Defining and diagnosing type 2 diabetes

Recommendations

Recommendation	Reference	Grade*
Individuals who are not at high risk of type 2 diabetes should be screened for risk of diabetes every three years from 40 years of age using the Australian type 2 diabetes risk assessment tool (AUSDRISK)	1 NHMRC, 2009	C
Aboriginal and Torres Strait Islander people should be screened annually with blood testing (fasting plasma glucose, random venous glucose or glycated haemoglobin [HbA1c]) from 18 years of age	2 RACGP and NACCHO, 2018	Good Practice Point
Individuals with any one of the following risk factors: • AUSDRISK score of ≥12 • all people with a history of a previous cardiovascular event (acute myocardial infarction or stroke) • women with a history of gestational diabetes mellitus • women with polycystic ovary syndrome • patients on antipsychotic drugs should be screened		
• with fasting blood glucose (FBG) or HbA1c	1 NHMRC, 2009	B
• every three years	1 NHMRC, 2009	C
Individuals with impaired glucose tolerance test or fasting glucose (not limited by age) should be screened:		
• with FBG or HbA1c	1 NHMRC, 2009	B
• every 12 months	1 NHMRC, 2009	C

*Refer to 'Explanation and source of recommendations' for explanations of the levels and grades of evidence.

Defining type 2 diabetes

Diabetes is a group of disorders and the 10th leading cause of death in Australia.[3] There are four clinical classes of diabetes:[4]

- **type 1 diabetes** – results from ß-cell destruction due to an autoimmune process usually leading to insulin deficiency
- **type 2 diabetes** – results from a progressive insulin secretory defect on the background of insulin resistance
- **gestational diabetes mellitus (GDM)** – defined as glucose intolerance with onset or first recognition during pregnancy
- **other specific types of diabetes** – for example, monogenic diabetes and diabetes secondary to other causes (refer below).

Type 2 diabetes is a chronic and progressive medical condition that results from two major metabolic dysfunctions: insulin resistance followed by pancreatic islet cell dysfunction, causing a relative insulin deficiency. These occur due to modifiable lifestyle-related risk factors interacting with non-modifiable and genetic risk factors.[5]

The relative insulin deficiency leads to chronic hyperglycaemia and multiple disturbances in carbohydrate, protein and fat metabolism.[5]

Who is at risk of type 2 diabetes?

Type 2 diabetes is the most common form of diabetes in Australia. Five per cent of adults have a diagnosis of type 2 diabetes, although this is likely to be an underestimate of the true prevalence.[6] Additionally, almost one in six adults are affected by impaired glucose tolerance (IGT) or impaired fasting glucose (IFG).[3]

Clinical suspicion for type 2 diabetes needs to remain high, as type 2 diabetes is often asymptomatic and is increasingly developing in younger people (refer to the section 'Early-onset type 2 diabetes').[4] Causes of secondary diabetes, such as diseases of the exocrine pancreas (eg pancreatic cancer, cystic fibrosis, haemochromatosis), metabolic, or drug-induced causes (eg treatment of human immunodeficiency virus [HIV]), should also be considered in the presence of symptoms suggestive of diabetes.[3]

Type 2 diabetes in specific populations

There is a higher prevalence of type 2 diabetes among Australians from lower socioeconomic backgrounds compared with higher socioeconomic groups,[6] and certain ethnic groups are more at risk: people with Pacific Islander, Southern European or Asian backgrounds are more than twice as likely as other Australians to develop diabetes within five years.[7]

Aboriginal and Torres Strait Islander people are almost four times more likely to have diabetes than non-Indigenous Australians,[6] and type 2 diabetes is a direct or indirect cause of 20% of Aboriginal and Torres Strait Islander people deaths.[8] Furthermore, the average age of diabetes onset is younger for Aboriginal and Torres Strait Islander people than non-Indigenous Australians,[9] and in some populations, Aboriginal children and adolescents have rates of type 2 diabetes that are 6–20 times higher than non-Indigenous youth.[10]

Assessing diabetes risk

Patients should be assessed for diabetes risk every three years from 40 years of age using the Australian type 2 diabetes risk assessment tool (AUSDRISK; Table 1).[1]

Aboriginal and Torres Strait Islander point

Given the high background prevalence of type 2 diabetes in Aboriginal and Torres Strait Islander adults, AUSDRISK has limited use as a screening tool in this population.

