns beside the statements for addition of responses. The experts had to choose "Agree" for a "Yes" or "Disagree" for a "No" for each statement and were free to add comments and suggestions in the specified column if required. Statements with at least 80% agreement were considered to have reached concordance and those that did not reach concordance were modified as per the panel's inputs and recirculated in the Round 2.

Round 2

The statements that did not reach concordance in Round 1 were circulated among the experts by email. The responses were collected and analysed in the same manner as in Round 1. Statements not reaching 80% concordance were retained for discussion in Round 3.

Round 3

Round 3 was a direct interaction round among the experts in person, with one member acting as the facilitator. The panellists were encouraged to discuss the statements until an agreement was reached to modify, eliminate, or retain the statement in the recommendations. Two endocrinologists could not participate in the Round 3 due to personal reasons, though they were part of the initial 2 rounds. The remaining 15 endocrinologists participated in all 3 rounds.

Two hundred sixteen recommendation statements were circulated through email to all 17 panel members in Round 1. 80% concordance was achieved for 209 recommendation statements in Round 1. The remaining 7 were recirculated in Round 2, but these could not achieve 80% concordance again. These 7 were again discussed at length in Round 3 along with all the other recommendation statements and accepted with amendments.

Diagnosis

Classification of diabetes

Type 1 diabetes mellitus (T1DM) and T2DM, both are heterogeneous diseases with varying manifestations and disease progressions. Although, traditional definitions categorized T1DM as juvenile onset and T2DM as adult onset, both diseases can occur at any age. The right categorisation of the type of diabetes is important for appropriate management [9].

T1DM vis-à-vis T2DM

A newly diagnosed adult with T1DM may experience a short duration of illness (1–4 weeks) or a more slowly evolving process which may be misinterpreted as T2DM. The distinguishing characteristics of a patient with T1DM include acute onset, diagnosis relatively at a younger age (< 30 years), lower body mass index (BMI), unintentional weight loss, ketoacidosis, family history of autoimmune disease and/or insulin dependence at an early age and, presence of blood or urine ketones as mentioned in Figure 2. Temporary remission of insulin requirements is more common in adult patients with T1DM [9, 10].

The characteristics of a patient with T2DM are either slow onset of symptoms or no symptoms; diagnosed usually at more than 30 years of age, but

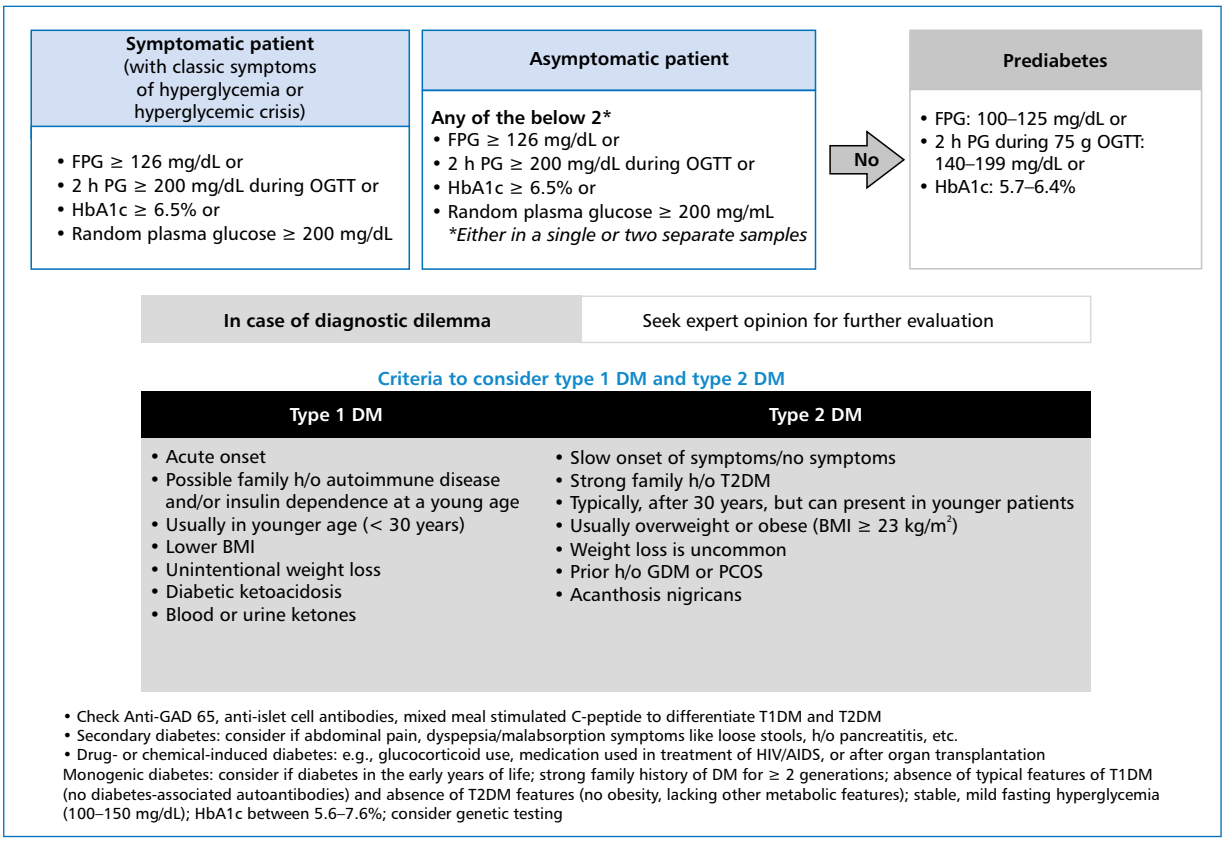


Figure 2. Diagnosis of Diabetes in a Non-Pregnant Adult (≥ 18 years) (Adapted from ADA Diabetes Care 2022)
BMI — body mass index; FPG — fasting plasma glucose; GDM — gestational diabetes mellitus; HbA1c — glycated hemoglobin; OGTT — oral glucose tolerance test; PCOS — polycystic ovarian syndrome; T1/2DM — type 1/2 diabetes mellitus

can present in younger individuals also; overweight, or obese (BMI ≥ 23 kg/m^2), weight loss is uncommon; a strong family history of T2DM or a prior history of gestational diabetes mellitus (GDM) or polycystic ovary syndrome (PCOS) and acanthosis nigricans [9].

Patients with monogenic diabetes can sometimes be mistaken for having T1DM. Pancreatic cancer may present with diabetes and weight loss. Distinguishing T1DM and T2DM in a young adult with newly diagnosed diabetes can be challenging at times [10].

Until 90s, T2DM was considered as a disease of middle-aged and older people. In recent decades, its prevalence is consistently raising among adults under 30 years. Onset of T2DM in a young adult herald an increased duration of the disease and the risk of both micro- and macrovascular complications [11].

There are various etiologies of T2DM. T2DM is characterised by relative insulin deficiency due to malfunction of pancreatic β-cells and insulin resistance. Majority of the patients with T2DM have obesity. Seemingly non-obese patients may have increased abdominal fat deposition which may lead to T2DM. Patients with T2DM seldom present with diabetic ketoacidosis (DKA), which is usually associated with stress of another illness such as infection, myocardial infarction (MI), or use of certain drugs [9].

Delay in diagnosis of T2DM

T2DM is a gradually progressing disease, and in the initial stages, the characteristic osmotic symptoms may not be severe enough to get noticed, making it undiagnosed for many years, at times [9].

Biochemical tests

Diagnosis of diabetes and prediabetes depends on plasma glucose criteria, which is measured as fasting plasma glucose (FPG) value or the 2-hour plasma glucose (2h PG) value during the oral glucose tolerance test (OGTT), or glycated hemoglobin (HbA1c) criteria (Fig. 2) [9]. One of the major challenges in the diagnosis of diabetes, especially in developing counties like India, is observed to be lack of standardization of laboratory techniques [12].

Diabetes is confirmed when fasting (defined as at least 8 hours of no caloric intake) plasma glucose ≥ 126 mg/dL or 2h PG is ≥ 200 mg/dL during OGTT (a glucose load of 75 g anhydrous glucose dissolved in water) or HbA1c is ≥ 6.5% [9].

The condition is diagnosed as pre-diabetes when HbA1c value is between 5.7–6.4%; FPG levels between 100–125 mg/dL, and the 2h PG value during 75 g OGTT between 140–199 mg/dL [9].

A random plasma glucose of ≥ 200 mg/dL in a patient with classic symptoms of hyperglycemia or hyperglycemic crisis is diagnostic of diabetes [9].

Unless there is a clear clinical diagnosis (patient in a hyperglycemic crisis or classic symptoms of hyperglycemia and a random plasma glucose ≥ 200 mg/dL or FPG ≥ 126 mg/dL or HbA1c is ≥ 6.5%), two abnormal screening test results are required, either from the same sample or in two separate test samples to establish the diagnosis of T2DM. It is advised that the second test, which can be either a repeat of the first test or a different test, must be carried out right away if two distinct test samples are being used [9].

Measuring only HbA1c could lead to under-diagnosis in people with low mismatches and over-diagnosis in those with high mismatches. Additional OGTT and/ /or FPG to complement HbA1c should be performed to establish confirmatory diagnosis [13–16]. When diagnosis of diabetes by HbA1c is in doubt, FPG and/ /or 2h PG should be used for diagnosis of diabetes [17]. Patients with diabetes should undergo a laboratory assessment of HbA1c at their initial visit if data is not available within the last three months, and thereafter every subsequent visit at 3 months [18].

Diabetes specific autoantibodies are the diagnostic test of choice to distinguish between T1DM and T2DM in patients with new onset hyperglycemia where the type of diabetes is ambiguous [19].

Circulating pancreatic autoantibodies, anti-glutamic acid decarboxylase (Anti-GAD); Insulin autoantibodies (IAA); Insulinoma-associated-2 autoantibodies (IA-2); Islet cell cytoplasmic autoantibodies (ICA) and Zinc transporter 8 autoantibodies (ZnT8Ab) suggest that the individual is at risk of or has developed T1DM [19].

Biomarkers: C-peptide

C-peptide is a helpful and broadly utilized tool to evaluate pancreatic beta cell function and to differentiate T1DM, T2DM, and maturity-onset diabetes of the young (MODY). Although C-peptide is useful in classifying diabetes, it must always be interpreted in clinical context of disease duration, comorbidities, and family history [20, 21].

Physical indicators of insulin resistance, such as acanthosis nigricans and skin tags can be found in 60 to 90% of young people with T2DM [10]. Monogenic form of diabetes should be considered if the patient does not seem to fit with T1DM or T2DM [22].

Recommendations

A. Burden of diabetes in India is mainly due to the increasing prevalence of overweight/obesity and unhealthy lifestyles. **B**

B. FPG and 2h PG are more accurate to diagnose diabetes than HbA1c. **B**

C. Take into consideration the factors that may impact hemoglobin glycation independently of glycemia. **B**

D. If there is marked discordance in HbA1c and plasma glucose levels, then plasma blood glucose criteria to be used to diagnose diabetes. **B**

E. For the diagnosis of diabetes, FPG with no caloric intake for at least 8 hours must be ≥ 126 mg/dL; 2h PG must be ≥ 200 mg/dL during OGTT and HbA1c must be ≥ 6.5%. **B**

F. A diagnosis of pre-diabetes is made when the HbA1c value is between 5.7–6.4%, FPG level is between 100–125 mg/dL, and 2h PG test value during 75 g OGTT is between 140–199 mg/dL. **B**

G. A random plasma glucose of ≥ 200 mg/dL in a patient with classic symptoms of hyperglycemia or hyperglycemic crisis is diagnostic of diabetes. **B**

H. Two abnormal test results from the same sample or in two separate test samples is required to make a diagnosis of diabetes where a state of hyperglycemia is uncertain. **B**

I. History of DKA, ketonuria, blood ketones, age, weight loss, time course for symptoms, severity of symptomes and family history at presentation may help distinguish T1DM and T2DM. **B**

J. DKA usually suggests T1DM, although it can occur in T2DM and secondary diabetes. Irrespective of the type of diabetes, all patients with DKA should be treated with insulin and referred to an expert. **B**

K. Circulating pancreatic autoantibodies ICA, IAA, glutamic acid decarboxylase 65-kilodalton isoform (GAD65), IA-2, and ZnT8 suggest that the individual is at risk of or has developed T1DM. **B**

L. Diabetes-specific autoantibody testing may be considered for all patients when diagnosis is doubtful (T1DM or T2DM). **B**

M. Fasting C-peptide may help to differentiate T1DM and T2DM. Euglycemia needs to be achieved before this and testing should not delay insulin treatment. **B**

N. Acanthosis nigricans, skin tags aid in clinically differentiating T2DM from T1DM to a certain degree. **B**

O. Monogenic diabetes should be considered if diabetes in early adulthood, strong family history of DM for ≥ 2 generations; absence of typical features of T1DM (no diabetes-associated

autoantibodies) and absence of T2DM features (no obesity, lacking other metabolic features); stable, mild fasting hyperglycemia (100–150 mg/dL), HbA1c between 5.6–7.6%. Genetic testing should be considered for these patients. **A**

P. When there is a diagnostic dilemma, it is important to seek expert opinion for further evaluation of the type of diabetes. **E**

Lab testing

The follow-up visit should include most components of the initial comprehensive medical evaluation. HbA1c and serum creatinine should be evaluated during the initial consultation if a report within past 3 months is not available and every 3 months thereafter. FPG and 2h PG (or a random blood glucose) are recommended at every visit [18].

Evaluation of complete blood count (CBC), lipid profile [including total cholesterol, low-density lipoproteins (LDL), and high-density lipoproteins (HDL) and triglycerides], liver function tests, spot urinary albumin-to--creatinine ratio (UACR), and estimated glomerular filtration rate (eGFR) are recommended at the initial visit and at least annually thereafter [18].

