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Brazilian guideline for screening and diagnosis of type 2 diabetes: a position statement from the Brazilian Diabetes Society



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Abstract

Background Patients with type 2 diabetes (T2D) often experience prolonged periods of asymptomatic hyperglycemia, which significantly increases the risk of developing chronic complications related to diabetes. Screening programs for individuals at high risk for T2D provide valuable opportunities not only for early diagnosis but also for detecting intermediate hyperglycemic states, commonly referred to as prediabetes. Interventions aimed at preventing diabetes in this group can successfully delay or even avoid the onset of the disease and its associated burdens. This review is an update of the Brazilian Diabetes Society (Sociedade Brasileira de Diabetes [SBD]) evidence-based guideline for diagnosing diabetes and screening T2D.

Methods The methodology was previously published and defined by the internal institutional steering committee. The working group drafted the manuscript by selecting vital clinical questions for a narrative review, utilizing MEDLINE via PubMed to identify relevant studies. The review assessed the best available evidence, including randomized clinical trials (RCTs), meta-analyses, and high-quality observational studies related to the diagnosis of diabetes.

Results and conclusions Fifteen specific recommendations were formulated. Screening is recommended for adults aged 35 and older or younger individuals with obesity and additional risk factors. For children and adolescents, screening is recommended starting at age ten or the onset of puberty if they are overweight or obese and have additional risk factors. Fasting plasma glucose (FPG) and HbA1c are recommended as initial screening tests. The oral glucose tolerance test (OGTT) is recommended for high-risk individuals with normal HbA1c and FPG or those with prediabetes. The 1-h OGTT is preferred over the 2-h OGTT, as it is both more practical and a superior test. A structured approach to reevaluation intervals is provided.

Keywords Practice guidelines: type 2 diabetes mellitus, Prediabetic state, Blood glucose, Glycated hemoglobin, Oral glucose tolerance test, Diagnosis, Early diagnosis, Disease prevention

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Background

Patients with type 2 diabetes (T2D) can often have asymptomatic hyperglycemia for long periods, which increases the risk of developing diabetes-related chronic complications. According to the International Diabetes Federation (IDF) Atlas (10th edition), 44.7% of the adults living with diabetes are unaware of their status [1]. In Brazil, the most recent data indicated that approximately 30% of individuals with diabetes remain undiagnosed [2]. Therefore, it is crucial to create screening strategies for individuals more prone to developing T2D. Screening programs for T2D are also valuable opportunities to identify individuals with intermediate hyperglycemic states, frequently known as prediabetes. Interventions to prevent diabetes in this group may successfully avoid or postpone the diagnosis and its potential burden.

While the need for screening programs for T2D is clear, there is ongoing debate about the optimal sequence of diagnostic tests for this purpose, who should be screened, and the frequency of tests. Fasting plasma glucose (FPG), 2-h oral glucose tolerance test (OGTT), and hemoglobin A1c (HbA1c) have been the most common tests used in screening programs [3]. However, recently, the IDF issued a Position Statement recommending the incorporation of the 1-h OGTT (1 h-OGTT) in the diagnostic criteria for T2D and intermediate hyperglycemia [4].

The 21st IDF Atlas reports that Brazil ranks as the 6th country globally in the number of patients with diabetes between 20 and 79 years of age and the 8th in the number of undiagnosed diabetes cases. In addition, Brazil currently holds the highest prevalence of T2D among the youth populations [1]. Therefore, improving screening strategies is crucial in our population as a significant public health measure. In this Position Statement, the Brazilian Diabetes Society (Sociedade Brasileira de Diabetes [SBD]) suggests a screening algorithm for T2D.

Methodology

This review is an English-translated update of part of the 2024 Guidelines of the SBD, and the methodology was approved for publication by the internal institutional steering committee. This working group drafted the manuscript, selecting vital clinical questions for a narrative review using MEDLINE via PubMed and the MeSH terms [diabetes], [diagnosis], [HbA1c], [oral glucose tolerance test], [screening], [prediabetes], and [fasting glucose]. The best available evidence was reviewed, including randomized clinical trials (RCTs), meta-analyses, and high-quality observational studies related to the diagnosis of diabetes.

Level of evidence: Three levels of evidence were considered: A—Data from more than one RCT or a meta-analysis of RCTs with low heterogeneity ($I^2 < 40\%$). B—Data from a meta-analysis with high levels of heterogeneity ($I^2 \ge 40\%$), a single RCT, a prespecified subgroup analysis, extensive observational studies, or meta-analyses of observational studies. C—Data from small or nonrandomized studies, exploratory analyses, other guidelines, or expert consensuses.

Degree of recommendation: A poll was sent to the working group for each defined recommendation. The frequency of the responses was analyzed, and a degree of recommendation was obtained based on the following criteria: I—More than 90% of the panel agreed; IIa—Between 70 and 90% of the panel agreed; IIb—Between 50 and 70% of the panel agreed; and III—Most of the panelists advised against the recommendation. The terminology for the four degrees of recommendation was as follows:

I—IS RECOMMENDED
IIa—SHOULD BE CONSIDERED;
IIb—MAY BE CONSIDERED;
III—IS NOT RECOMMENDED.

Recommendations

Initial screening: who should screen

R1: Screening for diabetes in asymptomatic adults IS RECOMMENDED for all individuals aged 35 years or older; younger adults (between 18 and 34 years of age) with either overweight or obesity and any additional risk factor (Table 1); or individuals classified at high or very high risk of T2D, according to the Finnish Diabetes Risk Score (FINDRISC).



- Screening for T2D in asymptomatic individuals is recommended based on evidence showing that early detection and treatment of T2D can significantly reduce the risk of complications, including cardiovascular disease, neuropathy, and nephropathy [5]. Moreover, screening can identify prediabetes, providing an opportunity for early intervention through lifestyle modifications and preventive measures [6]. Screening strategies and preventive measures are cost-effective in high-risk individuals [7, 8].
- A cross-sectional study conducted in the US (National Health and Nutrition Examination Survey) showed that

Table 1 Screening for type 2 diabetes or prediabetes in asymptomatic adults

·Age 35 and older (universal)

•Younger adults (18–34 years of age) with overweight or obesity ($BMl \ge 25 \text{ kg/m}^2$)* who has one or more of the following risk factors:

- O Family history of type 2 diabetes in a first-degree relative
- O History of cardiovascular disease
- O Hypertension
- O HDL cholesterol less than 35 mg/dL
- O Triglycerides greater than 250 mg/dL
- O Polycystic ovary syndrome
- O Acanthosis nigricans
- O Physical inactivity

Screening for type 2 diabetes should also be done in these situations:

- O High or very high FINDRISC score
- O Previous prediabetes diagnosis
- O History of gestational diabetes
- O Individuals using hyperglycemia-inducing medications (e.g., corticosteroids)

Note: Individuals with pancreatitis, HIV or diseases associated with diabetes mellitus should also undergo screening to identify secondary diabetes

Adapted from reference 17

*consider ≥ 23 kg/m² in individuals with purely Asian background

the number needed to screen (NNS) is significantly higher in individuals under 35 than in those aged 35 to 80. This study compared the frequency of positive screening (diabetes diagnosis) and NNS in universal screening across age groups (with 5-year intervals). The differences were most pronounced between the 30–34 and 35–39 age groups (prevalence of 1.3% and NNS of 80 in the 30–34 group vs. 3.4% and 31 in the 35–39 group) [9].

- The prevalence of diabetes mellitus becomes significant at age 35 and increases steadily with age. In Brazil, according to VIGITEL 2023 data, the prevalence of diabetes is 0.5% among individuals aged 18 to 24, 2.4% among those aged 25 to 34, 5.5% among those aged 35 to 44, 10.4% among those aged 45 to 54, 22.4% among those aged 55 to 64, and 30.3% among individuals aged 65 or older [10].
- There is an association between prediabetes and cardiovascular risk. A study with 505 individuals aged 19 to 88 years demonstrated that HbA1c and FPG levels characteristic of prediabetes are associated with a higher cardiovascular risk, justifying screening to identify individuals who should be targeted for evaluation and intervention [11].
- Screening is cost-effective. From the perspective of the American healthcare system, in adults with an average age of 48 years and a body mass index (BMI) of 30 kg/m², the cost of screening and intervention with metformin and lifestyle modification for identified cases of diabetes and prediabetes over three years would be lower than the cost of not screening and not diagnosing people with diabetes [12].
- The presence of additional risk factors increases the risk of T2D. A sub-analysis of the STAND study evaluated, through OGTT and HbA1c, the

