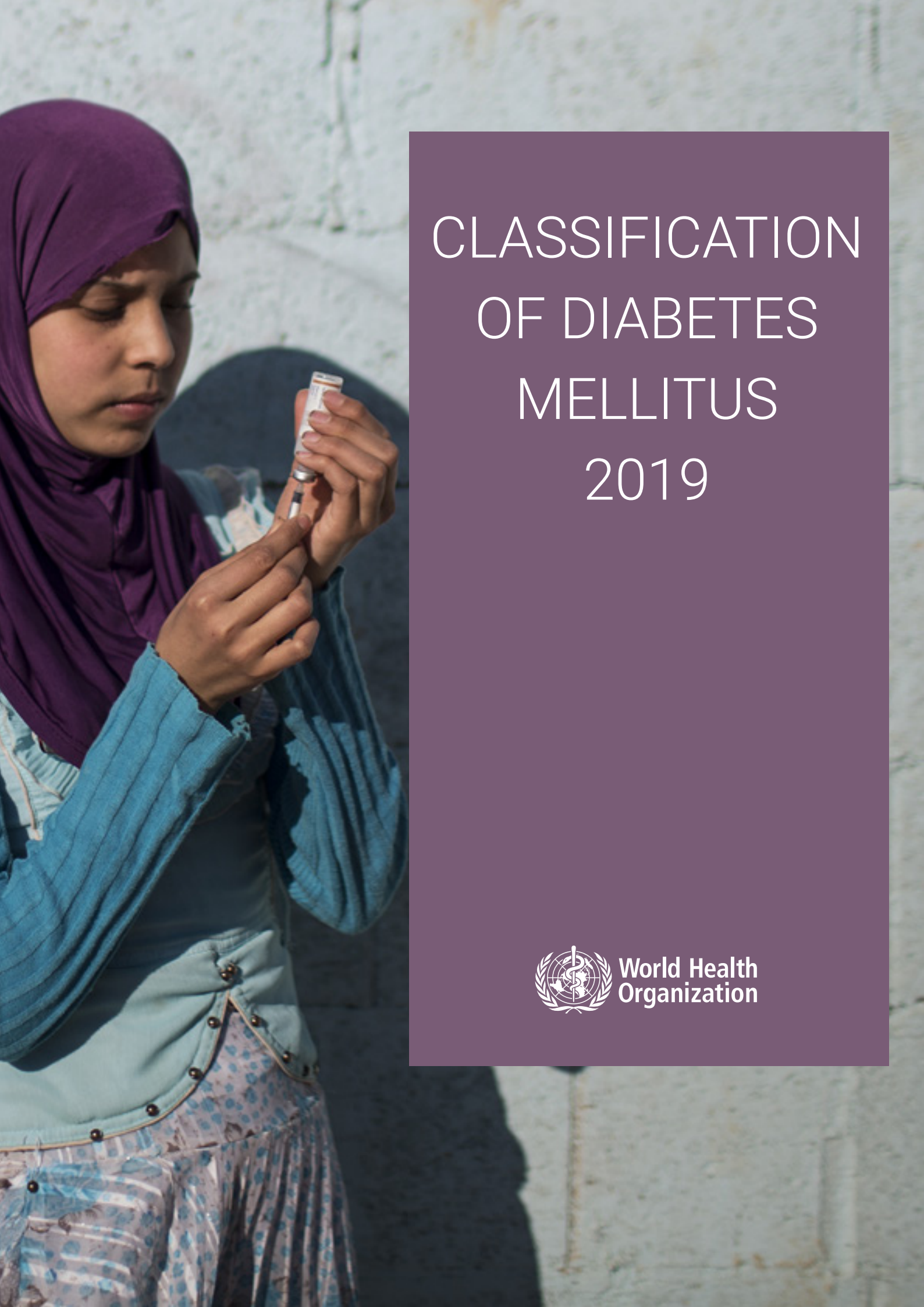

CLASSIFICATION OF DIABETES MELLITUS 2019

World Health Organization

Classification of diabetes mellitus

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Executive summary

This document updates the 1999 World Health Organization (WHO) classification of diabetes. It prioritizes clinical care and guides health professionals in choosing appropriate treatments at the time of diabetes diagnosis, and provides practical guidance to clinicians in assigning a type of diabetes to individuals at the time of diagnosis. It is a compromise between clinical and aetiological classification because there remain gaps in knowledge of the aetiology and pathophysiology of diabetes.