Serum sodium, serum potassium, serum creatinine, and eGFR should be evaluated more regularly in known cases of chronic kidney disease (CKD) or while starting or modifying drugs that influence renal function, such as angiotensin-converting enzyme inhibitors (ACEi), angiotensin receptor blockers (ARB), or diuretics. The risk of atherosclerotic cardiovascular disease (ASCVD), heart failure (HF), CKD and hypertension should also be assessed in all patients with diabetes at diagnosis and annually [18].

Vitamin B12

Clinical and biochemical vitamin B12 deficiency is quite common in patients with diabetes. Vitamin B12 deficiency may result from inadequate dietary intake, particularly in vegetarians and alcoholics, malabsorption caused by chronic atrophic gastritis, primarily in the elderly patients, pernicious anemia, coeliac disease, chronic pancreatitis, and medications like metformin (MF), which has been shown to lower vitamin B12 levels. These conditions can present with a variety of clinical manifestations, including dementia, peripheral neuropathy, subacute combined degeneration of the brain, and impaired memory. Patients with diabetes who have certain risk factors for vitamin B12 insufficiency should be screened for the condition and should take the recommended amount of vitamin B12 [23]. Vitamin B12 deficiency is widespread in the Indian population, particularly among those who have T2DM [24, 25].

Recommendations

A. HbA1c and serum creatinine to be done at initial visit if a report within the past 3 months is not available. **B**

B. HbA1c and serum creatinine to be done every 3–6 months thereafter as per clinical discretion. **B**

C. FPG and 2h PG (or a random plasma glucose) are recommended every visit. **B**

D. CBC, lipid profile, liver function tests, spot UACR, eGFR should be done at initial visit and at least annually thereafter. **E**

E. Serum sodium, serum potassium, serum creatinine and eGFR should be done more frequently in known cases of CKD, or at initiation and when changes in medications that affect kidney function such as ACEi, ARBs, or diuretics are made. **B**

F. Consider checking and replacing vitamin B12, if the patient has anemia, peripheral neuropathy, is a vegetarian, has symptoms of malabsorption, or is on MF. **B**

G. Risk of ASCVD, HF, CKD and hypertension should be assessed in all patients at diagnosis and annually. **B**

Physical activity or exercise

Regular physical activity (aerobic exercise and strength training) can keep a check on blood pressure (BP), cholesterol and glucose levels. It can also increase functional ability and well-being [26, 27]. Unless there are significant comorbidities or a short life expectancy, moderate-to-vigorous physical activity is advised, i.e. a mix of aerobic and resistance exercise for ≥ 150 min/week, for the prevention and treatment of diabetes [27].

All individuals with T2DM should be encouraged to engage in regular physical activity, reduce sedentary time, and break up sitting time with frequent activity breaks [28]. Leisure time activities such as walking, swimming, gardening, jogging, and yoga can reduce HbA1c significantly [29].

Any new physical activity needs to be introduced slowly and gradually increase the intensity and duration once they get accustomed to the activity. To maintain better levels of insulin sensitivity, it is advised that these exercises take place on at least 3 days of the week and people should not wait more than 2 days between activity sessions. For younger and more physically fit individuals, shorter durations, i.e. minimum 75 min/ /week of vigorous intensity or interval training may be sufficient [30]. Underlying undiagnosed cardiovascular disease (CVD) needs to be investigated and managed appropriately prior to starting any fitness training regimen for those who are at risk of CVD.

Recommendations

A. Physical activity should be introduced gradually, based on the patient's willingness, ability, and comorbidities. **B**

B. Intensity of the activity should be individualized to the specific goals. **B**

C. Patients should be encouraged to do a combination of aerobic exercises, resistance exercises and yoga. **C**

D. Most adults with diabetes should engage in ≥ 150 min of moderate-to-vigorous intensity aerobic activity per week, spread over at least 3 days/ /week, with no more than 2 consecutive days without activity. Shorter durations (minimum 75 min/week) of vigorous intensity or interval training may be sufficient for younger and more physically fit individuals. **B**

E. Active lifestyle and non-sedentary activities like walking, yoga, housework, gardening, swimming, and dancing, using stairs instead of elevators, walking or bicycling instead of motor vehicle to travel short distances should be promoted. **B**

Medical nutrition therapy (MNT)

To control diabetes effectively, nutrition therapy is essential [31]. Determining what to eat and adhering to a meal plan are often the most challenging aspects of the diabetes treatment strategy [32]. Since each patient with diabetes has a unique set of eating habits, preferences, and metabolic goals, there is no universally applicable ideal percentage of calories for the consumption of carbohydrates, proteins, and fats. Therefore, the macronutrient distribution should be determined by an individual's assessment of these factors [33].

Registered dietitian

Ideally, a registered dietician should recommend every patient with diabetes, a customized MNT at the time of diagnosis or shortly later, as well as during the follow-up visits. Dietitians should ideally execute three to six MNT interactions over the first six months and then decide whether more MNT sessions are required, based on an individual evaluation. Dietitians should conduct at least one MNT follow-up appointment each year based on the convincing evidence that, continued MNT sessions continued reductions and maintenance of HbA1c. Individual nutrition needs should be addressed based on personal and cultural preferences, health literacy and numeracy, access to healthful food choices, willingness and ability to make behavioural changes, and also barriers to change. Reducing calorie intake while maintaining a healthy eating pattern is recommended to promote weight loss [33]. Where dietitian is not available, the physician can teach the person with diabetes, the basics and nuances of diabetes diet, using simple examples from daily local food menus and audio-visual aids.

Honey and jaggery are not recommended as alternative sweetener for sucrose [14, 15]. Intake of honey for eight weeks raised HbA1c and lowered waist circumference in patients with T2DM [34, 35].

Weight loss

For people with T2DM, a 5% weight loss is advised to see a progressive clinical benefit [36]. With lifestyle programmes, significant weight reduction may be achieved by creating an energy deficit of 500–750 kcal/ /day, which is typically 1,500–1,800 kcal/day for males and 1,200–1,500 kcal/day for women when adjusted for the individual's baseline body weight [37].

Counselling

All individuals with diabetes are advised to get nutrition counselling that focuses on lowering or maintaining glycemic targets, accomplishing weight management targets, and reducing cardiovascular (CV) risk factors within specific treatment objectives [36]. Less focus should be placed on the outcome of counselling and more on the development of behaviours that promote long-term weight loss or weight management [33].

Dietary counselling, adherence to a calorie--restricted diet, and regular exercise have all been linked to decreased risks of incident diabetes in Indian males with impaired glucose tolerance. Rural and urban communities from South and North India have benefited from MNT-based model meals and community health initiatives, which have led to favourable dietary pattern modifications and improvements in a number of parameters including BMI, waist circumference, FPG, and others [38]. In obese Asian Indian individuals with any kind of prediabetes, a stepwise diabetes prevention programme reduced the probability of developing diabetes within three years [39]. These studies, along with a few others involving Indians at risk of diabetes, highlighted the advantages of adopting dietary strategies like consuming lots of fibre-rich foods, high-protein meal replacements, switching from polished white rice to whole grain brown rice, and eating more fruits and vegetables [40, 41]. Diet should include pulses, legumes, unprocessed vegetables, and low-fat dairy [15].

Table 1. Recommendations for Distribution of Carbohydrate, Proteins, and Fats in Eating Plan

Carbohydrate, protein, and fat distribution should be based on individualized assessment of current eating patterns, preferences, and metabolic goals. Diet should include pulses, legumes, unprocessed vegetables, and low-fat dairy			
Carbohydrates	**Proteins**	**Fats**	**Others**
• Carbohydrate content in the food should be 50–60% of total calorie intake • Complex carbohydrates should be preferred over refined products like *maida* • White rice in meals and breakfast (dosa and idly) to be substituted with brown rice, roti with whole grain wheat flour, oats, millets (ragi, jowar, bajra, foxtail millet, etc.), quinoa, wherever feasible	• For people with diabetes without kidney disease- average daily protein intake is 1–1.5 g/kg body weight/ day or 15–20% of total calories	• Fat intake should be < 30% of total calorie intake • Oils with high monounsaturated fatty acid (MUFA) and polyunsaturated fatty acid (PUFA), vegetable oils are to be used • Foods high in saturated fat (butter, coconut oil, margarine, ghee) should be avoided • Intake of saturated fatty acids should be < 10% of total calories/day	• Consumption of foods with low glycaemic index to be encouraged • Fibre intake should be 25–40 g/day • 4–5 small portions of fresh fruits/vegetables should be included in the diet • Fruit juices to be avoided • Overall salt consumption should be < 5 g/day or preferably even less • Diabetic modifications to local cuisines that are practical to be encouraged than fancy nonlocal cuisines that are impractical

Recommendations

A. Refer to a qualified dietitian if facilities exist; if no facilities exist, provide appropriate information (leaflets, websites). **B**

B. Focused MNT at diagnosis and as needed throughout life and during times of changing health status to achieve treatment goals. **E**

C. Carbohydrate, protein, and fat distribution should be based on individualized assessment of current eating patterns, preferences, and metabolic goals* (Tab. 1). **B**

D. Diet and lifestyle changes to achieve 5% weight loss should be recommended wherever appropriate. **B**

E. Diet should be individualized to a person's needs and preferences taking cultural diversity and cuisines into consideration. **B**

F. Energy deficit of 500 kcal/day can be considered to achieve a weight loss of 1–2 kg/month where appropriate. **A**

G. Dietary counselling should reiterate the basic principles of the constituents of food products at 1st visit and every visit in the 1st year and thereafter as needed. **B**

H. The average daily level of protein intake for people with diabetes without kidney disease is typically 1–1.5 g/kg body weight/day or 15–20% of total calories. **B**

I. Fad diets like ketogenic diet, time restricted eating or intermittent fasting may work only short term. **B**

J. There is no proven role of dietary supplements to achieve weight loss. **A**

K. Honey and jaggery are not recommended as alternative sweeteners for sucrose. **B**

L. Diet should include pulses, legumes, unprocessed vegetables, and low-fat dairy. **B**

M. Bitter gourd juice, methi and jackfruit powder are not proven remedies for controlling blood glucose levels (no large-scale studies to justify their efficacy and safety). **B**

Lifestyle advice

Comprehensive lifestyle modifications and pharmacotherapy should begin at diagnosis in patients with diabetes [26]. Lifestyle modification must always accompany other forms of therapy [11]. A multifaceted, ongoing lifestyle optimization programme is crucial for all patients with diabetes. The key components of lifestyle therapy include MNT, healthy eating habits, regular and adequate physical exercise, enough sleep, psychological support, and quitting smoking [26].

Alcohol and tobacco

Alcohol and substance abuse counselling should be offered as required. A crucial aspect of lifestyle advice

is smoking cessation and abstaining from all tobacco products. In individuals who are having trouble quitting smoking, nicotine replacement therapy and other pharmacologic therapies (e.g. sustained-release bupropion and varenicline) should be evaluated. Patients who are unable to quit smoking on their own should be referred to structured programmes [26].

Sleep

Adequate sleep is essential for maintaining good energy levels, general wellbeing, and overall health. Hence, an average sleep of around 6–9 hours of timely sleep every night is recommended. Individuals who sleep for 6 to 9 hours a night have less cardio metabolic risk factors, and those who get less sleep have risk of increased insulin resistance, hypertension, hyperglycemia, dyslipidemia, and an increase in inflammatory cytokines [26].

Recommendations

A. Lifestyle advice is to be given to all people with T2DM at diagnosis and periodically. **B**

B. Patients with diabetes who drink alcohol should be advised to avoid or limit alcohol intake and those who smoke should be advised smoking cessation and not to use any tobacco products. **A**

C. Patients with diabetes should be advised to avoid sugar sweetened beverages. **B**

D. Patient with diabetes may be advised judicious use of artificial sweeteners (aspartame — 40 mg/ /kg of body weight/day; neotame — 2 mg/kg of body weight/day; saccharin — 5 mg/kg of body weight/day; acesulfame — 15 mg/kg of body weight/day). **B**

E. Advise all patients with diabetes to get 6-9 hours of timely sleep. **A**

Glycemic goals

Assessment of glycemic control

For obvious reasons, optimal glycemic control is the crucial aspect in managing diabetes. Glycemic objectives should be tailored to each patient based on factors such as the duration of diabetes, age, life expectancy, concomitant illnesses, known CVD or advanced microvascular problems, hypoglycemia unawareness, and individual patient considerations [42].

HbA1c reflects the average glycemia over about 3 months. All patients with diabetes should have regular HbA1c testing at initial evaluation and as part of ongoing therapy. Patient's glycemic goals can be met and maintained if HbA1c levels are measured every three months [42]. To ensure that glycemic objectives are attained and maintained, patients with T2DM must be thoroughly monitored regularly regardless of the therapy they are getting [26].

Glycemic targets

Many non-pregnant adults should aim for a HbA1c of < 7% without experiencing any significant hypoglycemia. Pre-prandial and peak postprandial capillary plasma glucose should be between 80–130 mg/dL and <180 mg/dL respectively; however, more, or less stringent glycemic goals may be appropriate for specific patients [43, 44]. According to the most recent advanced technologies and treatments for diabetes (ATTD) international time in range (TIR) consensus (2019), most people with T2DM should aim to spend > 70% of their time per day (approx. > 17 h) in TIR (70–180 mg/dL), with time below range (TBR) < 70 mg/dL < 4% and time above range (TAR) > 180 mg/dL being less than 25% of time per day [45]. Less stringent targets are recommended for older or high-risk people, as well as for adults under the age of 25. However, glycemic objectives should always be tailored to the individual and rarely, it depends on how CGM and the data it produces are used personally. A strong relationship exists between HbA1c and %TIR. Lower the HbA1c, higher the TIR [45].

