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Clinical Practice Guidelines

Screening for Type 1 and Type 2 Diabetes

Canadian Diabetes Association Clinical Practice Guidelines Expert Committee

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KEY MESSAGES

- In the absence of evidence for interventions to prevent or delay type 1 diabetes, screening for type 1 diabetes is not recommended.
- Screening for type 2 diabetes using a fasting plasma glucose (FPG) and/or glycated hemoglobin (A1C) should be performed every 3 years in individuals ≥40 years of age or in individuals at high risk using a risk calculator.
- Diabetes will be diagnosed if A1C is ≥6.5% (see Definition, Classification and Diagnosis chapter, p. S8).
- Testing with a 2-hour plasma glucose (2hPG) in a 75 g oral glucose tolerance test (OGTT) should be undertaken in individuals with an FPG of 6.1–6.9 mmol/L and/or an A1C of 6.0%–6.4% in order to identify individuals with impaired glucose tolerance (IGT) or diabetes.
- Testing with a 2hPG in a 75 g OGTT may be undertaken in individuals with an FPG 5.6–6.0 mmol/L and/or A1C 5.5%–5.9% and ≥1 risk factor in order to identify individuals with IGT or diabetes.

The clinical spectrum of diabetes ranges from a low-risk to a higher-risk individual or to the symptomatic patient who needs immediate treatment. Screening for diabetes implies testing for diabetes in individuals without symptoms who are unaware of their condition. Screening for diabetes will also detect individuals at increased risk for diabetes (prediabetes) or individuals with less severe states of dysglycemia who may still be at risk for type 2 diabetes. Screening strategies vary according to the type of diabetes and evidence of effective interventions to prevent progression of prediabetes to diabetes and/or reduce the risk of complications associated with diabetes. The growing importance of diabetes screening is undeniable (1).

In contrast to other diseases, there is no distinction between screening and diagnostic testing. Therefore, to screen for diabetes and prediabetes, the same tests would be used as for diagnosis of both medical conditions (see Definition, Classification and Diagnosis chapter, p. S8).

Screening for Type 1 Diabetes

Type 1 diabetes mellitus is primarily a result of pancreatic beta cell destruction due to an immune-mediated process that is likely incited by environmental factors in genetically predisposed individuals. An individual's risk of developing type 1 diabetes can be estimated by considering family history of type 1 diabetes with attention to age of onset and sex of the affected family members (2) and profiling immunity and genetic markers (3). The loss of pancreatic beta cells in the development of type 1 diabetes passes through a subclinical prodrome that can be detected reliably in first- and second-degree relatives of persons with type 1 diabetes by the presence of pancreatic islet autoantibodies in their sera (4). However, in a recent large study, one-time screening for glutamic acid decarboxylase antibodies (GADAs) and islet antigen-2 antibodies (IA-2As) in the general childhood population in Finland would identify 60% of those individuals who will develop type 1 diabetes over the next 27 years. Initial positivity for GADAs and/or IA-2As had a sensitivity of 61% (95% confidence interval [CI] 36–83%) for type 1 diabetes. The combined positivity for GADAs and IA-2As had both a specificity and a positive predictive value of 100% (95% CI 59–100%) (5). Ongoing clinical studies are testing different strategies for preventing or reversing early type 1 diabetes in the presence of positive autoimmunity. Given that the various serological markers are not universally available and in the absence of evidence for interventions to prevent or delay type 1 diabetes, no widespread recommendations for screening for type 1 diabetes can be made.

Screening for Type 2 Diabetes

Adults

Undiagnosed type 2 diabetes may occur in >2.8% of the general adult population (6), and the number increases to >10% in some populations (7,8). Tests for hyperglycemia can identify these individuals, many of whom will have, or will be at risk for, preventable diabetes complications (5,6). To be effective, population-based screening would have to involve wide coverage and would have the goal of early identification and subsequent intervention to reduce morbidity and mortality. Using various multistaged screening strategies, the ADDITION-Europe study showed that 20% to 94% of eligible people in primary care practices attended the first blood glucose test of the screening process, and diabetes was detected in 0.33% to 1.09% of the target populations, which was lower than expected (9). In the subsequent ADDITION-Europe cluster randomized trial of intensive multifaceted cardiovascular risk factor management vs. routine diabetes care among screening-identified type 2 diabetes patients, intensive management did not reduce cardiovascular events (hazard ratio 0.83; 95% CI 0.65–1.05) or all-cause mortality (hazard ratio 0.91;