While acknowledging the progress that is being made towards a more precise categorization of diabetes subtypes, the aim of this document is to recommend a classification that is feasible to implement in different settings throughout the world. The revised classification is presented in Table 1.

Unlike the previous classification, this classification does not recognize subtypes of type 1 diabetes and type 2 diabetes and includes new types of diabetes (“hybrid types of diabetes” and “unclassified diabetes”).

Table 1 : Types of diabetes

Type of diabetes	Brief description	Change from previous classification
Type 1 diabetes	β-cell destruction (mostly immune-mediated) and absolute insulin deficiency; onset most common in childhood and early adulthood	Type 1 sub-classes removed
Type 2 diabetes	Most common type, various degrees of β-cell dysfunction and insulin resistance; commonly associated with overweight and obesity	Type 2 sub-classes removed
Hybrid forms of diabetes		New type of diabetes
Slowly evolving, immune-mediated diabetes of adults	Similar to slowly evolving type 1 in adults but more often has features of the metabolic syndrome, a single GAD autoantibody and retains greater β-cell function	Nomenclature changed – previously referred to as latent autoimmune diabetes of adults (LADA)
Ketosis-prone type 2 diabetes	Presents with ketosis and insulin deficiency but later does not require insulin; common episodes of ketosis, not immune-mediated	No change
Other specific types		
Monogenic diabetes - Monogenic defects of β-cell function - Monogenic defects in insulin action	Caused by specific gene mutations, has several clinical manifestations requiring different treatment, some occurring in the neonatal period, others by early adulthood Caused by specific gene mutations; has features of severe insulin resistance without obesity; diabetes develops when β-cells do not compensate for insulin resistance	Updated nomenclature for specific genetic defects
Diseases of the exocrine pancreas	Various conditions that affect the pancreas can result in hyperglycaemia (trauma, tumor, inflammation, etc.)	No change
Endocrine disorders	Occurs in diseases with excess secretion of hormones that are insulin antagonists	No change
Drug- or chemical-induced	Some medicines and chemicals impair insulin secretion or action, some can destroy β-cells	No change
Infection-related diabetes	Some viruses have been associated with direct β-cell destruction	No change
Uncommon specific forms of immune-mediated diabetes	Associated with rare immune-mediated diseases	No change
Other genetic syndromes sometimes associated with diabetes	Many genetic disorders and chromosomal abnormalities increase the risk of diabetes	No change
Unclassified diabetes	Used to describe diabetes that does not clearly fit into other categories. This category should be used temporarily when there is not a clear diagnostic category especially close to the time of diagnosis	New types of diabetes
Hyperglycaemia first detected during pregnancy		
Diabetes mellitus in pregnancy	Type 1 or type 2 diabetes first diagnosed during pregnancy	No change
Gestational diabetes mellitus	Hyperglycaemia below diagnostic thresholds for diabetes in pregnancy	Defined by 2013 diagnostic criteria
Diagnostic criteria for diabetes: fasting plasma glucose ≥ 7.0 mmol/L or 2-hour post-load plasma glucose ≥ 11.1 mmol/L or Hba1c ≥ 48 mmol/mol **Diagnostic criteria for gestational diabetes**: fasting plasma glucose 5.1–6.9 mmol/L or 1-hour post-load plasma glucose ≥ 10.0 mmol/L or 2-hour post-load plasma glucose 8.5–11.0 mmol/L		

Introduction

Since 1965 the World Health Organization has periodically updated and published guidance on how to classify diabetes mellitus (hereafter referred to as "diabetes") *(1)*. This document provides an update on the guidance last published in 1999 *(2)*.

