

National Clinical Practice Recommendations for Management of Diabetes Mellitus 2019 Ministry of Health & Population

Prepared by
(National Diabetes Committee)

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صحة



For further information please contact : SANOFI Egypt
3, EL Massareh St., Zekitoun, Cairo , Egypt , P.O. BOX : 1486
Tel.: +202 22860000-22860060 Fax: + 202 22860107- 22860112
www.sanofi.com

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FORWARD



Non-communicable diseases are major health threats that are responsible for more than 85% of all deaths over Egypt. A great percentage of these deaths results from consequently developed complications that could be avoided with early detection, diagnosis and proper management.

In Egypt, people are following a lifestyle, which is reflected negatively on their health. That includes; low engaging in physical activities, smoking, increase salt and sugar intake and consuming processed food rather than fresh vegetables and fruits. As a result, they suffer from obesity and many serious health problems.

The Egyptian ministry of health exerts enormous efforts in collaboration with other ministries, national and international organization to minimize the risks and consequences of NCDs. We have the ability to decrease the incidence of NCDs through a collaborative approach, which includes cost-effective strategies. This plan provides a framework that clarifies the specific role of each ministry or involved partner

Furthermore, these strategies outline the clear actions of Egyptian ministry of health and population to control the increasing challenge facing Egypt regarding Diabetes, Hypertension, heart diseases, cancer, and respiratory diseases

Finally, I would like to confirm my complete support to implement the plan that aimed at achieving the nine national NCDs targets adopted by Egypt, based on the nine voluntary global targets. Besides, I would like to express my deep gratitude to all professors and experts who worked on this plan and their goal to improve public health of all Egyptians.

Minister of Health and Population
Prof. Hala Zayed

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**National Clinical Practice
Recommendations for Management of
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2018

Ministry of Health Introduction

The 2018 Egyptian clinical practice recommendations for diabetes care is intended to provide public health guidance, clinicians and patients the general treatment goals, pharmacological agents for managing hyperglycaemia in type 2 diabetes and tools to evaluate the quality of care, for the use in primary and secondary health-care setting. The recommendations are based on an extensive review of the clinical diabetes literature, supplemented with latest WHO, IDF, NICE and ADA/EASD guidelines.

They also propose treatment goals substantiated by extensive scientific evidence on which therapeutic decisions can be based and treatment quality evaluation tools adapted to the Egyptian

The project proposes to share common treatment models and goals for the care of persons with diabetes in our practical national framework with all medical and non-medical professionals involved in diabetes care. Egyptian Clinical Practice Recommendations for Diabetes Mellitus can be deemed as a scientific landmark for integrated management, disease management, professional accreditation and hospital's daily need to create effective and efficient diagnostic and care pathways where the level of scientific tests behind every recommendation has been classified.

The document enlarges on "desirable" goals in the management of most diabetes; individual preferences, co-morbidities and other factors related to the individual patient characteristics, to justify the various decisions. Moreover, the Clinical Practice Recommendations are not designed to prevent either further diagnostic investigations or patient management by other specialists, when required.

There are many international guidelines for diabetes mellitus with its pragmatic features, systematic updates and recommendations furnished with evidence levels.

However, not always can treatment standards, which suit other populations and social and healthcare situations, be applied to

the Egyptian culture; moreover, there are certain divergent views in the international diabetological community and a national stand concerning the clinical application of these points is required.

On the basis of indications provided by the International Diabetes Federation (The IDF) does not recommend 'reinventing the wheel', but does strongly encourage the redesign of the wheel to suit local circumstances), derived guidelines have thus been drafted for obvious reasons related to the rational use of both human and economic resources. Furnished with levels of evidence and recommendations, they are based on the critical evaluation of the ADA, other international guidelines and various European Guidelines and when necessary, the primary sources available in literature, adapting them and targeting them at the Egyptian culture. Process and outcome indicators have been added to the recommendations whenever possible.

References:

- 1- World Health Organization 2018 (CC BY-NC-SA 3.0 IGO; <https://creativecommons.org/licenses/by-nc-sa/3.0/igo>).
- 2- International Diabetes Federation 2017. (ISBN: 978-2-930229-85-0)
- 3- NICE 2018. (HYPERLINK "<https://www.nice.org.uk/terms-and-conditions>" \l "notice-of-rights" <https://www.nice.org.uk/terms-and-conditions#notice-of-rights>)
- 4- Management of Hyperglycemia in Type 2 Diabetes, 2018. A Consensus Report by the American Diabetes Association (ADA) and the European Association for the Study of Diabetes (EASD) (<https://doi.org/10.2337/dci18-0033>)

GRADING OF SCIENTIFIC EVIDENCE

Evidence Levels and Recommendation Strength (Adopted from ADA)

Evidence Levels:

Evidence type I

Evidence obtained from large controlled randomized clinical trials and/or from systematic reviews of randomized trials.

Evidence type II

Evidence obtained from one randomized trial with an appropriate pattern.

Evidence type III

Evidence obtained from non-randomized cohort studies with either concurrent or historical controls or their Meta-analysis.

Evidence type IV

Evidence obtained from either retrospective case control studies or their meta-analysis.

Evidence type V

Evidence obtained from case studies ("series of cases") without a control group.

Evidence type VI

Evidence based on the opinions of either authoritative experts or expert committees, as specified in both the guidelines and consensus conference, or based on the opinions of team members that drafted these guidelines.

Recommendation Strength:

Strength A

The performance of a special procedure or diagnostic investigation is highly recommended. This strength indicates a special recommendation backed by scientific evidence of good quality, though not necessarily type I or II.

Strength B

It is based on the doubt that the special procedure or intervention in question must always be recommended, but it is deemed that its performance must be carefully considered.

Strength C

There is a basic uncertainty either for or against the recommendation to perform the procedure or intervention.

Strength D

The procedure's performance is not recommended.

Strength E

There are strong recommendations against the procedure.

Classification & Diagnostic criteria

Classification

The classification of diabetes includes four clinical classes:

- **Type 1 diabetes** (results from B-cell destruction, usually leading to absolute insulin deficiency).
 - **Type 2 diabetes** (results from a progressive insulin secretory defect on the background of insulin resistance).
 - Other specific types of diabetes due to other causes, e.g., genetic defects in B-cell function, genetic defects in insulin action, diseases of the exocrine pancreas (such as cystic fibrosis), and drug or chemical induced (such as after organ transplantation).
- Gestational Diabetes Mellitus (GDM diagnosed during pregnancy). Assigning a type of diabetes to an individual often depends on the circumstances present at the time of diagnosis, with individuals not necessarily fitting clearly into a single category. For example, some patients cannot be clearly classified as having type 1 or type 2 diabetes. Clinical presentation and disease progression may vary considerably in both types of diabetes.

The traditional paradigms of type 2 diabetes occurring only in adults and type 1 diabetes only in children are no longer accurate, as both diseases occur in both cohorts.

Occasionally, patients with type 2 diabetes may present with Diabetic Ketoacidosis (DKA). Children with type 1 diabetes typically present with the hallmark symptoms of polyuria/polydipsia and occasionally with DKA. The onset of type 1 diabetes may be variable in adults and may not present with the classic symptoms seen in children.

However, difficulties in diagnosis may occur in children, adolescents and adults, with the true diagnosis becoming more obvious over time.

The diagnostic criteria for diabetes currently proposed by the WHO and IDF

- Fasting glucose ≥ 126 mg/dL (7.0 mmol/L)
- OR 2-hour glucose following ingestion of 75-g glucose load ≥ 200

mg/dL (11.1 mmol/L)

- OR random plasma glucose in symptomatic patient ≥ 200 mg/dL (11.1 mmol/L)
- OR HbA1c $\geq 6.5\%$ (48 mmol/mol)
- Fasting is defined as no caloric intake for at least 8 hours.
- The 2-hour postprandial glucose test should be performed using a glucose load containing the equivalent of 75-g anhydrous glucose dissolved in water.

General target for glucose control of T2D

- The general target for glucose control in T2D should be $< 7\%$ (53 mmol/mol), pre-prandial capillary blood glucose from 80 to 130 mg/dl and postprandial capillary blood glucose less than 160-180 mg/dl.
- Lower HbA1c targets are desirable or at least should be considered, as long as hypoglycemia and weight gain can be avoided using appropriate treatments.
- Values of HbA1c above 8% (64 mmol/mol) are generally unacceptable.
- Blood glucose below 54 mg/dl (3 mmol/L) should be always avoided.
- Consider relaxing the target HbA1c level on a case-by-case basis, with particular consideration for people who are older or frail, who are unlikely to achieve longer-term risk-reduction benefits, people with a reduced life expectancy, for whom tight blood glucose control poses a high risk of the consequences of hypoglycemia and for whom intensive management would not be appropriate, for example, people with significant comorbidities.

Monitoring

In adults with type 2 diabetes, measure HbA1c levels at:

- 3–6-monthly intervals (tailored to individual needs), until the HbA1c is stable on unchanging therapy.
 - 6-monthly intervals once the HbA1c level and blood glucose lowering therapy are stable.
- remove and add:

The diagnostic criteria for prediabetes currently proposed by the WHO and IDF

- Fasting glucose 100-125 mg/dL (6.1-7.0 mmol/L)
- OR 2-hour glucose following ingestion of 75-g glucose load 140-199 mg/dL (7.8-11.0 mmol/L)
- OR HbA1c 5.7-6.4%

Screening for type 2 diabetes

- Screening programmes are recommended for people at high risk of diabetes identified during a medical check up (opportunistic screening). (VI, B)
- Screening programmes should be based on Fasting Plasma Glucose. It has a more favourable cost/efficacy ratio than those based on OGTT. (VI, B)
- In case of normal screening tests, high risk subjects should be re-examined annually; moreover, they must be provided with useful instructions to both change their lifestyle and to reduce diabetes risk factors. (VI, B)

Subjects with a high risk of diabetes

- 1- IFG, IGT or past gestational diabetes
 - 2- Age ≥ 45 years, especially with BMI ≥ 25 kg/m² or abdominal obesity
 - 3- Age < 45 years, overweight (BMI ≥ 25 kg/m²) and one or more of the following conditions:
 - First degree relative with type 2 diabetes.
 - Arterial hypertension ($\geq 140/90$ mmHg) and/or antihypertensive treatment.
 - Low levels of HDL cholesterol (< 35 mg/dl)
 - Polycystic ovarian syndrome or other insulin-resistant conditions like Acanthosis nigricans.
- Women who delivered a baby weighting > 4 kg.
 - Children aged > 10 years, with BMI > 85 th percentile and two of the following conditions:
 - First or second degree relative with type 2 diabetes and mother with gestational diabetes.
 - Signs of insulin-resistance or associated conditions (hypertension,

dyslipidemia, Acanthosis nigricans, polycystic ovarian syndrome).
• Maternal history of diabetes or GDM during the child's gestation

Screening and diagnosis of gestational diabetes(GDM)

- Screen for undiagnosed type 2 diabetes at the first prenatal visit in those with risk factors, using standard diagnostic criteria (B)
- Screen for GDM at 24–28 weeks gestation in pregnant women not previously known to have diabetes (B)
- Screen women with GDM for persistent diabetes at 6–12 weeks postpartum, using OGTT, non-pregnancy diagnostic criteria (E)

Two approaches may be followed for GDM screening at 24–28 weeks:

1. Two-step approach:

- A. Perform initial screening by measuring plasma or serum glucose 1 h after a 50-g oral glucose load. A glucose threshold after 50-g load of > 140 mg/dl identifies 80% of women with GDM, while the sensitivity is further increased to 90% by a threshold of > 130 mg/dl.
 - B. Perform a diagnostic 100-g OGTT on a separate day in women who exceed the chosen threshold on 50-g screening. The 100-g OGTT should be performed in the morning after an overnight fast of at least 8 h. The diagnosis of GDM is made if at least two of the four plasma glucose levels are met or exceed
- | | |
|---------|-----------|
| Fasting | :95mg/dl |
| 1h | :180mg/dl |
| 2h | :155mg/dl |
| 3h | :140mg/dl |

2. One-step approach:

- (may be preferred in clinics with high prevalence of GDM): Perform a diagnostic 75-g OGTT in all women to be tested at 24–28 weeks. The 100-g OGTT should be performed in the morning after an overnight fast of at least 8 h.

To make a diagnosis of GDM, at least two of the following plasma glucose values must be found:

Fasting: 92 mg/dL (5.1 mmol/L)

1 h: 180 mg/dL (10.0 mmol/L)

2 h: 153 mg/dL (8.5 mmol/L)

Screening is not required when all the following characteristics are present:

1- Age < 25 years.

2- Normal pre-pregnancy weight.

3- Negative family history for diabetes mellitus.

4- Negative case history for impaired glucose tolerance.

5- Obstetric history with no unfavourable outcome.

Glucose tolerance should be reassessed in all women with gestational diabetes 6 - 12 weeks after delivery with an OGTT with subsequent screening for the development of diabetes or pre-diabetes. (VI, B)

Prevention/Delay of Type 2 Diabetes

- Avoiding overweight and performing regular physical exercise (30 min a day or 150 min a week) is the most appropriate way of reducing the risk of type 2 diabetes mellitus in subjects with Prediabetes. (I, A)

- Subjects with Prediabetes must be given counselling concerning weight loss of 5–10% of body weight and for increasing physical activity such as walking. (I, A)

- Subjects with Prediabetes must be encouraged to change their diet habits:
 - Reduce the total intake of fat (< 30% of the daily energy intake) and especially of saturated fatty acids (< 10% of the daily calorie intake).
 - Increase the intake of vegetable fibre (at least 15 g/1,000 kcal).

(I, A)

- Monitoring for the development of diabetes in those with pre-diabetes should be performed annually.

Pharmacological treatment though less effective, can be considered for obese subjects with IGT in whom the lifestyle interventions have either failed or cannot be applied. (I, B), and metformin should be

the only drug considered for use in diabetes prevention.

Diabetes care

Ideally diabetics must be cared for by both the general practitioner and the diabetes team, which, coordinated by a Diabetologist, comprises doctors, nurses, dieticians and mental health professionals skilled in implementing an integrated disease management approach designed to treat a chronic disease. (VI, B)

Diabetics must actively participate in the care plan, which is drafted like a personalized therapeutic alliance between the patients, his/her family and diabetes team members. The patient's age, education and employment, physical exercise practiced, diet habits, social and economic conditions, personality, cultural factors and the presence of other diseases or complications of diabetes will be focused. (VI, B)

By applying diversified strategies and techniques to suit the patient's age, social status and cultural level, the care plan must include an education program centered on self-management of diabetes to provide appropriate knowledge on problem-solving methods applied to disease management. The care plan implementation requires that every aspect of the plan be clarified and agreed on between the patient and the diabetes team, beside the definition of achievable goals. (VI, B)

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A complete medical evaluation should be performed to classify the diabetes, detect the presence of diabetes complications, review previous treatment and risk factor control in patients with established diabetes, assist in formulating a management plan, and provide a basis for continuing care

Laboratory tests appropriate to the evaluation of each patient's medical condition should be performed.

Screening Recommendation

- Consider screening those with type 1 diabetes for other autoimmune diseases (thyroid, vitamin B12 deficiency, celiac) as appropriate (B)

Initial evaluation:

A diabetic patient's first evaluation should include a complete medical check up that also check chronic complications typical of the disease and laboratory tests to define the patient's general clinical conditions. If diabetes had already been diagnosed, the treatment established and the degree of glycemic control obtained must be reassessed and the disease management plan must be redrafted, if necessary, once key points have been defined. (VI, B)

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Table (3) The diabetic patient initial evaluation:

		INITIAL VISIT	EVERY FOLLOW-UP VISIT	ANNUAL VISIT
PAST MEDICAL AND FAMILY HISTORY	Diabetes history - Characteristics at onset (e.g., age, symptoms) - Review of previous treatment regimens and response - Assess frequency/causes/severity of past hospitalizations	✓	✓	
	Family history - Family history of diabetes in a first-degree relative - Family history of autoimmune disorder	✓		
	Personal history of complications and common comorbidities - Macrovascular and microvascular - Common comorbidities - Presence of hemoglobinopathies or anemias - High blood pressure or abnormal lipids - Use dental visit - Use alcohol and/or drugs - Visits to specialists	✓	✓	✓
	Interval history Changes in medical/family history since last visit		✓	✓
	Social history - Assess lifestyle and behavior patterns - Eating patterns and weight history - Sleep patterns and physical activity - Family history with carbohydrate counting in type 1 diabetes - Tobacco, alcohol, and substance use - Identify existing social supports - Interval history - Changes in social history since last visit	✓	✓	✓
Medications and Vaccinations	- Medication-taking behavior - Medication intolerance or side effects - Complementary and alternative medicine use - Vaccination history and needs	✓	✓	✓
Technology Use	- Assess use of health apps, online education, patient portals, etc. - Glucose monitoring (meter/CGM) results and data use - Review insulin/pump settings	✓	✓	✓
Screening	Psychosocial conditions - Screen for depression, anxiety, and disordered eating; refer for further assessment or intervention if warranted - Consider assessment for cognitive impairment	✓		✓
	Diabetes self-management education and support - History of diabetes/diabetes educator visits - Screen for barriers to diabetes self-management - Refer or offer social resources and support as needed	✓	✓	✓
	Hypoglycemia Timing of episodes, awareness, frequency and causes	✓	✓	✓
	Pregnancy planning For women with childbearing capacity, review contraceptive needs and preconception planning	✓	✓	✓

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		INITIAL VISIT	EVERY FOLLOW-UP VISIT	ANNUAL VISIT
PHYSICAL EXAMINATION	- Height, weight, and BMI, growth/pubertal development in children and adolescents - Blood pressure determination - Orthostatic blood pressure measures (when indicated) - Fundoscopic examination (refer to eye specialist) - Thyroid palpation - Skin examination (e.g., acanthosis nigricans, insulin injection or infusion sites, lipodystrophy) - Comprehensive foot examination - Visual inspection (e.g., skin integrity, callus formation, foot deformity or ulcer formation) - Screen for PAD (pedal pulses, reflexes, ABI if diminished) - Determination of temperature, vibration or pinprick sensation, and 10-g monofilament exam	✓	✓	✓
	- A1C (if the results are not available within the past 3 months) - If not performed/available within the past year - Lipid profile, including total LDL and HDL cholesterol and triglycerides^a - Liver function tests^b - Spot urinary albumin-to-creatinine ratio - Serum creatinine and estimated glomerular filtration rate^c - Thyroid-stimulating hormone in patients with type 1 diabetes^d - Vitamin B12 (per methotrexate when indicated) - Serum potassium levels in patients on ACE inhibitors, ARBs, or diuretics^e	✓	✓	✓
ASSESSMENT AND PLAN	Goal setting - Set A1C/blood glucose target and monitoring frequency - If hypertension diagnosed, establish blood pressure goal - Incorporate new members to the care team as needed - Diabetes education and self-management support needs	✓	✓	✓
	Cardiovascular risk assessment and staging of CKD - History of ASCVD - Presence of ASCVD risk factors (see Table 3.2) - Staging of CKD (see Table 10.1)^f	✓	✓	✓
	Therapeutic treatment plan - Lifestyle management - Pharmacologic therapy - Referrals to specialists (including dietitian and diabetes educator) as needed - Use of glucose monitoring and insulin delivery devices	✓	✓	✓
		✓	✓	✓

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Diagnostic investigations and specialist consultations

- ECG in the adult, if clinically required.
- Ophthalmological consultation for annual dilated eye examination.
- Family planning for women of childbearing age.
- Specialist consultation for feet, if required.
- Dental examination.
- Other specialist consultations and services, if required.

