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DIABETES MELLITUS: AN EVOLVING GLOBAL CHALLENGE IN ENDOCRINOLOGY

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ABSTRACT

Diabetes mellitus (DM) represents one of the most pressing global health challenges of the 21st century, with a rapidly rising prevalence that spans across socioeconomic and geographic boundaries. This review provides a comprehensive overview of the current understanding of diabetes mellitus, including its classification, pathophysiology, epidemiology, and the evolving landscape of diagnosis and management. Type 1 and Type 2 diabetes, while distinct in etiology, both contribute significantly to morbidity and mortality through acute and chronic complications affecting multiple organ systems. We explore the genetic, environmental, and lifestyle factors contributing to the development of diabetes, as well as the growing impact of urbanization and aging populations. Advances in pharmacologic therapies, including novel glucose-lowering agents and personalized treatment strategies, are examined alongside technological innovations such as continuous glucose monitoring and insulin delivery systems. Furthermore, we address the global disparities in diabetes care, highlighting the need for integrated health policies, preventive strategies, and equitable access to resources. As diabetes mellitus continues to evolve as a global public health issue, a multidisciplinary and forward-thinking approach is essential to curb its impact and improve patient outcomes worldwide.

KEYWORDS: diabetes mellitus, Type 1 diabetes, Type 2 diabetes, global health, pathophysiology, management, endocrinology, public health.

INTRODUCTION

Diabetes mellitus (DM) is a complex, chronic metabolic disorder that has emerged as one of the most significant global public health challenges of the 21st century. Characterized by persistent hyperglycemia, diabetes results from defects in insulin secretion, insulin action, or a combination of both. It is not a single disease but rather a heterogeneous group of disorders with varying etiologies, pathophysiologies, and clinical manifestations. The most prevalent forms include Type 1 diabetes mellitus (T1DM), Type 2 diabetes mellitus (T2DM), and gestational diabetes mellitus (GDM), along with less common monogenic and secondary types.

The global burden of diabetes is alarming. According to the International Diabetes Federation (IDF), the number of people living with diabetes has more than tripled over the past two decades and is expected to exceed 700 million by 2045 if current trends continue. T2DM accounts for approximately 90–95% of all cases and is closely linked to rising rates of obesity, sedentary lifestyles, unhealthy diets, and population aging. T1DM, though less prevalent, typically manifests in childhood or adolescence and poses significant lifelong management challenges. GDM, increasingly recognized for its impact on maternal and fetal outcomes, also raises the future risk of T2DM for both mother and child.

The pathophysiology of diabetes is multifaceted. In T1DM, autoimmune destruction of pancreatic β-cells leads to absolute insulin deficiency. T2DM, on the other hand, involves a combination of insulin resistance in peripheral tissues and a progressive decline in β-cell function. Recent research has also highlighted the roles of chronic inflammation, gut microbiota, genetic predisposition, and epigenetic modifications in the development and progression of both types of diabetes.

Beyond hyperglycemia, diabetes is associated with a broad range of acute and chronic complications that significantly impact quality of life and life expectancy. These include microvascular complications such as retinopathy, nephropathy, and neuropathy, as well as macrovascular complications such as coronary artery disease, stroke, and peripheral arterial disease. The long-term management of diabetes, therefore, requires a comprehensive, multidisciplinary approach encompassing not only glycemic control but also cardiovascular risk reduction, complication screening, and lifestyle modification.

Despite considerable advancements in our understanding of diabetes and the development of novel diagnostic tools and therapeutic strategies—including continuous glucose monitoring, insulin analogs, oral antidiabetic agents, and incretin-based therapies—significant disparities remain in access to care, especially in low- and middle-income countries. Additionally, the increasing prevalence of diabetes in children and adolescents, coupled with the high incidence of undiagnosed cases, underscores the need for early detection and preventive strategies.