Aboriginal or Torres Strait Islander people should instead proceed directly to blood testing for diabetes, in conjunction with other opportunistic screening (such as for cardiovascular risk assessment) from 18 years of age.[2]

An AUSDRISK score of ≥12 or more is considered 'high risk' for developing type 2 diabetes (Table 1). The following people are also considered at high risk, **regardless** of AUDRISK score:[1,11]

- people aged ≥40 years who are overweight or obese
- people of any age with IGT or IFG
- people with a first-degree relative with diabetes
- all patients with a history of a cardiovascular event (eg acute myocardial infarction, angina, peripheral vascular disease or stroke)
- people of high-risk ethnicity/background (eg Pacific Islands, Indian subcontinent)
- women with a history of GDM
- women with polycystic ovary syndrome (PCOS)
- people taking antipsychotic medication
- Aboriginal and/or Torres Strait Islander people.

It is recommended that all patients at high risk are tested every three years for diabetes with either FBG or HbA1c (refer to 'Diagnosing diabetes in asymptomatic patients').[1,11] People with IGT or IFG should be tested annually.[1] For recommended management of people at high risk of developing diabetes, refer to the section 'Preventing progression to type 2 diabetes'.

Refer to the section 'Type 2 diabetes, reproductive health and pregnancy' for recommendations on screening in pregnancy.

Aboriginal and Torres Strait Islander point

Aboriginal and Torres Strait Islander adults who are obese are seven times as likely as those of normal weight or underweight to have diabetes (17% compared with 2.4%).[2]

The AusDiab study found that body mass index (BMI), waist circumference and waist-to-hip ratio all had similar correlations with diabetes and cardiovascular disease (CVD) risk.[12] However, a later study of diabetes risk in an Aboriginal community found that in women, central obesity (defined as waist circumference ≥88 cm) or BMI ≥25 kg/m^2 were better predictors of type 2 diabetes and CVD risk; many women with 'normal' BMIs were found to be centrally obese. For men, a BMI ≥25 kg/m^2 was a better predictor than BMI ≥30 or waist circumference ≥102 cm.[13]

Table 1. AUSDRISK tool for assessing type 2 diabetes risk[7]

AUSDRISK score	Risk of developing type 2 diabetes within five years*
≤5	1 in 100
6–8	1 in 50
9–11	1 in 30
12–15	1 in 14
16–19	1 in 7
≥20	1 in 3

*The overall score may overestimate the risk of diabetes in those aged <25 years and underestimate the risk in Aboriginal and Torres Strait Islander people.[1]

Impaired fasting glucose and impaired glucose tolerance

The definition of diabetes is based on a collection of symptoms and agreed glycaemic measures associated with escalating retinopathy risk. Patients with elevated glucose not high enough to be diagnosed with type 2 diabetes might have either IFG or IGT, also known as 'dysglycaemic states' or 'intermediate hyperglycaemia'. IFG is identified by a FBG test, and IGT can be identified by a two-hour oral glucose tolerance test (OGTT) – refer to Figure 1.[14]

These states are not considered benign, and they reflect a risk of developing diabetes in the future; however, IFG and IGT have been shown to regress over three years in 18% of cases, if patients follow standard (ie non-intensive) lifestyle recommendations.[15]

As CVD risk is distributed across a continuum of post-challenge glucose levels, any degree of post-challenge hyperglycaemia may be associated with the development of premature CVD.[16]

Refer also to the section 'Preventing progression to type 2 diabetes'.

Diagnosing type 2 diabetes

Three laboratory tests can be used to diagnose type 2 diabetes:

- FBG
- HbA1c
- OGTT.

Notes about the use of each in making a diagnosis can be found in Table 2.