Glycemic control

Evaluating glycemic control:

Two primary techniques available for health providers and patients to assess the effectiveness of the management plan on glycemic control are:

- Patient self-monitoring of blood glucose (SMBG)
- A1C

A. Self-monitoring of blood glucose (SMBG)

- Blood glucose self-monitoring is an essential factor in the self management of diabetes both to achieve the therapeutic goals and to reduce the risk of acute hypoglycaemia. (VI, B)
- Daily self-monitoring is essential for type 1 diabetics under intensive insulin therapy. (II, A)
- Blood glucose self-monitoring by varying frequency and testing modes is useful for type 2 diabetics under insulin therapy. (III, B)
- Self-monitoring frequency must be adjusted to intercurrent events and increased in clinical conditions, such as an intercurrent disease, unnoticed episodes of hypoglycaemia, hypoglycaemia at night and changes in hypoglycaemic treatment. (VI, B)

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- The patient must be taught to self-monitor blood glucose; moreover, glucometer accuracy must be periodically checked and treatment must be adjusted to suit measured values, even resorting to a commonly agreed algorithm. (VI, B)
- Recommendations for glucose monitoring in patients on multiple-dose insulin (MDI) or insulin pump therapy should do SMBG prior to meals and snacks, occasionally postprandially, at bedtime, prior to exercise, when they suspect low blood glucose, after treating low blood glucose until they are normoglycemic, and prior to critical tasks such as driving (B)
- SMBG is especially important for patients treated with insulin to monitor for and prevent asymptomatic hypoglycemia and hyperglycemia

Monitoring

In adults with type 2 diabetes, measure HbA1c levels at:

Ø 3–6-monthly intervals (tailored to individual needs), until the HbA1c is stable on unchanging therapy.

Ø 6-monthly intervals once the HbA1c level and blood glucose lowering therapy are stable.

N.B.

In clinics where HbA1c test is not available or lacking standardization, it is advisable to depend on self monitoring of plasma glucose for glycemic control.

Glycemic goals:

Diabetes treatment must be speedily adjusted for every patient to obtain near normal blood glucose concentrations and stable HbA1c values < 7%. In patients who decide to be pregnant HbA1c should be < 7%. These values will enable prevention of both the incidence and progression of micro- and macro-vascular complications. (I, A)

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Less stringent A1C goals such as <8% may be appropriate for patients with a history of severe hypoglycaemia, limited life expectancy, advanced microvascular or macrovascular complications, extensive co-morbid conditions, and those with longstanding diabetes in whom the general goal is difficult to attain despite appropriate glucose monitoring, and effective doses of multiple glucose-lowering agents including insulin. (VI, B), Consider age when setting glycemic goals in children and adolescents with type 1 diabetes, with less stringent goals for younger children. (E) Algorithms for insulin therapy are recommended for Intensive Care patients as they facilitate the achievement of glycemic goals. (II, B)

Glycemic goals for non-pregnant adults with diabetes:

- HbA1c < 7.0%.
- Fasting and pre-prandial capillary plasma glucose 80–130 mg/dl.
- Post-prandial capillary plasma glucose < 180 mg/dl.
- Post-prandial plasma glucose must be tested 2 hours after the meal's start.

N.B.

Glycemic goals should be individualized, based on a patient's duration of diabetes, age, life expectancy, co-morbid conditions, known cardiovascular disease (CVD) or advanced microvascular complications, unawareness of hypoglycemia, and other considerations

The recommendation for glycemic control in children and adolescents with type 1 diabetes:

In selecting glycemic goals, the long-term health benefits of achieving a lower A1C should be balanced against the risks of hypoglycemia and the developmental burdens of intensive regimens in children and youth.

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Special consideration should be given to the unique risks of hypoglycemia in young children.

For young children (<7 years old), glycemic goals may need to be modified since most at that age have a form of “hypoglycemic unawareness,” including immaturity of and a relative inability to recognize and respond to hypoglycemic symptoms; this places them at greater risk for severe hypoglycemia.

While it was previously thought that young children were at risk for cognitive impairment after episodes of severe hypoglycemia, current data have not confirmed this.

Furthermore, new therapeutic modalities, such as rapid and long-acting insulin analogs, technological advances (e.g., low glucose suspend), and education may mitigate the incidence of severe hypoglycemia.

These goals apply to all pediatric age groups:

- Plasma blood glucose before meals 90–130 mg/dl
- Plasma glucose at bedtime/overnight 90–150 mg/dl
- A1C < 7.5%

Regarding goals for glycemic control for women with GDM:

Due to alterations in red blood cell turnover that lower the normal A1C level in pregnancy, the A1C target in pregnancy is < 6% if this can be achieved without significant hypoglycemia. (B)

Recommendations is to target the following maternal capillary glucose concentrations:

- pre-prandial: < 95 mg/dl and either
- 1-h post meal: < 140 mg/dl
- or
- 2-h post meal: <120 mg/dl

For women with preexisting type 1 or type 2 diabetes who become pregnant, it is recommended the following as optimal glycemic goals, if they can be achieved without excessive hypoglycemia:

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- premeal, bedtime, and overnight glucose 60–99 mg/dl
- peak postprandial glucose 100 –129 mg/dl
- A1C <6.0%

N.B.

This recommendation must take in consideration that individualizing care is needed.

Medical nutrition therapy (MNT)

General recommendations:

- Nutrition therapy is recommended for all people with type 1 and type 2 diabetes as an effective component of the overall treatment plan (A)
- To achieve therapeutic goals, people with diabetes or prediabetes must receive personalized medical nutrition therapy by a dietitian, preferably a diabetes team member trained in the diabetes field. (III,B)
- Nutrition consultation must consider people with prediabetes or diabetes mellitus' personal requirements and intention to change. (VI, B)
- Vegetables, beans, fruit and cereal typical of the Mediterranean diet must be added to the diet of people with type 1 and 2 diabetes mellitus. The intake of fibre rich food with a low Glycemic Index must be encouraged especially when a diet is rich in carbohydrates. (I, A)
- There is no evidence to recommend the use of “diabetic diets” for diabetics. (VI, D)
- Evidence suggests there is no ideal percentage of calories from carbohydrate, protein, and fat for all people with diabetes (B)
- Therefore, macronutrient distribution should be based on individualized assessment of current eating patterns, preferences, and metabolic goals (E)

- Intensive lifestyle programs with frequent follow-up are required to achieve significant reductions in excess body weight and improve clinical indicators
- Several studies have attempted to identify the optimal mix of macronutrients for meal plans of people with diabetes

Overweight and Obesity

- Weight loss is recommended in all overweight (BMI 25.0 – 29.9 kg/m²) or obese (≥ 30.0 kg/m²) adults. (I,A)
- The main approach to weight loss is a change in lifestyle, which involves reducing calorie intake and increasing physical exercise. A moderate reduction in calorie intake (300–500 kcal/day) and a moderate increase in energy consumption (200–300 kcal/day) ensure slow but progressive weight loss (0.45–0.90 kg/week). (I,A)
- Moderate physical exercise must be recommended to suit the patient's physical fitness when the program starts. This exercise must then be gradually increased in duration and frequency to 30–45 min a day of moderate aerobic exercise for 3–5 days a week (goal: 150 min/week). Higher levels of physical exercise at least 1 h a day of moderate activity (walking) or 30 min a day of more vigorous exercise (jogging) can be required to obtain effective long-term weight loss. (VI,B)

Carbohydrates:

- The daily intake of carbohydrates with the diet must provide 45–60% of total daily calories. (VI,C)
- Considering these limits, the patient's metabolic features will suggest the most appropriate intake for type 1 and 2 diabetics. (I,A)
- Diets with a low-carbohydrate content (specifically reduced below 130 g/day) are not recommended for diabetics. (III,B)
- Both the quantity and quality of carbohydrates in food can influence the glycemic response. Controlling total carbohydrate intake with

either an exchange diet or the carbohydrate count is a key strategy to obtain glycemic control in patients under insulin therapy with a daily multiple injections (basal-bolus). (I,A)

- Assessing the quantity, quality and distribution of the daily intake of carbohydrates can facilitate achieving optimal glycemic control. All patients treated with hypoglycemic drugs, especially with insulin therapy, require the time of intake and drug dosage to be evaluated and adapted to the quantity and nature of carbohydrates taken. (III,B)

Sucrose:

- The total intake of sucrose should not exceed 10% of the total energy daily introduced with food. A more restrictive intake can be useful for people who need to lose weight. (I,A)

The Glycemic index

can be a useful indicator in the choice of food rich in carbohydrates to be added to the diet of diabetics. (III,B)

Fibres:

- People with type 1 and 2 diabetes must be encouraged to consume food with high-fibre content. (I,A)
- The ideal fibre content in the diet should be more than 40 g/day (or 20 g / 1,000 kcal / day); most of it should be soluble. (I,A)
- Daily consumption of either vegetables or fruit and a weekly intake of beans can meet minimum fibre requirements. (III,B)

Proteins:

- In patients with no history of nephropathy, the protein intake should provide 10–20% of the total energy daily supplied by food. (VI,B)
- Individuals with any degree of chronic renal failure must limit protein intake to the recommended dose (0.6–0.8 g / kg) to reduce

the risk of nephropathy developing any further. (I,A)

Fats:

- Fat intake should be < 30% of the total energy daily supplied by food. (III,B)
- The daily intake of saturated fat must be less than 10% of total calories. A lesser amount (<7%) can be useful if LDL cholesterol is >100 mg/dl. (I,A)
- Oils rich in monounsaturated fatty acids (MUFA) are an important source of fat. Depending on the patient's preferences, they can provide 10–20% of the total energy daily introduced with food. (III,B)
- The intake of trans fatty acids must be minimized (<1%). (VI,B)
- Polyunsaturated fatty acids (PUFA) must not contribute over 10% of the total energy daily supplied by food. (III,B)
- **Cholesterol** introduced with the diet must not exceed 300 mg/day. It can be further reduced if LDL cholesterol is >100 mg/dl. (I,A)
- In overweight patients, a fat intake below 30% of the total energy daily introduced can facilitate weight loss. (IV,C)

Sweeteners:

- Calorie-free sweeteners (i.e. saccharin, aspartame, acesulfame-K, sucralose) are safe when taken in moderate daily doses. (I,A)

Diet supplements:

- Habitual intake of supplements, such as antioxidants (i.e. vitamin E, C and B-carotene) is not recommended when there is no evidence of their long-term efficacy and safety. (I,D)
- The intake of food that is naturally rich in antioxidants, microelements and other vitamins must be encouraged. Hence diabetics must be encouraged to daily eating fruit and vegetables. (III,B)

Salt:

- Like the population at large, diabetics must be recommended to take less than 6 g/day of salt. (I,A)

Specific nutritional interventions in type 1 diabetics:

Patients treated with either rapid acting insulin analogues or insulin pumps must adjust the pre-prandial insulin bolus to suit carbohydrates contained in meals. (I,A)

Patients treated with fixed doses of insulin must maintain carbohydrate intake at meals constant both concerning quantity and time. (III,B)

Pharmacological treatment

Type 1 diabetes

- Most people with type 1 diabetes should be treated with MDI injections (3 - 4 injections per day of basal and prandial insulin) (A)
- Most people with type 1 diabetes should be educated in how to match prandial insulin dose to carbohydrate intake, pre-meal blood glucose, and anticipated activity (E)
- Most people with type 1 diabetes should use insulin analogs to reduce hypoglycemia risk (A)
- Keep close control of blood glucose to reduce the risk of chronic complications. (I,A)
- The prescription of self-management algorithms for insulin therapy can facilitate the achievement of glycemic goals. (II,B)
- When HbA1c values are higher than the goal, appropriate treatment variations should be speedily implemented to rapidly reach and maintain good glycemic control in time. (VI,B), taking into account the patient's possible poor adhesion to the prescribed therapy. (I,A)

Type 2 diabetes

- Close monitoring of blood glucose to reduce the risk of chronic complications. (I, A)
- When HbA1c concentrations are higher than the glycemic goal, appropriate treatment variations must be speedily implemented to rapidly reach and maintain good blood glucose control in time. (VI, B)
- The revolutionary advance in the number of blood glucose-lowering medications has led to some confusion for both practitioners and patients regarding the most appropriate way to treat diabetes. We agree that the choice of specific antihyperglycemic agents should be based primarily on their A1C lowering capacity, demonstrated safety (especially hypoglycaemia) and efficacy in long-term studies, tolerability and expense. Specific effects of individual therapies on cardiovascular disease risk factors, such as hypertension or dyslipidemia, are also considered important.
- Metformin, if not contraindicated and if tolerated, is the preferred initial pharmacological agent for type 2 diabetes (A)
- In newly diagnosed type 2 diabetic patients with markedly symptomatic and/or elevated blood glucose levels or A1C, consider insulin therapy, with or without additional agents, from the outset (E)
- It is essential to combine two or more oral hypoglycemic drugs in patients who lack good control with monotherapy. (I,A)
- It is essential to start either basal or multi-injection insulin therapy when blood glucose control is inadequate even with multi-oral therapy. (I,A)
- Take into account possible poor adherence to the prescribed treatment. (I,A)
- A patient-centered approach is stressed, taking into account patient preferences, cost and potential side effects of each class, effects on body weight, and hypoglycemia risk.
- Due to the progressive nature of type 2 diabetes, insulin therapy is eventually indicated for many patients with type 2 diabetes. (B)

Key priorities for implementation

Education

- All guidelines consider diabetes education as one of the cornerstones of diabetes management.
- Group education seems to work well for people with T2D at the time of diagnosis, with an annual review of their progress.
- Education should be evidence-based, suit the needs of the individual, have specific aims and learning objectives and support the learner plus family and caregivers in developing attitudes, beliefs, knowledge and skills to self-manage diabetes.
- The “Train the Trainer” centers should be familiar with this kind of program and teach it during their courses.
- The program should be if possible conducted by a trained diabetes educator.
- Every primary care unit should facilitate the training of at least one of their health professionals to become a diabetes educator.
- Patients with T2D should attend this diabetes education periodically.

Lifestyle changes

- Persons with T2D must improve their lifestyle from the time of diagnosis to reach the metabolic targets as soon as possible, this could be achieved by reducing BW by about 10 % of total BW.

Physical activity

- All guidelines consider physical activity or exercise as part of lifestyle modifications.
- Some specify moderate aerobic physical activity such as walking for at least 150 minutes per week at intervals of no longer than 48 hours.
- A more intensive physical activity program including at least 275 minutes per week may be needed to assist weight loss and avoid regain.

Diet

- All guidelines recommend a hypocaloric diet for overweight or obese people with T2D in order to aim for a normal body weight or to achieve a clinically significant reduction in body weight. This means that moderately obese people have to lose at least 10 kg and therefore it is recommend that their daily caloric intake should be limited to 800 to 1200 calories (low-calorie diet) in order to achieve the necessary weight loss within 6 months.
- Severely obese people may not be able to achieve this with diet and may need bariatric surgery.
- The health care provider can start by giving simple advice on diet changes such as to avoid snacks, sweets and eating out (where size and content of meals cannot be controlled) and reduce the daily caloric intake by 500 to 600 calories. Referral to a dietician if available can be very useful to learn how to translate the caloric restriction into feasible meals and how to manage some barriers for caloric restriction such as emptiness and hunger.
- The patient should be advised to prefer high-fiber and low-glycemic index foods.
- Three to five daily portions of vegetables and/or fruits, fish, grains and monounsaturated fats are good choices.
- Sugar, sweets and sweetened beverages should be avoided.