Severe and/or frequent hypoglycemia is an absolute indication for the change of treatment regimens, and also setting higher glycemic goals [42]. A less-intensive glycemic goal is advised for those with severe comorbid diseases, advanced diabetic complications, or significant cognitive or functional impairments. Overly strict blood glucose management in elderly individuals with more severe illness may not offer many advantages but may carry some danger [46].

Recommendations

A. HbA1c in most non-pregnant adults with diabetes should be < 7%. **A**

B. FPG in most non-pregnant adults with diabetes should be between 80–130 mg/dL. **B**

C. Post prandial blood sugar (1–2 hours after meal) in the majority non-pregnant adults with diabetes should be between 80–180 mg/dL. **B**

D. HbA1c in older adults who are otherwise healthy with few coexisting chronic illnesses and intact cognitive function and functional status should be < 7.0–7.5%. **B**

E. Less stringent HbA1c goals < 8% may be appropriate for patients with limited life expectancy or when benefits of the treatment are lesser than the harms of treatment. **B**

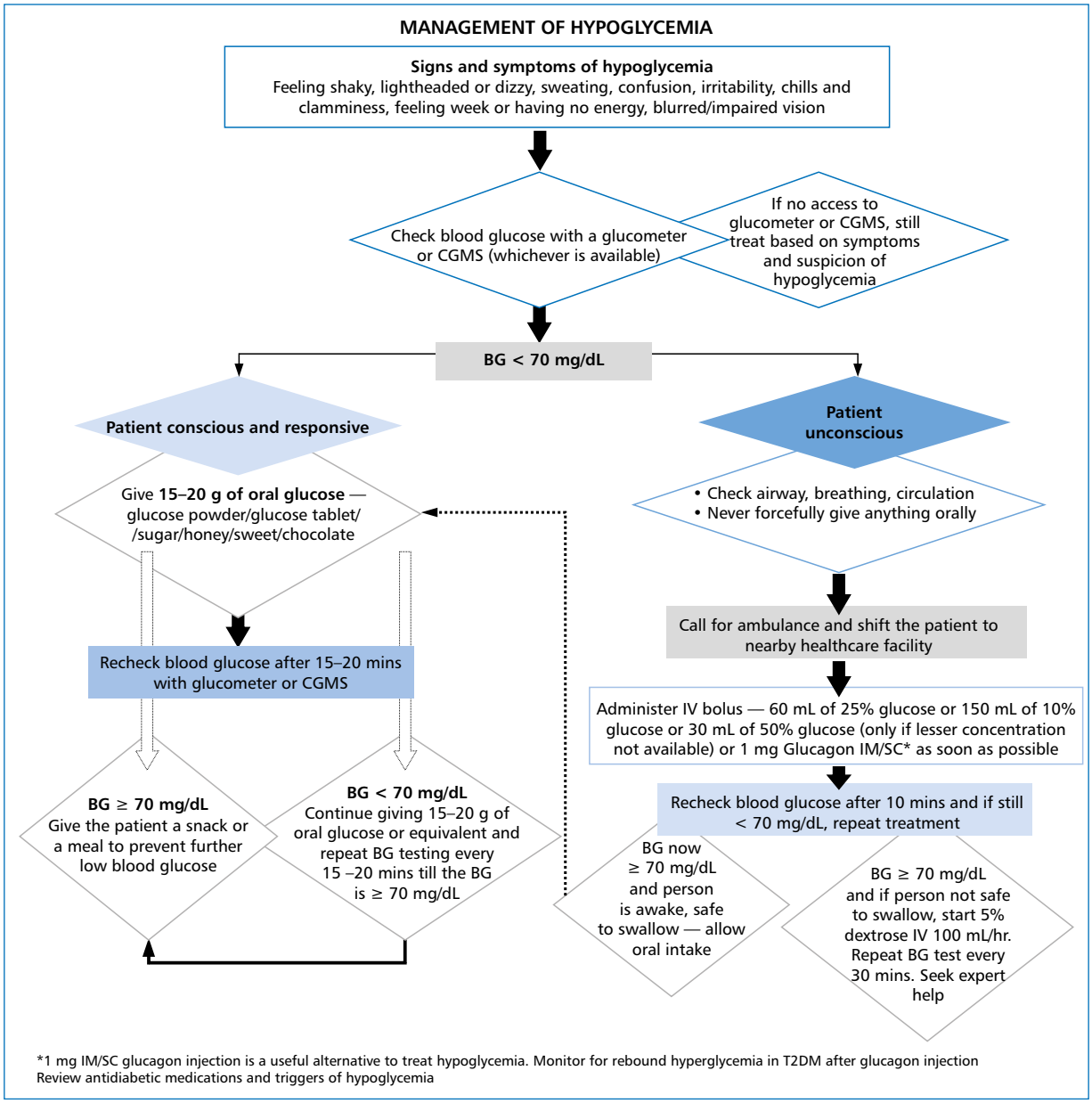


Figure 3. Management of Hypoglycemia
BG — blood glucose; CGMS — continuous glucose monitoring system; IV — intravenous; T2DM — type 2 diabetes mellitus

F. Glycemic goals for some older adults might be relaxed as part of individualized care, but hyperglycemia or hyperglycemia complications should be avoided in all patients. **B**

G. HbA1c goals need to be individualized based on the duration of diabetes, age, life expectancy, comorbid conditions, existing CVD, microvascular complications, profession, patient preference, and awareness about hypoglycemia during hypoglycemic episodes. **B**

Hypoglycemia

Hypoglycemia is a major challenging factor in the glycemic management of an individual with diabetes. Level 1 hypoglycemia is termed when blood glucose is < 70 mg/dL and ≥ 54 mg/dL. Level 2 hypoglycemia is when the blood glucose is < 54 mg/dL and Level 3 hypoglycemia is when a severe incident is defined by changed mental or physical status needing help for treatment of hypoglycemia [42].

Hypoglycemia symptoms include shakiness, anger, disorientation, tachycardia, and hunger (Fig. 3). For

patients with diabetes, hypoglycemia symptoms can be uncomfortable or scary. Hypoglycemia at Level 3 might result in unconsciousness, seizures, coma, or even death. At each visit, doctors should assess the patient's risk of hypoglycemia, especially if they are on insulin or an insulin secretagogue [47].

Management

Management of hypoglycemia is summarised in Figure 3. Most episodes of hypoglycemia can be self-treated by ingestion of glucose or carbohydrate-containing juice, soft drinks, candy, other snacks, or a meal. A good amount of carbohydrate (15–20 g) can be given again in 15–20 minutes if necessary. Since the glycemic response to oral glucose is transient, it is often advised to consume a larger snack or meal soon after the plasma glucose level is corrected to normal range with oral glucose. When a hypoglycemic patient is unable to consume carbohydrates orally, or in case of severe hypoglycemia, intravenous glucose is necessary [42, 48].

Fast-acting carbohydrates should be given to patients when their blood glucose falls below the normal range, which is < 70 mg/dL. Although pure glucose ingestion is preferred to correct hypoglycemia, any form of carbohydrate that contains glucose is recommended to raise the blood glucose levels rapidly [42].

When someone is unable or unwilling to take glucose or foods orally, hypoglycemia can be treated using glucagon injection intramuscularly (IM) or subcutaneously. Both the patients and the caregivers (family members, roommates, school personnel, childcare providers, institution staff, or co-workers, etc.), should be primed about the usage of glucagon which includes glucagon storage and how to give it [42].

For treating hypoglycemia with intravenous glucose, the use of 5%, 10% or 25% glucose solutions is preferable over the use of 50% glucose because the use of hyperosmolar solutions, such as 50% glucose increases the risk of extravasation damage [49].

In order to reduce hypoglycemia, hypoglycemia avoidance education, re-evaluation, and treatment regimen adjustments should be made [42]. Precipitating causes need to be investigated at the earliest opportunity and appropriately managed. Education about hypoglycemia prevention and treatment should be part and parcel of every visit to the doctor.

Recommendations

A. Blood glucose < 70 mg/dL is hypoglycemia and any hypoglycemia requiring 3rd party assistance or blood glucose < 54 mg/dL is severe hypoglycemia. **B**

B. Risk or occurrence of hypoglycemia should be assessed at every visit. **C**

C. In a scenario of hypoglycemia or potential hypoglycemia, if there is no access to glucometer or continuous glucose monitoring (CGM) to check blood glucose levels, patient should be treated based on symptoms and suspicion of hypoglycemia. **B**

D. Oral glucose (15–20 g) or equivalent is to be given for conscious patients with blood glucose < 70 mg/dL. If there is continued hypoglycemia (blood glucose < 70 mg/dL) after 15 min, then repeat 15–20 g of oral glucose. Repeat oral glucose 15–20 g and recheck blood sugar after 15–20 mins till the blood glucose is ≥ 70 mg/dL. Once ≥ 70 mg/dL, give a snack or a meal to prevent further hypoglycemia. **B**

E. Unconscious person with hypoglycemia should be administered intravenous (IV) bolus — 60 mL of 25 % dextrose or 150 mL of 10% dextrose or 30 mL of 50% dextrose (only if lesser concentration is not available due to risk of extravasation injury) or 1 mg of Glucagon IM as soon as possible. **B**

F. After treatment of hypoglycemia in an unconscious person as above, with IV dextrose, recheck the plasma glucose after 10 mins and if still < 70 mg/dL, repeat treatment. Once plasma glucose ≥ 70 mg/dL, and the patient is awake and safe to swallow, allow oral intake of 15–20 g glucose (glucose powder/tablet/honey/sugar/sweet/chocolate). Once plasma glucose ≥ 70 mg/dL, and if the patient is not safe to swallow, start 5% dextrose IV 100 mL/h. Repeat plasma glucose monitoring every 30 mins and seek help from an expert. **B**

G. Be vigilant for hypoglycemia in patients with impaired or declining cognition, advanced age, co-morbidities (renal or hepatic impairments), decreased food intake due to any reason. **B**

H. Hypoglycemic unawareness is defined as having blood glucose < 70 mg/dL without symptoms. These patients should be referred to an expert. **E**

Remission

Remission in individuals with T2DM refers to a return to normal or near normal blood glucose levels. It can be achieved occasionally with the use of either established and newly developed medication treatments, lifestyle changes, or metabolic surgery [50].

Types and definition of remission

The 3 categories of remission are partial remission, complete remission, and prolonged remission.

According to ADA consensus report 2022, "Partial" remission to be considered when hyperglycemia below diagnostic thresholds for diabetes was maintained without active pharmacotherapy for at least 1 year. "Complete" remission to be considered when normal glucose levels are achieved without pharmacotherapy for 1 year. "Prolonged" remission to be considered when a complete remission persisted for 5 years or more without pharmacotherapy [51].

A partial remission is defined as HbA1c < 6.5% (< 48 mmol/mol) and/or FPG 100–125 mg/dL (5.6 to 6.9 mmol/L) whereas a complete remission calls for normal HbA1c value < 5.7% and FPG readings < 100 mg/dL (5.6 mmol/L), respectively [51].

A change in lifestyle, further medicinal or surgical procedures, or a combination of these methods may be used to put diabetes into remission. Depending on the intervention, a therapy may or may not need to be stopped before a diagnosis of remission is made [51, 52].

A diagnosis of remission can only be made when all glucose-lowering medications have been stopped for a period long enough to enable the effects of the medication to fade and to evaluate the impact of the drug's absence on HbA1c readings. Some individuals with diabetes may experience an improvement in their blood sugar levels to the normal range, either of their own will or as a result of medical treatments. In some circumstances, this improvement can last even after the use of glucose-lowering medications has been discontinued. Presently, with emerging therapies, such lasting improvement could be achieved [51].

The T2DM metabolic control therapies have advanced significantly in recent years. When T2DM in adults occurs initially, short-term pharmacological treatment may sometimes restore near normal glycemic control, allowing medication to be discontinued. The strongest evidence for the reversal of "glucose toxicity" and restoration of glycemic control comes from early, intensive insulin treatment, while it can also happen with alternative therapies [50].

Recommendations

A. Remission of diabetes is sustained metabolic improvement in T2DM to near normal levels, i.e. return of HbA1c to < 6.5% spontaneously or following an intervention, persisting for at least 3 months in the absence of usual glucose lowering pharmacotherapy. **B**

B. Complete remission is maintenance of normal glucose levels without pharmacotherapy for 1 year. **B**

C. Prolonged remission is a complete remission persisting for ≥ 5 years without pharmacotherapy. **B**

D. Remission of T2DM may be possible with rigorous dietary and lifestyle changes within the first 6 years after the diagnosis of T2DM, if not established on insulin. **B**

Obesity and T2DM

Pathophysiology of T2DM

Obesity plays a crucial part in the onset and progression of T2DM. Ectopic fat deposition (visceral fat, skeletal muscle, liver, pancreatic cells, and other organs) is thought to play a role in the pathophysiology of T2DM. As subcutaneous fat expands to its maximum, this can result in hepatic and peripheral insulin resistance as well as progressive β-cell failure, which in turn leads to hyperglycemia [53]. People with BMI ≥ 30 kg/m^2 have increased lifetime risk of developing diabetes, spending more time with the disease, and dying earlier due to the disease [54].

Table 2. Distribution of BMI Stratified for India (Adapted from [56])

Body type	BMI
Underweight	Less than 18.5 kg/m^2
Normal or lean	18.5–22.9 kg/m^2
Overweight	23.0–24.9 kg/m^2
Obese	Greater than or equal to 25 kg/m^2
Morbid obesity	Greater than or equal to 35 kg/m^2

BMI — body mass index

Assessment of obesity

Obesity is a significant contributing factor for the increasingly prevalent metabolic syndrome and T2DM among Asian Indians, The BMI cut-off criteria for overweight and obesity in Indian T2DM patients is 23–24.9 kg/m^2 and ≥ 25 kg/m^2, respectively (Tab. 2) [55, 56].