This review aims to provide a comprehensive and up-to-date synthesis of the current knowledge surrounding diabetes mellitus. It will explore the epidemiology, pathophysiology, diagnostic criteria, clinical features, and complications of diabetes, as well as recent advances in treatment and future directions in research and public health. By examining diabetes through both clinical and global health lenses, this article seeks to underscore the urgent need for coordinated, innovative, and equitable approaches to tackle this evolving endocrine and societal challenge.[2]

Classification of Diabetes Mellitus

Diabetes mellitus (DM) is a group of metabolic disorders characterized by chronic hyperglycemia resulting from defects in insulin secretion, insulin action, or both. The classification of diabetes has evolved over time as understanding of its pathophysiology has improved. According to the American Diabetes Association (ADA) and the World Health Organization (WHO), diabetes is broadly classified into the following main categories[4]:

1. Type 1 Diabetes Mellitus (T1DM)

Type 1 diabetes mellitus is primarily an autoimmune disorder in which the body's immune system mistakenly attacks and destroys the insulin-producing β-cells of the pancreas. This results in an absolute insulin deficiency. It commonly presents in childhood or adolescence but can occur at any age. T1DM accounts for approximately 5–10% of all diabetes cases.

Subtypes

- **Type 1A**: Autoimmune-mediated; associated with autoantibodies such as GAD (glutamic acid decarboxylase), IA-2, or ZnT8.
- **Type 1B**: Idiopathic; not associated with autoantibodies, more common in certain ethnic groups (e.g., African and Asian descent).

Clinical features include rapid onset of symptoms such as polyuria, polydipsia, weight loss, and often diabetic ketoacidosis (DKA) at diagnosis.

2. Type 2 Diabetes Mellitus (T2DM)

Type 2 diabetes mellitus is the most common form, accounting for about 90–95% of all diabetes cases. It is characterized by a combination of insulin resistance and progressive β-cell dysfunction leading to relative insulin deficiency. T2DM typically develops in adults but is increasingly seen in children and adolescents due to rising obesity rates and sedentary lifestyles.

Risk factors include obesity, physical inactivity, family history, ethnicity (higher risk in African, Hispanic, Native American, and Asian populations), and aging.

Clinical onset is often insidious, and many patients remain undiagnosed for years. Complications may be present at diagnosis due to prolonged hyperglycemia.

3. Gestational Diabetes Mellitus (GDM)

Gestational diabetes mellitus is defined as glucose intolerance of varying severity with onset or first recognition during pregnancy. GDM affects approximately 7–14% of pregnancies and is associated with adverse maternal and fetal outcomes, including macrosomia, preeclampsia, and neonatal hypoglycemia.

Women with GDM have an increased risk of developing T2DM later in life, and their offspring are also at elevated risk for obesity and glucose intolerance.

4. Other Specific Types of Diabetes

This category includes a variety of uncommon forms of diabetes resulting from specific genetic, endocrinologic, or environmental factors.

Examples include

- **Monogenic Diabetes Syndromes**
  - *Maturity-Onset Diabetes of the Young (MODY)*: A group of autosomal dominant inherited forms of diabetes due to single-gene mutations affecting β-cell function.
  - *Neonatal Diabetes*: Occurs in the first 6 months of life and may be transient or permanent.
- **Diseases of the Exocrine Pancreas**
  - Includes conditions such as pancreatitis, cystic fibrosis, and pancreatic cancer that damage pancreatic tissue and impair insulin production.
- **Endocrinopathies**
  - Such as Cushing's syndrome, acromegaly, and pheochromocytoma, which antagonize insulin action.
- **Drug- or Chemical-Induced Diabetes**
  - Induced by medications such as glucocorticoids, thiazides, atypical antipsychotics, or exposure to toxins.
- **Infections and Genetic Syndromes**
  - Certain viral infections and chromosomal abnormalities (e.g., Down syndrome, Turner syndrome) may be associated with diabetes.

Emerging Classifications and Phenotypic Clusters

Recent research has proposed new subclassifications of diabetes based on phenotypic clusters, incorporating age at onset, insulin resistance, autoimmunity, and β-cell function. These approaches aim to improve prediction of disease progression and response to treatment. However,

such stratifications are not yet standard in clinical practice.[6]

Etiology of Diabetes Mellitus

The etiology of diabetes mellitus (DM) is multifactorial, involving a complex interplay of genetic, environmental, and lifestyle factors. The underlying causes differ between the major types of diabetes—Type 1, Type 2, and other less common forms—but all result in hyperglycemia due to impaired insulin production, insulin action, or both.

1. Etiology of Type 1 Diabetes Mellitus (T1DM)

Type 1 diabetes is primarily an autoimmune disorder in which the body's immune system targets and destroys the insulin-producing β-cells of the pancreas, leading to absolute insulin deficiency.