Blood glucose management

Individualized care

- Adopt an individualized approach to diabetes care that is tailored to the needs and circumstances of adults with type 2 diabetes, taking into account their personal preferences, comorbidities, risks from polypharmacy, and their ability to benefit from long-term interventions because of reduced life expectancy.
- Such an approach is especially important in the context of multi-morbidity.
- Reassess the person's needs and circumstances at each review.

- Take into account any disabilities, including visual impairment, when planning and delivering care for adults with type 2 diabetes.
- Several factors affect the choice of glucose-lowering medications, particularly in the setting of patient-centered care. In addition to CVD, effect on weight, hypoglycemic risk, treatment cost, and other patient-related factors that may influence treatment selection.

Drug treatment

Initial drug treatment (Monotherapy)

- Offer metformin as the initial drug treatment for adults with type 2 diabetes.
- Titration from 500 to 2000 mg per day, and administration with or after meals.
- Metformin should not be used in patients with an eGFR <30 ml/minute/1.73m² and dose reduction should be considered when the eGFR is <45 ml/minute/1.73m².
- Caution should be taken when conditions are present that may reduce eGFR.
- In adults with type 2 diabetes, if metformin is contraindicated or not tolerated, consider initial drug treatment with: Dipeptidyl Peptidase-4 (DPP-4) inhibitor or Pioglitazone or a Sulfonylurea (Glibenclamide should be avoided in patients aged 60 years and older).
- Some guidelines consider that any glucose lowering drug (GLD) with approved indication as monotherapy can be used and the choice would depend on the profile of the drug (efficacy, safety and local cost-effectiveness) and the preference of the patient (compliance, quality of life and affordability) e.g. sodium-glucose cotransporter 2 (SGLT2) Inhibitors , GLP1 A.

First intensification of drug treatment (Dual therapy)

- Second glucose lowering drug should be added if monotherapy with metformin is not sufficiently effective to reach the HbA1c target

or fails afterwards.

- The best choice of add-on is an SU (Glibenclamide should be avoided in patients aged 60 years and older), a DPP4 inhibitor or a SGLT2 inhibitor.
- GLP1 receptor agonist can be used if weight loss is a priority and the drug is affordable.

Second intensification of drug treatment (Triple therapy)

- Third glucose lowering drug should be added if the dual therapy is not sufficiently effective to reach or maintain the HbA1c target.
- The most common choice to add to the dual therapy is basal insulin.
- GLP1 receptor agonist can be added instead, if weight loss is indicated or has been insufficient.
- Triple therapy with three oral glucose lowering drug may be effective before adding an injectable.
- In adults with type 2 diabetes, a GLP-1 mimetic in combination with insulin should be offered by specialist.

Implications of New Evidence from Cardiovascular Outcomes Trials

- Because of the new evidence for the benefit of specific medications to reduce mortality, heart failure (HF), and progression of renal disease in the setting of established CVD, their use was considered compelling in this patient group.
- Therefore, an important early step is to consider the presence or absence of ASCVD, HF, and CKD, conditions in aggregate affecting 15–25% of the population with type 2 diabetes.
- Thus, we recommend that providers consider a history of CVD very early in the process of treatment selection.
- Among patients with type 2 diabetes who have established ASCVD, SGLT2 inhibitors or GLP-1 receptor agonists with proven

cardiovascular benefit are recommended as part of glycemic management.

- Among patients with ASCVD in whom HF coexists or is of special concern, SGLT2 inhibitors are recommended.
- For patients with type 2 diabetes and CKD, with or without CVD, consider the use of an SGLT2 inhibitor shown to reduce CKD progression or, if contraindicated or not preferred, a GLP-1 receptor agonist shown to reduce CKD progression.

Initial combination therapy

- The baseline HbA1c threshold to start with the initial combination therapy varies from 7.5% to 9% (58-75 mmol/mol).
- In particular, the mechanism of action of the other drug should be complementary to metformin and there should not be unacceptable added side effects.
- Therefore, the combination with a SU (Glibenclamide should be avoided in patients aged 60 years and older), a DPP4 inhibitor or an SGLT2 inhibitor may be the preferred option.

Initial insulin therapy

- Most guidelines recommend the use of insulin alone or in combination with other glucose lowering drugs (GLDs) when persons with T2D are unstable, with symptoms and signs of acute decompensation including dehydration, acute weight loss, acute illness, very high glucose levels and presence of ketones.
- Basal insulin should be preferred and it can be temporary.
- Most insulin algorithms start with 10 unit or 0.2 units/kg and titrate once or twice weekly at 1 to 2 units each time to achieve a target fasting blood glucose between 70 and 130 mg/dL.

Insulin-based treatments

Start insulin therapy for adults with type 2 diabetes from a choice of a number of insulin types and regimens:

- NPH insulin injected once or twice daily according to need.
- Consider starting both NPH and short-acting insulin (particularly

if the person's HbA1c is 9.0% or higher), administered either: separately or as a pre-mixed (biphasic) human insulin preparation.

- Consider, as an alternative to NPH insulin, using long acting insulin analogues e.g. detemir, glargine U100, U 300 or degludec as it will reduce the frequency of injections from twice to once daily or when the person's lifestyle is restricted by recurrent symptomatic hypoglycemic episodes or when the person would otherwise need twice-daily NPH insulin injections in combination with oral glucose-lowering drugs.

- Consider pre-mixed (biphasic) preparations that include short-acting insulin analogues, rather than pre-mixed (biphasic) preparations that include short-acting human insulin preparations, if a person prefers injecting insulin immediately before a meal or hypoglycemia is a problem or blood glucose levels rise markedly after meals.

- Consider switching to long acting insulin analogues from NPH insulin in adults with type 2 diabetes: who do not reach their target HbA1c because of significant hypoglycemia or who experience significant hypoglycemia on NPH insulin irrespective of the level of HbA1c reached or who cannot use the device needed to inject NPH insulin but who could administer their own insulin safely and accurately if a switch to one of the long-acting insulin analogues was made and for whom switching to one of the long-acting insulin analogues would reduce the number of daily injections.

- Monitor adults with type 2 diabetes who are on a basal insulin regimen (NPH insulin, long acting insulin analogues) for the need for short-acting insulin before meals (or a pre-mixed [biphasic] insulin preparation).

- Monitor adults with type 2 diabetes who are on pre-mixed (biphasic) insulin for the need for a further injection of short-acting insulin before meals or for a change to a basal bolus regimen, if blood glucose control remains inadequate.

Therapeutic education

(Diabetes self management)

- People with diabetes must be instructed to self-manage their disease both at the time of diagnosis and later, to suit requirements. (III,B)

- Education on the self-management of diabetes must be guaranteed by the team's healthcare personnel that are specially qualified with ongoing professional training to conduct educational activities. (VI,B)

- All diabetes teams must have at least one healthcare operator who is specifically trained in therapeutic education. (VI,B)

- When there is no educator, we encourage other team members to acquire this competence. (VI,B)

- Education on the self-management of diabetes must also focus on psychosocial issues because emotional wellness is strongly associated with the positive outcome of treatment. (III,B)

- Education on the self-management of diabetes must be appropriately acknowledged and paid as an integrated intervention system in the framework of National Health Services (UK). (VI,B)

Psychosocial evaluation applied to diabetes care

- A preliminary evaluation of the psychological and social condition especially depression must be performed at the first examination and, anyhow, when adherence to the therapeutic regime is inadequate. (VI,B)

- The psychosocial evaluation should study the attitude towards the disease and subsequent expectations, diabetes related complications, medical management and quality of life (both in a broad sense and related to the disease), economic, social and emotional resources and the patient's psychiatric history, if any. (VI,B)

- Psychological treatment is better inserted in the framework of routine treatment than administered only when a specific problem or worsening in the psychic condition are detected. (VI,B)

Intercurrent Illness

- When there is an intercurrent disease, pharmacological treatment must be reviewed and adjusted to suit either concomitant blood glucose alterations or the new risk profile induced by the disease in progress. (III, B)
- The stress of illness, trauma, and/or surgery frequently aggravates glycemic control and may precipitate diabetic ketoacidosis (DKA) or non-ketotic hyperosmolar state. Any condition leading to deterioration in glycemic control necessitates more frequent monitoring of blood glucose and urine or blood ketones. Vomiting accompanied by ketosis may indicate DKA, a life-threatening condition that requires immediate medical care to prevent complications and death; the possibility of DKA should always be considered. Marked hyperglycemia requires temporary adjustment of the treatment program and, if accompanied by ketosis, frequent interaction with the diabetes care team. The patient treated with oral glucose-lowering agents or MNT alone may temporarily require insulin.
- Adequate fluid and caloric intake must be assured. Infection or dehydration is more likely to necessitate hospitalization of the person with diabetes than the person without diabetes. The hospitalized patient should be treated by a physician with expertise in the management of diabetes, and recent studies suggest that achieving very stringent glycemic control may reduce mortality in the immediate post-myocardial infarction period.
- Aggressive glycemic management with insulin may reduce morbidity in patients with severe acute illness.

Hypoglycemia

- Oral glucose (15 g) is the choice treatment for mild and moderate hypoglycemia, though equivalent doses of any form of carbohydrates containing glucose can be used for this purpose; the effects of treatment should be evident within 15 min after ingestion. (VI, B)
- The effect of treatment during a hypoglycemic condition can only be temporary. Hence, blood glucose must be tested every 15 min

till at least two normal values are found without the administration of further treatment between two tests. (VI,B)

- The intra venous administration of hypertonic glucose solutions (20–33%) is the choice treatment for acute hypoglycemia when there is venous access, failing which; either intramuscular or subcutaneous administration of glucagon is recommended. (VI,B).
- Glucagon must be available for all patients with a significant risk of acute hypoglycemic episodes (i.e. diabetics under insulin therapy who lack good glycemic control due to either unstable blood glucose concentrations or the onset of sudden hypoglycemic episodes with no forewarning). The administration of glucagon does not require the attendance of a healthcare professional. (VI, B)

Vaccinations

- Yearly administer the Influenza vaccine to diabetics aged over 6 months. (III, B)
- Administer the pneumococcal vaccine to diabetic adults at least once in a lifetime. A single revaccination is recommended for subjects aged > 64 years who had their first vaccination at least 5 years before. Other indications for revaccination are nephrotic syndrome, chronic renal failure and other immunocompromised conditions (i.e. organ transplant). (III,B)

Diabetes managed care

- Achieving diabetes care goals includes cooperation between the diabetes team, the general practitioner, in the framework of well defined care pathways based on an integrated multidisciplinary and multi-professional approach that is implemented with the patient's informed consent. (III,B)
- It is to be hoped that facilities directly involved in diabetes care have appropriate information systems with a special data storage system designed to store common basic data by format and plot to encourage data sharing and the definition and use of clinical indicators. (VI,B)

Either a specialized team or a diabetologist should be consulted when there is:

- Newly diagnosed diabetes;
- Insulin-treated diabetes;
- Diabetes without good glycemic control;
- Gestational diabetes either during pregnancy or in view of a pregnancy;
- Diabetes developing either acute or chronic complications. (III)

Prevention and Management of Diabetic Complications

(I) Cardiovascular diseases

- CVD is the major cause of mortality for individuals with diabetes. It is also a major contributor to morbidity and direct and indirect costs of diabetes. Type 2 diabetes is an independent risk factor for macrovascular disease and its common coexisting conditions (e.g., hypertension and dyslipidemia) are also risk factors.

Blood pressure management

- Salt restriction strategies such as avoiding the addition of table salt are useful to help control high blood pressure.
- Add medications if lifestyle advice does not reduce blood pressure to below 140/80 mmHg (below 130/80mmHg if there is kidney, eye or cerebrovascular damage).
- Monitor blood pressure every 1–2 months, and intensify therapy if the person is already on antihypertensive drug treatment, until the blood pressure is consistently below 140/80 mmHg (below 130/80mmHg if there is kidney, eye or cerebrovascular damage).
- Treatment for hypertension should include drug classes demonstrated to reduce CV events in patients with diabetes: ACE Inhibitors, Angiotensin receptor blockers (ARBs), Thiazide-like

diuretics and Dihydropyridine calcium channel blockers.

- Multiple-drug therapy is generally required to achieve BP targets. However, combinations of ACE inhibitors and ARBs and combinations of ACE inhibitors or ARBs with direct renin inhibitors should not be used.
- An ACE inhibitor or ARB, at the maximally tolerated dose indicated for BP treatment, is the recommended first-line treatment for hypertension in patients with diabetes and urinary albumin-to-creatinine ratio ≥ 300 mg/g creatinine or 30-299 mg/g creatinine.

Dyslipidemia

- All people with T2D and established CVD should start treatment with a statin (secondary prevention).
- They would benefit from the highest recommended dose of atorvastatin or rosuvastatin, or the statin should be selected and up-titrated to reach an LDL cholesterol target <70 mg/dL (1.8 mmol/L).
- All people with T2D and without established CVD who are ≥40 years old and have LDL cholesterol >100 mg/dL (2.6 mmol/L), should start treatment with a statin (primary prevention).
- People with T2D and without established CVD who have LDL cholesterol >70 mg/dL (1.8 mmol/L) may also benefit from statin therapy, particularly if they have a high 10-year CVD risk calculated with a validated risk score (primary prevention).
- If the target of LDL cannot be reached in spite of maximum tolerated dose of statin, we should consider the addition of combined therapy with statin as ezetimibe or PCSK9 inhibitor (if affordable).
- When statin therapy is started it should be maintained lifelong.
- People with levels of triglycerides >500 to 1000 mg/dL (5.7-11.4 mmol/L) despite lifestyle changes and improved glycemic control should start a fibrate to prevent acute pancreatitis.

Antiplatelet treatment

- Most guidelines recommend low-dose aspirin (75-350 mg/d) for people with T2D and established CVD (secondary prevention).
- Some guidelines suggest that aspirin could do more benefit than harm in those without established CVD but with a high CVD risk (primary prevention) but emphasize that there is still no good evidence for this.

3- Coronary heart disease: screening and management

- In asymptomatic patients, routine screening for coronary artery

disease (CAD) is not recommended, as it does not improve outcomes as long as cardiovascular disease (CVD) risk factors are treated (A)

- In patients with known CVD, consider ACE inhibitor therapy (C) and use aspirin and statin therapy (A) (if not contraindicated) to reduce the risk of cardiovascular events
- In patients with a prior MI, β -blockers should be continued for at least 2 years after the event (B)
- The following diagnostic investigations are also recommended for diabetics with a high cardiovascular risk (they must be repeated every 1–3 years, depending on the results obtained):
 - Carotid Doppler ultrasound;
 - Doppler ultrasound of the lower limbs (with Winsor Index < 0.9 or if arteries are not compressible) patients might need ischemia provocative tests (exercise ECG or exercise stress scintigraphy/ echocardiography) (VI, B)

(II) Diabetic nephropathy: screening and management

General recommendations

- Optimize glycemic control to reduce the risk and/or slow down the progress of nephropathy. (I, A)
- Optimize pressure control to reduce the risk and/or slow down the progress of nephropathy. (I, A)
- To be consistent with newer nomenclature intended to emphasize the continuous nature of albuminuria as a risk factor, the terms “microalbuminuria” (30–299 mg/24 h) and “macroalbuminuria” (>300 mg/24 h) will no longer be used, but rather referred to as persistent albuminuria at levels 30–299 mg/24 h and levels ≥300 mg/24 h. Normal albumin excretion is currently defined as <30 mg/24 h

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- Diabetic nephropathy occurs in 20-40% of patients with diabetes
- Persistent albuminuria in the range of 30-299 mg/24 h has been shown to be an early stage of diabetic nephropathy in type 1 diabetes and a marker for development of nephropathy in type 2 diabetes
- It is a well-established marker of increased CVD risk
- To reduce the risk or slow the progression of nephropathy, optimize glucose control (A)
- At least once a year, quantitatively assess urine albumin excretion and estimated glomerular filtration rate in patients with type 1 diabetes duration of ≥ 5 years and in all patients with type 2 diabetes
- An ACE inhibitor or ARB for the primary prevention of diabetic kidney disease is not recommended in diabetic patients with normal blood pressure and albumin excretion < 30 mg/24 h (B)
- Either ACE inhibitors or ARBs (but not both in combination) are recommended for the treatment of the non-pregnant patient with modestly elevated (30-299 mg/24 h) (C) or higher levels (> 300 mg/24 h) of urinary albumin excretion (A)
- When ACE inhibitors, ARBs, or diuretics are used, monitor serum creatinine and potassium levels for the development of increased creatinine or changes in potassium (E)
- Continued monitoring of urine albumin excretion to assess both response to therapy and progression of disease is reasonable (E)
- When eGFR is < 60 mL/min/1.73 m², evaluate and manage potential complications of CKD (E)
- For people with diabetes and diabetic kidney disease (albuminuria > 30 mg/24 h), reducing dietary protein below usual intake not recommended (A)
- Correct any lipid profile alterations to both slow down the progress of nephropathy and reduce the associated cardiovascular risk. (I, B)
- Dihydropyridine calcium channel blockers (DCCB) as frontline treatment are not more effective than the placebo in slowing down the progress of nephropathy. Their use in nephropathy should be

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- limited to the role of additional therapy to further reduce blood pressure in patients already treated with ACE-inhibitors or ARBs. (III,B)
- The use of non-dihydropyridine calcium channel blockers (NDCCB), beta blockers and diuretics can be considered to control blood pressure in patients who do not tolerate ACE-inhibitors and/or ARBs. (VI,B)
 - A nephrology consultation is required GFR is < 60 mL/min per 1.73 m² or if there is any difficulty in managing either hypertension or hyperkalemia. (III,B)

(III) Diabetic retinopathy: screening and management

General recommendations

- Diabetic retinopathy is a highly specific vascular complication of both type 1 and type 2 diabetes, with prevalence strongly related to duration of diabetes
- Diabetic retinopathy is the most frequent cause of new cases of blindness among adults aged 20–74 years
- Optimizing glycemic control reduces the risk and progress of retinopathy. (I, A)
- Optimizing pressure control reduces the risk and progress of retinopathy. (I, A)

Screening

- Adults with type 1 diabetes should first have their fundus examined with pupil dilation by either an ophthalmologist or a trained health-care professional within 5 years after the onset of diabetes. (III, B)
- Patients with type 2 diabetes should first have their fundus examined with pupil dilation by either an ophthalmologist or a trained health-care professional soon after the diagnosis of diabetes. (III, B)
- If there is no evidence of retinopathy for one or more eye exams, then exams every 2 years may be considered. If diabetic retinopathy is present, subsequent examinations for type 1 and type 2 diabetic

patients should be repeated annually by an ophthalmologist or optometrist. If retinopathy is progressing or sight threatening, then examinations will be required more frequently (B)

- Subsequent examinations for type 1 and type 2 diabetic patients are generally repeated annually
- Exams every 2 years may be cost effective after one or more normal eye exams, and in a population with well-controlled type 2 diabetes there was essentially no risk of development of significant retinopathy with a 3-year interval after a normal examination
- Examinations will be required more frequently if retinopathy is progressing
- Diabetic women who plan on starting a pregnancy should undergo a complete eye examination and be monitored throughout pregnancy (at least every 3 months until delivery) and during the first year after delivery. (III,B)
- Screening is not recommended in women with gestational diabetes mellitus because they do not have a high risk of developing diabetic retinopathy. (III,D)

Diagnosis

Retinal fluorangiography is not recommended as a diagnostic tool for diabetic retinopathy. (VI,D) Retinal fluorangiography must be performed in view of laser treatment in all cases, whose lesions require a pathogenetic interpretation that cannot be provided on the basis of the clinical examination.