Among patients with both T2DM and overweight or obesity and who have inadequate glycemic, BP, lipid control and other obesity related medical conditions, a modest and sustained weight loss improves them and may reduce the need for medications to control these risk factors. As supplements to food and exercise, there are pharmaceuticals for both short- and long--term weight control. When deciding on medication regimens, one must consider how each prescription will affect weight. Medications linked to varied degrees of weight reduction include MF, glucosidase inhibitors, sodium-glucose cotransporter 2 inhibitors (SGLT-2i), glucagon-like peptide 1 receptor agonists (GLP-1RA),

and amylin mimics. While insulin secretagogues, thiazolidinediones, and insulin are frequently linked to weight gain, dipeptidyl peptidase 4 inhibitors (DPP-4i) have no effect on weight [37].

Management

Long-term (> 12 weeks) therapy for adult obesity is possible with the lipase inhibitor orlistat, which is available over the counter (OTC) in dosages of 60 mg and 120 mg [37]. Glycemic control and lipid parameters significantly improve with orlistat medication and diet [57]. In overweight or obese patients with T2DM, orlistat (120 mg) appears to enhance glycemic control and not just weight loss alone. An increase in insulin sensitivity, a slower and less complete digestion of dietary fat, a decrease in postprandial plasma non-esterified fatty acids, a reduction in visceral adipose tissue, and stimulation of GLP-1 secretion in the lower small intestine are some of the hypothesised mechanisms underlying this effect [58].

Surgery for the treatment of obesity can aid in T2DM improvement and long-lasting weight loss. Metabolic surgery may be considered as an option in adults with a BMI of 30.0–34.9 kg/m^2 (> 27.5 kg/m^2 in Asians) who are suffering from T2DM and are unable to lose weight permanently or cure their comorbid conditions and hyperglycemia with nonsurgical treatments. Metabolic surgery should be performed in high volume centres with multidisciplinary teams knowledgeable and skilled in managing obesity, diabetes, and gastrointestinal (GI) surgery [37].

Recommendations

A. Overweight and obesity cut-off points for Indian T2DM patients are BMI 23–24.9 kg/m^2 and ≥ 25 kg/m^2 respectively. **B**

B. Consider medication's effect on weight when choosing glucose-lowering medications in patients with T2DM who are overweight or obese. **B**

C. Wherever indicated, the weight loss agent to be considered is Tab. Orlistat 60–120 mg thrice daily. **B**

D. For patients with BMI ≥ 27.5 kg/m^2 who do not achieve desired weight loss, glycemia control and improvement in comorbidities with nonsurgical methods, referring them to an expert for metabolic surgery may be considered as an option. **A**

Management of hyperglycemia

The key to manage diabetes is the implementation of a personalised approach that is tailored to the needs of T2DM patients, considering their preferences, comorbidities, risks associated with polypharmacy, and possibilities of benefiting from long-term therapy. A strategy like this is crucial when dealing with multimorbidity [59]. One must also consider the effectiveness, risk of hypoglycemia, influence on weight, cost and access, side effects, and patient preferences along with the consequences on CV and renal comorbidities while selecting the appropriate drug [59, 60].

It is important to consider the medications' effect on weight when treating T2DM patients individually (Tab. 3). Patients with T2DM who are obese should be prescribed weight-loss or weight-neutral medications. Weight reduction is encouraged by MF, SGLT-2i, GLP-1RA, alpha-glucosidase inhibitor (AGI), and amylin mimics. Fixed-ratio insulin/GLP-1RA combo treatments and DPP-4i seem to have negligible effect on weight. Weight gain is associated with thiazolidinediones, insulin, and insulin secretagogues [sulfonylureas (SU), meglitinides] [61]. The optimal first-choice medications for people who are at elevated risk of ASCVD, HF, and or CKD are GLP-1RA and SGLT-2i. As some newer anti-diabetic medications can be more expensive, the agents used will have an impact on care associated with costs [59, 62].

Pharmacologic therapy

First-line of pharmacotherapy should begin as soon as T2DM is identified; for many individuals, this will involve MF monotherapy along with lifestyle changes, unless there are contraindications. In some situations, such as in those who have a known or elevated risk of CV or renal problems, additional or alternative medicines may be taken into consideration [60]. MF is a safe, time tested, cost-effective drug recommended as first line therapy unless there are contraindications for its use. A dose of 500 mg MF to be taken once a day, and the dose should be increased gradually to prevent any GI adverse effects. The dose can be increased to 500 mg twice a day after 1–2 weeks up to their three-month HbA1c check and increased further to 1000 mg twice daily if they are still not reaching their goals [26, 59].

In individuals with contraindications for MF or intolerance, a medication from a different class should be considered as initial therapy based on patient considerations [62]. Majority of the patients may require dual combination medication to attain their target HbA1c level when HbA1c is ≥ 1.5–2% above the glycemic target. Insulin has the advantage of being effective where other agents are not. Insulin should be considered as part of any combination regimen when hyperglycemia is severe, especially if catabolic features (weight loss, hypertriglyceridemia, ketosis) are present. It is usual practice to start insulin therapy for individuals who have blood glucose levels of ≥ 300 mg/dL (16.7 mmol/L) or

Table 3. Criteria to Choose an Agent

Hypoglycemia	Weight	Cost	ASCVD or at high risk of ASCVD	HF	CKD/albuminuria
Low risk of hypoglycemia	**Weight neutral**	**Low cost**	GLP-1RA or SGLT2i based on glycemic needs	SGLT2i	SGLT2i or GLP-1RA
DPP4i, GLP-1RA, SGLT2i, Pio, AGI	MF, DPP4i, AGI	MF, SU, Pio, meglitinides, human insulin, some DPP4i, some SGLT2i, AGI			
Increased risk of hypoglycemia	**Weight loss**	**High cost**	If Hba1c above the target, consider SGLT2i for patients on GLP-1RA and vice versa		
SU, meglitinides and insulin	GLP-1RA, SGLT2i	GLP-1RA, some DPP4i, some SGLT2i, analogue insulins			
	Weight gain				
	SU, Pio, meglitinides and insulin				

AGI — alpha glucosidase inhibitor; ASCVD — atherosclerotic cardiovascular disease; CKD — chronic kidney disease; DPP4i — dipeptidyl peptidase 4 inhibitor; GLP-1RA — glucagon-like peptide-1 receptor agonist; HF — heart failure; MF — metformin; Pio — pioglitazone; SGLT2i — sodium/glucose contransporter-2 inhibitor; SU — sulfonylurea

HbA1c >10% (86 mmol/mol) or if the patient exhibits symptoms of hyperglycemia (i.e. polyuria or polydipsia) or signs of catabolism (weight loss). Simplifying the regimen or switching to noninsulin medications is frequently feasible once glucose toxicity resolves [60].

Glycemic management of non-pregnant adult with T2DM

Choice of any glycemic agents should be assessed by considering the individual patient characteristics, patient preferences, any contraindications to the drug, glucose-lowering efficacy, risk of hypoglycemia, affordability, effect on body weight and other factors such as comorbidities. This patient centric approach is recommended for diabetes management. As shown in the Figure 4, the hyperglycemic agents are classified as.

First-line agents

If HbA1c ≥ 6.5%, MF is usually the initial pharmacotherapy in people with T2DM along with lifestyle modification. Titration of MF can be done to maximum tolerated dose, i.e. up to 2 g/day.

If HbA1c ≥ 8.5–9%, consider dual therapy by adding a second agent to MF which should be chosen based on individual patient characteristics, efficacy, and safety profile of other antihyperglycemic agents like SU, DPP-4i, SGLT-2i, GLP-1RA, pioglitazone [14, 15].

Consider insulin therapy if the patient has an active infection, renal or hepatic impairment or hospitalized or having weight loss or undergoing surgery or planning pregnancy.

Glycemic levels should be assessed periodically. If glycemic targets are not achieved within 3 months of initiating first-line agents, consider addition of 2nd or 3rd line as appropriate.

Although MF is usually the first line agent to tackle hyperglycemia, SGLT2i or GLP-1A would be justified as first line agents instead of MF, if HF, high risk of ASCVD, diabetic kidney disease (DKD) or obesity exist, especially if HbA1c is not high, i.e. < 7%. If in doubt about this choice, it is recommended to seek expert opinion.

Second-line agents

Choice of glucose lowering agent at any stage, be it first line, second line, third line, fourth line antihyperglycemic agents should be made again based on individual patient characteristics, patient preferences, any contraindications to the drug, glucose-lowering efficacy, risk of hypoglycemia, affordability, effect on body weight and other factors [63]. The recommended second–line agents for T2DM include either oral or injectable GLP--1RA, SGLT-2i, DPP-4i, SU, AGIs, meglitinides, pioglitazone and insulin.

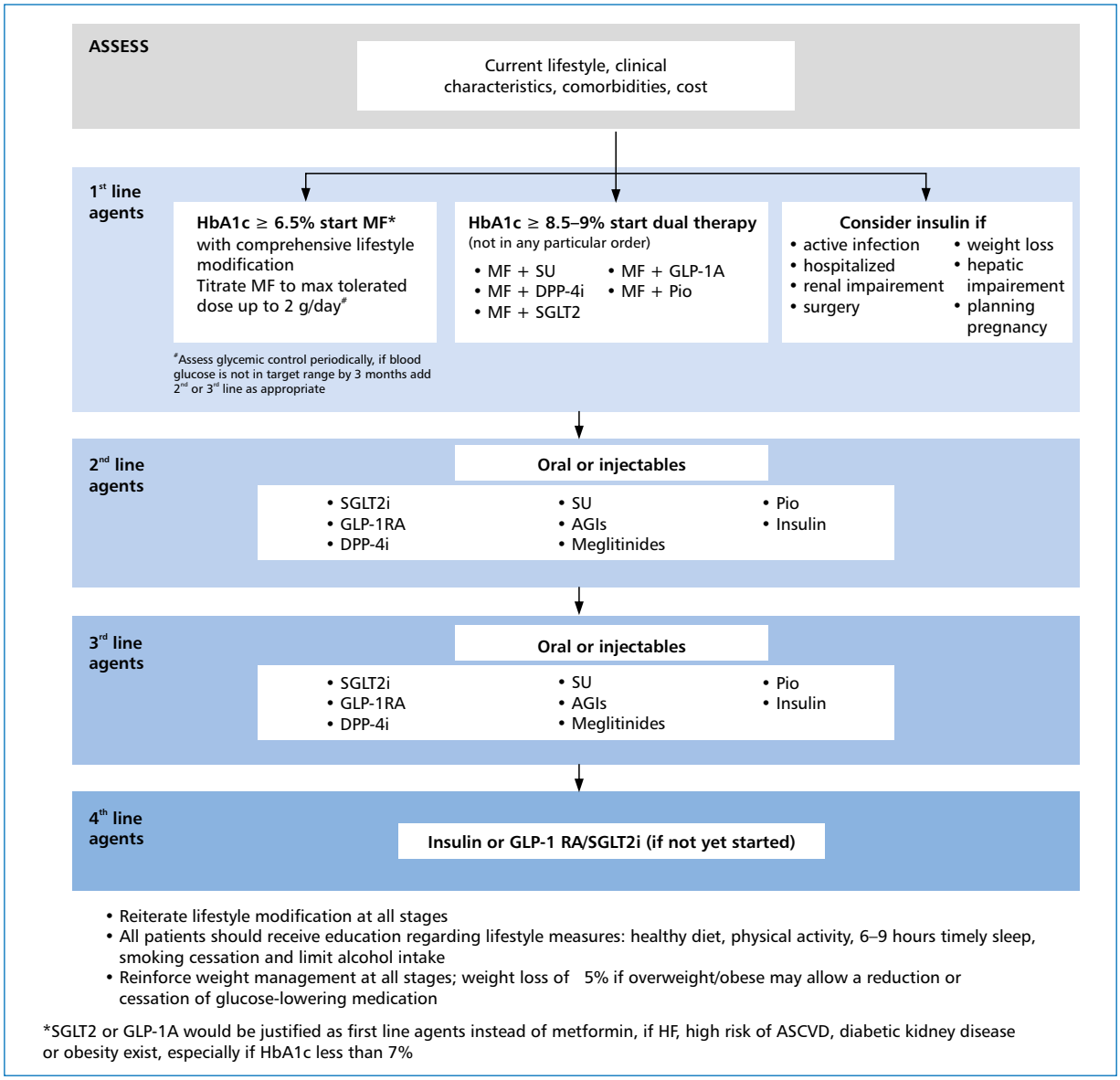


Figure 4. Glycemic Management of Non-Pregnant Adult with T2DM
AGI — alpha glucosidase inhibitor; ASCVD — atherosclerotic cardiovascular disease; DPP4i — dipeptidyl peptidase 4 inhibitor; GLP-1 — glucagon-like peptide-1; GLP-1RA — glucagon-like peptide-1 receptor agonist; HF — heart failure; MF — metformin; Pio — pioglitazone; SGLT2i — sodium/glucose contransporter-2 inhibitor; SU — sulfonylurea; T2DM — diabetes mellitus;

Third-line agents

Oral or injectable GLP-1RA, SGLT-2i, DPP-4i, SU, AGIs, meglitinides, pioglitazone and insulin are considered as third line agents.

Fourth-line agents

Insulin or GLP-1RA/SGLT-2i are options for fourth line antihyperglycemic medications (if not yet started).

At all phases of therapy, it is strongly recommended to reinforce on lifestyle changes and weight control since a weight loss of > 5% in cases of overweight or obesity may allow for a decrease or discontinuation of antihyperglycemic drugs. All T2DM patients should be educated on lifestyle modifications such as a healthy diet, physical activity, 6–9 hours timely sleep, smoking cessation, and limiting alcohol intake.