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Table 1
Risk factors for type 2 diabetes

- Age ≥40 years
- First-degree relative with type 2 diabetes
- Member of high-risk population (e.g. Aboriginal, African, Asian, Hispanic or South Asian descent)
- History of prediabetes (IGT, IFG or A1C 6.0%–6.4%)*
- History of gestational diabetes mellitus
- History of delivery of a macrosomic infant
- Presence of end organ damage associated with diabetes:
  - Microvascular (retinopathy, neuropathy, nephropathy)
  - Macrovascular (coronary, cerebrovascular, peripheral)
- Presence of vascular risk factors:
  - HDL cholesterol level <1.0 mmol/L in males, <1.3 mmol/L in females*
  - Triglycerides ≥1.7 mmol/L*
  - Hypertension*
  - Overweight*
  - Abdominal obesity*
- Presence of associated diseases:
  - Polycystic ovary syndrome*
  - Acanthosis nigricans*
  - Psychiatric disorders (bipolar disorder, depression, schizophrenia†)
  - HIV infection‡
  - OSA§
- Use of drugs associated with diabetes:
  - Glucocorticoids
  - Atypical antipsychotics
  - HAART‡
  - Other (see Appendix 1)
- Other secondary causes (see Appendix 1)

A1C, glycated hemoglobin; *HAART,* highly active antiretroviral therapy; *HDL,* high-density lipoprotein; *HIV,* human immunodeficiency virus-1; *IFG,* impaired fasting glucose; *IGT,* impaired glucose tolerance; *OSA,* obstructive sleep apnea.

* Associated with insulin resistance.

† The incidence of type 2 diabetes is at least 3 times higher in people with schizophrenia than in the general population (25,26). Using data collected in 1991, the prevalence of diabetes was assessed in >20,000 individuals diagnosed with schizophrenia. The rate of diagnosed diabetes was 9% to 14%, exceeding rates for the general population prior to the widespread use of new antipsychotic drugs (27).

‡ HIV and HAART increase the risk of prediabetes (IGT) and type 2 diabetes by 1.5- to 4-fold compared to the general population (28).

§ OSA is an independent risk factor for diabetes (hazard ratio 1.43) (29).

95% CI 0.69–1.21) (10). Of note, a very high proportion of the routine care group also received optimal cardiovascular risk factor management, which may have diluted any potential benefits. In ADDITION-Cambridge, population-based screening for type 2 diabetes was not associated with a reduction in all-cause, cardiovascular or diabetes-related mortality within 10 years compared to a no-screening control group. However, the low rate of type 2 diabetes in the screened population (3%) was likely too small to affect overall population mortality (11). Nonetheless, there is no current evidence of clinical benefit to support a strategy of population-based screening for type 2 diabetes.

Although the relatively low prevalence of diabetes in the general population makes it unlikely that mass screening will be cost effective, testing for diabetes in people with risk factors for type 2 diabetes or with diabetes-associated conditions is likely to result in more benefit than harm and will lead to overall cost savings (12–17). Routine testing for type 2 diabetes is, therefore, justifiable in some but not all settings (18,19). Screening individuals as early as age 40 years in family physicians' offices has proved to be useful in detecting unrecognized diabetes (20).

While fasting plasma glucose (FPG) and/or glycated hemoglobin (A1C) are the recommended screening tests, a 75 g oral glucose tolerance test (OGTT) is indicated when the FPG is 6.1 to 6.9 mmol/L (14) and/or A1C is 6.0% to 6.4%. It may be indicated when the FPG is 5.6 to 6.0 mmol/L and/or A1C is 5.5% to 5.9% and suspicion of type 2 diabetes or impaired glucose tolerance (IGT) is high (e.g. for individuals with risk factors listed in Table 1) (Figure 1).

People with prediabetes, especially those with IGT or an A1C of 6.0% to 6.4%, not only are at increased risk of developing type 2 diabetes, but they also have an increased risk of macrovascular complications, particularly in the context of the metabolic syndrome (21). These individuals would benefit from cardiovascular risk factor reduction strategies (1). Members of high-risk ethnic populations (Table 1) should be screened for prediabetes and type 2 diabetes using the recommended screening tests, such as FPG, OGTT and A1C. However, the high prevalence of hemoglobinopathies among these populations may considerably reduce the accuracy of A1C as a reliable screening tool in these populations. Furthermore, high-risk ethnic groups may have A1C levels that are slightly higher than those of Caucasians at the same level of glycemia, and more studies may help determine ethnic-specific A1C thresholds for diabetes diagnosis (see Definition, Classification and Diagnosis chapter, p. S8).