Specifically:

- Pathogenetic interpretation of macular edema;
- Detection of suspicious neovascularizations;
- Exact definition of ischemic retinal areas;
- Study of the macula in cases of clinically unjustified impaired vision. (VI, B)

Refer to the ophthalmologist in case of:

- Sudden loss of vision;
- Evidence of retinal detachment;
- Vessel neoformation;
- Preretinal or retinal bleeding;
- Presence of rubeosis iridis;
- Unexplained deterioration in visual acuity;
- Hard exudates within one diameter of the foveal disk;
- Macular edema;
- Unexplained retinal findings;
- Early stage proliferative or worsening retinopathy.(VI,B)

Treatment

- Laser treatment reduces the risk of impaired vision in patients with high-risk retinal lesions. (I,A)
- Anti-vascular endothelial growth factor (VEGF) therapy is indicated for diabetic macular edema (A)
- The presence of retinopathy is not a contraindication to aspirin therapy for cardio-protection, as this therapy does not increase the risk of retinal hemorrhage (A)

Follow-up

- Testing frequency must be: every 2 years, if there is no diabetic retinopathy; yearly, if there is mild to moderate background diabetic retinopathy (VI,B); earlier (3-6 months), if either new lesions are detected or if lesions have worsened, compared to the last follow up, if there is exudate within one diameter of the foveal disk, if the patient has a high risk of progress (rapid improvement in glycemic control, presence of arterial hypertension or renal complications). (VI,B)

(IV) Diabetic neuropathy: screening and management

General recommendations

- Optimizing glycemic control reduces the risk of the onset and progress of neuropathy. (I, A)
- Screening for neuropathy must be performed on all type 2 diabetics at the time of diagnosis and on type 1 diabetics after 5 years of disease duration. Subsequent testing must be performed annually. (VI,B)

Distal symmetrical polyneuropathy

- Screening for chronic distal symmetrical sensitive and motor polyneuropathy must use simple clinical tests, such as pressure sensitivity testing with the 10 g single filament and vibratory sensibility testing on the big toe with a tuning fork, preferably performed within a structured score-based system. (I, A)
- Screening for distal symmetrical polyneuropathy does not require electrophysiological testing, which is instead useful towards a differential diagnosis, when clinical characteristics are atypical. (VI, B)
- If distal symmetrical polyneuropathy is diagnosed, the diabetic should be inserted in a specific educational programme to prevent ulceration and amputation of diabetic feet. (III,B)

Autonomic neuropathy

- Screening for autonomic neuropathy must be performed with a detailed case history integrated by cardiovascular reflex testing, since symptoms are non specific and do not allow a diagnosis of autonomic dysfunction. (VI,B)
- Cardiovascular tests are very useful when symptoms suggest autonomic dysfunction, when there is a high cardiovascular risk or a risk of microangiopathic complications (diabetic retinopathy or nephropathy), before major surgery, when planning a physical

exercise programme and, in diabetics with poor glycemic control. (VI,B)

Pharmacological treatment

- Pain generated by peripheral neuropathy can be relieved by tricyclic antidepressants, anticonvulsants, serotonergic, noradrenergic and opiates (I,A)

Drugs to treat symptomatic DPN

- Tricyclic drugs : Amitriptyline 10-75 mg at bedtime, Nortriptyline 25–75 mg at bedtime, Imipramine 25-75 mg at bedtime
- Anticonvulsants: Gabapentin 300-1,200 mg t.i.d., Carbamazepine 200-400 mg t.i.d, Pregabalin 100 mg t.i.d.,
- 5-hydroxytryptamine and norepinephrine uptake inhibitor: Duloxetine 60–120 mg daily
- Substance P inhibitor: Capsaicin cream 0.025-0.075% applied t.i.d. or q.i.d.

Erectile dysfunction

- Erectile dysfunction (ED) is an endothelial dysfunction equivalent; hence, it implies a strong risk of atherosclerotic complications. This involves the need for cardiovascular diagnostic investigations. (I,A)

Foot care

Screening and prevention

All patients with diabetes mellitus must undergo a complete examination of the foot at least once a year. Feet must be examined in high-risk patients on every visit. (VI,B), this could be done by diabetologist or primary care physician trained to look for the presence of neuropathy, ischemia or deformity.

- Risk factors for diabetic foot must be defined at the time of screening. The subsequent follow up can be scheduled to suit the risk and presence of lesions. (VI,B)
- All diabetics must have an educational programme on the diabetic

foot. (I,A) It should be presented in a structured and organized manner. This plays an important role in the prevention of foot problems.

- In the absence of a multidisciplinary foot care team, foot lesions are more likely to lead to amputation. All patients with diabetes should have access to structured diabetic foot care. Otherwise, referral in the right time to the right place should be arranged. , if feasible a diabetic foot care team should include doctors specialized in diabetic foot care, health-care professional qualified in the educational field and trained in diabetic foot care (podiatrist and/or nurses). (VI,B)
- The elderly (age >70 years) require special attention, especially if they live alone, if they have a long-disease duration and if they have impaired vision and financial problems, since they have a higher risk of foot lesions. (III, B)
- Patients with feet at risk of lesions must be prescribed appropriate footwear and orthotic devices that reduce peak plantar pressure. (II, B)

Foot examination

- The foot examination should include the evaluation of the case history of past ulcers and amputations, examination, palpation, evaluation of the perception of pressure (with the 10 g Semmes–Weinstein monofilament) and of vibration (with the tuning fork 128-Hz or with the biothesiometer). (I,A)
- Screening for peripheral arteriopathy should include a history for claudication, assessment of the pedal pulses and measurement of the ankle–brachial index (ABI). (III,B)

Risk categorization:

Following examination of the foot, each patient can be assigned to any of the following risk category, which should guide the subsequent management:

A- Low Risk: where all of the following are present: Normal

Sensation, good pulses, no previous ulcer, no foot deformity and normal vision.

B- Moderate Risk: where any of the following is present: Losses of sensation, absent pulse or previous vascular surgery, significant visual impairment, physical disability e.g stroke, gross obesity...etc.

C- High Risk: where any of the following is present:

- Previous ulcer or previous amputation.
- Absent pulse and neuropathy.
- Callus in addition to other risk factor as foot deformity, neuropathy or absent pulse.

D- Active foot Disease: where foot ulceration is present, mild to moderate infection or acute charcot .

E- Limb threatening conditions: as critical limb ischemia and severe infection.

Management plan according to risk categorization:

A- Low risk Patients:

- Annual foot check.
- Education about nail and skin care, appropriate footwear and the warning signs that necessitate emergency consultation other than his ordinary annual exam.

B- Moderate Risk Patients:

- Regular check up every 4-12 weeks and management accordingly.
- Patient with visual impairment or physical disability who would otherwise fit into low risk group: nail care regularly by trained foot care nurse could be substituted.

C- High Risk Patients:

- Regular check up every 4 weeks and management accordingly.
- Referral to diabetic foot clinic is to be considered for careful

assessment, treatment of any non ulcerative pathology, plantar pressure measurement and orthotic advice as well as vascular assessment.

D- Active Foot Disease:

ii) Management of Diabetic Foot Ulcer:

Should have contact to diabetic foot team (hospital based).

Multidisciplinary approach of the DFU includes:

- Relief of pressure and protection of the ulcer: Off-loading is the cornerstone in ulcers with increased biomechanical stress using total contact casting, other casting techniques, removable cast walker or half shoes according to availability.
- Restoration of skin perfusion: Arterial revascularization procedures: results do not differ from people without diabetes, but distal revascularization procedures (angioplasty or bypass-surgery) are needed more frequently.
- Treatment of infection:
 - Superficial ulcer with skin infection to be treated with debridement with removal of all necrotic tissue and oral antibiotics targeted at *Staphylococcus aureus* and streptococci
 - Deep (limb-threatening) infection for surgical drainage as soon as possible (emergency referral) with removal of necrotic or poorly vascularized tissue, including infected bone and revascularization if necessary with broad-spectrum antibiotics intravenously, aimed at Gram-positive and negative micro-organisms, including anaerobes
- Metabolic control and treatment of co-morbidity.
 - Optimal diabetes control, if necessary with insulin (blood glucose <140 mg/dl)
 - Treatment of edema and malnutrition.
- Local wound care
 - Frequent wound inspection

- Frequent wound debridement (with scalpel)
- Control of exudate and maintenance of moist environment

ii) CHARCOT'S FOOT

Clinical diagnosis of Charcot's foot needs high index of suspicion. It is based on the appearance of a red, swollen edematous and possibly painful foot in the absence of infection.

Total contact casting and non-weight bearing are effective treatments for acute Charcot's foot. Evidence level 3

E- Limb threatening situations:

- Critical limb ischemia or severe infections are the indications of hospital admission.
- Patients should be referred for admission into the hospital receiving surgical emergency departments.

(A) Diabetes care in specific populations

A-1 Diabetes care in children and adolescents

Screening and management of chronic complications

Nephropathy yearly screening for micro-albuminuria should be initiated at the age of 10 or after 5 years of disease duration. (III,B), annually from age 11 yr with 2 yr of diabetes duration and from 9 yr with 5 yr of duration (E)

- Once confirmed, persistent high levels of microalbuminuria must be treated with a titrated ACE-inhibitor, if possible, till microalbuminuria is normalized. (IV,B)
- Hypertension management of normal–high-pressure values must include, when appropriate, an intervention on diet and on physical exercise focused on weight control and on increased physical exercise. Pharmacological treatment should be started, if pressure goals are not achieved after 3–6 months of intervention on the lifestyle. (III,B)
- ACE-inhibitors must be taken into account as initial treatment of

hypertension. (III,B)

Dyslipidemia Prepubertal children:

- Fasting lipid profile must be tested on all children aged > 2 years on diagnosis of diabetes (after appropriate glycemic control has been reached) with a family history of hypercholesterolemia (total cholesterol > 240 mg/dl), positive family history of cardiovascular events before the age of 55 or unknown family history. If the family history is negative, the first lipid screening should be performed at puberty (>12 years). If values are within acceptable risk levels (LDL cholesterol < 100 mg/dl), the test should be repeated every 5 years. (III,B)
- Pubertal children (>12 years): the fasting lipid profile must be tested on diagnosis of diabetes (after appropriate glycemic control is achieved). If values are within acceptable risk levels (LDL cholesterol < 100 mg/dl), the test must be repeated every 5 years. (III,B)
- Treatment of dyslipidemia must be based on the fasting lipid profile (especially on LDL cholesterol) evaluated after appropriate glycemic control is achieved.
- The goal of treatment is a LDL cholesterol value < 100 mg/dl. (III,B)
- Initial treatment must include both optimizing glycemic control and medical nutrition therapy to reduce the diet's saturated fat content. (VI, B)
- The addition of pharmacological agents is recommended when LDL cholesterol is > 160 mg/dl and in patients with LDL cholesterol 130–159 mg/dl, considering the cardiovascular risk profile, after nutrition therapy and lifestyle changes have failed. (III,B)

Retinopathy

- Initial eye examination should occur shortly after diagnosis to detect cataracts or major refractive errors that require treatment for binocular vision (E).
- Screening for retinopathy as for microalbuminuria should start

from 11 yr with 2 yr of diabetes duration and from 9 yr with 5 yr of duration and after 2 yr of diabetes duration in an adolescent (E).

- Minimum assessment for retinopathy should be by ophthalmoscopy through dilated pupils by an experienced observer (E).
- For those with duration less than 10 yr, minimal background retinopathy on fundal photography and reasonable glycemic control, biennial assessment by fundal photography, can occur (E). The first ophthalmologic evaluation must be scheduled at the onset and, if it is normal, repeated when the child is 10 years old and has had diabetes for 3–5 years. (III, B)
- A yearly follow-up is generally recommended after the age of 10 years. The frequency of retinopathy screening in general should occur annually but should be more frequently if there are high-risk features for visual loss, less frequent controls can be deemed acceptable, if proposed by the ophthalmologist. (VI,B)

Exercise

- Blood glucose monitoring is key for the active child with diabetes so that trends in glycemic responses can be identified. Records should include notes of their blood glucose, the timing, duration and intensity of exercise as well as the strategies used to maintain glucose concentrations in the normal range. Measurements of glucose should be taken before, during, and after the end of exercise with particular attention paid to the direction of change in glycemia.
- Tailor insulin regimen to activity.
- Discuss the percentage reductions in insulin before exercise.
- Discuss type and amount of carbohydrate required for specific activities.
- Advise about risk of late hypoglycemia and reduction in long-acting/basal insulin.
- Consume up to 1.5 g CHO/kg body mass/h of strenuous or longer-duration exercise when circulating insulin levels are high.
- Monitoring several hours after exercise and before bed is particularly critical on days where strenuous activities occur as

nocturnal hypoglycemia is common.

- Strenuous exercise is dangerous and should be avoided if pre-exercise blood glucose levels are high (≥ 250 mg/dL) with ketonuria/ketonemia. Give approximately 0.05 U/kg or 5% of total daily dose (TDD; including all meal bolus doses and basal insulin/basal rate in pump) and postpone exercise until ketones have cleared (E).
- Dehydration is a risk unless sugar-free fluids also are consumed.

Summary recommendations for physical activity

- Arrive at a good level of metabolic control: neither hyperglycemia nor ketonuria. Eventually measure blood glucose concentration before the activity
- Always carry some sugar
- Increase the intensity and duration of the activity in a progressive fashion
- In the few hours preceding the exercise, ingest slowly absorbing carbohydrates in order to replenish the liver and muscle glycogen reserves
- In the case of unforeseen physical activity, increase glucose consumption immediately before, during, and after the activity
- In the case of foreseen activity, decrease the insulin dose during and after intense muscular activity
- Do not inject the insulin at a site that will be heavily involved in the muscular activity
- Avoid physical exercise at the time of the peak action of insulin
- If the activity is of the prolonged endurance type, be certain to ingest glucose-sweetened water or carbohydrates just before, during, and after the exercise
- Measure the blood glucose before retiring on the evening after major physical activity in order to avoid hypoglycemia during the night
- Evaluate the effect after every modification in insulin dose and every change in nutritional status
- Make the people accompanying you aware of the procedures and treatment of severe hypoglycemia (glucagon injection)

A-2 Diabetes care during intercurrent illness

The diabetes care team should provide clear guidance to patients and families on how to manage diabetes during intercurrent illnesses to avoid the complications of

- Ketoacidosis;
- Dehydration;
- Uncontrolled or symptomatic hyperglycemia;
- Hypoglycemia.

General principles

- Never stop insulin (A).
- The insulin dose may need to be increased or decreased (A).
- The most common mistake made by health care providers and caregivers who are unfamiliar with diabetes is to advise the omission of insulin because the child is ill and not eating, thus increasing the risk of diabetic ketoacidosis (DKA). When vomiting occurs in a child with diabetes, it should always be considered a sign of insulin deficiency until proven otherwise (E).
- More frequent monitoring is required of BG and ketones. BG should be monitored at least every 3–4 h including through the night and sometimes every 1–2 h.
- If episodes of hyperglycemia, ketosis, and vomiting recur, with or without infection, it should be recognized that this may be because of omission or inadequate administration of insulin. Insulin omission is particularly problematic during adolescence.
- Loss of appetite: Replacing meals with easily digestible food and sugar-containing fluids provide energy and help prevent further ketosis. Antipyretics such as paracetamol, acetaminophen, ibuprofen, etc. should be used in case of fever
- Maintaining hydration
- Hyperglycemia, fever, excessive glycosuria, and ketonuria increase fluid losses.