Combination therapy

Maintenance of glycemic targets with monotherapy may be possible for only few years, after which combination therapy is essential. To reach their desired HbA1c, many patients need dual or triple combination medication. It has traditionally been recommended to add drugs to MF in a stepwise manner for a clear

evaluation of the advantages and disadvantages of novel treatments as well as to minimise potential side effects and expense. Dual therapy, as first line is used to achieve glycemic targets more quickly, and then it is used to extend the duration of the glycemic impact [60].

More rigorous early combination therapy offers some advantages and should be considered, if necessary, during a shared decision-making process with patients. First, more intense therapy with two or more agents, including insulin may be beneficial and should be considered during a collaborative decision-making process with patients, if necessary. For example, in patients presenting with HbA1c readings 1.5–2.0% above goal, combination treatment should be taken into consideration. Finally, the addition of high glycemic efficacy medications or medicines to reduce CV/renal risk (e.g. GLP-1RAs, SGLT-2i) may allow for weaning off the present regimen, particularly drugs that may raise the risk of hypoglycemia. Therefore, treatment intensification need not necessarily follow a sequential addition of therapy instead, the regimen should be adjusted to coincide with patient-centred treatment goals [60].

Based on the patient's clinical features and preferences, additional medications may be added to the initial therapy. The important clinical criteria include existence of proven ASCVD or indicators of high ASCVD risk, HF, CKD, other comorbidities, risk of certain adverse medication effects, as well as safety, tolerability, and cost. Similar factors are considered when treating individuals who need a third medication to reach their glycemic targets. An SGLT-2i or GLP-1RA with demonstrated CVD benefit is advised as part of the glucose-lowering regimen independent of HbA1c and MF use, in patients with ASCVD or indicators of high ASCVD risk (such as patients under the age of ≥ 55 with coronary, carotid, or lower-extremity artery stenosis > 50% or left ventricular hypertrophy), HF, or CKD [60].

Recent systematic reviews and network meta-analyses reveal that adding particular GLP-1RAs and insulin regimens to MF-based background treatment results in a significant HbA1c reduction. Treatment plans must always be regularly evaluated for effectiveness, side effects, and patient burden. Patients may need treatment reduction or discontinuation frequently due to inefficiency, unpleasant side effects, cost, or a change in glycemic objectives [60].

Individuals who have long standing diabetes may require more potent injectable drugs. The inclusion of basal insulin, either human neutral protamine Hagedorn (NPH) or one of the long-acting insulin analogues, to oral drug regimens is a well-established technique that is beneficial for many patients. Recent research also supports the use of GLP-1RAs in patients who are not at glycemic target. Although the majority of GLP-1RAs are injectable, semaglutide is currently marketed as an oral version. In trials evaluating the addition of an injectable GLP-1RA or insulin in individuals requiring further glucose reduction, the glycemic effectiveness of injectable GLP-1RA was comparable to or better than that of basal insulin. In these studies, GLP-1RAs had worse GI side effects than insulin but a decreased risk of hypoglycemia and favourable benefits on body weight. In light of these findings, GLP-1RAs are recommended for individuals who need the potency of an injectable medication for glucose management with the added benefit of weight loss and less hypoglycemia with potential cardio-renal benefits. In patients who are intensified to insulin therapy, combination therapy with a GLP-1RA has been proven to have superior efficacy and durability of glycemic treatment impact with lesser weight gain and lesser hypoglycemia than intensification with insulin therapy alone without GLP-1RA. However, cost and tolerability are crucial factors to consider while using GLP-1RA [60].

Table 4. Indications for Insulin Therapy in Patients with T2DM

Indications for Insulin therapy in patients with T2DM
• Acute illness
• Infection/sepsis
• Surgery
• Planning pregnancy and during pregnancy
• In-hospital management of hyperglycemia
• Glucose toxicity
• Contraindications to or failure to achieve goals with oral antidiabetic medications, and a need for flexible therapy
• Uncontrolled diabetes (persistently HbA1c level remains above the set target despite other antidiabetic drugs)
• Hepatic or renal impairment

HbA1c — glycated hemoglobin; T2DM — type 2 diabetes mellitus

Insulin therapy

Insulin is the most effective anti-hyperglycemic medication [26]. The use of insulin treatment is necessary for many patients who are diagnosed with T2DM [60]. Indications of insulin include acute illness or surgery, pregnancy, glucose toxicity, contraindications to or failure to achieve goals with oral antidiabetic medications, and a need for flexible therapy (Tab. 4) [64]. When hyperglycemia is severe, insulin should be considered as a component of any combination treatment, especially if the patient is symptomatic or if any catabolic characteristics, such as weight loss or ketosis, are present. Insulin has the benefit of being successful

when other medicines may not be [43]. Before beginning insulin therapy, a number of issues should be considered, including the patient's motivation, CV and end-organ difficulties, age, the risk of hypoglycemia, the patient's general health state, and cost [26].

Patients with long-standing uncontrolled T2DM and who are on two or more oral anti-hyperglycemic medications and are less likely achieving their target HbA1c with a third medication, an addition of a GLP-1RA, may successfully decrease blood glucose levels, although many patients may eventually need insulin [26].

Insulin usage is an exhaustive topic in itself and will be covered in a separate document elaborately.

Recommendations

A. Pioglitazone is to be avoided in patients with or at risk of HF and osteoporosis and macular oedema. **B**

B. Insulin therapy should be considered in all patients failing to achieve glycemic targets on 3 oral agents. A three-step protocol involving initiation, titration, and intensification is recommended for all patients requiring insulin. **B**

C. MF and other glucose lowering agents, except pioglitazone should be continued after initiation of insulin for ongoing glycemic and metabolic benefits. Sulphonylureas may be discontinued with twice a day or more Insulin regimens. **A**

D. Antidiabetics with low risk of hypoglycemia are DPP-4i, GLP-1RA, SGLT-2i, pioglitazone, AGI. **B**

E. Antidiabetic drugs that cause weight gain: SU, thiazolidinedione, meglitinides, insulin. **B**

F. When cost is a constraint, the choice of antidiabetic drugs could be MF, SU, meglitinides, thiazolidinedione, human insulin, some DPP-4is and some SGLT-2is. **B**

BP Management

People with T2DM often have hypertension, which is a significant risk factor for ASCVD and microvascular problems [65]. The type and length of diabetes, age, sex, race or ethnicity, BMI, history of glycemic management, and presence of renal disease, all affect the prevalence of hypertension in patients with diabetes [66].

At each regular clinical appointment, BP should be checked in these patients. The BP targets should be tailored to each person with diabetes and hypertension through a process of collaborative decision-making that considers CV risk, potential side effects of antihypertensive drugs, and patient preferences [18, 65].

Home monitoring of BP should be part of the disease self-management program [67]. It is a helpful tool to enhance the management of hypertension and related healthcare outcomes [68]. Indicators of white coat hypertension, masked hypertension, or other differences between office and true BP can be found by self-monitoring of home BP and 24-hour ambulatory BP monitoring. Home BP monitoring may also improve patient medication adherence, thereby lowering their risk of CVD [65].

For patients, whose BP is > 120/80 mmHg, a lifestyle intervention must include weight loss. When necessary, a dietary pattern should be recommended similar to the dietary approaches to stop hypertension (DASH) programme, which includes increasing potassium intake while lowering sodium intake, drinking alcohol sparingly, and increased physical activity [65]. In individuals with hypertension, quitting of smoking also results in a considerable decrease in both systolic and diastolic BP [6].

BP target of < 130/80 mmHg may be recommended for those with diabetes and hypertension who are at greater CV risk (existing ASCVD or 10-year ASCVD risk ≥ 15%) [65]. Patients with diabetes and hypertension who have a reduced risk of CVD (10-year ASCVD risk < 15%) should target BP of < 140/90 mmHg [65].

Pharmacological management

The recommended first-line treatment for hypertension in adults with diabetes and coronary artery disease (CAD) is ACEi or ARBs. The recommended first-line treatment for hypertension in individuals with diabetes and UACR ≥ 300 mg/g creatinine or 30––299 mg/g creatinine is an ACEi or ARB, at the highest tolerable dose. If one class is intolerable, the other ought to be used in its place [65].

Initial treatment for patients with albuminuria (UACR ≥ 30 mg/g) should be with an ACEi or ARB to lower the risk of developing progressive kidney disease. In patients already receiving ACEi or ARB therapy, continuing it can have CV benefits without significantly raising the risk of end-stage renal disease (ESRD) until kidney function declines to eGFR 30 mL/min/1.73 m^2. Patients with eGFR < 30 mL/min/1.73 m^2 should be provided a long-acting loop diuretic, such as torsemide [66].

Patients on an ACEi, ARB, or diuretic should get their serum potassium, creatinine/eGFR, and potassium levels checked at least annually [65]. Patients with resistant hypertension who are receiving traditional pharmacological therapy with three agents, including a diuretic, but still don't reach BP goals should be referred to a specialist [66].

Recommendations

A. BP should be measured at every routine clinical visit. **A**

B. All hypertensive patients with diabetes should be encouraged to monitor their BP at home. **A**

C. BP targets should be individualized in patients with diabetes and hypertension to address CV risk, potential adverse effects of antihypertensive medications, and patient preferences. **B**

D. BP target for individuals with diabetes and hypertension:
- At higher risk of CVD (10-year ASCVD risk > 15%) is < 130/80 mmHg. **B**
- At lower risk of CVD (10-year ASCVD risk < 15%) is < 140/90 mmHg. **A**

E. If BP > 120/80 mmHg, advice lifestyle intervention, i.e. weight loss (when indicated), healthy eating pattern, reducing salt intake to < 5 g/day, moderation of alcohol intake, increasing physical activity and quitting smoking. **A**

F. ACEi or ARBs should be used as 1st line agents for hypertension in people with diabetes and CAD, and patients with diabetes and UACR ≥ 30 mg/g. **B**

G. Serum creatinine/eGFR, serum sodium and serum potassium levels should be monitored at least annually in patients on ACEi, ARB, or diuretic. **B**

H. When BP targets not met with 3 classes of antihypertensive medications or suspecting secondary causes of hypertension in people with diabetes, refer to an endocrinologist for further evaluation. **E**

Lipids management

Patients with T2DM have an increased prevalence of lipid abnormalities, contributing to their elevated risk of ASCVD. Diabetic dyslipidemia is a controllable risk factor which is essential to prevent CVD in people with T2DM [70]. Regulating atherogenic cholesterol particle concentrations is essential to prevent macrovascular disease or ASCVD. Early and aggressive therapy of dyslipidemia aids in lowering the risk of ASCVD in T2DM [26].

Lipid testing is important in clinical practice for CV risk assessment and treatment. Despite the fact that we spend the vast majority of our time not fasting, fasting samples have long been considered the gold standard for measuring triglycerides and cholesterol because fasting is thought to reduce variability and allow for a more accurate derivation of the commonly used Friedewald-calculated LDL cholesterol [71].

Postprandial effects do not reduce, but rather exacerbate, lipid-CVD risk relationships. Most lipid levels alter little after a meal as compared to fasting. In patients with diabetes, fasting may mask abnormalities in triglyceride-rich lipid metabolism, which is critical in identifying those with persistent residual risk after statin medication. Non-fasting tests are safe, convenient, and practical, with potential economic benefits and are sufficient for screening for CV risk. Currently, fasting panel testing is suggested in cases of excessively high triglycerides, and before initiating therapy in individuals with inherited lipid diseases [71].

Lipid profile (total cholesterol, LDL, HDL, and triglycerides) should be obtained in people at diabetes diagnosis or during the initial medical examination, and then every year or more frequently if indicated [65]. Lipid profile is recommended when individuals initiate statins or other lipid-lowering therapy. They should get evaluated 4–12 weeks after starting the statin therapy or changing the dose, and then every year thereafter. This aids in tracking prognosis and ensure medication adherence [65].

To improve the lipid profile and lower the risk of ASCVD in patients with diabetes, lifestyle changes focusing on weight loss (if indicated), DASH eating pattern, reduction of saturated fat and trans-fat, increase of dietary n-3 fatty acids, viscous fibre, and plant stanols/sterols intake, and increased physical activity should be advised. Lifestyle therapy may have to be intensified for patients with elevated triglyceride levels (> 150 mg/dL and/or low HDL < 40 mg/dL for men, < 50 mg/dL for women. In patients with extremely high triglycerides and poor glycemic control, glycemic management may also help to reduce plasma lipid levels [65].

Pharmacological therapy

Statins are cardio protective and excellent choice of medications to lower LDL cholesterol. High-intensity statin treatment achieves a ≥ 50% decrease in LDL cholesterol, and moderate-intensity statin regimens produce 30–49% reductions in LDL cholesterol. Low-dose statin medication is typically not suggested in patients with diabetes, although it is occasionally the only statin dose that a patient may take. If a patient does not tolerate the desired statin intensity, the maximally tolerated statin dosage should be utilised [65].

Statins, along with lifestyle management, may be appropriate for individuals with diabetes aged 20–39 years who have additional ASCVD risk factors (Tab. 5). Use moderate-intensity statin treatment in addition to lifestyle management for individuals with diabetes aged 40–75 years who do not have ASCVD. It is permissible to

use high-intensity statin medication in individuals with diabetes who are at higher risk, particularly those with multiple ASCVD risk factors or those aged 50–70 years. To lower LDL cholesterol levels by 50% or more in persons with diabetes with a 10-year ASCVD risk of 20% or higher, it may be appropriate to add ezetimibe to maximally tolerated statin medication. High-intensity statin medication should be coupled with lifestyle therapy for individuals of all ages with diabetes and ASCVD [65]. If LDL cholesterol is ≥ 70 mg/dL on maximum tolerated statin dosage in patients with diabetes and ASCVD, who are regarded extremely high risk using certain criteria, consider adding further LDL-lowering treatment (such as ezetimibe or PCSK9 inhibitor) [65].