- prevalence of T2D and prediabetes in 193 young adults aged 18 to 40 years, with a median age of 33.8 years, a median BMI of 33.9 kg/m 2 , and one additional risk factor. The prevalence of T2D and prediabetes were 4.7% and 18.1%, respectively [13].
- Risk assessment questionnaires for T2D help identify people under 35 who would benefit most from screening. The Brazilian Ministry of Health recommends using the FINDRISC [13] to stratify the risk of developing T2D.
- The FINDRISC tool assesses the likelihood of developing T2D based on factors such as age, BMI, waist circumference, physical activity, dietary habits, family history of diabetes, history of hyperglycemia during pregnancy, or treatment for hypertension [14, 15]. This targeted approach helps efficiently identify individuals most likely to benefit from early screening with a blood test (FPG, HbA1c, and OGTT) and intervention, optimizing healthcare resources and improving outcomes. FINDRISC has a maximum score of 26 and classifies individuals into risk levels as follows: low (<7 points), slightly elevated (7-11 points), moderate (12-14 points), high (15-20 points), and very high (more than 20 points). The full table for calculating the FINDRISC score is available in Table 2 and can also be accessed at https://findrisc.com/#findrisc.
- The risk of T2D is higher in ethnic minorities. However, since the Brazilian population is highly ethnically admixed, the panelists considered it inappropriate to include ethnicity as a risk factor for diabetes in Brazil.
- T2D screening allows for early detection of the disease, which can reduce the risk of its related chronic complications. It also identifies individuals with a higher propensity to develop diabetes who

Table 2 FINDRISC scale

TYPE 2 diabetes risk assessment form—FINDRISC

- 1. Age
- () Under 45 years (0 point)
- () 45 to 54 years (2 points)
- () 55 to 64 year (3 points)
- () over 64 years (4 points)
- 2. Body mass index
- () Below 25 kg/m² (0 point)
- () 25 to 30 kg/m² (1 point)
- () Greater than 30 kg/m² (3 points)
- 3. Waist Circumference measured at the line of the belly button

MEN

- () Less than 94 cm (0 point)
- () 94 to 102 cm (3 points)
- () More than 102 cm (4 points)
- WOMEN
- () Less than 80 cm (0 point)
- () 80 to 88 cm (3 points)
- () more than 88 cm (4 points)
- 4. Do you practice any daily physical activity for at least 30 min during work and/or during your free time (including the daily life activities)?
- () Yes (0 point)
- () No (2 points)
- 5. How often do you eat greens, vegetables and fruits?
- () Every day (0 point)
- () Not every day (1 point)
- 6. Do you regularly take or have already taken medication for high blood pressure?
- () No (0 point)
- () Yes (2 points)
- 7. Have you already presented elevated glycemia (blood sugar) (e.g., in a routine examination, during a health problem or during pregnancy)?
- () No (0 point)
- () Yes (5 points)
- 8. Do you have a family member who has been diagnosed with diabetes (type 1 or type 2)?
- () No (0 point)
- () Yes: at least one of your grandparents, aunt, uncle or first cousins (but not any of your parents, brothers or sisters) (3 points)
- () Yes: at least one of your parents, brothers, sisters or children (5 points)

Total Score:

may benefit from effective prevention strategies, such as lifestyle modifications.

In a validated computer simulation model using data from the ADDITION-Europe study, it was assumed that screening could anticipate the diagnosis of diabetes in 3 to 6 years. Earlier initiation of intensified treatment in individuals with T2D was estimated to lead to a reduction in all-cause mortality and cardiovascular events, with an absolute risk reduction (ARR) of 3.3%, a relative risk reduction (RRR) of 29%, and, over 6 years, a 4.9% ARR and a 38% RRR [16].

R2: Screening for type 2 diabetes in asymptomatic children and adolescents IS RECOMMENDED after the age of 10 or after the onset of puberty (whichever comes first) in those who are overweight (BMI at 85th percentile

or higher) or obese (BMI at the 95th percentile or higher) with, at least one additional risk factor (Table 3).



- In a population-based study including young people aged 10 to 19 years from five centers in the US, the prevalence of T2D in youth was 0.34/1,000 among 1.7 million in 2001, increasing to 0.46/1,000 among 1.8 million young people in 2009. In 2009, T2D prevalence was 0.17/1,000 in Caucasians, 0.79/1,000 in Hispanics, 1.06/1,000 in Blacks, and 1.2/1,000 in Native Americans. From 2001 to 2009, T2D prevalence increased by 30.5% (18).
- According to the ERICA study, the prevalence of T2D and prediabetes in Brazil was 3.3% and 22%,

Table 3 Screening for type 2 diabetes or prediabetes in asymptomatic children and adolescents

Screening should be considered in youth* with overweight (BMI \geq 85th percentile) or obesity (BMI \geq 95th percentile) who have one or more additional risk factors:

- Maternal history of diabetes or gestational diabetes (GDM) during the child's gestation
- Family history of type 2 diabetes in first- or second-degree relative
- Signs of insulin resistance or insulin resistance-related conditions (acanthosis nigricans, hypertension, dyslipidemia, polycystic ovary syndrome, or small-for-gestational-age birth weight)

respectively, among 37,854 adolescents aged 12 to 17 years [19].

- T2D in children and adolescents is characterized by insulin resistance (IR) and decreased insulin secretion, similar to adults. The increase in T2D prevalence in this age group is strongly associated with obesity, especially in girls [20]. Approximately 70% to 90% of affected patients have obesity, with 38% having severe obesity. Obesity and family history appear to have an additive effect on disease risk [21]. In the ERICA study, obese adolescents had a 59% higher chance of T2D.
- IR development is also associated with genetic factors and ethnicity [22]. More than 75% of children and adolescents with T2D usually have at least one first- or second-degree relative affected by this disease [23]. Low birth weight also increases the risk of IR in adulthood by seven times [24].
- Children with T2D are generally asymptomatic or oligosymptomatic for long periods, justifying the need for screening in high-risk individuals. The average age at T2D diagnosis is 13 years, coinciding with the period of highest IR. In the most extensive study on T2D in youth (Treatment Options for Type 2 Diabetes in Adolescents and Youth − TODAY), 65% of the patients with T2D were female, with a mean age of 14 years; they were in Tanner stage III, had a BMI Z-score of 2.15, a positive family history of diabetes in 89.4%, and 26.3% had blood pressure ≥ 90th percentile [25].
- The risk of T2D in adolescents and children is higher in ethnic minorities in the US. However, considering the ethnically admixed Brazilian population, we do not think it appropriate to include ethnicity as a risk factor in T2D screening criteria for children and adolescents in our population.

How to screen for type 2 diabetes and prediabetes:

R3: For the diagnosis of T2D, it is RECOMMENDED to use Fasting Plasma Glucose (FPG), HbA1c, 1-h OGTT or 2 h-OGTT. The diagnostic criteria are FPG≥126 mg/dL,

Table 4 Criteria for the diagnosis of diabetes:

Tests	Normal	Prediabetes	DM
Fasting glucose (mg/dL)	< 100	100–125	≥126
Random glucose (mg/ dL) + symptoms	-	-	≥200
1 h-OGTT (mg/dL)	< 155	155-208	≥209
2 h-OGTT (mg/dL)	< 140	140-199	≥200
HbA1c (%)	< 5.7	5.7-6.4	≥6.5

HbA1c≥6.5%, 1-h OGTT glucose≥209 mg/dL, or 2-h OGTT glucose≥200 mg/dL (Table 4).



- In 1997, The Report of the Expert Committee on the Diagnosis and Classification of Diabetes defined the FPG and 2-h OGTT (2 h-OGTT) cutoffs for diagnosing diabetes and prediabetes based on three population cohorts that assessed the association between glycemic levels and the development of diabetic retinopathy [26–32].
- A cohort study demonstrated a continuous relationship between glycemic levels and the development of diabetic retinopathy. However, a threshold differentiates individuals at higher risk for diabetes-related complications from those at lower risk, which establishes the diagnostic cutoff for diabetes [33]. Notably, this threshold is inconsistent across studies, and variations in retinopathy prevalence between populations may partly account for the differing thresholds. These variations highlight the need for population-specific research to understand better the optimal thresholds for diagnosing and managing diabetes-related complications like retinopathy [34].
- The Emerging Risk Factors Collaboration study, which evaluated 121 prospective studies involving 1.27 million adults with individual records of cardiovascular complications, showed that in individu-

^{*}After the onset of puberty or after 10 years of age, whichever occurs earlier. Adapted from reference 17

- als without a history of diabetes, the risk of coronary heart disease was significantly higher in those with FPG≥126 mg/dL compared to those with FPG≤100 mg/dL. Known diabetes diagnosis or FPG≥126 mg/dL, regardless of other factors, doubled the risk of coronary heart disease, stroke, and vascular-related deaths [35].
- FPG and HbA1c are complementary measures, as subjects may have elevated levels of one or both biomarkers. FPG reflects glucose homeostasis in the post-absorptive state, and HbA1c reflects average glycemia over 2-3 months. The FPG value is strongly correlated with the HbA1c value [36].
- The use of HbA1c \geq 6.5% as a diagnostic criterion for diabetes was suggested in 2009 by the International Expert Committee based on population studies that evaluated fasting glucose and 2 h-OGTT [37, 38]. An analysis of data from nine studies across five countries, with 44,623 participants aged 20 to 79 years, showed an increased odds ratio (OR) between HbA1c levels and the presence of diabetic retinopathy (OR for HbA1c 6.5-6.9% vs HbA1c 4-4.4% = 16.8 [95% CI: 2.3–123.7]; p=0.01) [32].
- The HbA1c cutoff of 6.5% has a sensitivity (Se) of 47-67% and a specificity (Sp) of 98-99% for diagnosing diabetes, compared to the 2 h-OGTT. Brazilian data also corroborate the low Se and high Sp of HbA1c for diagnosing diabetes relative to the 2 h-OGTT [38-41].
- A meta-analysis of 17 studies evaluating the accuracy of HbA1c and FPG for diabetes diagnosis, using the 2 h-OGTT as the gold standard, showed that the Se, Sp, positive predictive value, and negative predictive value of HbA1c \geq 6.5% were 50% (95% CI 42–59%), 97.3% (95% CI 95.3–98.4), 18.3% (95% CI 11.1– 30.5), and 51% (95% CI 43-60%), respectively. For FPG \geq 126 mg/dL, the respective values were 59.4% (95% CI 46.6–71%), 98.8% (95% CI 96.5–99.6%),