Key etiological factors include

- **Genetic Predisposition**
  - Strongly associated with specific HLA class II alleles (e.g., HLA-DR3, DR4, and DQ8).
  - Family history increases risk, but heritability is lower than in Type 2 diabetes.
- **Autoimmunity**
  - Presence of autoantibodies such as anti-GAD (glutamic acid decarboxylase), IA-2, insulin autoantibodies (IAA), and ZnT8.
- **Environmental Triggers**
  - Viral infections (e.g., enteroviruses like Coxsackievirus B).
  - Early exposure to cow's milk proteins or low vitamin D levels (hypothesized).
  - Stress and other environmental insults may precipitate onset.

2. Etiology of Type 2 Diabetes Mellitus (T2DM)

Type 2 diabetes results from a combination of insulin resistance and progressive β-cell dysfunction. It has a strong genetic component but is largely influenced by environmental and lifestyle factors.

Key etiological factors include

- **Genetic Susceptibility**
  - Polygenic inheritance; multiple gene variants associated with β-cell function, insulin signaling, and fat metabolism.
  - Family history is a significant risk factor.
- **Insulin Resistance**
  - Often linked to obesity, particularly visceral (abdominal) fat.
  - Adipose tissue secretes adipokines and proinflammatory cytokines that impair insulin signaling.
- **β-Cell Dysfunction**
  - Progressive decline in insulin secretion despite increasing insulin resistance.
- **Lifestyle Factors**
  - Physical inactivity, high-calorie diets, consumption of processed and sugary foods.
  - Chronic stress, poor sleep patterns.
- **Other Risk Factors**
  - Age (risk increases with age), ethnicity (higher risk in African, Hispanic, South Asian, and Native American populations), and low birth weight (fetal programming hypothesis).

3. Etiology of Gestational Diabetes Mellitus (GDM)

GDM occurs due to insulin resistance that develops during pregnancy, typically in the second or third trimester. This resistance is partly physiological but may exceed the pancreatic β-cell's capacity to compensate.

Key etiological factors include

- **Placental Hormones**
  - Hormones such as human placental lactogen, estrogen, and cortisol antagonize insulin action.
- **Preexisting Insulin Resistance**
  - Women with obesity or polycystic ovary syndrome (PCOS) are at higher risk.
- **Genetic and Ethnic Factors**
  - Family history of diabetes and certain ethnic backgrounds are associated with higher risk.

4. Etiology of Other Specific Types of Diabetes

These forms of diabetes are due to identifiable secondary causes:

- **Monogenic Diabetes (e.g., MODY)**
  - Caused by single-gene mutations affecting β-cell function (e.g., HNF1A, HNF4A, GCK).
  - Typically presents at a young age, with autosomal dominant inheritance.
- **Pancreatic Disorders**
  - Chronic pancreatitis, hemochromatosis, cystic fibrosis, and surgical removal of the pancreas.
- **Endocrine Disorders**
  - Conditions like Cushing's syndrome, acromegaly, pheochromocytoma (excess counter-regulatory hormones).
- **Drug- or Chemical-Induced**
  - Glucocorticoids, thiazide diuretics, atypical antipsychotics, and immunosuppressants.
  - Exposure to toxins such as streptozotocin or pentamidine.
- **Infections**
  - Congenital rubella, cytomegalovirus, and others can damage β-cells.
- **Genetic Syndromes**
  - Such as Down syndrome, Turner syndrome, and Prader-Willi syndrome.

Signs and Symptoms of Diabetes Mellitus

The clinical presentation of diabetes mellitus varies depending on the type of diabetes, the duration of the disease, and the presence of complications. While some individuals may be asymptomatic and diagnosed incidentally through routine blood testing, others may present with classic symptoms of hyperglycemia or diabetes-related complications.[6]

1. Common Symptoms of Hyperglycemia (Seen in Both Type 1 and Type 2 Diabetes)

These symptoms result from the effects of high blood glucose levels and osmotic diuresis:

- **Polyuria**: Increased urination due to osmotic effect of excess glucose in the urine.
- **Polydipsia**: Excessive thirst resulting from dehydration caused by polyuria.
- **Polyphagia**: Increased hunger, often associated with weight loss due to the body's inability to utilize glucose effectively.
- **Unexplained weight loss**: Particularly in Type 1 diabetes due to catabolism of fat and muscle.
- **Fatigue and weakness**: Due to lack of cellular glucose uptake.
- **Blurred vision**: Caused by osmotic changes in the lens due to fluctuating glucose levels.
- **Slow-healing wounds or frequent infections**: Hyperglycemia impairs immune function and wound healing.
- **Tingling or numbness in hands or feet**: A sign of diabetic neuropathy, more common in long-standing Type 2 diabetes.