Hypertriglyceridemia management

The most effective treatments to control hypertriglyceridemia are to make lifestyle changes such as abstaining from alcohol, eating less quickly digested carbs, losing weight, and controlling blood glucose levels [65, 72]. Severe hypertriglyceridemia (fasting triglycerides ≥ 500 mg/dL and especially > 1,000 mg/dL) may necessitate pharmacologic treatment (fibric acid derivatives and/or fish oil) and dietary fat restriction to lower the risk of severe pancreatitis [65].

In adults with moderate hypertriglyceridemia (fasting or non-fasting triglycerides 175–499 mg/dL), clinicians should address and treat lifestyle factors (obesity and metabolic syndrome), secondary factors (diabetes, chronic liver, or kidney disease and/or nephrotic syndrome, hypothyroidism), and medications that raise triglycerides. The addition of icosapent ethyl to a statin in individuals with ASCVD or other CV risk factors who have reduced LDL cholesterol, but increased triglycerides (135–499 mg/dL) might be considered to minimise CV risk [65].

Combination treatment with statins and fibrates is linked with an increased risk of aberrant transaminase levels, myositis, and rhabdomyolysis (more prevalent with higher statin dosages and renal failure), and it is not known to enhance ASCVD outcomes and is typically not advised [65]. Dual peroxisome proliferator-activated receptors α/γ (PPAR α/γ) dual agonist (Saroglitazar) is a newer medication for controlling many pathogenetic variables in diabetic atherogenic dyslipidemia [73]. Saroglitazar may be an effective and safe treatment option for people with T2DM who have hypertriglyceridemia [74].

Recommendations

A. Most lipid levels differ minimally after a meal compared with fasting, hence measuring non-fasting lipids has no disadvantage with respect to risk assessment and may be preferred for convenience. **B**

B. For individuals not on statins or other lipid-lowering therapy, it is important to obtain a lipid profile at the time of diabetes diagnosis/at initial medical evaluation, and every year thereafter, or more frequently if indicated. **E**

C. Lifestyle modification — weight loss, dietary changes, and increased physical activity — should be recommended to improve the lipid profile and reduce the risk of developing ASCVD in patients with diabetes. **A**

D. Dietary and lifestyle changes, including weight loss and abstinence from alcohol are recommended for patients with hypertriglyceridemia. **C**

E. Lipid profile should be done at initiation of statins or other lipid-lowering therapy, 4–12 weeks after initiation or a change in dose, and annually thereafter, to monitor response to therapy/medication adherence. **E**

F. For individuals with elevated triglyceride (≥ 150 mg/dL) and/or low HDL cholesterol (< 40 mg/dL for men, < 50 mg/dL for women) intensify lifestyle therapy and optimize glycemic control. **C**

G. In patients with diabetes with 10-year ASCVD risk of ≥ 20%, ezetimibe is to be added to the maximally tolerated statin therapy to reduce LDL cholesterol by ≥ 50%. **C**

H. In patients with diabetes and ASCVD considered very high risk using specific criteria, and LDL cholesterol ≥ 70 mg/dL on maximally tolerated statin dose, consider adding ezetimibe or PCSK9 inhibitor (use restricted due to higher cost). **A**

I. If fasting triglycerides are ≥ 500 mg/dL, then evaluate the patient for secondary causes of hypertriglyceridemia. Consider medical therapy to reduce the risk of pancreatitis and referral to an endocrinologist. **C**

J. In patients with moderate hypertriglyceridemia (fasting or non-fasting triglycerides 175–499 mg/dL), address and treat lifestyle factors (obesity and metabolic syndrome), secondary factors (diabetes, chronic liver, or kidney disease and/or nephrotic syndrome, hypothyroidism), and medications that raise triglycerides. **C**

K. In patients with ASCVD or other CV risk factors on statin therapy with controlled LDL cholesterol but elevated triglycerides (135–499 mg/dL), consider adding icosapent ethyl to reduce CV risk. **A**

L. Combination of a statin and fibrate does not improve ASCVD outcomes compared with a statin alone and is generally not recommended for CV risk reduction alone. **A**

M. Dual PPAR inhibitor (saroglitazar) is an effective and safe therapeutic option for improving hypertriglyceridemia in patients with T2DM. Although saroglitazar improves triglycerides, there are no CV outcome trials yet. **B**

N. Statin therapy is contraindicated in pregnancy and women planning pregnancy. **B**

CVD (cardiovascular disease)

Early identification of metabolic syndromes, such as obesity, elevated BP, hypertriglyceridemia, reduced HDL cholesterol, borderline high-risk LDL cholesterol and impaired FPG and interventions to reduce the CVD risks are the major goals of the primary prevention of CVD [75].

Diabetes-related ASCVD is the primary cause of morbidity and death. Hypertension and dyslipidemia, co-occur frequently with T2DM and are established risk factors for ASCVD. Diabetes is an independent risk factor for ASCVD. Aspirin has been found to be useful in lowering CV morbidity and mortality in high-risk individuals with a history of MI or stroke (secondary prevention) and is strongly recommended for secondary prevention [65, 76, 77].

Aspirin may be advised as primary prevention in individuals aged ≥ 50 years who have diabetes and at least one other major risk factor, such as family history of premature ASCVD, hypertension, dyslipidemia, smoking, CKD, or albuminuria and are not at increased risk of bleeding (older age, anemia, renal disease). But, when individuals experience ASCVD, aspirin is indicated for secondary prevention since the benefit outweighs the risk [65, 76, 77].

In secondary prevention, aspirin provides a larger absolute decrease in major vascular events, stroke, and coronary events [78]. Low-dose aspirin treatment has been shown to be effective in the secondary prevention of major CV events [79]. Usually higher doses of aspirin (> 75 mg/day) are not suggested since they do not improve event prevention and are linked with increased risk of GI bleeding [80].

Atypical cardiac symptoms (unexplained dyspnoea, chest discomfort); signs or symptoms of associated vascular disease such as carotid bruits, transient ischemic attack (TIA), stroke, claudication, or peripheral arterial disease; or electrocardiogram (ECG) abnormalities such as Q waves should be considered when investigating CVD [65].

As part of comprehensive CV risk reduction and glucose-lowering regimens, new glucose-lowering medicines, SGLT-2i, and GLP-1RA are suggested as first-line treatment in patients with T2DM who have developed CVD or are at high or very high CV risk [27, 65, 81].

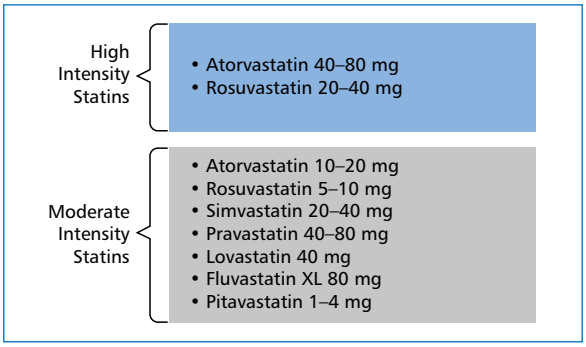
Any SGLT-2i with demonstrated CV benefit is recommended in patients with T2DM and established ASCVD or its risk factors, or DKD, to reduce the risk of major adverse CV events and hospitalisation for HF. For an additive decrease in the risk of adverse CV and renal events, combined treatment with an SGLT-2i and a GLP-1RA with demonstrated CV benefit may be used. A SGLT-2i with proven effectiveness is advised in patients with T2DM and established HF with lower ejection fraction to minimise the risk of increasing HF and CV mortality [65, 82, 83].

To minimise the risk of CV events in individuals with established ASCVD, particularly CAD, an ACEi or ARB is suggested [65]. Treatment with ACEi/ARB before the initial diagnosis of obstructive CAD was associated with a lower incidence of acute MI, smaller infarct size, improved heart function, and lower incidences of non-fatal stroke and composite major adverse cardiac and cerebral event (MACCE) in patients with diabetes and hypertension [84].

Table 5. Recommendations to Statin Therapy in Primary and Secondary Prevention of ASCVD

Comorbidity	Age	Recommended therapy
Patients with diabetes and ASCVD	All ages	Start high-intensity statin therapy + Lifestyle changes
Patient with diabetes and additional ASCVD risk factors	20–39 years	Initiate statin therapy + Lifestyle changes
Patient with diabetes without ASCVD	40–75 years	Start moderate intensity statin therapy + Lifestyle changes
Patients with diabetes with multiple ASCVD risk factors	50–70 years	Start high intensity statin therapy

Adapted from ADA Diabetes Care 2022



MF may be continued for lowering blood glucose in people with T2DM who have stable HF if their eGFR is > 30 mL/min/1.73 m^2. However, it is not suggested in unstable or hospitalised patients with HF [68]. MF can be continued (or started) with an eGFR of 60 mL/min/1.73 m^2, while renal function should be monitored regularly (every 3–6 months). MF dosage should be examined and lowered (by 50% or to half-maximal dose) in patients with eGFR < 45 mL/min/1.73 m^2, and renal function should be regularly monitored (every 3 months). MF should not be started and stopped if the eGFR is < 30 mL/min/1.73 m^2 [85].

Recommendations

A. Aspirin (75 mg/day) may be used for primary prevention in patients with diabetes who are at increased CV risk, after a comprehensive discussion with the patient on the benefits vs. risk of bleeding. **A**

B. Aspirin (75 mg/day) is used for secondary prevention in patients with diabetes and history of ASCVD. **A**

C. Routine screening for CAD is not recommended in asymptomatic patients as it does not improve outcomes as long as CVD risk factors are treated. **A**

D. Investigations are to be considered when there are typical or atypical cardiac symptoms (unexplained dyspnoea, chest discomfort); signs or symptoms of associated vascular disease including carotid bruits, TIA, stroke, claudication, or PAD; or ECG abnormalities (Q waves). **E**

E. In individuals with T2DM with established ASCVD or established kidney disease, SGLT-2i or GLP-1RA with demonstrated CVD benefit need to be considered for comprehensive CV risk reduction and/or glucose-lowering benefits. **A**

F. In individuals with T2DM and established ASCVD with multiple ASCVD risk factors, or DKD, a SGLT-2i with demonstrated CV benefit is strongly recommended. **A**

G. In individuals with T2DM and established HF, a SGLT-2i with proven benefit is recommended to reduce risk of worsening HF and CV death. **A**

H. In individuals with T2DM and established ASCVD, multiple ASCVD risk factors, or DKD, a SGLT-2i with demonstrated CV benefit is recommended to reduce the risk of major adverse CV events and/or hospitalization for HF. **A**

I. In individuals with known ASCVD, particularly CAD, an ACEi or ARB therapy is recommended to reduce the risk of CV events. **A**

J. In patients with T2DM and stable HF, MF may be continued for glucose lowering if eGFR remains > 30 mL/min/1.73 m^2, but should be avoided in unstable or hospitalized patients with HF. **B**

Chronic kidney disease (CKD)

CKD is diagnosed when there is a sustained increase in urine albumin excretion (often known as albuminuria), as well as a low eGFR or other signs of kidney impairment. CKD is the major cause of ESRD, which necessitates dialysis or kidney transplantation. Furthermore, the presence of CKD significantly increases CV risk and health-care expenses in persons with diabetes. It affects 20–40% of patients with diabetes. It may be present at the time of diagnosis in T2DM patients [86].

To assist treatment options, eGFR and albuminuria must be measured. The UACR in a random spot urine collection can be used to screen for albuminuria (should be done at least once a year to enable timely diagnosis of CKD), monitor progression of CKD, detect superimposed kidney diseases such as acute kidney injury (AKI), assess risk of CKD complications, dose drugs appropriately, and to determine whether nephrologist referral is required. The eGFR should be measured in all patients with T2DM, independent of therapy. Patients with urine albumin levels of ≥ 300 mg/g creatinine and an eGFR of 30–60 mL/min/1.73 m^2 should be evaluated twice annually to guide medication [86].

If the UACR is 3 mg/mmol, adults with CKD and T2DM can be given an ARB or an ACEi (titrated to the highest permitted dose that the person can tolerate). Adults using an ARB or an ACEi can also be given an SGLT-2i if their ACR is > 30 mg/mmol and they fulfil the requirements in the marketing authorization (including relevant eGFR thresholds) [59].

Albuminuria and eGFR in persons with renal disease may fluctuate due to CKD progression, a secondary cause of kidney disease, AKI, or pharmaceutical effects. Serum potassium levels should be checked on a regular basis in patients on diuretics and those with an eGFR < 60 mL/min/1.73/m^2 who are using ACEi, ARBs, or mineralocorticoid receptor antagonists. Diuretics, ACEi, and ARBs have the potential to lower intravascular volume, renal blood flow, and/or glomerular filtration. Slight elevations in serum creatinine (up to 30% over baseline) caused by ACEi and ARBs should not be mistaken with AKI. Hyperkalemia during the first year of ACEi/ARB medication is uncommon in persons with eGFR greater > 60 mL/min/1.73 m^2, but significantly more prevalent in people with lower eGFR [87].

As kidney disease progresses, it needs more active evaluation and treatment, which may entail referral to a nephrologist or specialist [88]. Refer to a nephrologist

if there is uncertainty about the etiology of kidney disease, if there are difficult management issues (anemia, secondary hyperparathyroidism, significant increases in albuminuria despite good BP control, metabolic bone disease, resistant hypertension or electrolyte disturbances), or if there is advanced kidney disease (eGFR < 30 mL/min/1.73 m^2 that would require renal replacement therapy) as early recommendation [86, 89].