- 47.82% (95% CI 19.1-119.7%), and 41.1% (95% CI 30.5-55.5%) [42].
- HbA1c levels may also vary according to ethnicity and the studied population due to factors independent of medication adherence and access to healthcare, like differences in red cell survival, intra and extracellular glucose balance, and genetic determinants of hemoglobin glycation. Africandescendant individuals may have higher HbA1c levels than expected for their glycemic profile, resulting in false-positive diabetes diagnoses [43, 44].
- The HbA1c measurement can avoid the risk of intraindividual variability observed in plasma glucose (PG) measurements and the need to fast. The values of HbA1c, regardless of the methodology used, may not be reliable in the presence of some conditions that alter the life expectancy of erythrocytes (for example, the use of erythropoietin, hemolytic anemia), severe iron deficiency anemia, and recent blood transfusions. Sickle cell anemia or other hemoglobin variants, such as fetal hemoglobin (HbF) and hemoglobins S, C, D, and E, can also interfere with HbA1c results. The factors that may interfere in the glycation of hemoglobin and, therefore, may limit the use of HbA1c for the diagnosis of diabetes are summarized in Table 5. To use HbA1c values as a diagnostic tool for diabetes, it is necessary to employ the global standardization method proposed by the National Glycohemoglobin Standardization Program (NGSP) [45-47].
- Recently, an IDF expert committee re-evaluated the accuracy and applicability of the 1 h-OGTT for diagnosing prediabetes and diabetes. 1 h-OGTT is more practical than 2 h-OGTT. A meta-analysis of 15 studies, with 35,551 individuals of Caucasian, Native American, Asian, and Mexican American descent, identified that the 1 h-OGTT cutoff of 209 mg/dl is equivalent to the 2 h-OGTT cutoff of 200 mg/dl for diagnosing diabetes [48]. The IDF recommends that

Table 5 Limiting factors for the use of HbA1c for diagnosing diabetes mellitus

Iron deficiency and hemolytic anemia Iron supplementation Vitamin B12 deficiency Use of erythropoietin Recent blood transfusion Chronic liver disease Genetic changes in hemoglobin: hemoglobinopathies, HbF, methemoglobin

Chronic kidney failure (shortened red cell survival and/or formation of Carbamylated hemoglobin)

Increase in intraerythrocytic pH

Splenectomy

Medicines that reduce hemoglobin half-life such as antiretrovirals, ribavirin and dapsone

Use of acetylsalicylic acid (ASA) in high doses

Hypertriglyceridemia

Table 6 Accuracy of fasting, 1-h and 2-h plasma glucose in OGTT for identification of diabetes and prediabetes regarding the referred studies

	Fasting glucose	1 h-glucose	2 h-glucose
For T2D			
Sai Prasann N et al	AUC=0.59	AUC=0.72	AUC = 0.62
Oh TJ et al	AUC=0.61	AUC=0.74	AUC = 0.63
Peddinti G et al Botnia Prospective Study	Se 55% Sp 64% AUC=0.63	Se 75% Sp 68% AUC=0.75	Se 56% Sp 73% AUC=0.68
Saunajoki et al	AUC=0.71	AUC=0.81	AUC = 0.72
For preDM			
Sai Prasann N et al	AUC=0.56	AUC=0.68	AUC = 0.64

AUC: area under the curve, Se: sensitivity, Sp: specificity

- 1 h-OGTT glucose \geq 209 mg/dl should be a criterion for diagnosing diabetes [4].
- All diagnostic methods have methodological limitations. FPG requires fasting, can be affected by acute conditions, and has lower reproducibility than HbA1c. The OGTT is more costly, uncomfortable, and time-consuming, but has higher Se. For its use, a diet including at least 150 g of carbohydrates per day is required for three days before the test. HbA1c is more expensive, does not account for individual variability in the protein glycation process, and has lower diagnostic Se than other methods [36, 49].
- Diagnostic criteria for type 2 diabetes have not been investigated specifically in children and adolescents and are based on adult definitions. However, hemoglobin A1c (HbA1c) is recognized by the International Society for Pediatric and Adolescent Diabetes (ISPAD) and the American Diabetes Association (ADA) as a valid diagnostic tool [17, 50]. Kim et al. evaluated 190 children and adolescents with obesity or asymptomatic glucosuria who underwent an oral glucose tolerance test (OGTT) to assess the accuracy of HbA1c as a diagnostic tool for diabetes. The study concluded that an HbA1c threshold of≥6.5% was appropriate for diagnosing type 2 diabetes in this population, although the ideal cutoff was identified as 6.15% [51]. A study involving a multiethnic cohort of 1,156 children and adolescents with obesity assessed the utility of HbA1c for diagnosing diabetes and associated risks. Participants underwent HbA1c measurement and a 2-h oral glucose tolerance test (2 h-OGTT), with 218 followed up for approximately two years. Results showed that 47% of those with HbA1c levels in the "at risk" range (5.7–6.4%) and 62% with $HbA1c \ge 6.5\%$ were classified as having prediabetes or diabetes

- by 2 h-OGTT. The optimal HbA1c threshold for detecting diabetes was 5.8% (78% specificity, 68% sensitivity), while a 1% increase in baseline HbA1c was associated with a 13-fold higher risk of prediabetes or diabetes. This study indicates that HbA1c can be a useful clinical tool for identifying T2D when combined with FPG and 2 h-PG. However, relying solely on HbA1c for diagnosing prediabetes and T2D may be insufficient, to avoid missed or delayed identification [52]. Although a lower cutoff might be more appropriate for this age group, setting the HbA1c threshold at 6.5% for diagnosing diabetes, in conjunction with other criteria, is unlikely to result in an excessive number of inappropriate diabetes diagnoses.
- A longitudinal study (1965-2007) of a highrisk Indigenous American cohort examined the relationship between childhood HbA1c, 2 h-PG levels, and diabetes-related complications. Children with overweight and obesity that had HbA1c compatible with pre-diabetes levels had a higher incidence of retinopathy than those with normal HbA1c (7.9 vs. 2.5 cases per 1,000 person-years; risk difference 5.4; P=0.002). Elevated HbA1c levels, analyzed as a continuous variable, were also significantly linked to increased retinopathy risk (HR 1.53 per %). While A1c, 2 h-PG, and FPG were similarly effective in predicting albuminuria, 2 h-PG slightly outperformed HbA1c in predicting retinopathy (AUC 0.73 vs. 0.69; P = 0.046). Overall, higher childhood glycemia was associated with an increased risk of albuminuria and retinopathy [53].

Important note:

Plasma glucose measurement for the diagnosis of diabetes mellitus – preanalytical standards of performance

PG measurement must be performed in venous blood. Ideally, the blood sample should be immediately centrifuged to obtain plasma. When performing a fast plasma separation is impossible, blood should be stored in a tube containing glycolysis inhibitor substances such as sodium fluoride. Samples that cannot be immediately centrifuged should be kept refrigerated for a maximum period of 30 min [54]

R4: For screening prediabetes or intermediate hyperglycemia, it is RECOMMENDED to use Fasting Plasma Glucose (FPG), HbA1c, 1-h OGTT, or 2-h OGTT. Prediabetes is defined as FPG between 100–125 mg/dL, HbA1c between 5.7–6.4%, 1-h OGTT glucose between 155–208 mg/dL, or 2-h OGTT glucose between 140–199 mg/dL (Table 4).