2. Specific Features in Type 1 Diabetes Mellitus

- **Abrupt onset of symptoms**, especially in children or adolescents.
- **Diabetic ketoacidosis (DKA)** may be the first presentation, characterized by:
  - Nausea and vomiting
  - Abdominal pain
  - Kussmaul respiration (deep, labored breathing)
  - Fruity-smelling breath (due to ketones)
  - Altered mental status or coma (in severe cases)

3. Specific Features in Type 2 Diabetes Mellitus

- **Gradual onset** of symptoms; often diagnosed incidentally.
- May be **asymptomatic** for years.
- More likely to present with:
  - **Chronic complications** (e.g., neuropathy, retinopathy, nephropathy) at diagnosis.
  - **Recurrent infections** (e.g., urinary tract infections, skin infections).
  - **Acanthosis nigricans** (hyperpigmented, velvety skin, usually in the neck or axilla), indicative of insulin resistance.

4. Gestational Diabetes Mellitus (GDM)

- Often **asymptomatic** and detected through routine prenatal screening (e.g., oral glucose tolerance test).
- In some cases, may present with:
  - Excessive fetal growth (macrosomia)
  - Polyhydramnios
  - Recurrent urinary tract infections
  - Fatigue and increased urination, which may be difficult to distinguish from normal pregnancy symptoms.

5. Symptoms of Acute and Chronic Complications

Acute Complications

- **Diabetic Ketoacidosis (DKA)** – mostly in T1DM.
- **Hyperosmolar Hyperglycemic State (HHS)** – more common in T2DM; characterized by extreme hyperglycemia, dehydration, and altered consciousness without significant ketosis.

Chronic Complications May Present As

- **Visual disturbances** (due to diabetic retinopathy or cataracts).
- **Numbness, burning, or pain in extremities** (diabetic neuropathy).
- **Swelling, foamy urine** (early signs of diabetic nephropathy).
- **Claudication or chest pain** (peripheral artery disease or coronary artery disease).

Diagnosis of Diabetes Mellitus

The diagnosis of diabetes mellitus (DM) is based on the presence of chronic hyperglycemia confirmed through standardized laboratory tests. Diagnostic criteria are established by leading health organizations such as the American Diabetes Association (ADA) and the World Health Organization (WHO). The choice of test may vary based on the clinical context, availability, and patient factors.[10]

1. Diagnostic Criteria for Diabetes Mellitus (ADA 2024 Guidelines)

A diagnosis of diabetes can be made if any one of the following criteria is met **on two separate occasions**, unless symptoms are clearly present:

Test	Diagnostic Threshold
Fasting Plasma Glucose (FPG)	≥ 126 mg/dL (7.0 mmol/L)
2-hour Plasma Glucose (OGTT)	≥ 200 mg/dL (11.1 mmol/L) after 75g oral glucose
Hemoglobin A1c (HbA1c)	≥ 6.5% (48 mmol/mol)
Random Plasma Glucose	≥ 200 mg/dL (11.1 mmol/L) **with classic symptoms**

Note: Fasting is defined as no caloric intake for at least 8 hours. The oral glucose tolerance test (OGTT) should be conducted using 75g anhydrous glucose dissolved in water.

2. Diagnostic Criteria for Prediabetes (Intermediate Hyperglycemia)

Identifying prediabetes is important for early intervention to prevent progression to diabetes:

Test	Prediabetes Range
Fasting Plasma Glucose	100–125 mg/dL (5.6–6.9 mmol/L)
2-hour Plasma Glucose (OGTT)	140–199 mg/dL (7.8–11.0 mmol/L)
HbA1c	5.7–6.4% (39–46 mmol/mol)

3. Additional Tests and Considerations

- **Autoantibody Testing**: Helpful in distinguishing Type 1 from Type 2 diabetes, especially in atypical cases or young adults (e.g., GAD, IA-2, ZnT8 antibodies).
- **C-Peptide Levels**: Used to assess endogenous insulin production. Low levels suggest Type 1 diabetes.
- **Urine Testing**
  - **Glucosuria**: May indicate hyperglycemia but is not diagnostic.
  - **Ketones**: Present in diabetic ketoacidosis (T1DM) or under metabolic stress.
- **Continuous or Flash Glucose Monitoring**: Used in management, not diagnosis.