Recommendations

A. For screening of CKD, urinary albumin, spot UACR and eGFR should be assessed in all patients with T2DM regardless of treatment at diagnosis and annually. **B**

B. Patients with diabetes with urinary albumin ≥ 30 mg/g creatinine and/or an eGFR 30–60 mL/ /min/1.73 m^2 should be monitored twice annually to guide therapy. **B**

C. To reduce the risk or slow the progression of CKD, SGLT-2i can be used (up to eGFR: 30) for optimal glycemic control and ACEi or ARB for optimal BP control. **A**

D. When ACEi, ARBs or diuretics are used, serum creatinine and serum potassium levels need to be monitored periodically. **A**

E. Refer to a nephrologist, if eGFR is < 30 mL/ /min/1.73 m^2, the etiology of kidney disease is uncertain (small kidneys on ultrasonography, casts in urine, microscopic hematuria), proteinuria in the nephrotic range, difficult management issues, and rapidly progressing kidney disease or nephropathy in the absence of retinopathy. **A**

Diabetic retinopathy (DR)

DR is a specific vascular consequence of diabetes, and its incidence is significantly connected to the length of diabetes as well as the level of glycemic control. Chronic hyperglycemia, nephropathy, hypertension, and dyslipidemia are other risk factors for or associated with retinopathy [90]. Regular follow-up with early identification and treatment of vision-threatening retinopathy allows for the avoidance of up to 98% of DR-related visual loss [91].

Optimizing glycemic management can lower the chance of developing DR or delay its development. To lessen the risk of or slow the development of DR, BP and serum cholesterol management must be considered [90]. A considerable number of people with diabetes experience proliferative alterations or diabetic macular oedema (DME), which necessitate treatment [91].

Whether visual signs are present or not, routine follow-up is mandatory. Programs that employ retinal photography (in conjunction with remote reading or the use of a validated assessment tool) might increase access to DR screening and may be a suitable screening technique for DR that can aid in prompt referral for a thorough eye exam when necessary [90]. Retinal photography is a screening technique for retinopathy, but it is not a replacement for a thorough eye exam, which should be performed at least initially and then at regular intervals as advised by an ophthalmologist [91].

The ophthalmologist's screening techniques have a much greater specificity for DR identification [92]. Regular screening every 1–2 years may be recommended if there is no sign of retinopathy, and the blood glucose is under control. An ophthalmologist should repeat dilated retinal examinations at least once a year if there is any indication of DR. More regular check-ups will be necessary if the retinopathy is developing or sight- threatening [93].

Patients with any degree of DME and moderate or severe non-proliferative DR, or any proliferative DR should be referred to an ophthalmologist immediately [90–92].

Women with pre-existing diabetes who are thinking about getting pregnant or who are already pregnant should be advised about the risk of developing and progressing DR during term, as pregnancy is linked to a rapid advancement of DR. Rapid initiation of intensive glycemic control in the presence of retinopathy has been linked to retinopathy deterioration [90]. In patients with pre-existing diabetes, eye examinations should be performed before pregnancy, during the first trimester, and these individuals should be examined every trimester and for one year postpartum as suggested by the degree of retinopathy [90].

Recommendations

A. To reduce the risk or slow the progression of DR, optimize glycemic, BP control and serum lipid control. **A**

B. Retinal photography and grading or comprehensive eye examination should be done by an ophthalmologist at diagnosis. **B**

C. If there is no evidence of retinopathy and glycemia is well controlled, screening for DR should be done every 1–2 years. **B**

D. When there is DR (any level), an annual dilated retinal examination should be done by an ophthalmologist. Retinopathy that is progressing or sight-threatening will require more frequent retinal examination. **B**

E. Appropriate screening strategies for DR are programs that use retinal photography to improve access to DR screening. **B**

F. Maculopathy, macular oedema, moderate or severe non-proliferative DR, or any proliferative DR or any uncertainty in grading images should be referred to an ophthalmologist specialized in retinal problems. **A**

G. Women who are planning pregnancy or who have become pregnant should be counselled about the risk of development and/or progression of DR. **B**

H. Eye examinations should occur before pregnancy and in the 1st trimester in patients with pre-existing T2DM. Patients should then be monitored every trimester and for 1 year postpartum, as indicated by the degree of retinopathy. **B**

Diabetic neuropathy

Diabetic neuropathies are a heterogeneous group of disorders with varying clinical presentations, and it is an exclusion diagnosis. Non-diabetic neuropathies can occur in people with diabetes. Approximately 50% of diabetic peripheral neuropathies (DPN) are asymptomatic, hence early detection and therapy of neuropathy is crucial [90]. Diabetes-related peripheral neuropathy elevates the risk of foot ulceration and amputation [94]. The most prevalent kind of diabetic neuropathy is distal symmetric polyneuropathy (DSPN). Simple physical examination screening tests, such as the 10-g monofilament on the dorsal portion of the great toe bilaterally and vibration sensitivity with a 128 Hz tuning fork, work quite well in identifying neuropathy and forecasting its occurrence. A thorough history, evaluation of temperature, pinprick sensation, and vibration with a 128-Hz tuning fork (for large-fibre function) should all be part of the evaluation. Annual 10-g monofilament testing should be performed on all patients to detect at-risk foot for ulceration and amputation [90, 94, 95].

Individuals with T2DM should be screened for peripheral neuropathy upon diagnosis and yearly afterwards [90, 94]. Symptoms differ depending on the type of sensory fibres implicated. The involvement of tiny fibres causes the most typical early symptoms, which include pain and dysesthesia (unpleasant sensations of burning and tingling). When big fibres are implicated, numbness and loss of protective sensation (LOPS) may occur. LOPS signifies the presence of distal sensorimotor polyneuropathy, which is a risk factor for diabetic foot ulceration [90, 95].

Pinprick and temperature sensation are used to measure small-fibre function and vibration perception, whereas 10-g monofilament is used to assess large-fibre function and protective sense [90]. The 10-g monofilament is an effective clinical test for diagnosing severe or advanced neuropathy and identifying individuals who are at elevated risk of ulceration and amputation [95, 96].

Diabetic autonomic neuropathies impact the part of the nervous system that controls internal body functions and can damage the heart (cardiac autonomic neuropathy), the GI tract, and the genitourinary system, as well as cause sexual dysfunction [95]. Autonomic neuropathy symptoms and signs should be evaluated in patients with microvascular problems, which should be thoroughly elicited during the history and physical examination. The most common clinical manifestations of diabetic autonomic neuropathy are hypoglycemia unawareness, resting tachycardia, orthostatic hypotension, gastroparesis, constipation, diarrhoea, fecal incontinence, erectile dysfunction (ED), neurogenic bladder, and sudomotor dysfunction with increased or decreased sweating [90]. Autonomic neuropathy diagnosis and treatment may relieve symptoms, minimise sequelae, and enhance quality of life (QOL) [95].

Consider treating individuals who are experiencing neuropathic pain with duloxetine, pregabalin or gabapentin to improve their QOL [95]. Those with asymmetrical neuropathy presentations, higher motor deficits, fast increasing neuropathy symptoms are indications that often require more thorough examination and referral for further neurological evaluation [94, 95, 97].

Recommendations

A. Assess all patients with T2DM for DPN at diagnosis and annually thereafter. **B**

B. DSPN is assessed by a careful history and assessment of either temperature or pinprick sensation and vibration sensation using a 128-Hz tuning fork. **B**

C. Annual 10-g monofilament testing is indicated in all to identify feet-at-risk of ulceration and amputation. **B**

D. Assess symptoms and signs of autonomic neuropathy in patients with microvascular complications. **E**

E. Optimize glucose control to prevent and to slow the progression of neuropathy in patients with T2DM. **A**

F. Assess and treat patients to reduce pain related to DPN, symptoms of autonomic neuropathy and improve QOL. **B**

G. Initial pharmacologic treatments for neuropathic pain in diabetes are pregabalin, duloxetine, or gabapentin that need to be titrated appropriately. **B**

H. Refer to an endocrinologist or neurologist in case of intractable pain despite 2 agents. **E**

I. ED in T2DM can be due to neurological, vascular, or psychological causes and also medication. ED may warrant expert review by an endocrinologist. **B**

Foot care

Foot ulcers and amputation, an outcome of diabetic neuropathy and/or peripheral artery disease (PAD) are important causes of morbidity and mortality among patients with diabetes. Early detection and treatment of feet at risk of ulceration and amputations can delay or avoid negative consequences. It is critical to obtain a prior history of neuropathy symptoms such as pain, burning, numbness, and vascular disease symptoms such as leg fatigue, claudication [90].

Additional key assessments in the history include previous foot ulceration or amputation; neuropathic or peripheral vascular symptoms; poor eyesight or renal replacement treatment; and tobacco use, which is a risk factor not just for vascular disease but also for neuropathy [98].

Foot examinations should involve skin examination, assessment of foot abnormalities, neurological evaluation (10-g monofilament testing with at least one additional evaluation, such as pinprick, temperature, or vibration), and vascular evaluation, which should include pulses in the legs and feet. For people with claudication symptoms or diminished or missing pedal pulses, an ankle-brachial index and additional vascular examination are required. Individuals with diabetes should get a full foot assessment at least once a year to detect risk factors for ulcers and amputations [90].

Patients having a history of ulcers or amputations, foot abnormalities, insensate feet, or PAD may require more regular comprehensive foot assessments. Ankle-brachial index (ABI) testing should be performed on individuals with PAD signs and symptoms (initial screening for PAD should include history of reduced walking speed, leg tiredness, claudication, and pedal pulse evaluation) [90].

People with diabetes who have indications or symptoms of vascular disease or no pulses on screening foot examination should undergo ABI pressure testing and be sent to a vascular specialist if necessary [98]. In order to give patients, the best care possible, physicians from a range of disciplines are typically needed [99].

In high-risk patients with diabetes, such as those with substantial neuropathy, foot abnormalities or a history of amputation, customised therapeutic footwear is indicated [100]. Appropriate therapeutic footwear with proven pressure reduction can help avoid the recurrence or aggravation of plantar foot ulcers [90].

Recommendations

A. Assess current symptoms of neuropathy (pain, burning, numbness) and vascular disease (leg fatigue, claudication). **B**

B. Local examination of the foot must include inspection of the skin, assessment of foot deformities, neurological assessment (10-g monofilament testing with at least 1 other assessment, i.e. pinprick, temperature, vibration), and vascular assessment, including peripheral pulses and should be done at every visit. **B**

C. Obtain a past history of ulceration, amputation, Charcot foot, angioplasty or vascular surgery, cigarette smoking, retinopathy, and renal disease. **B**

D. Annual comprehensive foot evaluation to be done to identify risk factors for ulcers and amputations. **B**

E. ABI and further vascular assessment as appropriate should be advised for patients with symptoms of claudication or decreased/absent pedal pulses. **C**

F. Patients with high-risk feet and/or foot ulcers should be referred to multidisciplinary centres with podiatric, orthopedic facilities. **B**

G. Provide general preventive foot self-care education to all patients with diabetes, including advice to not walk bare footed. **B**

H. Recommend specialized therapeutic footwear for high-risk patients, including those with severe neuropathy, foot deformities, ulcers, callous formation, poor peripheral circulation, and history of amputation. **B**

Non-alcoholic fatty liver disease (NAFLD)

NAFLD is defined as the ectopic accumulation of fat in the liver when no other causes of secondary liver fat accumulation are present [101] whereas non-alcoholic steatohepatitis (NASH) is the inflammatory subtype of NAFLD and is associated with disease progression, development of cirrhosis, and need for liver transplant [102]. NAFLD and T2DM commonly coexist, increasing the risk of poor hepatic and extra-hepatic consequences [103]. Furthermore, T2DM has been linked to a faster development of NAFLD to NASH,

cirrhosis, or hepatocellular cancer (HCC). Non-invasive techniques, such as elastography or fibrosis biomarkers, can be used to estimate the risk of fibrosis, but referral to a liver specialist may be required for definitive diagnosis. The liver biopsy is the gold standard for determining the existence of NASH [18].

The major anomaly in NAFLD is mildly raised serum aminotransferases, which are related with greater BMI, waist circumference, triglyceride levels, and decreased HDL cholesterol levels. Weight loss, glycemic management, and pharmacotherapy for hyperglycemia or dyslipidemia are all effective for the management of NAFLD. Treatment with pioglitazone and vitamin E for biopsy-proven NASH has been demonstrated to improve liver histology, but the implications on long-term clinical outcomes remain unknown [18].

Patients with T2DM or prediabetes with increased liver enzymes (alanine aminotransferase) or fatty liver on ultrasonography should be checked for NASH and liver fibrosis [18].

SGLT-2i like empagliflozin, dapagliflozin, canagliflozin, ipragliflozin, and luseogliflozin, some GLP-1RA such as liraglutide, exenatide and dulaglutide [104] dual PPAR α/γ agonist saroglitazar seem to improve NASH [105]. Weight loss in obese individuals with NASH is known to improve NASH and the clinical outcomes [106].

Recommendations

A. Patients with T2DM or prediabetes with increased liver enzymes (alanine aminotransferase) or fatty liver on ultrasonography should be checked for NASH and liver fibrosis. **C**

B. Exclude other pathology such as viral hepatitis and autoimmune hepatitis. In case of any doubt with diagnosis or management, refer to an expert. **B**

C. Non-invasive tests, such as elastography or fibrosis biomarkers, may be used to assess risk of fibrosis, but referral to a liver specialist and liver biopsy may be required for definitive diagnosis. **B**

D. Treatment with pioglitazone and vitamin E for biopsy-proven NASH has been demonstrated to improve liver histology, but the implications on long-term clinical outcomes remain unknown. **B**

E. SGLT-2i like empagliflozin, dapagliflozin, canagliflozin, ipragliflozin, and luseogliflozin some GLP-1RA such as liraglutide, exenatide and dulaglutide, dual PPAR α/γ agonist saroglitazar seem to improve NASH. **C**

F. Weight loss in obese individuals with NASH is known to improve NASH and the clinical outcomes. **B**

Immunizations for adults with T2DM

The coronavirus disease 2019 (COVID-19) pandemic has highlighted the significance of regular immunizations for those living with diabetes. Preventing avoidable infections not only decreases morbidity but also hospitalizations, which may reduce the risk of contracting diseases like COVID-19. Children and adults with diabetes should be immunised in accordance with age-appropriate recommendations (Tab. 6) [18].