Class 1 Level B

Summary of evidence:

- When conducting tests for the diagnosis of diabetes, Individuals with mild hyperglycemia who do not meet the criteria for diabetes may be identified. According to the IDF, these cases constitute "intermediate hyperglycemia," which includes "impaired fasting glucose" (IFG) for cases where mild dysglycemia occurs in fasting and "impaired glucose tolerance" (IGT) for situations where mild hyperglycemia is observed after an OGTT, without meeting the criteria for diabetes [4]. The SBD and the American Diabetes Association (ADA) use the term "prediabetes" for these individuals [17]. Although not all individuals in this group will progress to diabetes, the term "prediabetes" has become widely accepted, easy to understand, and commonly used by healthcare professionals.
- In the RCTs of diabetes prevention in Asia, Europe, and the United States, the annual rates of progression to diabetes in individuals with prediabetes based on FPG, 2 h-OGTT, and HbA1c that did not receive intervention ranged from 5.8% to 18.3% [55–59].
- A meta-analysis that comprised 103 prospective cohort studies with up to 24 years of follow-up reported a cumulative incidence of diabetes of 31% for IFG in 12 years (relative risk: 4.32), 41% for IGT in 12 years (relative risk: 3.61), and 31% for individuals with HbA1c between 5.7% and 6.4% in 10 years (relative risk, 5.5) [60].
- A direct association between 1 h-OGTT glucose ≥ 155 mg/dL and the incidence of T2D in subsequent years has been observed in several prospective studies, such as the San Antonio Heart Study, GHO, and Botnia, which evaluated 1,611, 853, and 2,603 individuals, respectively [4, 61–63].
- Although some studies used different cutoffs for predicting T2D with the one h- OGTT, the value of 155 mg/dL represents an appropriate point in terms of Se and Sp for predicting T2D in diverse ethnic populations, as shown in Table 5.
- Fiorentino et al. evaluated 392 individuals without diabetes at two time points: at baseline with the 1 h-OGTT and hyperinsulinemic-euglycemic clamp and after 5.2±0.9 years. The hazard ratio (HR) for developing diabetes in individuals with 1 h-OGTT glucose≥155 mg/dL was 4.02 (95% CI 1.06–15.26), possibly due to lower insulin sensitivity and beta-cell dysfunction [64].

R5: It is RECOMMENDED that the initial screening approach for diabetes be determined by FPG and HbA1c simultaneously in the same blood sample. Sequential testing may also be considered according to local availability, ease of access, and cost.



Summary of evidence:

- FPG and HbA1c measurements are more practical than performing an OGTT. Additionally, starting with FPG and HbA1c prevents unnecessary glucose overload in individuals with positive tests.
- Ideally, FPG and HbA1c should be measured simultaneously for initial T2D screening in settings with adequate financial and technical resources. Simultaneous measurements are convenient, allowing screening from a single fasting blood sample. However, HbA1c testing is more costly and requires a standardized methodology and trained personnel [65].
- The criteria for diabetes mellitus diagnosis may not always align. FPG and HbA1c are complementary, reflecting different aspects of glucose homeostasis [42, 66]. In a systematic review of 117 population-based studies, the concordance rate between FPG and HbA1c for diabetes mellitus diagnosis was 29–39% worldwide, including Brazil [67].
- In situations where HbA1c cannot be used due to factors affecting its accuracy and in settings with partial financial and technical feasibility, isolated FPG measurement is acceptable for initial T2D screening.

An algorithm to guide T2D screening is provided in Fig. 1.

R6: When diabetes cannot be diagnosed using FPG and HbA1c, or when these tests indicate prediabetes, the OGTT is RECOMMENDED to identify undetected cases of T2D or to assess the future risk of developing T2D.



Summary of evidence:

 The OGTT can detect additional cases of diabetes not identified by other methods. Among those diagnosed with diabetes through the 2 h-OGTT, 31% had normal FPG, and 20% had IFG. These individuals

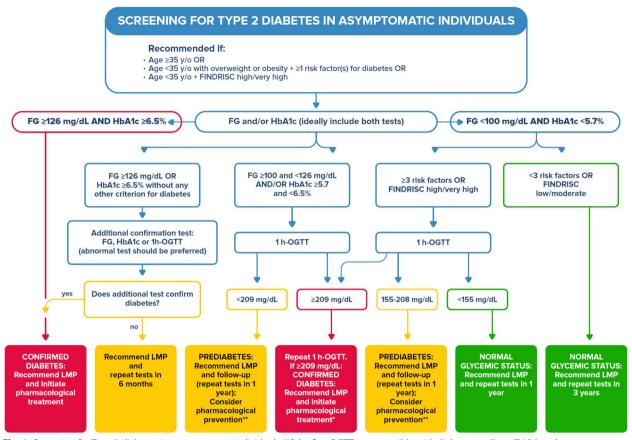


Fig. 1 Screening for Type 2 diabetes in asymptomatic individuals. *If the first OGTT is compatible with diabetes mellitus (DM) but there is no diagnostic confirmation, screening should be repeated in 6 months. **In individuals with prediabetes and fasting glucose (FG), OGTT (1 or 2 h), and HbA1c values close to the criteria established for DM, earlier repetition of screening (between 6 and 12 months) should be considered. LMP: Lifestyle Modification Program.

had a higher risk of premature death (HR of 1.8 in men and 2.6 in women) [68]. The Se of HbA1c for detecting diabetes diagnosed by OGTT is 47–67%. Performing OGTT in high-risk individuals increases diabetes detection [69].

Meijnikman et al. evaluated the performance of OGTT versus HbA1c in 1,241 individuals with overweight and obesity. Among them, 47.3% of newly diagnosed patients and 44.2% of prediabetes cases would have been missed if OGTT had not been done, respectively. These data suggest that not performing an OGTT results in a significant underdiagnosis of T2D in an overweight and obese adult population [70].

R7. In individuals with normal FPG and HbA1c, with three or more risk factors for T2D, or with a high/very high FINDRISC score, the OGTT IS RECOMMENDED to further investigate for diabetes and prediabetes.



Summary of evidence:

- OGTT has a higher sensitivity than FPG and HbA1c and therefore can detect additional cases of T2D in high-risk individuals [36, 42, 49].
- Performing OGTT in individuals with normal FPG and HbA1c but multiple risk factors allows the identification of those who would benefit most from diabetes prevention measures, such as nutritional guidance and physical activity. This can be useful for individual actions or government preventive programs. The accuracy of fasting, 1-hour and 2-hour plasma glucose in Oral Glucose Tolerance Test for identification of diabetes and prediabetes are described in Table 6.

R8: When an OGTT is indicated, the 1-h OGTT is RECOMMENDED over the 2 h-OGTT as it has superior accuracy in identifying prediabetes and T2D, with a lower cost and higher feasibility.

Class 1 Level B

- In 1979, the National Diabetes Data Group (NDDG) recommended intermediate glucose values during the 2 h-OGTT (30 min, 1 h, and 1.5 h) for diagnosing diabetes. Due to the impracticality of these intermediate measures and the satisfactory reproducibility and Se of the 2-h measurement for diagnosing T2D, the other points on the OGTT curve were abandoned. This decision was not based on the ability to predict prediabetes, future diabetes, or chronic diabetes complications [71, 72].
- More recently, studies have shown that the 1 h-OGTT has similar reproducibility to fasting glucose and the 2 h-OGTT, and it can identify individuals with diabetes and retinopathy similarly, as well as have good accuracy in identifying prediabetes and predicting the progression to T2D [73–76].
- Observational studies have examined the proportion of individuals with standard glucose tolerance (normal FPG and 2 h-OGTT) but with 1 h-OGTT values≥155 mg/dL across different ethnic groups. The prevalence ranged from 11 to 16% in young obese individuals and from 25 to 42% in high-risk populations. This group does not exhibit a completely normal glucose profile and represents an intermediate stage of metabolic dysfunction. In the RISC study, those with normal FPG and 2 h-OGTT but elevated 1 h-OGTT showed higher insulin resistance and progressed more frequently to IGT (determined by the 2 h-OGTT) over three years than others [4, 77].
- The 1 h-OGTT is superior to the 2 h-OGTT in detecting individuals at risk for developing T2D. In the San Antonio Heart Study, the glycemic profile of 1,611 Mexican Americans without diabetes was evaluated using the OGTT. The 1 h-OGTT had higher Se (75%) than FPG (31.6%) and the 2 h-OGTT (45.6%) for predicting T2D, and a higher positive predictive value (45.9%, 41.2%, and 39.1%, respectively) over a 7 to 8-year followup, though with lower Sp [61]. In this sample, 16.7% of normoglycemic individuals by FPG and 2 h-OGTT but with 1 h-OGTT≥155 mg/dL developed T2D within 7–8 years. The annual risk of T2D was significantly higher in individuals with 1 h-OGTT≥155 mg/dL than in others (2.2% vs. 0.39% per year) [61, 78]. The initial 1 h-OGTT was superior to the 2 h-OGTT and FPG as a predictor for the development of T2D.
- The 1 h-OGTT results in earlier detection of T2D and prediabetes, increasing the possibility of inter-