4. Screening Recommendations

- **Type 2 Diabetes**
  - Adults aged ≥35 years should be screened every 3 years.
  - Screen earlier and more frequently if risk factors are present: obesity, family history, hypertension, dyslipidemia, gestational diabetes, or high-risk ethnicity.
- **Type 1 Diabetes**
  - No routine screening in the general population.
  - Consider autoantibody testing in first-degree relatives of individuals with T1DM.
- **Gestational Diabetes**
  - Screen at 24–28 weeks of gestation using a one- or two-step OGTT approach.
  - Early screening is advised in high-risk women.

5. Differential Diagnosis

It is important to distinguish between different types of diabetes to guide appropriate treatment:

Type	Key Features
Type 1 DM	Autoantibodies positive, low C-peptide, young onset
Type 2 DM	Overweight/obese, insulin resistance, family history
MODY	Young onset, strong family history, non-insulin-dependent
Secondary DM	Related to drugs, pancreatic disease, or endocrinopathies

Treatment of Diabetes Mellitus

The treatment of diabetes mellitus (DM) aims to achieve optimal glycemic control, prevent acute complications, and reduce the risk of long-term microvascular and macrovascular complications. The approach to treatment depends on the type of diabetes, the individual's overall health, age, duration of disease, presence of complications, and personal preferences. Management involves a combination of lifestyle interventions, pharmacotherapy, monitoring, and education.

1. General Principles of Diabetes Management

- **Glycemic Targets (ADA Guidelines)**
  - HbA1c < 7% for most adults
  - Preprandial glucose: 80–130 mg/dL (4.4–7.2 mmol/L)
  - Postprandial glucose: <180 mg/dL (10.0 mmol/L) at 1–2 hours after meals
- **Key Components**
  - Lifestyle modifications
  - Pharmacologic therapy
  - Blood glucose monitoring
  - Management of comorbidities (hypertension, dyslipidemia)
  - Regular screening for complications
  - Patient education and self-care

2. Lifestyle Modifications

- **Dietary Therapy**
  - Emphasis on balanced, nutrient-rich diet with low glycemic index foods
  - Reduce intake of refined sugars and saturated fats
  - Portion control and carbohydrate counting
  - Diet plans tailored by registered dietitians or certified diabetes educators
- **Physical Activity**
  - At least 150 minutes/week of moderate-intensity aerobic activity (e.g., brisk walking)
  - Resistance training 2–3 times/week
  - Helps improve insulin sensitivity and weight control
- **Weight Management**
  - Aim for 5–10% weight loss in overweight or obese individuals with T2DM
  - Bariatric surgery may be considered in select patients with BMI ≥35 kg/m²
- **Smoking Cessation and Alcohol Moderation**

3. Pharmacologic Therapy

A. Type 1 Diabetes Mellitus

- **Insulin Therapy is essential**
  - Multiple daily injections (MDI) of basal and bolus insulin or continuous subcutaneous insulin infusion (CSII) via insulin pump
  - Types of insulin:
    - Rapid-acting (e.g., lispro, aspart, glulisine)
    - Short-acting (e.g., regular insulin)

- Intermediate-acting (e.g., NPH)
- Long-acting (e.g., glargine, detemir, degludec)
- **Adjunct therapies**:
  - Pramlintide (amylin analog) in selected cases

B. Type 2 Diabetes Mellitus

- **First-line Therapy**
  - **Metformin**: Improves insulin sensitivity, reduces hepatic glucose production
- **Second-line and Add-on Agents**
  Depending on comorbidities (e.g., cardiovascular disease, chronic kidney disease, obesity), choose from:
  - **SGLT2 inhibitors** (e.g., empagliflozin, dapagliflozin): Cardiorenal benefits
  - **GLP-1 receptor agonists** (e.g., liraglutide, semaglutide): Weight loss, CV protection
  - **DPP-4 inhibitors** (e.g., sitagliptin, linagliptin): Well tolerated, modest effect
  - **Sulfonylureas** (e.g., glipizide): Cost-effective, risk of hypoglycemia
  - **Thiazolidinediones** (e.g., pioglitazone): Improve insulin sensitivity
  - **Basal insulin**: Introduced if oral agents are inadequate
- **Insulin therapy**: Initiated in cases of severe hyperglycemia, catabolic symptoms, or failure of multiple oral agents.