People with diabetes are at an increased risk of hepatitis B infection, as well as complications from influenza and pneumococcal illness [18]. Individuals with diabetes are more susceptible to pneumonia because of hyperglycemia, poor long-term diabetes control, prolonged diabetes duration, lower immunity, impaired lung function, pulmonary microangiopathy, higher risk of aspiration, and concomitant morbidity [107]. Vaccine recommendations are important due to the increased frequency of drug-resistant influenza and pneumococcal illness, as well as accompanying problems in the elderly. The advisory committee on immunization practices (ACIP) of the centres for disease control and prevention (CDC) recommends influenza, pneumococcal, and hepatitis B immunizations for individuals with diabetes. Tetanus-diphtheria-pertussis, measles-mumps-rubella, human papillomavirus, and shingles vaccinations are also recommended [18].

Recommendations

A. Provide age-appropriate vaccines for individuals with diabetes. **A**

B. Annual influenza vaccine is recommended for all individuals ≥ 6 months of age, especially those with diabetes. **A**

C. Diabetes patients aged 2 to 64 years should additionally receive a 23-valent pneumococcal polysaccharide vaccination. Additional PPSV23 immunisation is required at the age of ≥ 65, regardless of vaccination history. **A**

D. Depending on the vaccine, provide a 2- or 3-dose series of hepatitis B vaccination to unvaccinated people with diabetes aged 18 to 59 years. **A**

E. Consider giving a 3-dose series of hepatitis B vaccination to unvaccinated people with diabetes over the age of ≥ 60. **A**

Table 6. Highly Recommended Immunizations for Adult Patients with Diabetes (ACIP, CDC) (Adapted from ADA Diabetes Care 2022)

Vaccination	Age-group recommendations	Frequency
Hepatitis B	< 60 years of age; ≥ 60 consult with a healthcare professional	Two- or three-dose regimen
Human papilloma virus (HPV)	≤ 26 years of age; After speaking with a healthcare professional, those aged 27 to 45 may also receive the HPV vaccine	3 dosages given over 6 months
Influenza	All patients: It is suggested to avoid receiving the live attenuated influenza vaccination.	Annual
Pneumonia [PPSV23 (Pneumovax)]	Ages 19 to 64 should receive the Pneumovax vaccine	One dose
	≥ 65 years of age, acquire a second dose of Pneumovax after 65 years old and at least 5 years after receiving the first dose.	One dose; if PCV13 has been given, then give PPSV23 ≥ 1 year after PCV13 and ≥ 5 years after any PPSV23 at age < 65 years
Pneumonia [PCV13 (Prevnar)]	Adults ≥ 19 of age, those with a cochlear implant, a cerebrospinal fluid leak, or an immunocompromising condition (such chronic renal failure)	One dose
	19–64 years of age, immunocompetent, no recommendation	None
	≥ 65, 65 years old, immunocompetent, and engaged in shared decision-making with a healthcare professional	One dose
Tetanus, diphtheria, pertussis (TDAP)	All adults: pregnant women should get an additional dosage	Booster every 10 years
Zoster	≥ 50 years of age	

Pregnancy planning and preconception counselling

All women of reproductive age with diabetes should be advised about the necessity of reaching and maintaining euglycemia as safely as possible prior to conception and throughout pregnancy. Family planning should be discussed, and effective contraception should be provided and utilised until a woman's treatment regimen and HbA1c are optimal for pregnancy. Preconception counselling should emphasise the significance of obtaining glucose levels as near normal levels as safely achievable, preferably HbA1c < 6.5%, to lower the risk of congenital abnormalities, preeclampsia, macrosomia, premature birth, and other problems [108].

Prior to pregnancy, all drugs that are risky in pregnancy should be discontinued. In pregnancy, antihypertensives such as methyldopa, nifedipine, labetalol and clonidine are effective and relatively safe for treatment of hypertension. Statins should be avoided during pregnancy [108, 109].

In GDM, insulin is the preferable drug for treating hyperglycemia as per Diabetes Canada clinical practice guidelines and ADA guidelines. Prenatal vitamins containing at least 400 mg of folic acid are suggested before conception. Failure to meet the required folic acid intake during the peri-conceptional phase increases the risk of spina bifida in women with pre-existing diabetes. The percentage of neural tube malformations is reduced in women with pre-GDM who take supplements containing > 0.4 mg of folic acid [110, 111].

The ADA recommends FPG between 70–95 mg/dL and 1-hour postprandial glucose between 100––140 mg/dL, 2 h PG between 100–120 mg/dL in a pregnant woman with diabetes. HbA1c should be used as a supplementary indicator of glycemic control during pregnancy. In the second and third trimesters, HbA1c < 6% has the lowest risk of large-for-gestational-age new-borns, premature birth, and preeclampsia. It is optimal if a target of < 6% is met without significant hypoglycemia throughout pregnancy, however, it can be raised to 7% if hypoglycemia is a concern. When used in conjunction with pre- and postprandial blood glucose monitoring, CGM can aid in the achievement of HbA1c objectives in GDM [108].

GDM and management of T2DM in pregnancy are exhaustive topics and hence only the very basics are covered here as part of this consensus report.

Recommendations

A. Preconception counselling should be incorporated into routine diabetes care for all women with T2DM in the reproductive age group. **A**

B. Effective reversible contraception is recommended until the treatment regimen and HbA1c are optimized for pregnancy. **A**

C. Preconception counselling should be done to address the importance of achieving glucose levels as close to normal, ideally HbA1c < 6.5% to reduce the risk of congenital anomalies, preeclampsia, macrosomia, preterm birth, and other complications. **A**

D. Women with diabetes planning pregnancy or who have become pregnant should be counselled on the risk of development and/or progression of DR. **B**

E. Once a woman with diabetes decides to plan pregnancy in the near future, medications need to be optimized.

- All oral medications used for glucose control other than MF need to be stopped. **B**
- Insulin is safe in pregnancy and may be started if required for optimal glucose control. **A**
- Statins and ACEi or ARB need to be stopped. **B**
- Anti-hypertensive such as labetalol or nifedipine or methyldopa may be used instead of other anti- hypertensives that are not safe in pregnancy. **B**

F. Folic Acid 5 mg/day should be given to all women planning pregnancy (3 months prior to conception). **B**

G. Glucose targets are FPG < 95 mg/dL and 1-hour postprandial glucose < 140 mg/dL, 2h PG below < 120 mg/dL. **B**

H. HbA1c is slightly lower in pregnancy; the ideal target in pregnancy is < 6% if it can be achieved without significant hypoglycemia. The target may be relaxed to < 7% to prevent hypoglycemia. **B**

I. HbA1c targets in diabetes and pregnancy can be facilitated by CGM. **B**

Diabetes care in hospital

In hospitalised patients, hyperglycemia, hypoglycemia, and glucose fluctuation are linked to poor outcomes, including mortality. Careful care of inpatients with diabetes delivers direct and immediate advantages. Preadmission management of hyperglycemia in patients having elective surgeries, inpatient diabetes service with well-developed standards, and careful transition out of the hospital to prior outpatient management, all help to improve diabetes management in the hospital. Based on preadmission glycemia, inpatient therapy and discharge planning need to be planned. All individuals with diabetes or hyperglycemia should have their HbA1c levels checked after admission unless checked in the past 3 months. If HbA1c has not been evaluated in the previous three months, it should be done for all patients with diabetes or hyperglycemia admitted to the hospital [112].

In T2DM patients, measuring HbA1c on admission can help modify treatment regimens upon discharge [113]. In patients with T2DM, the HbA1c level at admission is an effective predictor of glycemic control and responsiveness to basal-bolus insulin therapy during hospitalisation [114].

Continuous intravenous insulin infusion is the most effective approach for meeting glycemic goals in the intensive care unit. Intravenous insulin infusions should be given according to proven written or computerised protocols that allow for pre-set changes in infusion rate, glycemic variations, and insulin dosage [112].

For the majority of critically sick patients, insulin treatment should be commenced to manage persistent hyperglycemia ≥ 180 mg/dL and aimed to a glucose range of 140–180 mg/dL. More stringent goals of 110–140 mg/dL may be reasonable for critically sick patients after surgery or patients undergoing cardiac surgery, as long as they can be met without causing substantial hypoglycemia. In patients with significant comorbidities and in inpatient care settings where regular glucose monitoring or careful nursing supervision is not possible, glucose values between 180–250 mg/dL may be tolerable. Glycemic levels > 250 mg/dL may be tolerated in terminally sick patients with a limited life expectancy [112].

For non-critical hospitalised patients with adequate nutritional intake, an insulin regimen including basal, prandial, and corrective components is the optimal therapy [114]. Similar patients with inadequate oral intake or who are prohibited from oral intake, basal insulin or a basal plus bolus correction regimen is the optimal therapy [114]. In the hospital care of T2DM patients undergoing general surgery, a basal-bolus insulin regimen is preferred over a subcutaneous sliding scale regular insulin regimen [113]. Subcutaneous sliding scale insulin regimens for hyperglycemia therapy in inpatients are strongly discouraged [112].

Oral anti-hyperglycemic medications are difficult to titrate for a quick effect, and they have adverse effects that limit their usage in the hospital. In certain scenarios, where there are no contraindications, selected DPP-4i like linagliptin and sitagliptin may be

continued in the hospitalized individual with T2DM. Oral agents may be restarted after hospital discharge if appropriate [115].

Recommendations

A. HbA1c test should be done in all patients with diabetes/or hyperglycemia (blood glucose > 140 mg/dL) admitted to the hospital if not done in the past 3 months. **B**

B. Insulin administration should be based on validated protocols that allows for adjustments of insulin dosage based on glycemic fluctuations. **B**

C. Insulin therapy should be initiated for treatment of persistent hyperglycemia (blood glucose ≥ 180 mg/dL). **A**

D. Target glucose range for majority of critically ill and non-critically ill patients is 140–180 mg/dL and more stringent goal of 110–140 mg/dL is for selected patients if it can be achieved without significant hypoglycemia. **A**

E. The preferred treatment for non-critically ill hospitalized patients with good nutritional intake is insulin regimen with basal, prandial and correction components. **A**

F. Use of sliding scale subcutaneous insulin regimen is strongly discouraged in the inpatient hospital setting. **A**

G. Continuous intravenous insulin infusion is the best method for achieving glycemic targets in the critical care setting, and preferably in patients who are nil-by-mouth. **B**

H. Usually, all orally administered antihyperglycemic agents have to be stopped with a very low threshold to start insulin. Few selective DPP-4i may be continued where appropriate, considering other comorbidities. **B**

Technology in diabetes

Diabetes technology refers to the hardware, devices, and software that people utilise to control diabetes, which might range from diet to blood glucose levels. Diabetes technology, when combined with education and follow-up, may enhance the lives and health of individuals with diabetes. The type(s) and selection of devices should be tailored to a person's personal needs, desires, skill level, and device availability [116].

Self-monitoring of blood glucose (SMBG) is an essential component of efficient insulin treatment. CGM has evolved as a tool for assessing glucose levels. Glucose monitoring enables patients to determine their unique response to medication and if glycemic objectives are being met safely. The frequency and timing of SMBG should be dictated by the patient's unique requirements and goals, or CGM usage should be considered [116].

CGM allows for the direct observation of glycemic excursions and daily profiles that can help with immediate therapy decisions and/or lifestyle modifications, assess glucose variability and identify patterns of hypo- and hyperglycemia. When used properly, real-time CGM in conjunction with multiple daily injections (MDI) and continuous subcutaneous insulin infusion (CSII) and other forms of insulin therapy is an useful tool to lower and/or maintain HbA1c levels and/or reduce hypoglycemia in adults and youth with diabetes [116]. The drawbacks include active usage in order to be effective, may induce anxiety, can have accuracy limitations, particularly the delay in registering blood glucose changes in dynamic situations, and allergies. Also, it is not yet widely available everywhere [117, 118].

Insulin pump therapy can be provided to those with T2DM who require MDI and are able to use the device safely. Insulin pump therapy may be recommended to pregnant women with GDM or T2DM patients who fail to achieve acceptable glycemic control with a basal/bolus regimen, have remarkably high insulin requirement, or exhibit chronic accelerated foetal development despite optimal conventional MDI regimen [119]. Other indications of insulin pump in T2DM include severe insulin resistance syndromes such as lipodystrophy, pregnancy, and insulin allergy [119].

The device should be chosen depending on the patient's circumstances, wishes, and needs. Traditional insulin pumps are an option for people on MDI as well as those with other kinds of diabetes that result in insulin insufficiency (those who have undergone a pancreatectomy and/or those with cystic fibrosis) [116].

Recommendations

A. Glucometers are important tools to monitor capillary glucose at the comfort of one's own home and considered wherever appropriate. **A**

B. Glucometer readings not to be used to diagnose T2DM. **B**

C. CGM is an invaluable tool in deriving information pertaining to glucose control, glucose variations, hypoglycemia, and the trends of the same, and may be recommended wherever required. **B**

D. Usually, insulin pumps are not required in T2DM. But if considered due to patient preference or clinical circumstances, refer to an endocrinologist. **B**

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Conflict of interest

None declared.

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