National Clinical Practice Recommendations for Management of Diabetes Mellitus 2018

- Liquids for hydration should contain salt and water and not just plain water if there are ongoing losses like vomiting or diarrhea. If appetite is decreased or the BG is falling below 180 mg/dL, sugar-containing fluids should be considered to avoid starvation ketosis (e.g., drinks, colas, ginger ale, etc.) It is best to shake the bubbles out of the sugar-containing soft drinks to minimize indigestion (E). Carbonated fluid does not affect the rate of gastric emptying, but alters the distribution of a meal within the stomach, causing a retention within the proximal part. (B)

- Elevated levels of ketones, whether associated with low BG (starvation) or high BG (insulin deficiency), contribute to nausea and vomiting, leading to decreased food and fluid intake, further elevated levels of ketones, and dehydration and ketoacidosis.

- Especially in young children with diabetes, intravenous fluids may be required if nausea, vomiting, or diarrhea are persistent.

Specific medical advice

- The underlying illness should be treated as it would be for a child without diabetes.
- Treating fever, malaise, and headache with antipyretics such as paracetamol or acetaminophen or ibuprofen is acceptable but not mandatory.
- Vomiting may be caused by (i) the illness itself (i.e., gastroenteritis, unclean food or food poisoning, surgical condition, or other illness); (ii) low BG; or (iii) lack of insulin resulting in high BG and ketosis.
- Unless food poisoning is suspected, consider treatment of vomiting with single injection or rectal administration of an antiemetic, such as phenegan suppositories, to help oral intake of carbohydrate, unless concerns about mental status exist. However, in the case of high BG and an excess of ketones, priority should be given to administering extra insulin. In this situation, the vomiting often stops once insulin therapy is begun because of reversal of ketosis (E).
- Oral medicines for symptomatic relief of vomiting or diarrhea have no proven efficacy and are therefore not usually recommended (E).

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Infections associated with hyperglycemia and/or ketosis

- Additional insulin doses of short- or rapid-acting insulin are required with careful monitoring to reduce BG, prevent ketoacidosis, and avoid hospital admission.
- The dose and frequency of injection will depend on the level and duration of hyperglycemia and severity of ketosis.
- If there is hyperglycemia with negative or small amounts of ketones, usual recommendations are to give an additional 5–10% of total daily dose (TDD) (or 0.05–0.1 U/kg) as short- or rapid-acting insulin. This may be repeated every 2–4 h based upon BG
- If there is hyperglycemia and more marked ketonuria (moderate to high), usual recommendations are to give an additional 10–20% of TDD (usually not more than 0.1 U/kg) as short- or rapid-acting insulin. This dose should be repeated every 2–4 h based upon frequent glucose and ketone results.
- The additional dose recommendation of 0.05–0.1 U/kg is a general recommendation for children with standard insulin requirements of approximately 1 U/kg/d. However, for children who have low requirements or adolescents with insulin resistance and high insulin requirements, the percentage calculations should be used rather than the 0.1 U/kg empirical additional dose (E).
- When patients in remission phase are ill (during the honeymoon phase), there may be a need to increase insulin up to 1 U/kg/d very quickly (E).
- During illness, it also may be necessary to increase basal insulin doses

(B) Diabetes care before and during pregnancy

- All diabetic women of childbearing age must be informed about the need to achieve good metabolic control before conception, the risk

of unscheduled pregnant and the need to schedule conception with effective contraception methods. (VI,B)

- Every diabetic woman who wishes to become pregnant must undergo screening and treatment for any complications (retinopathy, nephropathy, neuropathy, cardiovascular disease). (VI,B)

- Glycemic control must be optimized before the conception. The therapeutic goal is normal or near normal HbA1c levels, allowing for at most a 1% deviation from the upper normal limit. (III, B)

- Insulin therapy must be readily established in all women who fail to achieve the glycemic goal with nutritional therapy. Oral hypoglycemic agents must not be administered during pregnancy, due to the lack of enough data on the absence of teratogenous effects. (VI,B)

- Rapid acting insulin analogues: Aspart and Lispro can be either maintained or added to treatment during pregnancy; but data on the use of the rapid acting analogue glulisine during pregnancy is scarce; lastly, the use of long action analogues, which lack adequate safety data, is not recommended. (VI,B)

- The use of ACE-inhibitors, ARBs and statins is not allowed during pregnancy: hence, these drugs must be discontinued before conception. (VI,B)

- Insulin treatment must be readily started in women with gestational diabetes, if glycemic goals are not achieved after 2 weeks of nutritional treatment. (VI,B)

- Insulin patterns must be personalized in gestational diabetes: patterns include either 1 or 2 injections can be implemented, but intensive insulin treatment can be necessary to reach optimal blood glucose levels. (VI,B)

- Women with type 1 pregestational diabetes require multiple insulin injections.

- Intensive insulin treatment is usually required to reach glycemic targets, even in type 2 pregestational diabetes. (I,A)

- Women with diabetes during pregnancy must self-test glycemia at home (4–8 tests/day) with preprandial, postprandial (1 h after

the meal) and night time tests. Simplified self monitoring patterns can be used in gestational diabetes treated only with the nutritional therapy. (V, B)

- Ketosis must be avoided during pregnancy; hence, daily ketonuria testing on awakening is useful. (V, B)

- Nutrition treatment during pregnancy must be personalized, taking into account both the diet habit of diabetic women and the BMI before the pregnancy. The goals are appropriate maternal and fetal nutrition, appropriate calorie, vitamin and mineral intake and optimal glycemic control when there is no ketonuria. (VI,B)

(C) Diabetes care in the elderly

Glycemic control

- Glycemic goals should be individualized in elderly diabetics.

- If general conditions are good, HbA1c levels can be < 7.5%. (VI,B)

- In the diseased elderly (with complications, dementia, multiple diseases, a high risk of hypoglycemia and, in whom the risk of intensive glycemic control exceeds expected benefits) a less restrictive goal is recommended with HbA1c levels between 7.5 and 8.5%. (VI, B)

- In elderly diabetics the self-monitoring pattern should be designed to suit the degree of self-sufficiency; hence, individual functional, affective, cognitive capacities and on the risk of hypoglycemia. (VI,B)

- If oral hypoglycemic agents are prescribed in the elderly, chlorpropamide and glibenclamide are not recommended. (V,B)

- In elderly diabetics with serum creatinine > 1.5 mg/dl (> 1.4 mg/dl in women) or creatinine clearance levels indicating impaired kidney function metformin is not recommended, due to the higher risk of lactic acidosis. (IV, B)

- In elderly diabetics treated with metformin, serum creatinine should be tested at least once a year and at every dosage increase. Creatinine clearance should be tested in subjects aged >80 years or presenting a reduced muscular mass. (VI,C)

Cardiovascular risk and pharmacological treatment

- The cardiovascular risk must be evaluated in all elderly diabetics. (VI,B)
- Dyslipidemia in elderly diabetics must be corrected, compatibly with an overall evaluation of the patient's health condition. (II,B)
- If an elderly diabetic has LDL cholesterol >130 mg/dl, he needs both pharmacological therapy and lifestyle changes. The lipid profile must then be retested annually. (I,A)
- In elderly diabetics requiring antihypertensive pharmacological therapy, the treatment goal must be blood pressure<140/80, if it is well tolerated. A further drop in blood pressure (<130/80) can involve an additional advantage. (I,A)
- Considering that elderly subjects may poorly tolerate a pressure reduction (especially in case of past episodes of syncope, falls and orthostatic hypotension), antihypertensive treatment should be gradually established and titrated. (VI,B)
- In elderly diabetics treated with ACE-inhibitors or ARBS, kidney function and serum K should be tested within 1–2 weeks after the start of treatment, whenever the dosage is increased and, anyhow, at least once a year. (VI,B)
- Elderly diabetics treated with thiazides or loop diuretics require blood sodium and potassium testing within 1–2 weeks after the start of treatment, whenever the dosage is increased and, anyhow, at least once a year. (VI,B)

Functional evaluation

- Elderly patients with type 2 diabetes require a geriatric multidimensional evaluation and an evaluation of geriatric syndromes. (VI, B)

- The evaluation must include global/physical, cognitive and affective tests. (VI, B)
- The functional evaluation must be completed with the assessment of co morbidities and nutritional status. (VI, B)
- The elderly diabetic before performing physical exercise should be periodically evaluated; he must be informed about the beneficial effects of exercise and the resources available to increase the degree of exercise. (VI, B)
- Food intake, nutritional status and hydration should be periodically evaluated in elderly diabetics; they should be provided with nutrition therapy instructions that are appropriate for their social, economic and cultural condition, advice on diet contents and the potential advantages of body weight loss. The risk of calorie–protein malnutrition, which is rather frequent in the elderly, must always be evaluated. (VI, B)
- Elderly diabetics have a higher risk of depression; hence the need for special focus to recognize symptoms suggesting this diagnosis, both during an initial evaluation and in case of a worsened clinical condition that cannot otherwise be justified. (III, C)
- Elderly diabetics should be invited to keep an updated record of the drugs taken, which they must show their attending physician. (VI, C)
- The treating physician should take into account the possible presence of cognitive decline, both during the initial evaluation and when there is an otherwise unjustified decline in the clinical condition with, for instance, an increased difficulty to ensure safe care. (VI,C)
- Yearly screening of the elderly diabetic should include the search for symptoms of incontinence. (VI,C)
- The elderly diabetic should be questioned about any episodes of falls. In this case, the causes (i.e. drugs, environmental factors, etc.) will be investigated. (VI,C)
- During the initial evaluation, the elderly diabetic should be questioned on the possible presence of chronic pain. (VI,C)

(D) Diabetes care in specific situations

In-hospital Diabetes care

- The diagnosis of diabetes mellitus must be clearly entered in the case records of all diabetic patients who are admitted to hospital. (VI,B)
- If hyperglycemia is occasionally found during hospitalization, HbA1c testing should be performed to identify a condition of undiagnosed diabetes. (V,B)
- Capillary blood glucose must be monitored in all diabetics admitted to hospital and the results must be recorded to ensure their access to all attending team members. (VI,B)
- A treatment plan for hypoglycemia must be defined for every patient. Episodes occurring during hospitalization must be recorded in the case records. (VI,B)
- Admission is not the most appropriate time to establish an organized educational program centered on diabetes.
- However, the diabetic must be instructed on some basic aspects such as insulin injection and self-testing of blood glucose before discharge. (VI,B)
- Undiagnosed diabetics presenting hyperglycemia on admission to hospital must be referred to a diabetes care unit. (VI,B)

Glycemic goals

- During hospitalization, glycemic goals can be differentiated to suit the various clinical conditions:
 - Critical patients: blood glucose levels near 110 mg/dl and in any case <180 mg/dl; (II,B)
 - Non critical patients: preprandial blood glucose levels near 90–130 mg/dl, postprandial<180 mg/dl. (VI,B)
- Glycemic goals should be gradually achieved in some clinical conditions presenting a high risk of hypoglycemia. (VI,B)

Treatment

- Insulin therapy is the treatment of choice for non stabilized hospitalized diabetic patients; the use of the main oral hypoglycemic drugs (secretagogues, biguanides, and thiazolidinediones) has considerable limits in the hospital setting. (VI, B)
- Subcutaneous insulin treatment must preferably follow a scheduled scheme, which is frequently adapted to suit recorded blood glucose levels. This pattern can be integrated with a correcting algorithm based on blood sugar testing at the time of the injection. Insulin therapy only “when required” (sliding scale) is not recommended due to its poor efficacy. (IV, B)
- In critical patients and/or those who are unable to take food by mouth, during the perioperative period and in conditions of acute metabolic instability, insulin therapy must be delivered as continuous i.v. infusion, applying algorithms based on frequent blood glucose testing. (VI, B)
- Non critical patients who are expert in both self-delivery of insulin and blood glucose self-testing can be authorized to continue self management even during hospitalization, agreeing on the specific modes with the attending healthcare team. (VI,B)
- In patients already under treatment with an insulin pump (CSII), it can be useful to maintain this method even during hospitalization, as long as it can be correctly managed in the specific clinical situation. (VI,B)

(E) Diabetes care at school

- The diabetes team must draft a personalized care plan for the diabetic student with parents/guardians. (VI, B)
- An appropriate number of schoolteachers or other employees should be trained in procedures to be implemented for hypoglycemic episodes. These people must not necessarily be healthcare

professionals. (VI, B)

- Diabetic students must have instant access to whatever they need for diabetes treatment at all times and under supervision if it is necessary. (VI, B)
- The student must be able to test blood glucose in the classroom and to treat hypoglycemia either in the classroom or wherever he is for school activities, as included by his care plan. (VI, B)

Indicators

Introduction

Measurement, analysis and improvement, the measurement of professional performance and the subsequent feedback of information is essential in facilitating knowledge building and ongoing improvements in healthcare. The growing worldwide interest in indicators mirrors the need to measure processes and healthcare outcomes.

Hence, diabetic care unit must plan and implement monitoring, measurement and analysis actions required to prove product compliance with the standards of the best current scientific knowledge and, to steadily improve the efficacy of healthcare activities. The diabetic care unit should overcome the concept of one to- one duties, of attention focused on the single patient and, hence, on measurement of the efficacy of personal actions on individual parameters to build an information system designed to systematically collect individual data with the aim to measure the success of global performance. The goal is to highlight problems in an attempt to change the clinical, therapeutic, management and economic outcome. Indicators are variables that describe the complex phenomena of healthcare to facilitate decisions

concerning either implementing or maintaining changes.

An indicator requires quality attributes, in fact, it must:

- Measure important aspects of healthcare quality;
- Measure in a valid, precise, accurate, reproducible manner;
- Be speedily measurable in the framework of available resources;
- Be able to direct decisions;
- Be able to differentiate the various conditions;
- Obtain consensus regarding its meaning and mode of use.

Hence, the choice of indicators that can meet all quality requirements, either entirely or almost entirely is very important.

Note:

- Measurement methods must ensure that products comply with the current standards and expectations of reference subjects' privileged indicators obtained from data collected during daily activity management.

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**DIABETES IN
CHILDREN & ADOLESCENTS
EGYPTIAN GUIDELINES**



2018

Classification Of Diabetes In Children and Adolescents

The classification includes four clinical classes:

- Type 1 diabetes , results from Beta-cell destruction, usually leading to absolute insulin deficiency.
- Type 2 diabetes, results from a progressive insulin secretory defect on the background of insulin resistance.(Refer to section of type 2 diabetes)
- Other specific types of diabetes due to other causes e.g ,genetic defects in insulin action (monogenic forms of diabetes), diseases of the exocrine pancreas (such as cystic fibrosis), and drug - or chemical-induced diabetes (such as in the treatment of HIV/AIDS or after organ transplantation)
- Gestational diabetes mellitus (GDM) ; diabetes diagnosed during pregnancy that is not clearly overt diabetes.
- Type 1 diabetes is further subdivided into type1 A and type 1B.
- Type 1A diabetes ; this type is classified as immune mediated type1 diabetes (type 1A diabetes) and is responsible for the vast majority of cases of type1 diabetes. On the other hand, 5-10% of patients, have no evidence of an autoimmune phenomenon at disease onset, and are classified as idiopathic [type 1B] diabetes. Type 1B diabetes may be etiologically heterogeneous, including insulin secretory defects caused by extensive pancreatic islet cell destruction or Beta-cell dysfunction.

Clinical Presentations of type 1 diabetes:

1. A child presenting with a classical history of increasing polyuria, polydipsia and weight loss presents a straightforward diagnosis.
2. Other clinical presentations are the following:
 - Recent onset of enuresis in a previously toilet-trained child.
 - Vaginal candidiasis, especially in prepubertal girls.

- Vomiting and chronic weight loss, asthenia, and emaciation
 - Irritability and decreasing school performance.
 - Recurrent skin infections.
3. Emergency presentation as diabetic ketoacidosis with:
- Severe dehydration, repeated vomiting
 - Acetone detected on the breath.
 - Hyperventilation (Kussmaul respiration)
 - Disordered sensorium (disoriented, semicomatose or rarely comatose).
 - Shock (rapid pulse rate, poor peripheral circulation with peripheral cyanosis).

Partial Remission or Honeymoon Phase In Type 1 Diabetes

- In approximately 80 percent of children and adolescents, insulin requirements decrease transiently following initiation of insulin treatment
- A recent definition for partial remission is when the patient requires less than 0.5 unit of insulin per kg of body weight per day and has a HbA1c<7%.
- The partial remission phase commences within days or weeks of the start of insulin therapy and may last for weeks to months. During this phase, blood glucose levels are frequently stable within the normal range, despite fluctuations in diet and exercise. It is important for the families to be advised of the transient nature of the partial remission phase so as to avoid the false hope that the diabetes is spontaneously disappearing.

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Diagnostic criteria for all types of diabetes in children and adolescents are based on laboratory measurement of plasma blood glucose levels (BGL) and the presence or absence of symptoms (E). Finger prick BGL testing should not be used to diagnose diabetes (E).

- A marked elevation of the BGL confirms the diagnosis of diabetes, including a random plasma glucose concentration $\geq$ (200 mg/dL) 11.1 mmol/L or fasting plasma glucose $\geq$ ($\geq$ 126 mg/dL) 7.0 mmol/L in the presence of overt symptoms.

- If significant ketones are present in blood or urine, treatment is urgent, and the child should be referred to a diabetes specialist on the same day to avoid the development of ketoacidosis (A).

- The diagnosis of diabetes should not be based on a single plasma BGL in the absence of overt symptoms. If the diagnosis is in doubt, continued observation with fasting and/or 2 hour postprandial BGLs and/or an oral glucose tolerance test (OGTT) may be required (E). However, an OGTT is not needed and should not be performed if diabetes can be diagnosed using fasting, random, or postprandial criteria as excessive hyperglycemia can result (E).