Risk prediction tools for type 2 diabetes mellitus

A number of risk scores based on clinical characteristics have been developed to identify individuals at high risk of having undiagnosed diabetes. However, the impact of known risk factors

RECOMMENDATIONS

1. All individuals should be evaluated annually for type 2 diabetes risk on the basis of demographic and clinical criteria [Grade D, Consensus].

2. Screening for diabetes using FPG and/or A1C should be performed every 3 years in individuals ≥40 years of age or at high risk using a risk calculator [Grade D, Consensus]. More frequent and/or earlier testing with either FPG and/or A1C or 2hPG in a 75 g OGTT should be considered in those at very high risk using a risk calculator or in people with additional risk factors for diabetes [Grade D, Consensus]. These risk factors include:
   - First-degree relative with type 2 diabetes
   - Member of high-risk population (e.g. Aboriginal, African, Asian, Hispanic or South Asian descent)
   - History of prediabetes (IGT, IFG, or A1C 6.0%–6.4%)
   - History of gestational diabetes mellitus
   - History of delivery of a macrosomic infant
   - Presence of end organ damage complications associated with diabetes:
     - Microvascular (retinopathy, neuropathy, nephropathy)
     - Macrovascular (coronary, cerebrovascular, peripheral)
   - Presence of vascular risk factors:
     - HDL cholesterol <1.0 mmol/L in males, <1.3 mmol/L in females
     - Triglycerides ≥1.7 mmol/L
     - Hypertension
     - Overweight
     - Abdominal obesity
   - Presence of associated diseases:
     - Polycystic ovary syndrome
     - Acanthosis nigricans
     - Obstructive sleep apnea
     - Psychiatric disorders (bipolar disorder, depression, schizophrenia)
     - HIV infection
   - Use of drugs associated with diabetes:
     - Glucocorticoids
     - Atypical antipsychotics
     - HAART
     - Other (see Appendix 1)
   - Other secondary causes (see Appendix 1)

3. Testing with 2hPG in a 75 g OGTT should be undertaken in individuals with FPG 6.1–6.9 mmol/L and/or A1C 6.0%–6.4% in order to identify individuals with IGT or diabetes [Grade D, Consensus].

4. Testing with 2hPG in a 75 g OGTT may be undertaken in individuals with FPG 5.6–6.0 mmol/L and/or A1C 5.5%–5.9% and ≥1 risk factor(s) in order to identify individuals with IGT or diabetes [Grade D, Consensus].

Abbreviations:
2hPG, 2-hour plasma glucose; *A1C,* glycated hemoglobin; *FPG,* fasting plasma glucose; *HAART,* highly active antiretroviral therapy; *HDL,* high-density lipoprotein; *HIV,* human immunodeficiency virus-1; *IFG,* impaired fasting glucose; *IGT,* impaired glucose tolerance; *OGTT,* oral glucose tolerance test.