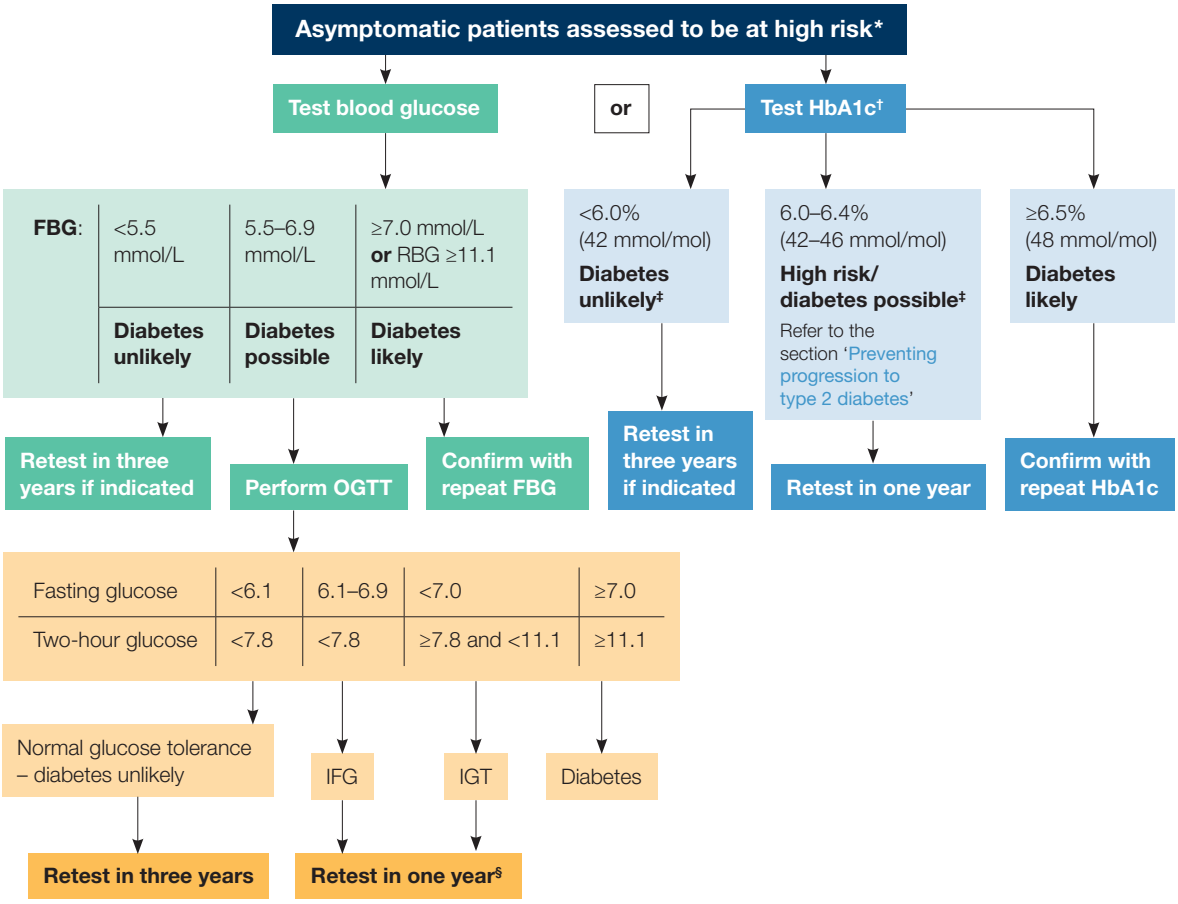
Diagnostic criteria differ depending on whether a patient is symptomatic or asymptomatic (refer below). Asymptomatic patients should be assessed for diabetes risk prior to testing, and screened as shown in Figure 1.