- vention and reducing the risk of complications. Most patients (74%) reach the cutoff for detecting T2D and prediabetes first with the parameters established for the 1 h-OGTT, compared to the 2 h-OGTT. In a study with 201 Native Americans, a glucose level \geq 209 mg/dL in the 1 h-OGTT was reached earlier than a glucose level \geq 200 mg/dL in the 2 h-OGTT (median of 1 year earlier) in people with T2D. The detection of prediabetes with a glucose level \geq 155 mg/dL in the 1 h-OGTT was also earlier than identifying a glucose level \geq 140 mg/dL in the 2 h-OGTT (median 1.6 years earlier) [79].
- The Botnia Prospective study, carried out in Finland with 2,603 subjects, has found that the 1 h-OGTT was superior to FPG and of 2 h-OGTT for detecting subjects at increased risk of developing T2D, with a Se of 75% and Sp of 73% and in predicting progression to T2D than FPG and the 2 h-OGTT, with a Se of 75% and Sp of 68%. The Se of FPG and the 2 h-OGTT were 55% and 56%, with 64% and 73% specificities, respectively. The 1 h-OGTT also outperformed a diabetes prediction model using multiple clinical risk factors and HbA1c [63]. A multicenter study combining the populations of the Botnia study (n=2,603) and Malmo Preventive Project (MPP) (n=2,386) identified the 1-h OGTT as the best predictor of T2D among 14 indices derived from the OGTT over a follow-up period of 5–23.5 years [63].
- Individuals who exhibit 1 h-OGTT≥155 mg/ dL (8.6 mmol/l) but two h-OGTT < 140 mg/dL (7.8 mmol/l) are at a significantly higher risk of developing diabetes and prediabetes compared to those with both 1 h-OGTT levels < 155 mg/dL (8.6 mmol/l) and 2 h-OGTT levels < 140 mg/dL (7.8 mmol/l). In the Israel Study of Glucose Intolerance, Obesity, and Hypertension (GOH Study), 1,970 people without diabetes were prospectively followed to assess the risk of diabetes. About 20 years after the initial assessment, the OR for diabetes in this high-risk group is 4.35 (95% CI: 2.50-7.73), and for prediabetes, the OR is 1.87 (95% CI: 1.09-3.26). These findings remain significant even after adjusting for sex, age, smoking status, BMI, blood pressure, FPG, and insulin levels [62].
- Based on these studies and the fact that the 1 h-OGTT is shorter than the 2 h-OGTT, providing greater practicality and potential economic advantage, the IDF expert committee recommended its preferential use for screening and diagnosing T2D [4]. Individuals with glucose ≥155 mg/dL in 1 h-OGTT without other glucose abnormalities could be a target for interventions to alter the natural progression of their condition and prevent the development of T2D, as well as its complications.

Important note:

Economic implications in adopting the 1 h-OGTT to detect prediabetes The primary prevention programs have demonstrated that lifestyle modification (LSM) is highly effective in delaying the onset of T2D and reducing associated morbidity in people with IGT. However, it is less effective in individuals with isolated IFG. The STOP DIABETES study has shown that LSM is effective in delaying the onset of T2D in people with prediabetes identified through a high 1 h-OGTT [80]. Andellini et al. conducted a health economic analysis using a Monte Carlo-based Markov simulation model to estimate the long-term cost-effectiveness of using the 1-h OGTT compared to the 2 h-OGTT for screening and assessing the risk of diabetes over 35 years. The primary outcome was the cost per quality-adjusted life year (QALY) gained. The base case model included 20,000 simulated patients over 35 years of follow-up. In the lifetime analysis, the 1 h-OGTT was projected to increase the number of years free from disease in 2 years per patient, delay the onset of T2D in 1 year per patient, to reduce the incidence of T2D complications (a 0.6 R per patient) and to increase the QALY gained (in 0.58 per patient). Even if the 1 h-OGTT diagnostic method resulted in higher initial costs associated with preventive treatment, long-term diabetes-related and complications costs were reduced, resulting in a lifetime saving of -31,225,719.82€. The incremental cost-effectiveness ratio was -8214.7€ per each QALY gained for the overall population. Therefore, screening for prediabetes with the 1 h-OGTT seems costeffective [81, 82]

Diagnosis of diabetes

R9: It IS RECOMMENDED to establish the diagnosis of diabetes mellitus when both FPG and HbA1c are respectively greater than or equal to 126 mg/dL and 6.5%.



Summary of evidence:

• In the Atherosclerosis Risk in Communities (ARIC) study, 12,268 participants (Caucasians and African-Americans) without a prior diabetes diagnosis were followed for 25 years to assess diabetes incidence. subgroups were prospectively analyzed (n=978): 1) those with confirmed diabetes (39%) according to both FPG and HbA1c criteria in the same sample and 2) those with only one abnormal test (61%). Confirmed cases showed moderate Se (54.9%) and high Sp (98.1%) for identifying new diabetes cases, which increased to 99.6% after 15 years. Confirmed diabetes cases were significantly associated with higher cardiovascular and renal disease incidence than unconfirmed cases. Prevalentdiagnosed diabetes was defined as self-reported physician diagnosis or current glucose-lowering medication use during follow-up. The authors concluded that confirming the diabetes diagnosis with two abnormal tests in a single sample had a high positive predictive value for subsequent diabetes diagnosis and was strongly associated with clinical outcomes, effectively identifying at-risk patients [69].

R10: If only one screening test for T2D meets diagnostic criteria, it is RECOMMENDED to perform an additional test, preferably repeating the abnormal test for confirmation.



Summary of evidence:

- Intra-individual variability of glycemic methods with a two-week interval between measurements was evaluated in 685 individuals over 20 years old without diabetes, included in NHANES III. The 2-h post-load glucose showed more significant variability (16.7%) compared to FPG (5.7%) and HbA1c (3.6%). The proportion of individuals with $FPG \ge 100 \text{ mg/dL}$, $FPG \ge 126 \text{ mg/dL}$, $FPG \ge 200 \text{ mg/dL}$ dL, 2-h post-load glucose≥140 mg/dL, 2-h postload glucose≥200 mg/dL, and HbA1c≥6.5% who had the same abnormality on the second result was 78%, 70.4%, 100%, 72%, 72%, and 83.3%, respectively. The prevalence of undiagnosed diabetes using only one FPG was 3.7%. With confirmation by a second sample, the prevalence was 2.8%, corresponding to a 24.4% reduction. For the 2-h OGTT, the prevalence of undiagnosed diabetes was 9% and 6.7%, with one or two abnormalities indicating a 26% reduction. These results suggest differences in diabetes prevalence estimates among epidemiological studies using one or two glycemic measurements [45].
- The diagnostic criteria for diabetes and prediabetes are described in Table 4.

R11: When typical hyperglycemic symptoms are present, it IS RECOMMENDED that the diagnosis of diabetes be established with a random plasma glucose greater than or equal to 200 mg/dL.



Summary of evidence:

 This panel suggests that to avoid delaying treatment initiation in acute situations, the diagnosis of DM can be established through random PG testing when typical symptoms of hyperglycemia are present, such as polyuria, polydipsia, and unexplained weight loss.

Follow up

R12: It IS RECOMMENDED that asymptomatic individuals with normal FPG and HbA1c and less than three risk factors, or low to moderate FINDRISC score, be re-evaluated at least every 3 years (Table 7).



R13: It IS RECOMMENDED that asymptomatic individuals with normal FPG and HbA1c but with three or more risk factors for diabetes or a high/very high FINDRISC score should also be re-evaluated at least after 12 months. (Table 7).



R14: It IS RECOMMENDED that after the initial screening for T2D, the re-evaluation of individuals with prediabetes be performed at least after 12 months (Table 7).



R15: After the initial screening for type 2 diabetes, it IS RECOMMENDED that individuals with only one laboratory test meeting the criteria for diabetes, without other abnormal tests, undergo re-evaluation at least after 6 months (Table 7).



Summary of evidence (recommendations 12–15):

- Evidence on the optimal screening interval for adults with initial normal laboratory results is limited. Cohort and modeling studies suggest that screening every 3 years may be a reasonable approach for adults with normal blood glucose levels. Therefore, we recommend a three-year interval for subsequent screening in people with < 3 risk factors or a low to moderate FINDRISC score. This frequency allows retesting possible false negatives before developing chronic complications [83, 84].
- A 12-month interval is suggested for individuals with prediabetes or average laboratory results but with ≥ 3 risk factors or a high/very high FINDRISC score, as they are more prone to developing T2D.

- Early re-evaluation in 6 to 12 months may be considered for those with prediabetes and test results close to diabetes diagnostic cutoffs. These individuals should be educated about the symptoms and signs associated with diabetes and advised to seek early medical care if they appear.
- A 6-month interval is suggested for individuals with one abnormal test to ensure timely diagnosis and intervention. This is the same testing frequency recommended by the 2023 Luso-Brazilian guidelines for individuals who already have diabetes, provided their condition is stable [85].
- These intervals may be shortened based on test availability and individualized decisions; however, extending the time between screenings is not recommended. A cost-benefit analysis of testing frequency is still lacking and should be conducted to determine the optimal testing frequency as a costeffective public health strategy.

Conclusions

Screening strategies for type 2 diabetes (T2D) are essential to prevent the development of diabetes-related chronic complications. This review presents the recommendations of the SBD for diagnosing diabetes and screening for T2D, considering the new approach from the IDF regarding the OGTT. The 1 h-OGTT was introduced to detect diabetes and prediabetes, with cutoff values of 209 mg/dL and 155 mg/dL, respectively. An algorithm has been provided to streamline the diagnostic process (Fig. 1), beginning with FPG and HbA1c. Universal screening is recommended starting at age 35, with earlier screening advised for high-risk individuals. Table 8 summarizes the final SBD recommendations for the diagnosis of diabetes and screening for T2D.