- The possibility of other types of diabetes should be considered in the child who has

- Negative diabetes-associated autoantibodies (B).

- An autosomal dominant family history of diabetes (maturity-onset diabetes of the young [MODY]).

- Age less than 12 months and especially in first 6 months of life (NDM [neonatal diabetes mellitus]).

- Mild-fasting hyperglycemia ([100-150 mg/dL] 5.5-8.5 mmol), especially if young, non-obese, and asymptomatic.

- A prolonged honeymoon period over 1 year or an unusually low requirement for insulin of $\leq$ 0.5 U/kg/day after 1 year of diabetes.

- Associated conditions such as deafness, optic atrophy, or

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syndromic features.

- A history of exposure to drugs known to be toxic to β -cells or cause insulin resistance (eg, immunosuppressive drugs such as tacrolimus or cyclosporin; glucocorticoids or some antidepressants).
- The differentiation between type 1, type 2, monogenic, and other forms of diabetes has important implications for both treatment and education (E).

Characteristics	Type 1	Type 2
Age	Throughout childhood	Pubertal (or later)
Onset	Most often acute, rapid	Variable : from slow, mild, often insidious to severe
Insulin dependence	Permanent, total, severe	Uncommon, but insulin required when oral hypoglycemic agents fail
Insulin secretion	Absent or very low	Variable
Insulin sensitivity	Normal	Decreased
Genetics	Polygenic	Polygenic
Race/ethnic distribution	All groups but wide variability of incidence	Certain ethnic groups are at particular risk
Frequency (% of all diabetes in young people)	Usually 90%	Most countries <10 % (Japan-80 %)

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Autoimmunity	Yes	No
Ketosis	Common	Rare
Obesity	No	Strong
Acanthosis Nigricans	No	Yes

Diagnostic tools, which may assist in confirming the diabetes type if the diagnosis is unclear, include:

- Diabetes-associated autoantibodies: glutamic acid decarboxylase 65 autoantibodies (GAD); Tyrosine phosphatase-like insulinoma antigen 2 (IA2); insulin autoantibodies (IAA); and β -cell specific zinc transporter 8 autoantibodies (ZnT8). The presence of one or more of these antibodies confirms the diagnosis of type 1 diabetes (A).
- Molecular genetic testing can help define the diagnosis and treatment of children with suspected monogenic diabetes and should be limited to those who on clinical grounds are likely to be positive (E).

Type2 diabetes mellitus in youth

T2DM in youth should be diagnosed using American Diabetes Association (ADA) criteria (A).

- Diagnosis can be made based on fasting glucose, or 2-hour glucose concentration during an oral glucose tolerance test (OGTT) or hemoglobin A1c (HbA1c) (B). In the absence of symptoms, testing should be confirmed with a repeat test on a different day. Clinicians should be aware of the weakness of each diagnostic test.
- Diabetes autoantibody testing should be considered in all pediatric patients with the clinical diagnosis of diabetes because of the high frequency of islet cell autoimmunity in otherwise "typical" T2DM (B).
- Pre-pubertal children are unlikely to have T2DM even if obese (A).

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- Antibodies will indicate the diagnosis of T1DM and an earlier need for insulin (A). Antibodies will indicate the need to consider the presence of other associated autoimmune disorders (A). Diabetes autoantibody testing should be considered in overweight/obese pubertal children with a clinical picture of T1DM (A).
- The presence of clinically relevant comorbidities should be assessed at the time of diagnosis (A), including hypertension, dyslipidemia, elevation of liver enzymes, and elevated urine albumin/creatinine ratio (ACR).
- Patients should be screened for obstructive sleep apnea (OSA), depression/anxiety, eating disorders, and impairment of cognition at the time of diagnosis (E).

Initial treatment

1. Lifestyle changes should be recommended at the time of diagnosis of T2DM (A).
2. Initial pharmacologic treatment of youth with T2DM should include metformin and insulin alone or in combination, depending on degree of hyperglycemia and metabolic disturbances, and presence or absence of ketosis/ketoacidosis (B).
 - a. Metabolically stable patients ($HbA1c < 8.5$ and no symptoms) should be started on metformin (A).
 - Begin with 500-1000 mg (or 850 mg when this is the lowest available dose) daily $\times 7$ to 15 days. Titrate once a week over 3 to 4 weeks, depending on patient tolerance, to a maximal dose of 1000 mg BID or 850 mg TID (extended release metformin product may be used where available).
 - In patients with ketosis/ketonuria/ketoacidosis, treatment with subcutaneous or intravenous insulin should be initiated to rapidly correct the metabolic abnormality (A). Once a day intermediate-acting or basal insulin (0.25-0.5 units/kg starting dose) is generally effective in attaining metabolic control. Metformin can be started along with insulin, once acidosis is resolved (E).

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• Transition onto metformin monotherapy can usually be achieved safely over 2 to 6 weeks (A).

3. The goal of treatment should be an HbA1c < 7.0% (<47.5 mmol/mol) (B).

4. Self-monitored blood glucose (SMBG) should be performed regularly. The frequency of SMBG should be individualized, based on the degree of glycemic control and available resources (E).

Glycemic control targets and glucose monitoring for children, adolescents, and young adults with diabetes

Regular self-monitoring of glucose (using accurate finger-stick blood glucose [BG] measurements, with or without continuous glucose monitoring [CGM] or intermittently scanned CGM [isCGM]), is essential for diabetes management for all children and adolescents with diabetes (A).

- Each child should have access to technology and materials for self-monitoring of glucose measurements to test enough to optimize diabetes care (B).
- Diabetes center personnel should advocate to nations, states, and health care funders to ensure that children and adolescents with diabetes have adequate glucose monitoring supplies (E).
- When finger-stick BGs are used, testing may need to be performed 6 to 10 times per day to optimize intensive control. Regular review of these BG values should be performed with adjustments to medication/nutritional therapies to optimize control (B).
- Real-time CGM data particularly benefit children who cannot articulate symptoms of hypoglycemia or hyperglycemia and those with hypoglycemic unawareness (A).
- For children, adolescents, and young adults aged ≤25 years we recommend **individualized targets**, aiming for the lowest achievable HbA1c without undue exposure to severe hypoglycemia balanced with quality of life and burden of care (E).

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• For children, adolescents, and young adults ≤25 years who have access to comprehensive care a target of HbA1c of <53 mmol/mol (7.0%) is recommended (E).

• A higher HbA1c goal (in most cases <58 mmol/mol [7.5%]) is appropriate in the following contexts:

- i. Inability to articulate symptoms of hypoglycemia.
- ii. hypoglycemia unawareness/history of severe hypoglycemia
- iii. Lack of access to analogue insulins, advanced insulin delivery technology, ability to regularly check BG, and CGM (E).
- iv. Individuals who are “high glycators,” in whom an at-target HbA1c would reflect a significantly lower mean glucose than 8.6 mmol/L (155 mg/dL) (E).

• A lower goal (6.5%) or 47.5 mmol/mol may be appropriate if achievable without excessive hypoglycemia, impairment of quality of life, and undue burden of care (E).

• A lower goal may be appropriate during the honeymoon phase of type 1 diabetes (E).

• For patients who have elevated HbA1c, a step-wise approach to improve glycemic control is advised including individualized attention to:

- _ Dose adjustments (E).
- _ Personal factors limiting achievement of the target (E).
- _ Assessment of the psychological effect of goal setting on the individual (E).

_ Incorporation of available technology to improve glucose monitoring and insulin delivery modalities (E).

• HbA1c measurement should be available in all centers caring for persons with diabetes (B).

• HbA1c measurements should be performed at least every 3 months (B).

• Examining variations in HbA1c between centers can assist in evaluating the care provided by health care centers including compliance with agreed standards to improve therapies and delivery of pediatric diabetes care (B).

Insulin

Insulin treatment in children and adolescents with diabetes must be started as soon as possible after diagnosis (usually within 6 hours if ketonuria is present) to prevent metabolic decompensation and diabetic ketoacidosis [A].

- Intensive insulin regimens delivered by combinations of multiple daily injections or pump therapy with differential substitution of basal and prandial insulin aiming to have optimal metabolic control have become the gold standard for all age groups in pediatric diabetology [E].
- **Insulin therapy must be individualized** for each patient in order to achieve optimal metabolic control [D/E].
- Improvements in glycemic control by intensive insulin treatment reduce the risks of acute and long-term complications [A]. There is no reason to believe this is not the case also in younger children [E].
- In all age groups, as close to physiological insulin replacement as possible and optimal glycemic control must be the aim using the locally available basal and prandial insulins [A].
- Although no insulin injection regimen satisfactorily mimics normal physiology, **premixed insulins are not recommended** for pediatric use [C]. When insulin is provided through a help organization, the recommendation should be to provide regular and NPH as separate insulins, not premixed [E].
- Whatever insulin regimen is chosen, it must be supported by **comprehensive education** appropriate for the age, maturity and individual needs of the child and family [A].
- Aim for appropriate insulin dosage throughout 24 hours to cover basal requirements and higher dosage of insulin in an attempt to match the glycemic effect of meals [E].
- Delivering prandial insulin before each meal is superior to

postprandial injection and should be preferred if possible [C].

- Daily insulin dosage varies greatly between individuals and changes over time. It therefore requires regular review and reassessment [E].
- The distribution of insulin dose across the day shows great individual variation. Regardless of mode of insulin therapy, doses should be adapted to the circadian variation based on the daily pattern of blood glucose [B].
- All children should have rapid-acting or regular insulin available for crisis management [E].
- It is essential that a small supply of spare insulin should be readily available to all children and adolescents so that the supply is uninterrupted [A].
- Children and adolescents should be encouraged to inject consistently within the same area (abdomen, thigh, buttocks, and arm) at a particular time in the day, but must avoid injecting repeatedly into the same spot to prevent lipohypertrophy [B].
- Insulins need to be administered by insulin syringes (or other injection devices) calibrated to the concentration of insulin being used [E].
- Regular checking of injection sites, injection technique and skills remain a responsibility of parents, care providers and health professionals [E].
- Health care professionals have the responsibility to advise parents, other care providers and young people on adjusting insulin therapy safely and effectively. This training requires regular review, reassessment and reinforcement [E].

Types Of Insulin:

Rapid acting insulin analogs

Type of insulin	Onset of action	Peak of action	Duration of action
Lispro			
Glulisine	10-15 min	60-90 min	4-5 hrs
Aspart			

Short acting insulin analogs

Type of insulin	Onset of action	Peak of action	Duration of action
Regular	30-60 min	2-4 hr	5-8 hrs

Intermediate acting insulin analogs

Type of insulin	Onset of action	Peak of action	Duration of action
NPH	1-3 hrs	5-8 hrs	12-16 hrs

Basal long-acting analogs

Insulin	Type	Onset	Peak or maximal action	Duration of action
Neutral protamine Hagedron®	Intermediate-acting	2-4 hours	4-12 hours	16-18 hours
Duquesin (Loven®), Novo Nordisk A/S, Baginord, Denmark™	Long-acting	2 hours	No peak	18-21 hours
Degludec® (Toujeo®), Novo Nordisk A/S™	Long-acting	>1 hour	No peak	>42 hours
Glargine 100 U/mL (Lantus®)™	Long-acting	Up to 4 hours	No peak	Up to 24 hours
Glargine 300 U/mL (Toujeo®)™	Long-acting	8 hours	No peak	Up to 36 hours

Notes: *Times depending on dose: 100 U/mL and 300 U/mL formulations of insulin degludec were demonstrated to be bioequivalent in terms of peak serum concentration achieved and area under the curve for blood concentration versus time.

Target Glycemia Control

Fasting BG	HbA1c	PPBG
100 - 130 mg/dL	≤ 7.5%	140 -180 mg/dL

Higher levels are acceptable in young age

Initial insulin dose:

- The insulin dose is individualized & adjustment of dose according to trials & errors.
- 0.5 - 1.0 U/kg/Day

How to classify the initial insulin dose?

Basal: 40-50% of total dose. Bolus: 50-60% of total dose.

Basal Insulin

- NPH or Detemir twice daily.
- Glargine or Degludec can be administered once daily.
- If it is decided to start with once daily basal insulin, it is usually administered at bedtime.
- Titration of basal insulin
- By observing glucose trends during periods of fasting.

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- The median glucose level before breakfast
- Any information on glucose levels during the night when glycemia is not contaminated by food or prandial insulin.

Bolus (Prandial) Insulin

- Typical doses:
 - 1 unit per 10 to 15 grams of carbohydrate.
- But in obese patients:
 - 1 unit per 5 grams of carbohydrate.
- While thin patients:
 - 1 unit per 20 grams of carbohydrate
- Titration of bolus insulin dose
 - For patients who use Regular (short-acting) insulin
Use 1500 rule. Divide 1500 by the total daily dose insulin, in units.
 - For patients who use the Rapidly acting Insulin analogues:
Use 1800 rule. Divide 1800 by the total daily dose result of division 1500 by total daily dose of insulin can give due to degree of decrease of blood sugar by giving one unit insulin.

When higher doses (basal and bolus) of insulin may be needed?

- If the patient has an infection.
- If the patient reduce his level of activity.
- If you are prescribed a medicine that changes insulin sensitivity (such as Prednisone).
- If the patient are under emotional stress.
- During adolescence (especially during the 1st 2 days of menstrual cycles in girls).
- During pregnancy.

When lower doses (basal and bolus) of insulin may be needed?

- If the patient become more active.

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- If the patient has problems with kidney function.
- If there is vomiting or diarrhea or decrease fluid intake.

Methods of Insulin Injection

Insulin syringes:

- Insulin syringes must have a measuring scale consistent with the insulin concentration.
- Injections by syringe are usually given into the deep SC tissue through a two-finger pinch of skin at a 45° angle. "A 90° angle can be used if the SC fat is thick enough."

Pen injector devices:

- Requires careful waiting of 15 seconds after pushing in the plunger helps to ensure complete expulsion of insulin through the needle.

Continuous subcutaneous

insulin injection (CSII) (Insulin Pump)

- Insulin pump use is increasing in younger age group, as clinicians become more comfortable as a more physiological insulin replacement therapy.

Factors Affecting Bioavailability & Absorption of SC Injected Insulin

1.Site of injection

- Abdominal injection (particularly if above the umbilicus) results in the quickest absorption.
- Arm injection results in quicker absorption than thigh or hip injection.

2.Depth of injection

- Intramuscular injections are absorbed more rapidly.

3.Insulin dose

- Higher doses have prolonged durations of action compared with lower doses.

4. Insulin mixing

- Regular insulin maintains its potency and time-action profile when it is mixed with NPH insulin; no insulin should be mixed with Insulin glargine or insulin detemir.

5. Exercise:

- Exercising a muscle group before injecting insulin into that area increases the rate of insulin absorption.

6. Heat application or Massage:

- Local application of heat or massage after an insulin injection increases the rate of insulin absorption.

Importance of self-monitoring of BG

- 1- Recognize and avoid hypoglycemia.
- 2- To adjust the dose of rapidly-acting insulin before meals.
- 3- Help achieve ideal blood glucose control.

Indication for testing for Ketones

- Any glucose reading is above 250 mg/dL.
- If your patient feels unwell and has symptoms of DKA.

Storage of Insulin

- Discard opened vials after one month.
- Refrigerate unopened vials not in use between 2-8 degrees.
- The expiration date applies to unopened, refrigerated insulin.
- Durable pens and dosing devices should NOT be refrigerated once in use.

Diabetic Ketoacidosis

Diagnostic criteria

- Dehydration:
 - Usually moderate to severe degree.
- Hyperglycemia (≥ 250 mg %).

- Metabolic Acidosis (with wide anion gap).
 - $\text{pH} < 7.3$. - $\text{HCO}_3^- < 15$ meq/L
- Ketonemia & Ketonuria.

Management of DKA

- Try to determine the underlying etiology and look for evidence of infection.
- Assess the degree of dehydration and vital data.
- Assess renal functions and serum electrolytes.
- Assess level of consciousness according to Glasgow coma scale.
- Put the patient on ECG monitor if available.
- If the patient is unconscious continuous nasogastric suction to empty the stomach and prevent aspiration.
- Insert 2 wide bore cannulas one for fluid infusion and one for insulin infusion.
- Additional calculations that may be informative:
 - Anion gap = $\text{Na} - (\text{Cl} + \text{HCO}_3^-)$
 - Normal anion gap in pediatrics is 12 ± 2 meq/L.
 - In DKA = 20-30 meq/L.
 - If > 35 meq/L think of concomitant lactic acidosis e.g. with sepsis
 - Corrected sodium =
 - Measured $\text{Na} + [2 \times (\text{Plasma glucose} - 5.6)] / 5.6 \text{ mmol/L}$
 - Effective osmolality = $2 \times (\text{Na} + \text{K}) + (\text{Plasma glucose} / 18)$.

Correction of Dehydration

1. Initial rehydration therapy:

- Start initial therapy without insulin infusion (for 1-2hrs)
- With hypotensive shock: 10-20 ml/Kg (Saline 0.9%) over 1 hr can be repeated till improvement of shock (Don't exceed 50 ml/kg over the 1st 4hrs)
- Without shock: 10 ml/Kg (Saline 0.9%) over 1 hr

2. Deficit and maintenance rehydration therapy:

• Volume of fluid needed:

- Deficit: in moderate dehydration(80ml/kg) and in severe dehydration (100ml/kg)
- Maintenance: 100ml/kg for the 1st 10kg, 50ml/kg for the next 10 kg & 20ml/kg thereafter
- Don't exceed 4 liters/day

• **Type of fluid:** starting fluid with normal saline in the 1st 4-6hrs. Changed to Dextrose 5% with normal saline when blood glucose (BG) falls below 250 mg% or rate of drop BG > 90mg% /hr. Dextrose may be increased to 10% or 12.5%.