Table 2. Diagnostic tests for type 2 diabetes

Diagnostic method	Use when diagnosing diabetes	Further notes
FBG	Fasting (eight hours)	May also be used to detect IFG
HbA1c	Non-fasting Abnormal HbA1c values generally should be repeated in asymptomatic patients and confirmed on a different day, unless two abnormal tests (eg FBG and HbA1c) are already available from the same day Note that HbA1c may lack accuracy (specificity and/or sensitivity) in the following cases, in which FBG or OGTT may assist diagnosis: • acute-onset glycaemic states such as post-traumatic type 2 diabetes (eg pancreatitis), rapid onset of glycaemia with sepsis and steroid use, etc • within four months post-partum • people with haemoglobinopathy or haemolysis, or advanced chronic kidney disease • people with iron deficiency (artificially elevated) • people who have recently had a blood or iron transfusion[17,18]	Not useful for assessment of IGT Threshold of 6.5% (48 mmol/mol) is linked to escalating microvascular disease, and HbA1c is a better predictor of macrovascular disease than FBG and two-hour post-glucose[19,20]
OGTT	Fasting (eight hours) 75 g glucose administered orally Blood is collected from a fasting venous sample and two-hour post-glucose challenge venous sample	Only method able to detect IGT. May concurrently detect IFG

FBG, fasting blood glucose; HbA1c, glycated haemoglobin; IFG, impaired fasting glucose; IGT, impaired glucose tolerance; OGTT, oral glucose tolerance test

Figure 1. Screening and diagnosing type 2 diabetes in asymptomatic people[1,21–23]



FBG, fasting blood glucose; HbA1c, glycated haemoglobin; IFG, impaired fasting glucose; IGT, impaired glucose tolerance; OGTT, oral glucose tolerance test; RBG, random blood glucose

Note: IGT and IFG cannot be diagnosed using HbA1c.

*Using AUSDRISK (score ≥12) or in specific high-risk categories

†Medicare Benefits Schedule (MBS) item number 66841 allows for diagnostic use only, once every 12 months. The request slip should be annotated as HbA1c or for Service Incentive Payment (SIP) and Practice Incentives Program (PIP) purposes. However, a confirmatory HbA1c test (MBS item number 66551) should be ordered before treatment initiation[21]

‡HbA1c results <6.5% do not exclude diabetes diagnosed by glucose tests[21]

§If confirmatory test is negative, repeat assessment one year or earlier if symptomatic

Diagnosing diabetes in symptomatic patients

The presence of symptoms suggestive of hyperglycaemia (refer below to 'Clinical symptoms suggestive of diabetes') with **one of the following** is confirmatory of a diagnosis of diabetes:

- a patient presenting with hyperglycaemic crisis
- a single elevated FBG ≥7.0 mmol/L
- single HbA1c ≥6.5%
- a random blood glucose ≥11.1 mmol/L.

A second laboratory test is not required to confirm the diagnosis, unless diagnostic uncertainty remains.

Clinical symptoms suggestive of diabetes

Symptoms of diabetes include:

- lethargy, polyuria, polydipsia
- frequent fungal or bacterial infections
- blurred vision
- loss of sensation (ie touch, vibration, cold)
- poor wound healing
- weight loss.

Clinical signs of insulin resistance

Signs of insulin resistance may include the following:[24]

- **Acanthosis nigricans** – typically characterised by hyperpigmentation (darkening of skin pigment) and usually accompanied by a velvety change in texture of the affected skin. Common sites are the neck and axillae.
- **Skin tags** – benign (non-cancerous) skin growths on the body or face. They can be smooth or wrinkled, skin-coloured or just slightly darker than skin colour and can vary in size.
- **Central obesity** – defined by a high waist-to-hip ratio, waist-to-thigh ratio and waist circumference.
- **Hirsutism** – excess facial and body hair, particularly on women.

Box 1 provides information about testing insulin levels.

Box 1. Testing insulin levels to assess insulin resistance

- There is no role for routinely testing insulin levels to assess insulin resistance in IGT, IFG or in the evaluation of type 2 diabetes.
- Patients with signs of insulin resistance should be screened for diabetes with FBG or HbA1c.

Diagnosing diabetes in asymptomatic patients

People who do not have symptoms of hyperglycaemia but who fall in the high-risk categories cited above, or people for whom there is clinical suspicion of diabetes, should be tested using FBG, HbA1c or OGTT (Box 2).

A second concordant laboratory result is required to confirm a diagnosis of diabetes in asymptomatic patients (Figure 1). It is recommended that the same laboratory test be repeated, using a new blood sample, for a greater likelihood of concurrence.