Table 7 Recommendations for follow-up in the screening for T2D

Clinical situation	Screening frequency
Asymptomatic individuals with only one criterium for diabetes	At least every 6 months
Prediabetes	At least once a year
Normal tests and 3 or more risk factors	At least once a year
Normal tests and FINDRISC high to very high	At least once a year
Normal tests and less than 3 risk factors	At least every 3 years
Normal tests and FIDRISC low to moderate	At least every 3 years

 Table 8
 Summary of recommendations

Recommendations	Class	Level
R1: Screening for diabetes in asymptomatic adults IS RECOMMENDED for all individuals aged 35 years or older; younger adults (between 18 and 34 years of age) with either overweight or obesity and any additional risk factor (Table 1); or individuals classified at high or very high risk of T2D, according to the Finnish Diabetes Risk Score (FINDRISC). R2: Screening for type 2 diabetes in asymptomatic children and adolescents IS RECOMMENDED after the age of 10 or after the onset of puberty (whichever comes first) in those who are overweight (BMI at 85th percentile or higher) or obese (BMI at the 95th percentile or higher) with, at least one additional risk factor (Table 2).	I	В
R3: For the diagnosis of T2D, it is RECOMMENDED to use Fasting Plasma Glucose (FPG), HbA1c, 1-hour OGTT or 2h-OGTT. The diagnostic criteria are FPG \geq 126 mg/dL, HbA1c \geq 6.5%, 1-hour OGTT glucose \geq 209 mg/dL, or 2-hour OGTT glucose \geq 200 mg/dL.	I	В
R4: For screening prediabetes or intermediate hyperglycemia, it is RECOMMENDED to use Fasting Plasma Glucose (FPG), HbA1c, 1-hour OGTT, or 2-hour OGTT. Prediabetes is defined as FPG between 100–125 mg/dL, HbA1c between 5.7–6.4%, 1-hour OGTT glucose between 155–208 mg/dL, or 2-hour OGTT glucose between 140–199 mg/dL.	1	В
R5: It is RECOMMENDED that the initial screening approach for diabetes be determined by FPG and HbA1c simultaneously in the same blood sample. Sequential testing may also be considered according to local availability, ease of access, and cost.	I	С

 Table 8 (continued)

R6: When diabetes cannot be diagnosed using FPG and HbA1c, or when these tests indicate prediabetes, the OGTT is RECOMMENDED to identify undetected cases of T2D or to assess the future risk of developing T2D.	1	В
R7: In individuals with normal FPG and HbA1c, with three or more risk factors for T2D, or with a high/very high FINDRISC score, the OGTT IS RECOMMENDED to further investigate for diabetes and prediabetes.	I	С
R8: When an OGTT is indicated, the 1-hour OGTT is RECOMMENDED over the 2h- OGTT as it has superior accuracy in identifying prediabetes and T2D, with a lower cost and higher feasibility.	I	В
R9: It IS RECOMMENDED to establish the diagnosis of diabetes mellitus when both FPG and HbA1c are respectively greater than or equal to 126 mg/dL and 6.5%.	I	В
R10: .If only one screening test for T2D meets diagnostic criteria, it is RECOMMENDED to perform an additional test, preferably repeating the abnormal test for confirmation.	I	В
R11: When typical hyperglycemic symptoms are present, it IS RECOMMENDED that the diagnosis of diabetes be established with a random plasma glucose greater than or equal to 200 mg/dL.	1	С
R12: It IS RECOMMENDED that asymptomatic individuals with normal FPG and HbA1c and less than three risk factors, or low to moderate FINDRISC score, be re - evaluated at least every 3 years (Table 7).	I	С

Table 8 (continued)

R13: It IS RECOMMENDED that asymptomatic individuals with normal FPG and HbA1c but with three or more risk factors for diabetes or a high/very high FINDRISC score should also be re-evaluated at least after 12 months. (Table 7).	I	С
R14: It IS RECOMMENDED that after the initial screening for T2D, the reevaluation of individuals with prediabetes be performed at least after 12 months (Table 7).	I	С
R15: After the initial screening for type 2 diabetes, it IS RECOMMENDED that individuals with only one laboratory test meeting the criteria for diabetes, without other abnormal tests, undergo re-evaluation at least after 6 months (Table 7).	I	С

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ADA	American Diabetes Association
ARIC	Atherosclerosis Risk in Communities
ARR	Absolute risk reduction
ASA	Acetylsalicylic acid
AUC	Area under the curve
BMI	Body mass index

CI Confidence interval DM Diabetes mellitus Diabetes Prevention Program DPP

Abbreviations

DPPOS Diabetes Prevention Program Outcomes Study

Diabetes Prevention Study DPS Fasting plasma glucose FPG **FINDRISC** Finnish Diabetes Risk Score Gestational diabetes

GDM HDL High-density lipoprotein HIV Human immunodeficiency virus HR Hazard ratio

HbA1c Hemoglobin A1c Fetal hemoglobin HbF

IDF International Diabetes Federation IFG Impaired fasting glucose IGT Impaired glucose tolerance Insulin resistance IR Lifestyle modification LSM NDDG National Diabetes Data Group

National Glycohemoglobin Standardization Program NGSP

NNS Number needed to screen NNT Number needed to treat

OD Odds ratio **OGTT** Oral glucose tolerance test

1 h-OGTT 1-Hour OGTT 2 h-OGTT 2-Hour OGTT

PG	Plasma glucose
QALY	Quality-adjusted life year
RCTs	Randomized clinical trials
Re	Relative risk reduction

SBD Sociedade Brasileira de Diabetes (Brazilian Diabetes

Society) Se Sensitivity Specificity. Sp T2D Type 2 diabetes

The Israel GOH Study Israel Study of Glucose Intolerance, Obesity, and

Hypertension

TODAY Treatment Options for Type 2 Diabetes in Adolescents

and Youth

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MR, LZ, CAN and RAC wrote the main manuscript text. WSSJ prepared the figure and tables. MCB reviewed and edited the whole manuscript. All authors reviewed the manuscript.

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References

- International Diabetes Federation. IDF Diabetes Atlas, 10th ed. Brussels, Belgium: international diabetes federation; 2021. https://diabetesatlas.org/.
- Tonaco LAB, Velasquez-Melendez G, Moreira AD, Andrade FCD, Malta DC, Felisbino-Mendes MS. Awareness of the diagnosis, treatment, and control of diabetes mellitus in Brazil. Rev Saude Publica. 2023;57:75.
- Bennett CM, Guo M, Dharmage SC. HbA(1c) as a screening tool for detection of Type 2 diabetes: a systematic review. Diabet Med. 2007;24(4):333–43.
- Bergman M, Manco M, Satman I, Chan J, Schmidt MI, Sesti G, et al. International diabetes federation position statement on the 1-hour post-load plasma glucose for diagnosing intermediate hyperglycemia and type 2 diabetes. Diab Res Clin Pract. 2024;209: 111589.
- Jonas DE, Crotty K, Yun JDY, Middleton JC, Feltner C, Taylor-Phillips S, et al. Screening for prediabetes and type 2 diabetes: updated evidence report and systematic review for the US preventive services task force. JAMA. 2021;326(8):744–60.
- Diabetes Prevention Program Research Group. Reduction in the incidence of type 2 diabetes with lifestyle intervention or metformin. N Engl J Med. 2002;346(6):393–403.
- Oliveira AF, Valente JG, Leite IC, Schramm JM, Azevedo AS, Gadelha AM. Cost-effectiveness of a national population-based screening program for type 2 diabetes: the Brazil experience. Diabetol Metab Syndr. 2010;2(1):14.
- 8. Herman WH, Ye W, Griffin SJ, Simmons RK, Davies MJ, Khunti K, et al. Costeffectiveness analysis of different screening strategies for type 2 diabetes. Diabetes Care. 2015;38(8):1795–803.
- 9. Chung S, Azar KM, Baek M, Lauderdale DS, Palaniappan LP. Reconsidering the age thresholds for type II diabetes screening in the US. Am J Prev Med. 2014;47(4):375–81.
- 10. Vigitel Brasil 2023: vigilância de fatores de risco e proteção para doenças crônicas por inquérito telefônico: estimativas sobre frequência e distribuição sociodemográfica de fatores de risco e proteção para doenças crônicas nas capitais dos 26 estados brasileiros e no Distrito Federal em 2023. Ministério da Saúde, Secretaria de Vigilância em Saúde e Ambiente, Departamento de Análise Epidemiológica e Vigilância de Doenças Não Transmissíveis. Brasília: Ministério da Saúde, 2023. 131 p. Disponível em: http://bvsms.saude.gov.br/bvs/publicacoes/vigitel_brasil_2023.pdf.
- Jesudason DR, Dunstan K, Leong D, Wittert GA. Macrovascular risk and diagnostic criteria for type 2 diabetes: implications for using FPG and HbA1c for cost-effective screening. Diabetes Care. 2003;26(2):485–90.
- Chatterjee R, Venkat Narayan KM, Lipscomb J, Phillips LS. Screening adults for prediabetes and diabetes may be cost-saving. Diabetes Care. 2010;33(7):1484–90.
- 13. Wilmot EG, Edwardson CL, Biddle SJ, Gorely T, Henson J, Khunti K, et al. Prevalence of diabetes and impaired glucose metabolism in younger'at