• **Duration:** 24-48 hrs according to plasma osmolality.

- If s.Osmolality $300 \leq 320 \longrightarrow$ Correct over 24 hrs
- If s.Osmolality $> 320 < 340 \longrightarrow$ Correct over 36 hrs
- If s.Osmolality > 340 or Initial s.Na⁺ > 150meq/L $\longrightarrow$ Correct over 48 hrs

Correction of Hyperglycemia & Ketonemia

1. By Insulin (Short Acting) Therapy As Follows:

- Insulin preparation: 50 U of regular insulin in 500ml normal saline.
- Onset: started 1-2 hrs after initial volume expansion (BG may decrease by 180-250mg% over the 1st 2hrs without insulin therapy).
- Don't start insulin therapy until serum K > 2.5 mEq/L.
- Don't give IV bolus of insulin (it increase risk of cerebral edema).
- Initial insulin dose: 0.1 U/Kg/hr (1ml/Kg/hr of insulin preparation) (>5 years) or 0.05 U/Kg/hr (0.5ml/Kg/hr of insulin preparation) (<5 years). • Insulin dose is then readjusted according to the rate of drop of BG.
- The ideal rate of drop of BG:(50-70 mg% / hr).
- If plasma glucose does not fall by 50 mg%: check hydration status, errors in insulin preparation, other possible causes that

impair response to insulin as infection if acceptable, insulin infusion could be doubled every hr. until glucose decline between 50 & 75 mg%/hr. is achieved.

2. S.C. or IM insulin (short or rapid acting insulin analog):

- In mild DKA, with good peripheral circulation, give initial dose SC 0.3 U/kg, followed 1 hr later by 0.1 U/kg every hr, or 0.15 - 0.2u/kg/2hr till acidosis is clear, (pH>7.3& HCO₃>15)., then decrease to 0.1 u/kg/2hr. until S.C. insulin replacement initiated.

Potassium Replacement

- If k<2.5mEq/L:
- give 1 mEq/kg of KCL over 1 hr withholding insulin infusion to be repeated until K > 2.5 mEq/L.
- If k 2.5 - < 3.5 mEq/L:
- give K 40-60 mEq/l as IVD until K ≥ 3.5 (monitor k hourly)
- If K 3.5 - 5 mEq/L:
- Start K+ replacement 40meq/L in IV fluids afer initial therapy & concurrent with starting insulin therapy.
- If K > 5.0 mEq/L:
- Wait till establishing adequate urine output.(1.5 cc/ kg / hr) and do not give K + monitor K hourly until K < 5.0 mEq/L.
- Put the patient on ECG monitor if available in cases of severe hypo or hyperkalemia.

Correction of acidosis

- Indications of bicarbonate therapy:
- Severe acidosis (pH<6.9) with shock.
- Life threatening hyperkalemia.
- Dose: 1-2 mEq/Kg over one hour IV drip

Indications of antibiotics in DKA

- Intravenous 3rd generation cephalosporin given to all patients except those who missed an insulin dose or who have no symptoms or signs of infections.

Criteria Of Resolution Of DKA:

- Clinical improvement of level of consciousness, tolerating oral feeding & no vomiting.
- Blood glucose <200mg%
- Serum bicarbonate >18 meq/l
- Venous pH > 7.3

Management of Hyperosmolar Hyperglycemia

- Blood glucose > 600 mg%
- Serum Bicarbonate > 15 mEq
- Urine ketones : small (mild)
- Consciousness : stupor or coma.

(Give same management as DKA, but use Half saline instead of normal saline)

Cerebral Edema

- Risk factors
- Younger age (< 5 years).
- New onset of diabetes.
- Longer duration of symptoms.
- Increased BUN at presentation.
- Severe acidosis at presentation.
- Failure to raise Na with improvement of the case.
- Rapid intake of fluids & rapid reduction of BG

How to avoid cerebral edema?

- Gradual correction of blood glucose: (not more than 90mg% / hr)
- Gradual correction of osmolality: (not more than 3mOsm/hr).
- Do not exceed the dose of fluids: 50ml/kg in the first 4hrs or 4L in

the 1st 24 hrs.

- Do not give insulin in the 1st hour of fluid treatment.

Treatment of cerebral edema:

- Move to ICU
- Raise head level of the bed.
- Restrict IV fluids to 2/3 maintenance.
- Mannitol: 1 gm/kg = 5 ml/kg mannitol 20% over 20 min. to be repeated after 30 min to 2 hrs if no response.
- If mannitol is not available or the osmolarity decrease in rate > 3mOsm/ hr., or decreased corrected Na⁺, give hypertonic saline 3% as 5-10ml / kg over 20 min to be repeated after 2 hrs if no response.
- Assess ventilation.

Indications of ICU admission in DKA

- Severe DKA
- Patient with altered level of consciousness
- Age < 5 years
- Renal impairment
- Cerebral Edema

Nutritional management in children and adolescents with Diabetes:

The guide to the distribution of macronutrients has been updated and re-enforces healthy eating patterns.

- The importance of meal-time routines with limitations on snacking has been emphasized in order to improve dietary quality and optimize glycemic outcomes.
- The impact of dietary fat and protein should be considered in the calculation of the meal-time insulin dose and how it is delivered.
- Continuous glucose monitoring is a useful tool for educating both the clinician and young person with diabetes on food related

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behaviors and the impact of specific meals on glucose levels.

- Assessment and management of hypoglycemia in children and adolescents with diabetes. Hypoglycemia is the commonest acute complication of type 1 diabetes. It may also occur in type 2 diabetes when treatment includes insulin or sulfonylurea therapy (B).
- Hypoglycemia presents a major physiological and psychological barrier for achieving optimal glycemic control and may result in significant emotional morbidity for patients and their caregivers (B).1
- Monitoring hypoglycemia is a key component of diabetes care as education about its causes, prevention, and treatment (A). Parents and caregivers need to be reassured that good glycemic control can be achieved without severe hypoglycemic events (B).
- Hypoglycemia is best defined as a fall in blood glucose level that exposes a patient to potential harm and there can be no single numerical definition of hypoglycemia for all patients and situations (E).
- The aim of diabetes treatment should be to maintain blood glucose level >3.9 mmol/L (70 mg/dL) while striving to achieve the best possible glycemic control without the occurrence of severe hypoglycemia (A).
- In clinical practice, a glucose value ≤ 3.9 mmol/L (70 mg/dL) is used as the clinical alert or threshold value for initiating treatment for hypoglycemia in diabetes because of the potential for glucose to fall further (E).
- Severe hypoglycemia is defined as an event with severe cognitive impairment (including coma and convulsions) requiring external assistance by another person to actively administer carbohydrates, glucagon, or take other corrective actions. Severe hypoglycemic coma is defined as a subgroup of severe hypoglycemia, as an event associated with a seizure or loss of consciousness (E).
- The incidence of severe hypoglycemic coma has fallen over

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the last 2 decades with a current rate of 3 to 7 per 100 patients years across international registries. Although lower hemoglobin A1c (HbA1c) was a risk factor for severe hypoglycemia, this association is no longer observed with contemporary therapy in recent surveys (B).2

- Young children remain at risk of severe hypoglycemia due to their reduced ability to communicate their needs (B).3
- Symptoms of hypoglycemia in the young result from adrenergic activation (eg, shakiness, pounding heart, sweateness) and neuroglycopenia (eg, headache, drowsiness, difficulty in concentrating). In young children, behavioral changes such as irritability, agitation, quietness, and tantrums may be prominent (B).

Treatment of hypoglycemia

- Severe hypoglycemia requires urgent treatment. In a hospital setting, this may include intravenous glucose (10% glucose, 2-3 mL/kg) (B). In the home or ambulatory setting, intramuscular (IM) or subcutaneous (SC) glucagon should be given (1 mg for children >25 kg and 0.5 mg for children <25 kg).
 - Glucagon should be readily accessible to all parents and caregivers, especially when there is a high risk of severe hypoglycemia. Education on administration of glucagon is essential (E). Intranasal glucagon is a promising alternative to IM glucagon and would provide an unmet need for an easily administered glucagon preparation.
 - Milder hypoglycemic events should be treated with oral glucose (10-15 g glucose). Depending on the circumstances, rapid acting glucose should be followed by additional carbohydrates to prevent recurrence of hypoglycemia (B).
- Treatment of hypoglycemia should increase the blood glucose by nearly 3 to 4 mmol/L (54-70 mg/dL). This can be accomplished by giving glucose tablets or sweetened fluids. Approximately 9 g of glucose is needed for a 30 kg child and 15 g for a 50 kg child (approximately 0.3 g/kg) (C).

Vaccination for diabetic patients

- Annually provide an influenza vaccine to all patients with diabetes ≥ 6 months of age.
- Administer pneumococcal polysaccharide vaccine 23 (PPSV23) to all patients with diabetes ≥ 2 years of age.

Complications of Type 1 Diabetes:

Microvascular Complications and their devastating effects:

- Nephropathy → End stage renal disease, Hypertension
- Retinopathy → Visual impairment, Blindness
- Neuropathy → Disabling pain, autonomic dysfunction

Screening of microvascular and macrovascular complications in children and adolescents:

1. Commence screening for microvascular complications at age 11 years (formerly 10 years) or after 5 years of diagnosis.
2. Screening for microvascular disease should be performed preconception and during each trimester of pregnancy.
3. Screen for lipid abnormalities in the non-fasting state.
4. Screen for renal disease by first morning albumin creatinine ratio as the preferred method.

Macrovascular Complications

- Diabetes is associated with a high risk of vascular disease including atherosclerosis and ischemic heart disease → primary cause of death among people with type 1 diabetes
- Peripheral vascular disease → Diabetic foot (uncommon)
- Devastating effects of microvascular diabetes complications are rare in children and uncommon in adolescents.

- Macrovascular complications are rare under the age of 30.
- Subclinical microvascular changes can be detected using sensitive testing methods during childhood and adolescence and predisposition to macrovascular complications starts early in life.
- **The role of the Pediatric Diabetologist is PREVENTION of the chronic complications and their devastating effects.**
 - **HOW? By early detection and intervention during the prolonged asymptomatic phase.**

Nephropathy

- **Microalbuminuria is considered to be a risk factor for diabetic nephropathy and progressive renal insufficiency in diabetics**
- **Microalbuminuria is diagnosed if:**
 - The albumin excretion rate (AER) is > 20 - 200 $\mu\text{g}/\text{min}$
 - The albumin excretion is 30 - 300 $\text{mg}/24$ hrs urine collection
 - The albumin/creatinine ratio (ACR) is > 30 $\mu\text{g}/\text{mg}$ in early morning urine sample.

Management:

- Improve glycemic control.
- Strongly discourage smoking.
- Encourage healthy exercise.
- Discourage excessive nutritional protein intake (recommended maximum of 1.0 - 1.2 g/kg body weight per day).
- Blood pressure lowering.
- ACE inhibitors with persistent micro-albuminuria

Dose:

- Children: 0.5 $\text{mg}/\text{kg}/\text{dose}$ q 12hr; maximum 6 $\text{mg}/\text{kg}/\text{day}$.
- Adolescents: 12.5 - 25 mg/dose q 12hr; maximum 450 mg/day .

Retinopathy

Management:

- Improve glycemic control.
- Strongly discourage smoking.
- Encourage healthy exercise.
- Laser therapy for vision threatening retinopathy.
- ACE inhibitor should be considered in progressive retinopathy.

Neuropathy

Includes peripheral sensory neuropathy and autonomic neuropathy

Detected by:

Appropriate history and examination for:

- Symptoms of numbness, pain, cramps and paresthesia
- Skin sensation, vibration sense and light touch
- Ankle reflexes.
- Postural change in blood pressure, and heart rate response to Valsalva maneuver (cardiovascular autonomic neuropathy).
- Post voiding residual urine in bladder by ultrasonography (urinary autonomic neuropathy).

Management:

- Improved glycemic control
- Strongly discourage smoking
- BMI reduction

Dyslipidemia:

Dyslipidemia is a preventable major risk factor for cardiovascular disease.

Dyslipidemia is present if one or more of the lipid or lipoprotein

levels are abnormal as follows:

- Total Cholesterol ≥ 200 mg/dl
- LDL-Cholesterol ≥ 100 mg/dl,
- HDL-Cholesterol < 40 mg/dl (males) & < 50 mg/dl (females),
- Triglycerides ≥ 150 mg/dl

When to start screening ?

- Lipid profile every 5 years starting at the age of 12 years or at age of 2 years if high risk.

Lipid profile is done only after initial glycemic control is achieved

Management:

The evolution of macrovascular disease may be reduced by:

- Improved glycemic control
- Avoiding smoking
- Participation in healthy exercise
- Blood pressure control
- Treatment of dyslipidemia by dietary changes and statins in non-responding cases.

Dose:

- <10 years old: Safety and efficacy not established.
- ≥ 10 years old: Initially 10 mg PO qDay, titrate at 4-week intervals;

not to exceed 20 mg PO qDay.

Nutritional Management In Children and Adolescents with Diabetes

Total daily energy intake should be distributed as follows:

1. Carbohydrate 50-55 % (Moderate sucrose intake up to 10% total energy)

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2. Fat 30-35%

- <10% saturated fat + trans fatty acids
- <10% polyunsaturated fat
- >10% monounsaturated fat (up to 20 % total energy)
- n-3 fatty acids (cis configuration): 0.15 g /day

3. Protein 10-15%

Vitamins, minerals and antioxidants

- Children with diabetes have the same vitamin and mineral requirements as other healthy children.

Artificial And Intense Sweeteners

- Water should be encouraged instead of sugary drinks.
- Products such as low fat yoghurt with intense sweeteners can be useful, especially for those who are overweight.
- Saccharin, aspartame, acesulfame K, cyclamates (in some countries), alitame and sucralose are used in low sugar, "light" or "diet" products to improve sweetness and palatability.
- There are no published scientific reports documenting harm from an intake of artificial sweeteners and it could be accepted in special situations.

Fasting in Ramadan

There are 2 opinions:

1. Obsolete prevention of fasting during Ramadan based on Fatwa of Alazhar Alsharif. Many Diabetic experts documented recurrent severe hypoglycemic and hyperglycemic attacks.

2. If the patient insists: Dividing the doses given into 2 doses of short or ultra-short insulin with one dose of long acting insulin. This only done for adolescence above 12 years with recent HA1c less than 8% and strict close follow up at least 7 times / day. If blood glucose below 80 mg/dl or above 200 mg/dl patient should break fast.

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Exercise

• Exercise is very beneficial and diabetes is no barrier to participation. Regular exercise and participation in sports, school trips, camps, etc should be encouraged. This should be recorded as part of the consultation record.

• While it is recognised that moderate intensity exercise increases the risk of hypoglycaemia, vigorous exercise might be associated with the release of adrenaline and glucagon which may provoke hyperglycemia and/or ketosis.

Sick-Days Management In Children and Adolescents with Diabetes:

• Children whose diabetes is under good metabolic control should not experience more illness or infections than children without diabetes. On the other hand, children with poor metabolic control may have altered immune function, increasing susceptibility to and delaying recovery from infection.

Diabetic children are in need for insulin during their illness, the same as during health or even, sometimes more. Some mothers consider that herchild's illness, with its associated anorexia and decreased food intake, is a good reason to stop or reduce insulin dose.

General Principles:

- Never stop insulin. The insulin dose may need to be increased or decreased.
- More frequent monitoring.
- Maintain hydration.
- Replace meals with easily digested food e.g. fluids. Choose the type of fluids according to blood glucose level.
- Treat the current illness and give symptomatic treatment as usual.
- When vomiting occurs in a child with diabetes, it should be always considered a sign of insulin deficiency unless it is proved otherwise.
- Consider treatment of vomiting with a single injection of antiemetic or rectal antiemetic suppository to help oral intake of carbohydrates.

InsulinTherapy:

- If BG readings are repeatedly low,decrease insulin dose by 10-20%.
- If BG readings are repeatedly high (> 250 mg/dl),check for ketones, and give extra insulin doses if needed.
- If there is hyperglycemia with negative or small amounts of ketones,usual recommendations are to give an additional 5-10% of TDD (total daily dose) or 0.05-0.1 U/kg as short/rapid acting insulin administered. This may be repeated every 2-4 hours based upon BG monitoring results.
- If there is hyperglycemia and more marked ketonuria (moderate to high), usual recommendations are to give an additional 10-20% of TDD(usually not more than 0.1 U/kg) as short-/rapid-acting insulin. This dose should be repeated every 2-4 hours; based upon frequent glucose and ketone results

Indications For Hospitalization During Illness

- The diagnosis is unclear.
- The child is young (<2-3 years) and exhausted.
- BG levels continue to be high inspite extra insulin.
- Persistent and heavy ketonuria.
- Severe or unusual abdominal pain.
- Persistent vomiting.
- Dehydration.
- Respiratory distress.

Diabetes Education

Recommendations

1. Every young person with diabetes and their parents/carers have a right to accessible, planned diabetes self-management education.
2. This includes all elements described in limited care.
3. Diabetes education should be delivered by an interdisciplinary

paediatric diabetes team (as a minimum a doctor, nurse and dietitian), acknowledging their different skills with a clear understanding of the special and changing needs of young people and their families as they grow through the different stages of life.

4. Diabetes education needs to be learner-centred and thus be adaptable to suit individual needs.
5. Diabetes management, facilitated by education, is unlikely to be successful without some degree of behavioural change in children, adolescents and their parents/carers.
6. The diabetes team should receive training in teaching and counselling techniques.
7. Diabetes education needs to be a continuous process and repeated for it to be effective.