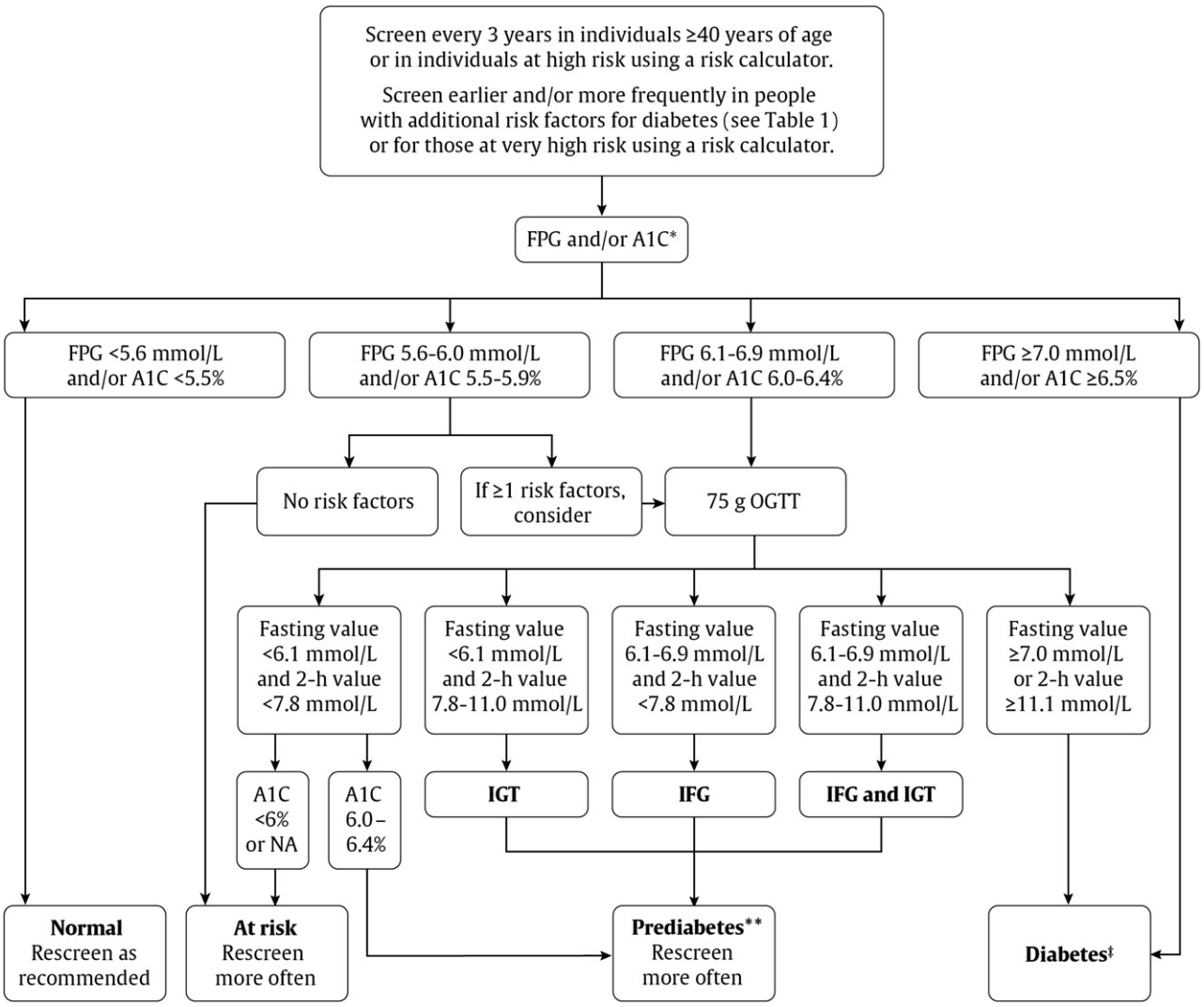

Figure 1. Screening and diagnosis algorithm for type 2 diabetes.
*If both fasting plasma glucose (FPG) and glycated hemoglobin (A1C) are available but discordant, use the test that appears furthest to the right side of the algorithm. **Prediabetes = impaired fasting glucose (IFG), impaired glucose tolerance (IGT), or A1C 6.0% to 6.4% (see Table 4 in Definition, Classification and Diagnosis of Diabetes, Prediabetes and Metabolic Syndrome, p. S8). ‡In the absence of symptomatic hyperglycemia, if a single laboratory test is in the diabetes range, a repeat confirmatory test (FPG, A1C, 2hPG in a 75 g OGTT) must be done on another day. It is preferable that the same test be repeated (in a timely fashion) for confirmation. If results of 2 different tests are available and both are above the diagnostic cutpoints, the diagnosis of diabetes is confirmed. NA = not available; OGTT = oral glucose tolerance test.

on having undiagnosed type 2 diabetes differs between populations of different ethnic origins, and risk scores developed in Caucasian populations cannot be applied to populations of other ethnic groups (22). Furthermore, the prevalence of individuals at risk for developing type 2 diabetes varies considerably according to the scoring system. Risk scoring systems must, therefore, be validated for each considered population in order to adequately detect individuals at risk and eventually implement efficacious preventative strategies (23). The Canadian Diabetes Risk Assessment Questionnaire (CANRISK) is a statistically valid tool that may be suitable for diabetes risk assessment in the Canadian population and is available on the Internet at www.phac-aspc.gc.ca/cd-mc/diabetes-diabete/canrisk/index-eng.php (24).

Other Relevant Guidelines

Definition, Classification and Diagnosis of Diabetes, Prediabetes and Metabolic Syndrome, p. S8
Reducing the Risk of Developing Diabetes, p. S16
Type 1 Diabetes in Children and Adolescents, p. S153
Type 2 Diabetes in Children and Adolescents, p. S163

Relevant Appendix

Appendix 1. Etiologic Classification of Diabetes Mellitus

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