- risk' UK adults: insights from the STAND program of research. Diabet Med. 2013;30(6):671–5.
- 14. Lindström J, Tuomilehto J. The diabetes risk score: a practical tool to predict type 2 diabetes risk. Diabetes Care. 2003;26:725–31.
- Barim EM, McLellan KCP, Ribeiro RS, Carvalho JAM, Lindstrom J, Tuomilehto J, et al. Tradução e adaptação transcultural para o português brasileiro do Escore Finlandês de Risco de Diabetes (FINDRISC) e avaliação da confiabilidade. Rev Bras Epidemiol. 2020;23:E200060.
- Griffin SJ, Borch-Johnsen K, Davies MJ, Khunti K, Rutten GE, Sandbæk A, et al. Effect of early intensive multifactorial therapy on 5-year cardiovascular outcomes in individuals with type 2 diabetes detected by screening (ADDITION-Europe): a cluster-randomized trial. Lancet. 2011;378(9786):156–67.
- 17 American Diabetes Association. classification and diagnosis of diabetes: standards of medical care in diabetes—2025. Diabetes Care. 2025;48(Suppl. 1):527–49.
- 18. Dabelea D. Prevalence of type 1 and type 2 diabetes among children and adolescents from 2001 to 2009. JAMA. 2014;311(17):1778–86.
- Telo GH, Cureau FV, Szklo M, Bloch KV, Schaan BD. Prevalence of type 2 diabetes among adolescents in Brazil: findings from study of cardiovascular risk in adolescents (ERICA). Pediatr Diabetes. 2019;20(4):389–96.
- Van Name MA, Cheng P, Gal RL, Kollman C, Lynch J, Nelson B, et al. Children and adolescents with type 1 and type 2 diabetes mellitus in the pediatric diabetes consortium registries: comparing clinical characteristics and glycaemic control. Diabet Med. 2020;37(5):863–7.
- Copeland KC, Zeitler P, Geffner M, Guandalini C, Higgins J, Hirst K, et al. Characteristics of adolescents and youth with recent-onset type 2 diabetes: the TODAY cohort at baseline. J Clin Endocrinol Metab. 2011;96(1):159–67.
- Eriksson J, Franssila-Kallunki A, Ekstrand A, Saloranta C, Widén E, Schalin C, et al. Early metabolic defects in persons at increased risk for noninsulin-dependent diabetes mellitus. N Engl J Med. 1989;321(6):337–43.
- 23. Rosenbloom AL, Silverstein JH, Amemiya S, Zeitler P, Klingensmith GJ. Type 2 diabetes in children and adolescents. Pediatr Diabetes. 2009;10(Suppl. 12):17–32.
- 24. Eyzaguirre F, Bancalari R, Román R, Silva R, Youlton R, Urquidi C, et al. Prevalence of components of the metabolic syndrome according to birthweight among overweight and obese children and adolescents. J Pediatr Endocrinol Metab. 2012;25(1–2):51–6.
- 25. TODAY Study Group. Effects of metformin, rosiglitazone, and lifestyle in youth with type 2 diabetes. N Engl J Med. 2012;366(24):2247–56.
- Expert Committee on the Diagnosis and Classification of Diabetes Mellitus. Report of the expert committee on the diagnosis and classification of diabetes mellitus. Diabetes Care. 2003;26(Suppl 1):S5–20.
- Martínez-Vizcaíno V, Cavero-Redondo I, Álvarez-Bueno C, Rodríguez-Artalejo F. The accuracy of diagnostic methods for diabetic retinopathy: a systematic review and meta-analysis. PLoS ONE. 2016;11(4): e0154411.
- Ito C, Maeda R, Ishida S, Harada H, Inoue N, Sasaki H. Importance of OGTT for diagnosing diabetes mellitus based on prevalence and incidence of retinopathy. Diabetes Res Clin Pract. 2000;49(2–3):181–6.
- McCance DR, Hanson RL, Charles MA, Jacobsson LTH, Pettitt DJ, Bennett PH, et al. Comparison of tests for glycated hemoglobin and fasting and two-hour plasma glucose concentrations as diagnostic methods for diabetes. BMJ. 1994;308:1323–8.
- Zhang X, Gregg EW, Williamson DF, Barker LE, Thomas W, Bullard KM, et al. A1C level and future risk of diabetes: a systematic review. Diabetes Care. 2010;33(7):1665–73.
- 31. Engelgau MM, Thompson TJ, Herman WH, Boyle JP, Aubert RE, Kenny SJ, et al. Comparison of fasting and 2-hour glucose and HbA1c levels for diagnosing diabetes: diagnostic criteria and performance revisited. Diabetes Care. 1997;20:785–91.
- Colagiuri S, Lee CMY, Wong TY, Balkau B, Shaw JE, Borch-Johnsen K, et al. Glycemic thresholds for diabetes-specific retinopathy: implications for diagnostic criteria for diabetes. Diabetes Care. 2011;34(1):145–50.
- 33. Sabanayagam C, Liew G, Tai ES, Shankar A, Lim SC, Subramaniam T, et al. Relationship between glycated hemoglobin and microvascular

- complications: Is there a natural cutoff point for the diagnosis of diabetes? Diabetologia. 2009;52(7):1279–89.
- Massin P. Hemoglobin A1c and fasting plasma glucose levels as predictors of retinopathy at 10 years: the French DESIR study. Arch Ophthalmol. 2011;129(2):188.
- Emerging Risk Factors Collaboration, Sarwar N, Gao P, Seshasai SR, Gobin R, Kaptoge S, Di Angelantonio E, et al. Diabetes mellitus, fasting blood glucose concentration, and risk of vascular disease: a collaborative metaanalysis of 102 prospective studies. Lancet. 2010;375(9733):2215–22.
- 36 Bonora E, Tuomilehto J. The pros and cons of diagnosing diabetes with A1C. Diabetes Care. 2011;34(Suppl 2):S194.
- Gillett MJ. International expert committee report on the role of the A1c assay in the diagnosis of diabetes. Diabetes Care. 2009;32(7):1327–34.
- Selvin E, Steffes MW, Gregg E, Brancati FL, Coresh J. Performance of A1C for the classification and prediction of diabetes. Diabetes Care. 2011;34(1):84–9
- Kumar PR, Bhansali A, Ravikiran M, Bhansali S, Dutta P, Thakur JS, et al. Utility of glycated hemoglobin in diagnosing type 2 diabetes mellitus: a community-based study. J Clin Endocrinol Metab. 2010;95(6):2832–5.
- 40. Kramer CK, Araneta MRG, Barrett-Connor E. A1C, and diabetes diagnosis: the Rancho Bernardo study. Diabetes Care. 2010;33(1):101–3.
- 41 Bennett CM, Guo M, Dharmage SC. HbA1c as a screening tool for detection of type 2 diabetes: a systematic review. Diabet Med. 2007;24(4):333–43.
- Kaur G, Lakshmi PVM, Rastogi A, Bhansali A, Jain S, Teerawattananon Y, et al. Diagnostic accuracy of tests for type 2 diabetes and prediabetes: a systematic review and meta-analysis. PLoS ONE. 2020;15(11): e0242415.
- 43. Karter AJ, Parker MM, Moffet HH, Gilliam LK. Racial and ethnic differences in the association between mean glucose and hemoglobin A1c. Diabetes Technol Ther. 2023;25(10):697–704.
- Ziemer DC, Kolm P, Weintraub WS, Vaccarino V, Rhee MK, Twombly JG, et al. Glucose-independent, black-white differences in hemoglobin A1c levels: a cross-sectional analysis of 2 studies. Ann Intern Med. 2010:152(12):770–7.
- Selvin E. Short-term variability in measures of glycemia and implications for the classification of diabetes. Arch Intern Med. 2007;167(14):1545.
- Weykamp C. HbA1c: a review of analytical and clinical aspects. Ann Lab Med. 2013;33(6):393–400.
- Gonzalez A, Deng Y, Lane AN, Benkeser D, Cui X, Staimez LR, et al. Impact of mismatches in HbA1c vs glucose values on the diagnostic classification of diabetes and prediabetes. Diabet Med. 2020;37(4):689–96.
- 48. Ahuja V, Aronen P, Pramodkumar TA, Looker H, Chetrit A, Bloigu AH, et al. Accuracy of 1-hour plasma glucose during the oral glucose tolerance test in diagnosis of type 2 diabetes in adults: a meta-analysis. Diabetes Care. 2021;44(4):1062–9.
- 49. Barr RG, Nathan DM, Meigs JB, Singer DE. Tests of glycemia for the diagnosis of type 2 diabetes mellitus. Ann Intern Med. 2002;137:263–72.
- Shah AS, Zeitler PS, Wong J, Pena AS, Wicklow B, Arslanian S, Chang N, Fu J, Dabadghao P, Pinhas-Hamiel O, Urakami T, Craig ME, Craig ME.ISPAD Clinical Practice Consensus Guidelines. Type 2 diabetes in children and adolescents. Pediatr Diabetes. 2022;23(7):872–902.
- Kim MS, Jo DS, Lee DY. Comparison of HbA1c and OGTT for the diagnosis of type 2 diabetes in children at risk of diabetes. Pediatr Neonatol. 2019;60(4):428–34.
- Nowicka P, Santoro N, Liu H, Lartaud D, Shaw MM, Goldberg R, Guandalini C, Savoye M, Rose P, Caprio S. Utility of hemoglobin A1c for diagnosing prediabetes and diabetes in obese children and adolescents. Diabetes Care. 2011;34:1306–11.
- Vazquez L, Vazquez Arreola E, Hanson RL, Sinha M. Glycemic measures in childhood as predictors of future diabetes-related microvascular complications in an indigenous american population. Diabetes Care. 2023;46(9):1659–67.
- World Health Organization. Use of glycated haemoglobin (HbA1c) in the diagnosis of diabetes mellitus: abbreviated report of a WHO consultation. Geneva: World Health Organization; 2011.
- 55. Knowler WC, Hamman RF, Edelstein SL, Diabetes Prevention Program Research Group, et al. Prevention of type 2 diabetes with troglitazone in the diabetes prevention program. Diabetes. 2005;54(4):1150–6.
- Knowler WC, Barrett-Connor E, Fowler SE, Diabetes Prevention Program Research Group, et al. Reduction in the incidence of type 2 diabetes with lifestyle intervention or metformin. N Engl J Med. 2002;346(6):393–403.