Self blood glucose monitoring

1. Self-monitoring of blood glucose (SMBG) is an essential tool in the optimal management of childhood and adolescent diabetes and, when financially possible, should be made available for all children with diabetes.
2. SMBG should be prescribed at a frequency to optimise each child's diabetes control, usually four to six times a day, because frequency of SMBG correlates with glycaemic control.
3. Without accurate monitoring, the risks of acute crises and long-term microvascular and macrovascular complications are greatly increased.
4. The acute and chronic complications of diabetes lead increased healthcare costs and personal disability.
5. Ketone testing should be available and performed: -During illness with fever and/or vomiting. -When blood glucose value above 14 mmol/l (250 mg/dl) in an unwell child or when persistent blood glucose levels above 14 mmol/l (250 mg/dl) are present. -When there is persistent polyuria with elevated blood glucose, especially

if abdominal pains or rapid breathing are present. -Blood ketone testing is preferred if available, especially for small children and -patients on insulin pumps.

6. Glucose monitoring records should not be used as a judgment but as a vehicle for discussing the causes of variability and strategies for Improving glycaemic control.

General Rules

- The increased frequency of SMBG is associated with improved HbA1c in patients with type 1 diabetes. This is thought to be because of both better insulin adjustment for food consumed and an improved ability to quickly correct out-of-target glucose values. In addition, early detection of lower glucose values prior to symptomatic hypoglycaemia may allow correction with a decreased risk of over correction and resultant hyperglycaemia.

- The use of SMBG during exercise may also allow improved insulin management and a decreased risk for hypoglycaemia during and following exercise.

Recommendations for Oriental Orthodox Christians with Diabetes as Regards Religious Fast

As all monotheist religions, Christianity has religious fasts imposed on its followers. Yet, not all Churches have similar fasts. The Orthodox Church, and in particular the Oriental Orthodox Church such as the Coptic Orthodox Church in Egypt, has a peculiar fast.

The main peculiarities of this fast are that it is imposed in a great number of days during the year. As an example, in the year 2014-

2015 there were 202 days of fast;(note that the Egyptian Church is following the Ancient Egyptian Calendar which starts on the 11th of September after the Nile flood). Besides, the severity, length and dates of the fast are variable. In essence, the fast entails total abstinence from food and beverages for a certain period followed by strictly vegetarian meals. Three main types of fast are practiced.

The first degree fast:

This is practiced before some main religious feasts (such as Easter) and every Wednesday and Fridays all over the year.This entails fasting from food and beverages from midnight to the sunset/or end of the Mass; followed by vegetarian meals and sea food is not allowed. (About 103 days in the year 2014-15).

The second degree fast:

This type of food is rich in carbohydrates, fats and salt. The main food recipes consumed are the typical Egyptian popular meals.

These include beans such as fava beans (foul medames), fava beans burger (falafel/taamia), smashed fava beans with green vegetables (bessara), black lentils (adss be gebba), yellow lentils, white beans etc.. These are slowly absorbed carbohydrates and have good vegetable protein content and are recommended to constitute a good bulk of the meal.

It also includes starchy foods such as potatoes, vegetables stuffed with rice, all types of pastas, rice, bread, vegetarian pizza, koshary (mixture of rice, pasta, peas, onion, black lentils and sauce) etc.. These items have a relatively moderate glycemic index and are recommended to be used with moderation.

Another food item is green vegetables which are either used for salads or cooked. When used in salads, we recommend using little amount of oil and table salt particularly for hypertensive patients. When cooked, we recommend avoiding frying, which is one of the most prevalent way of cooking; as it would contain a large amount of total fat and Trans fats due to the boiling of the used oils.

A popular food habit is the use of pickles, salted fishes and sesame seeds salads. The first two items should be avoided if the patient is hypertensive and the latter item should be used in moderation because of its high caloric content.

Fishes, when allowed constitute a healthy food item, unfortunately, unlike red meat; they have a low satiety index. Thus they are usually consumed with a lot of bread, potatoes or particularly rice. This should be avoided by consuming a lot of green salad to reach satiety.

Another food item is sweets prepared neither with eggs, milk nor milk products. To compensate for that, a greater amount of sugar is usually added. This habit should be certainly modified concerning the sugar content as well as the portions served. On the other hand, consuming fresh fruits in adequate portions should be encouraged. Counseling prior to the fast.

This should aim at depicting subjects who should be exempted to fast the first degree or second degree fast. It should assess the subject metabolic status, presence of complications, special needs or modifications of an intended fast. It should also entail modification of the therapeutic regimen.

Diabetes Education Before the Fast

Structured diabetes education is an essential tool for the management of diabetes during the fasting period and after breaking the fast. Diabetes education should also include performing glucose self-monitoring, nutritional education besides prevention, diagnosis and management of hypoglycemic and hyperglycemic episodes.

Recommendations for management of diabetes during Ramadan:

Patients can be stratified into their risk of hypoglycemia and/or complications prior to the start of the fasting period of Ramadan. Those at high risk of hypoglycemia and with multiple diabetic complications should be advised against prolonged fasting. Even in the lower hypoglycemia risk group, adverse effects may still occur.

- In order to minimize adverse side effects during fasting in patients with diabetes and improve or maintain glucose control, education and discussion of glucose monitoring and treatment regimens should occur several weeks prior to Ramadan.
- Agents such as metformin, thiazolidinediones and dipeptidyl peptidase-4 inhibitors appear to be safe and do not need dose adjustment.
- Most sulfonylureas may not be used safely during Ramadan except with extreme caution; besides, older agents, such as chlorpropamide or glyburide, should not be used.
- Reduction of the dosage of sulfonylurea is needed depending on the degree of control prior to fasting.

DIABETES EDUCATION DURING RAMADAN

Structured diabetes education is an essential tool for the management of diabetes during the fasting period and after breaking the fast during Ramadan. In a retrospective analysis by Bravis et al, patients who received diabetes education had less weight gain and fewer episodes of hypoglycemia compared with a group that did not receive education prior to Ramadan. Diabetes education, including the use of point-of-care (POC) glucose testing, resulted in fewer episodes of hypoglycemia between the start of Ramadan and the end of fasting. Diabetes education also helps to overcome certain barriers to diabetes care such as the misconception that puncturing

one's skin for blood glucose testing during the fast would break the fast.

USE OF GLUCOSE-LOWERING MEDICATIONS DURING RAMADAN

The preferred antidiabetic drugs during Ramadan are agents that provide sustained glucose control during prolonged fasting with low risk of hypoglycemia, especially during the fasting period. Table 1 lists the benefits and concerns of commonly used oral antidiabetic agents during Ramadan.

In general, it is recommended that insulin secretagogues should be avoided during periods of prolonged fasting due to the increased risk of hypoglycemia.

Recommendations for management of diabetes during Ramadan: update 2018

Table 1 Pharmacological oral agents for the treatment of type 2 diabetes during Ramadan

Generic name	Daily dosage (mg)	Advantages	Concerns
<u>Insulin secretagogues</u> Sulfonylureas Glipizide Glyburide Glimepiride Gliazide Gliazide MR Meglitinides Repaglinide Nateglinide	2.5–20 1.25–20 1–4 40–320 30–60 0.5–8 60–120	Lowers HbA1c by 1–2%, high initial response rate, no lag time before response, once-daily dosing, low cost Lowers HbA1c by 1–1.5%, shorter half-life than sulfonylureas	Hypoglycemia, weight gain, need caution in patients with renal and hepatic dysfunction and with sulfa allergy Hypoglycemia, weight gain, repeated (before meals) dosing, more expensive than sulfonylureas
<u>α-Glucosidase inhibitors</u> Acarbose Miglitol	25–150	Lowers HbA1c by 0.5–0.8% lowers postprandial glucose levels without causing hypoglycemia, weight neutral	Less effective in lowering glycemia than metformin or sulfonylureas, increased gas production and GI symptoms
<u>Insulin sensitizers</u> Biguanides Metformin	500–2000	Lowers HbA1c by 1–2%, weight neutral, high initial response rate, long record of relative safety, low risk of hypoglycemia, improved lipid profile, may reduce macrovascular events, low cost	Initial GI side effects common, risk of lactic acidosis, cannot be used in patients with renal dysfunction or hepatic dysfunction

Recommendations for management of diabetes during Ramadan: update 2018

Table 1 Pharmacological oral agents for the treatment of type 2 diabetes during Ramadan

Generic name	Daily dosage (mg)	Advantages	Concerns
Thiazolidinediones Pioglitazone	15–45	Lowers HbA1c by 0.8–1.5%, low risk of hypoglycemia, improved lipid profile	Weight gain, fluid retention causing peripheral edema and/or heart failure, expensive, risk of osteopenia in postmenopausal females
Incretin agents Dipeptidyl peptidase-4 inhibitors Sitagliptin Linagliptin Saxagliptin Alogliptin Anagliptin* Teneligliptin*	25–100 5 2.5–5 12.5–25 200–400 20–40	Lowers HbA1c by 0.6–1%, well tolerated, lowers postprandial glucose levels, weight neutral	More expensive and less potent than metformin and sulfonylureas, some agents require dose adjustment in patients with reduced renal function
Glucagon-like peptide 1 agonists Exenatide Liraglutide Exenatide ER Dulaglutide Albiglutide Lixisenatide*	5–10 mcg two times a day 0.6–1.8 mg daily 2 mg weekly 0.75–1.5 mg weekly 30 mg weekly 10 mcg daily	Lowers HbA1c by 0.8–2%, lowers postprandial glucose levels, weight loss, low risk of hypoglycemia, may reduce blood pressure, improved lipid profile	High rate of GI side effects, injectable, more expensive than sulfonylureas and metformin
SGLT-2 inhibitors Dapagliflozin Canagliflozin	5–10 mg daily 100–300 daily	Lowers HbA1c by 0.8–1.5%, low risk of hypoglycemia, weight loss, lower blood pressure	Increases risk of urinary tract infection and genital infections, expensive, risk of dehydration

Recommendations for management of diabetes during Ramadan: update 2018

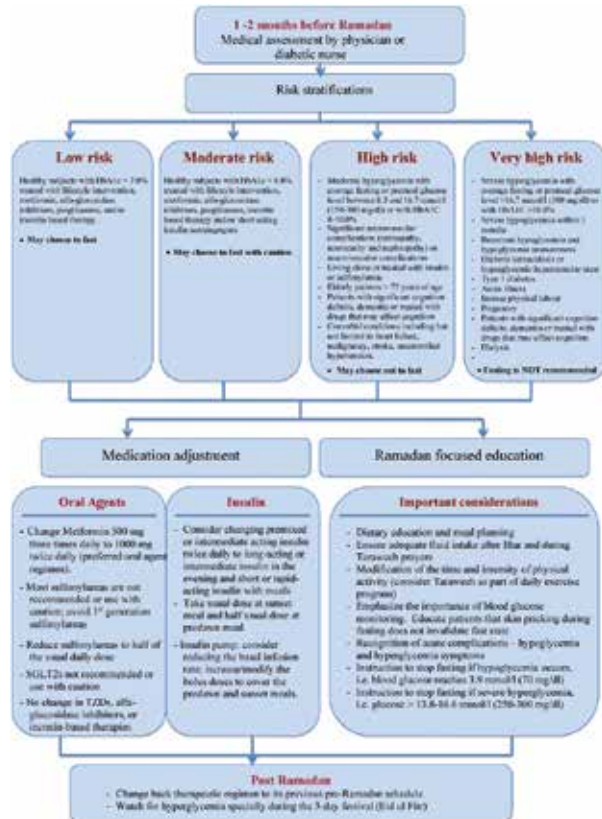


Figure 1 Management algorithm for people with type 2 diabetes intending to fast during Ramadan (HbA1c, glycated hemoglobin; SGLT-2, sodium glucose transporter-2 inhibitors; TZD, thiazolidinedione).

DATES CONSUMPTION

Daily consumption of dates is a deeply rooted tradition among Muslims, especially during the Ramadan. Most Muslims consume dates when they break their fast (Iftar), either alone or with other food items such as yoghurt. Some people also consume dates at the predawn meal (Suhoor). Dehydrated dates (Tamer) analysis revealed that they are rich in carbohydrates (total sugars: 44–88%), salts, minerals, vitamins, unsaturated fatty acids (0.2–0.5%), proteins (2–6%), and fibers (6–12%).

Consumption of 100 g of dates provides 50–100% of the recommended dietary fiber intake. In addition, dates have high fructose content with a 1:1 ratio of fructose and glucose. There is growing evidence of the beneficial effects of dates in improving glycemic and lipid control in patients with diabetes and a possible reduction in cardiovascular risk factors. More research; however, is needed to study the possible beneficial effects of dates on patients with diabetes during Ramadan.

TARAWEEH PRAYERS

Taraweeh prayers can be a strenuous physical activity that could result in dehydration and increased risk of hypoglycemia. Taraweeh prayers should be considered as a part of the daily exercise program. So patients are advised to monitor BG concentration, to eat starchy foods with Iftar, which are digested slowly, and to drink plenty of water before prayers. In addition, patients with diabetes should be advised to consume extra fluids and carbohydrates to treat hypoglycemic events during Taraweeh prayers. Patients with diabetes at risk or with a history of severe or recurrent hypoglycemia should be treated with agents with a low risk of hypoglycemia or advised to reduce the total daily dose of insulin during Ramadan and Taraweeh prayers.

MISCONCEPTIONS ABOUT DRAWING BLOOD AND INSULIN INJECTIONS DURING THE FAST

Contrary to the widespread belief among some Muslim communities that injection invalidates the fast, patients should be instructed that insulin injections have no nutrition value and that they are allowed, regardless of whether they are given by the subcutaneous, intramuscular, or intravenous route. There is a popular belief that pricking the finger for POC testing breaks the fast, which may lead to patients skipping glucose testing during Ramadan. Again, patients and family members should be educated that similar to injections, puncturing the skin with glucose monitoring devices are allowed, and that glucose monitoring may help in assessing glucose control and in recognizing hypoglycemia during Ramadan.

To prevent hypoglycemia in diabetes during fasting, healthcare providers need to emphasize the importance of regular glucose monitoring for maintenance of normoglycemia

LIFESTYLE CHANGES AFTER RAMADAN

The end of Ramadan is followed by a 3-day festival known as Eid ul-Fitr. This is usually marked with festivities, sharing of food, and sweet beverages. Patients with diabetes should be advised about the risks of hyperglycemia during this time, as many individuals overindulge in eating and drinking. When the month of Ramadan ends, the patients' therapeutic regimen should be adjusted and may be changed back to its previous schedule, if glycaemic control was satisfactory before Ramadan.

RECOMMENDATIONS FOR THE PREVENTION AND TREATMENT OF HYPOGLYCEMIA DURING RAMADAN

Box 1 Recommendations for prevention of hypoglycemia during Ramadan

- Blood glucose monitoring. Depending on treatment regimen, monitor glucose levels daily or several times a day. Patients treated with insulin and insulin secretagogues should measure glucose before, during, and after fasting (2–4 times daily)
- Consultation with diabetes healthcare provider for medication adjustment. Treatment regimen should be evaluated and modified according to glycemic control and risk of hypoglycemia, at least 1 month prior to Ramadan. Avoid or reduce sulfonylureas and/or insulin daily dosag
- Avoid skipping predrawn meals
- Avoid strenuous physical activity during fasting period
- Adjust medication dose and eat a snack in the presence of hypoglycemia (see box 2). Consider breaking the fast if there is severe or recurrent hypoglycemia
- Record blood glucose measures to determine patterns contributing to hypoglycemia

Box 2 Recommendations for treatment of hypoglycemia

The following are examples of 15 g of carbohydrate:

- 1/2 cup (four ounces) of apple or orange juice
- 1/2 cup (four ounces) of regular sweetened soda
- Three or four glucose tablets
- One serving of glucose gel—the amount equal to 15 g of carbohydrate
- 1 cup (eight ounces) of milk
- Five or six pieces of hard candy
- One tablespoon of sugar or honey

Editing Board



Dr. Asem M. Saf Eln Ahmed
MD, MRCP(UK), FRCP(Edin)
Professor of Internal Medicine &
Endocrinology, Cairo University



Prof. DR Abbas Orabi
Professor of diabetes &
Endocrinology zagazig university
Member of National diabetes
committee



Prof. Alaf Bassyouni
Prof. Of Internal Medicine, Head
of internal medicine department of
National Institute of Diabetes and
Endocrinology



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University



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Member of National Diabetes
Committee



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University



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Member of National Diabetes
Committee



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President of the Egyptian society
of diabetes and lipidology



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Endocrinology – Head of
Endocrinology Department, Ain
Shams University.



Dr. Nabil El Kafrawy
Head of Diabetes and
Metabolism Unit
Menoufia University



Dr. Nagwa Lachine
Prof of Diabetes Alex university



Dr. Nermin Shereba
Prof. of Diabetes & Endocrinology
– Ain Shams University



Dr. Reham Ghalab
Manager of the presidential
initiative for non communicable
diseases "100 million well" &
National Diabetes Committee
Coordinator



Prof. Dr. Salah El Ghazaly Harb
Prof. DR. Member of National
Diabetes Committee



Dr. Salah Sheibaya
Prof of Diabetes & Endocrinology
Ein shams university



Prof. Samir Helmy Assaad Khalil
Professor of Internal Medicine
Unit of Diabetology,
Lipidology & Metabolism
Faculty of Medicine,
Alexandria University



Dr. Samir Samney
Prof of Diabetes & Endocrinology
Cairo university



Dr. Yehia Ghanem
Prof. of Diabetes – Alex University

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