C. Gestational Diabetes Mellitus

- **Initial management**: Lifestyle modification, medical nutrition therapy
- **If glycemic targets are not met**
  - **Insulin** is the preferred pharmacologic treatment
  - Oral agents (e.g., metformin, glyburide) may be considered with caution

4. Blood Glucose Monitoring

- **Self-Monitoring of Blood Glucose (SMBG)**
  - Especially important in insulin-treated patients
  - Frequency based on treatment regimen and glycemic control
- **Continuous Glucose Monitoring (CGM)**
  - Recommended for T1DM and intensively managed T2DM
  - Improves glycemic outcomes and reduces hypoglycemia

5. Management of Comorbidities and Complications

- **Hypertension**
  - Target: <140/90 mmHg or <130/80 mmHg in high-risk individuals
  - ACE inhibitors or ARBs preferred
- **Dyslipidemia**
  - Statin therapy indicated based on age and cardiovascular risk
- **Antiplatelet Therapy**
  - Consider low-dose aspirin for secondary prevention of cardiovascular disease
- **Nephropathy, Retinopathy, Neuropathy**
  - Routine screening and early intervention
  - Use of SGLT2 inhibitors or GLP-1 RAs for renal protection

6. Patient Education and Psychosocial Support

- Diabetes self-management education and support (DSMES) programs
- Mental health evaluation for diabetes distress, depression, and anxiety
- Involvement of multidisciplinary care teams

CONCLUSION

Diabetes mellitus remains a complex and evolving global health challenge, with rising prevalence across both developed and developing nations. This chronic metabolic disorder, characterized by persistent hyperglycemia, affects nearly every organ system and significantly increases the risk of cardiovascular disease, kidney failure, blindness, and lower limb amputation.

Despite substantial advancements in our understanding of its pathophysiology and improvements in diagnostic tools and therapeutic options, the burden of diabetes continues to escalate. Effective management hinges on early diagnosis, personalized treatment strategies, comprehensive lifestyle modification, and continuous monitoring to prevent complications and improve quality of life.

Public health initiatives focused on prevention, education, and equitable access to care are crucial to mitigating the global impact of diabetes. Ongoing research into novel therapies, precision medicine, and digital health technologies offers hope for more effective, individualized care in the future. A collaborative effort between healthcare providers, policymakers, researchers, and patients is essential to reverse the current trajectory and ensure better outcomes for those living with diabetes.

REFERENCES

1. American Diabetes Association. Standards of Medical Care in Diabetes—2024. Diabetes Care., 2024; 47(Supplement_1): S1–S300. doi:10.2337/dc24-S001
2. World Health Organization. Diabetes. 2023. https://www.who.int/news-room/fact-sheets/detail/diabetes
3. Saeedi P, Petersohn I, Salpea P, et al. Global and regional diabetes prevalence estimates for 2019 and projections for 2030 and 2045: Results from the International Diabetes Federation Diabetes Atlas, 9th edition. Diabetes Res Clin Pract., 2019; 157: 107843. doi:10.1016/j.diabres.2019.107843
4. DeFronzo RA, Ferrannini E, Zimmet P, Alberti KGMM. International Textbook of Diabetes Mellitus, 4th Edition. Wiley-Blackwell, 2015.
5. Powers AC, D'Alessio D. Endocrine Pancreas and Pharmacotherapy of Diabetes Mellitus and

Hypoglycemia. In: Brunton LL, Hilal-Dandan R, Knollmann BC, eds. Goodman & Gilman's: The Pharmacological Basis of Therapeutics. 13th ed. McGraw-Hill, 2018.
6. Zheng Y, Ley SH, Hu FB. Global aetiology and epidemiology of type 2 diabetes mellitus and its complications. Nat Rev Endocrinol., 2018; 14(2): 88–98. doi:10.1038/nrendo.2017.151
7. Nathan DM, et al. Medical management of hyperglycemia in type 2 diabetes: a consensus algorithm for the initiation and adjustment of therapy. Diabetes Care., 2009; 32(1): 193–203. doi:10.2337/dc08-9025
8. Inzucchi SE, et al. Management of hyperglycemia in type 2 diabetes, 2015: a patient-centered approach. Diabetes Care., 2015; 38(1): 140–149. doi:10.2337/dc14-2441
9. International Diabetes Federation. IDF Diabetes Atlas, 10th Edition. 2021. https://diabetesatlas.org
10. Skyler JS, et al. Type 1 diabetes mellitus: pathogenesis and treatment. Lancet., 2017; 391(10138): 1261–1270. doi:10.1016/S0140-6736(17)31709-1