- 57. Knowler WC, Fowler SE, Hamman RF, Diabetes Prevention Program Research Group, et al. 10-year follow-up of diabetes incidence and weight loss in the diabetes prevention program outcomes study. Lancet. 2009;374(9702):1677–86.
- 58 Lindström J, Peltonen M, Eriksson JG, Finnish Diabetes Prevention Study (DPS), et al. Improved lifestyle and decreased diabetes risk over 13 years: long-term follow-up of the randomised Finnish Diabetes Prevention Study (DPS). Diabetologia. 2013;56(2):284–93.
- Yudkin JS, Montori VM. Diagnosis and management of prediabetes. JAMA. 2023;329(1):78–91.
- Richter B, Hemmingsen B, Metzendorf MI, Takwoingi Y. Development of type 2 diabetes mellitus in people with intermediate hyperglycaemia. Cochrane Database Syst Rev. 2018;10(10):CD012661.
- Abdul-Ghani MA, Abdul-Ghani T, Ali N, DeFronzo RA. One-hour plasma glucose concentration and the metabolic syndrome identify subjects at high risk for future type 2 diabetes. Diabetes Care. 2008;31(8):1650–5.
- Bergman M, Chetrit A, Roth J, Jagannathan R, Sevick M, Dankner R.
 One-hour post-load plasma glucose level during the OGTT predicts dysglycemia: observations from the 24year follow-up of the Israel Study of glucose intolerance, obesity and hypertension. Diabetes Res Clin Pract. 2016;120:221–8.
- Alyass A, Almgren P, Akerlund M, Dushoff J, Isomaa B, Nilsson P, et al. Modelling of OGTT curve identifies 1 h plasma glucose level as a strong predictor of incident type 2 diabetes: results from two prospective cohorts. Diabetologia. 2015;58(1):87–97.
- 64. Fiorentino TV, Marini MA, Andreozzi F, Arturi F, Succurro E, Perticone M, Sciacqua A, Hribal ML, Perticone F, Sesti G. One-hour postload hyperglycemia is a stronger predictor of type 2 diabetes than impaired fasting glucose. J Clin Endocrinol Metab. 2015;100(10):3744–51.
- 65. Little RR, Rohlfing CL. The long and winding road to optimal HbA1c measurement. Clin Chim Acta. 2013;15(418):63–71.
- Carson AP, Reynolds K, Fonseca VA, Muntner P. Comparison of A1C and fasting glucose criteria to diagnose diabetes among US adults. Diabetes Care. 2010;33(1):95–7.
- NCD Risk Factor Collaboration (NCD-RisC). Global variation in diabetes diagnosis and prevalence based on fasting glucose and hemoglobin A1c. Nat Med. 2023;29(11):2885–901.
- Selvin E, Steffes MW, Zhu H, Matsushita K, Wagenknecht L, Pankow J, et al. Glycated hemoglobin, diabetes, and cardiovascular risk in nondiabetic adults. N Engl J Med. 2010;362(9):800v11.
- Selvin E, Wang D, Matsushita K, Grams ME, Coresh J. Prognostic implications of single-sample confirmatory testing for undiagnosed diabetes: a prospective cohort study. Ann Intern Med. 2018;169(3):156.
- Meijnikman AS, De Block CEM, Dirinck E, Verrijken A, Mertens I, Corthouts B, Van Gaal LF. Not performing an OGTT results in significant underdiagnosis of (pre)diabetes in a high risk adult Caucasian population. Int J Obes. 2017;41(11):1615–20.
- Rushforth NB, Bennett PH, Steinberg AG, Miller M. Comparison of the value of the two- and one-hour glucose levels of the oral GTT in the diagnosis of diabetes in Pima Indians. Diabetes. 1975;24(6):538–46.
- Bartoli E, Fra GP, CarnevaleSchianca GP. The oral glucose tolerance test (OGTT) revisited. Eur J Intern Med. 2011;22(1):8–12.
- Briker SM, Hormenu T, DuBose CW, Mabundo LS, Chung ST, Ha J, et al. Metabolic characteristics of Africans with normal glucose tolerance and elevated 1-hour glucose: insight from the Africans in America study. BMJ Open Diabetes Res Care. 2020;8(1): e000837.
- 74. Kasturi K, Onuzuruike AU, Kunnam S, Shomaker LB, Yanovski JA, Chung ST. Two- vs one-hour glucose tolerance testing: predicting prediabetes in adolescent girls with obesity. Pediatr Diabetes. 2019;20(2):154–9.
- Paddock E, Looker HC, Piaggi P, Knowler WC, Krakoff J, Chang DC.
 One-hour plasma glucose compared with two-hour plasma glucose in relation to diabetic retinopathy in American Indians. Diabetes Care. 2018;41(6):1212–7.
- Saunajoki A, Auvinen J, Saarela V, Uusitalo JJ, Leiviskä I, Keinänen-Kiukaanniemi S, et al. Association of glucose metabolism and retinopathy signs in non-diabetic individuals in midlife-The Northern Finland Birth Cohort 1966 study. PLoS ONE. 2020;22:15.
- Manco M, Panunzi S, Macfarlane DP, Golay A, Melander O, Konrad T, et al. One-hour plasma glucose identifies insulin resistance and β-cell dysfunction in individuals with Normal glucose tolerance: cross-sectional

- data from the relationship between insulin sensitivity and cardiovascular risk (RISC) study. Diabetes Care. 2010;33(9):2090–7.
- Abdul-Ghani MA, Abdul-Ghani T, Stern MP, Karavic J, Tuomi T, Bo I, et al. Two-step approach for the prediction of future type 2 diabetes risk. Diabetes Care. 2011;34(9):2108–12.
- Ha J, Chung ST, Bogardus C, Jagannathan R, Bergman M, Sherman AS. One-hour glucose is an earlier marker of dysglycemia than two-hour glucose. Diabetes Res Clin Pract. 2023;203: 110839.
- STOP-NIDDM Trial Research Group. Acarbose for prevention of type 2 diabetes mellitus: The STOP-NIDDM randomized trial. Lancet. 2002;359(9323):2072–7.
- 81. Andellini M, Ferrario M, Mantovani LG. Health economic analysis of 1-hour vs 2-hour oral glucose tolerance test (OGTT) for screening and assessing risk of type 2 diabetes: a Monte Carlo-based Markov simulation model. Diabetologia. 2021;64(9):1854–62.
- 82. DECODE Study Group, on behalf of the European Diabetes Epidemiology Study Group. Will new diagnostic criteria for diabetes mellitus change the phenotype of patients with diabetes? Reanalysis of European epidemiological data. DECODE Study Group on behalf of the European Diabetes Epidemiology Study Group. BMJ. 1998; 317(7155): 371–5.
- Kato M, Noda M, Suga H, Matsumoto M, Kanazawa Y. Fasting plasma glucose and incidence of diabetes—implication for the threshold for impaired fasting glucose: results from the population-based Omiya MA cohort study. J Atheroscler Thromb. 2009;16(6):857–61.
- 84. Johnson SL, Tabaei BP, Herman WH. The efficacy and cost of alternative strategies for systematic screening for type 2 diabetes in the US population 45–74 years of age. Diabetes Care. 2005;28(2):307–11.
- 85. Bertoluci MC, Silva Júnior WS, Valente F, Araujo LR, Lyra R, de Castro JJ, Raposo JF, Miranda PAC, Boguszewski CL, Hohl A, Duarte R, Salles JEN, Silva-Nunes J, Dores J, Melo M, de Sá JR, Neves JS, Moreira RO, Malachias MVB, Lamounier RN, Malerbi DA, Calliari LE, Cardoso LM, Carvalho MR, Ferreira HJ, Nortadas R, Trujilho FR, Leitão CB, Simões JAR, Dos Reis MIN, Melo P, Marcelino M, Carvalho FD. 2023 UPDATE: Luso-Brazilian evidence-based guideline for the management of antidiabetic therapy in type 2 diabetes. Diabetol Metab Syndr. 2023;15(1):160. https://doi.org/10.1186/s13098-023-01121-x.

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