Diabetes comprises many disorders characterized by hyperglycaemia. According to the current classification there are two major types: type 1 diabetes (T1DM) and type 2 diabetes (T2DM). The distinction between the two types has historically been based on age at onset, degree of loss of β cell function, degree of insulin resistance, presence of diabetes-associated autoantibodies, and requirement for insulin treatment for survival *(3)*. However, none of these characteristics unequivocally distinguishes one type of diabetes from the other, nor accounts for the entire spectrum of diabetes phenotypes.

There are several reasons for revisiting the diabetes classification. Firstly, the phenotypes of T1DM and T2DM are becoming less distinctive with an increasing prevalence of obesity at a young age, recognition of the relatively high proportion of incident cases of T1DM in adulthood and the occurrence of T2DM in young people. Secondly, developments in molecular genetics have allowed clinicians to identify growing numbers of subtypes of diabetes, with important implications for choice of treatment in some cases. In addition, increasing knowledge of pathophysiology has resulted in a trend towards developing personalized therapies and precision medicine *(3)*. Unlike the previous classification, this classification does not recognize subtypes of T1DM and T2DM, includes new types of diabetes ("hybrid types of diabetes" and "unclassified diabetes"), and provides practical guidance to clinicians for assigning a type of diabetes to individuals at the time of diagnosis.

1. Diabetes: Definition and diagnosis

The term diabetes describes a group of metabolic disorders characterized and identified by the presence of hyperglycaemia in the absence of treatment. The heterogeneous aetio-pathology includes defects in insulin secretion, insulin action, or both, and disturbances of carbohydrate, fat and protein metabolism. The long-term specific effects of diabetes include retinopathy, nephropathy and neuropathy, among other complications. People with diabetes are also at increased risk of other diseases including heart, peripheral arterial and cerebrovascular disease, obesity, cataracts, erectile dysfunction, and nonalcoholic fatty liver disease. They are also at increased risk of some infectious diseases, such as tuberculosis.

Diabetes may present with characteristic symptoms such as thirst, polyuria, blurring of vision, and weight loss. Genital yeast infections frequently occur. The most severe clinical manifestations are ketoacidosis or a non-ketotic hyperosmolar state that may lead to dehydration, coma and, in the absence of effective treatment, death. However, in T2DM symptoms are often not severe, or may be absent, owing to the slow pace at which the hyperglycaemia is worsening. As a result, in the absence of biochemical testing, hyperglycaemia sufficient to cause pathological and functional changes may be present for a long time before a diagnosis is made, resulting in the presence of complications at diagnosis. It is estimated that a significant percentage of cases of diabetes (30–80%, depending on the country) are undiagnosed *(4)*.

Four diagnostic tests for diabetes are currently recommended, including measurement of fasting plasma glucose; 2-hour (2-h) post-load plasma glucose after a 75 g oral glucose tolerance test (OGTT); HbA1c; and a random blood glucose in the presence of signs and symptoms of diabetes. People with fasting plasma glucose values of ≥ 7.0 mmol/L (126 mg/dl), 2-h post-load plasma glucose ≥ 11.1 mmol/L (200 mg/dl) *(5)*, HbA1c ≥ 6.5% (48 mmol/mol); or a random blood glucose ≥ 11.1 mmol/L (200 mg/dl) in the presence of signs and symptoms are considered to have diabetes *(6)*. If elevated values are detected in asymptomatic people, repeat testing, preferably with the same test, is recommended as soon as practicable on a subsequent day to confirm the diagnosis *(6)*.

A diagnosis of diabetes has important implications for individuals, not only for their health, but also because of the potential stigma that a diabetes diagnosis can bring may affect their employment, health and life insurance, driving status, social opportunities, and carry other cultural, ethical and