Box 2. Diagnostic criteria for type 2 diabetes in asymptomatic patients

- HbA1c ≥6.5% (48 mmol/mol) on two separate occasions

or

- FBG ≥7.0 mmol/L or random blood glucose ≥11.1 mmol/L confirmed by a second abnormal FBG on a separate day

or

- OGTT before (fasting) and two hours after an oral 75 g glucose load is taken. Diabetes is diagnosed as FBG ≥7.0 mmol/L or two-hour post-challenge blood glucose ≥11.1 mmol/L

These tests are undertaken on venous blood samples.

Discordant testing

Due to the different physiological measures of glycaemia, confirmatory tests at times may give discordant results, especially if the second diagnostic test used is not the same as the initial one. For example, HbA1c levels may not be elevated in acute glycaemic states in newly diagnosed diabetes, such that a value of <6.5% (48 mmol/mol) does not exclude diabetes in the presence of an elevated blood glucose testing (≥7.0 mmol/L fasting or ≥11.1 mmol/L random).

When the results of more than one type of test are discordant, the result that is above the diagnostic cut-off point should be repeated to make the diagnosis.

Problems with the testing process, such as incorrect fasting or laboratory error, can also lead to discordant results.

Other types of diabetes

Alternative types of diabetes include the following.

Type 1 diabetes

Type 1 diabetes is typically considered a disease of children and the young; however, the majority of people with type 1 diabetes are adults, and as many as 42% of type 1 diabetes cases have their onset in people between 30 and 60 years of age.[25]

Consider type 1 diabetes if there is the presence of:

- ketosis/ketonuria (which may be absent)
- polyuria, polydipsia
- acute weight loss (>5% in less than four weeks)
- <50 years of age
- personal and family history of autoimmune disease
- acute onset of symptoms.

If suspicious of type 1 diabetes:

- Management of hyperglycaemia should not be delayed, and should include immediate assessment for possible ketosis and metabolic disorders such as hyperosmolar states while seeking specialist endocrinology assessment. If blood

ketone level is >1.5 mmol/L, seek help immediately. Blood ketones >0.5 mmol/L are abnormal in the presence of hyperglycaemia. Refer to the RACGP's position statement on emergency management of hyperglycaemia in primary care.

- Consider non-urgent confirmatory tests for glutamic acid decarboxylase (GAD) and/or insulinoma antigen-2 (IA-2) antibodies. These will be present in 90% of patients with type 1 diabetes. When measuring antibodies, higher rates of false negative results occur early in the development of type 1 diabetes. However, false negative results decrease when two different antibody tests are measured.
- Consider testing for plasma C-peptide level.[26] Levels <0.2 nmol/L on non-fasting sampling support the diagnosis of type 1 diabetes; however, the diagnostic accuracy of this test varies in early-onset type 1 diabetes. Specialist endocrinology evaluation will assist in the case of diagnostic uncertainty.

Latent autoimmune diabetes of adults

Latent autoimmune diabetes of adults (LADA – also called 'type 1.5' diabetes) is diabetes with ß-islet cell antibodies that occurs more commonly in adulthood. LADA often presents similarly to type 2 diabetes, but it involves a more rapid course of ß-cell destruction, a poorer metabolic response to non-insulin therapy and a more rapid progression to requiring insulin to control hyperglycaemia due to ß-cell failure.[27]

Monogenic diabetes

Monogenic diabetes is a collection of single-gene mutation disorders that account for 1–2% of diabetes cases. Cases usually develop before 25 years of age and are often non-insulin requiring. Monogenic diabetes can be misdiagnosed as either type 1 or type 2 diabetes.[28]

Monogenic diabetes is genetically heterogeneous, but all forms are dominantly inherited, unless they occur as a result of a de novo mutation. There is variance among the forms, with two main types: neonatal diabetes mellitus, occurring in the first six months of life (rare), and maturity-onset diabetes of the young (MODY). MODY subtypes may vary in the severity of hyperglycaemia. The most prevalent subtypes are due to mutations in the genes *HNF1A*, *GCK* and *HNF4A*. Not all forms of the MODY phenotype have yet been defined.[29] Suspected cases should be referred to a specialist endocrinologist, and management options and possible genetic diagnosis should be considered.[30]

Gestational diabetes mellitus

Refer to the section 'Gestational diabetes mellitus'.

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20635