Evidence Summary

Understanding diabetes

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Understanding diabetes

Diabetes refers to a group of metabolic conditions which are characterised by hyperglycaemia. Hyperglycaemia may occur due to defects in insulin secretion, insulin action or both. Chronic hyperglycaemia is associated with long term blood vessel damage.

This section aims to explain the different types of diabetes and their associated treatment.

Contents

What is diabetes?

Diabetes mellitus is a condition where high blood glucose levels (hyperglycaemia) occur. The normal range for blood glucose in a person who does not have diabetes is generally between 3 and 7.7mmol/L. This range is maintained during the individual's day to day activities.

Glucose is needed by the body for energy and is obtained from carbohydrate foods such as starches and sugars. The glucose is transported from the gut through the portal system to the body. Glucose that is not immediately used is transformed and stored in the liver. The regulation and storage of glucose is controlled by the hormone insulin.

Insulin is produced by the beta cells of the pancreas in response to a rise in blood glucose concentration. The hormone insulin is responsible for the uptake, storage and use of glucose by the body cells, thus supplying available energy for use in the body. Without sufficient insulin there will be impaired metabolism, not only of carbohydrates, but of protein and fats as well.

Classification of diabetes

The different types of diabetes have different causes and clinical presentation. The common feature for all types of diabetes is **hyperglycaemia**.

Primary diabetes

Type 1: An absolute deficiency of insulin. The exact trigger is unknown but it is an autoimmune response. Intensive insulin therapy is required for survival.[1]

Type 2: A combination of insulin resistance (a resistance by the cells of the body to the action of insulin, thereby reducing the effectiveness of insulin) and insulin deficiency. Type 2 diabetes is a progressive disease that requires ongoing monitoring and progression of therapy. Most people will need to take oral medication and/or injectable and eventually many will require insulin.[2]

Note: Pre diabetes is when the blood glucose level (BGL) is higher than normal but is not high enough for a diagnosis of diabetes. The person may be identified as having impaired fasting glucose and / or impaired glucose tolerance 2 hours post glucose load. These people have an increased risk of developing type 2 diabetes and have an increased cardiovascular risk.

Gestational diabetes

Diabetes occurring for the first time during pregnancy, and often lasting only for the duration of the pregnancy. Progression of type 2 diabetes later in life will occur in 5-50% of women with gestational diabetes mellitus (GDM). The lifetime risk of developing type 2 diabetes following a diagnosis of GDM is 60%.[3]

Secondary diabetes

Diabetes as a result of another disorder, for example: pancreatic disease, cystic fibrosis endocrine disorder, drugs, chemicals or other stresses.

Features of type 1 and type 2 diabetes

Type 1	Type 2
Characteristics	
10-15% of all people with diabetes	85-90% of all people with diabetes
no insulin produced	insulin resistance and insulin deficiency
family history	family history/ethnicity
due to damage to beta cells because of auto immune response	age, overweight/obese, lifestyle factors
generally occurs in younger people under 40 years but may occur at any age	usually occurs in older people over 40 years, however can occur at any age
Onset	
rapid onset (weeks / months)	gradual onset, often no symptoms (months or years)
Blood or urine ketones often present (due to lack of insulin)	ketones not usually present as some insulin still being produced
	may present with existing chronic complications
Treatment	
requires intensive insulin therapy either by multiple daily injections or insulin pump	varies depending on presenting health status
	requires lifestyle education, sometimes in combination with medications from diagnosis
	insulin therapy is often required after a few years

NB. Type 2 diabetes in children

Type 2 diabetes is rapidly increasing in children and adolescents, accounting for approximately 5 percent of diabetes in this age group in Australia.[2] Type 2 diabetes in children presents in a similar way as in adults eg there is insulin deficiency and resistance. Often children have a strong family history (present in over 80% of cases) and predominately they are obese. Aboriginal or Torres Strait Islander, Melanesian, Polynesian, Chinese, Southeast Asian, Middle Eastern or from the Indian sub-continent people have higher risk. Whilst type 2 diabetes is often asymptomatic it may present with ketosis and even mild to moderate ketoacidosis in this group. Type 2 diabetes may have a prolonged asymptomatic phase and so screening for complications should start at diagnosis. Children are at risk for macrovascular complications due to the underlying metabolic syndrome associated with type 2 diabetes.[4]

For further information, refer to the factsheets, *'What is type 1 diabetes'*, *'What is type 2 diabetes'* and 'G*estational diabetes'*.

Prevalence and burden of diabetes

Globally, diabetes has been named as the major threat to human health and productivity.[5] An estimated 1.2 million (6%) Australian adults aged 18 years and over had diabetes in 2014-15, based on self-reported data.[6] At least 1.5million Australians currently have diabetes with 280 people developing diabetes each day. Diabetes is the fastest growing chronic disease nationally.[6]

Aboriginal people are 4 times more likely to have diabetes than non-Aboriginal people.[7] Costs of diabetes are rising rapidly with an 86% increase in healthcare expenditure allocated to diabetes between 2000-01 and 2008-09 from $811 million to $1,507 million. The healthcare sector where the largest increase took place was hospital admitted patients for which expenditure more than doubled in this period.[8]

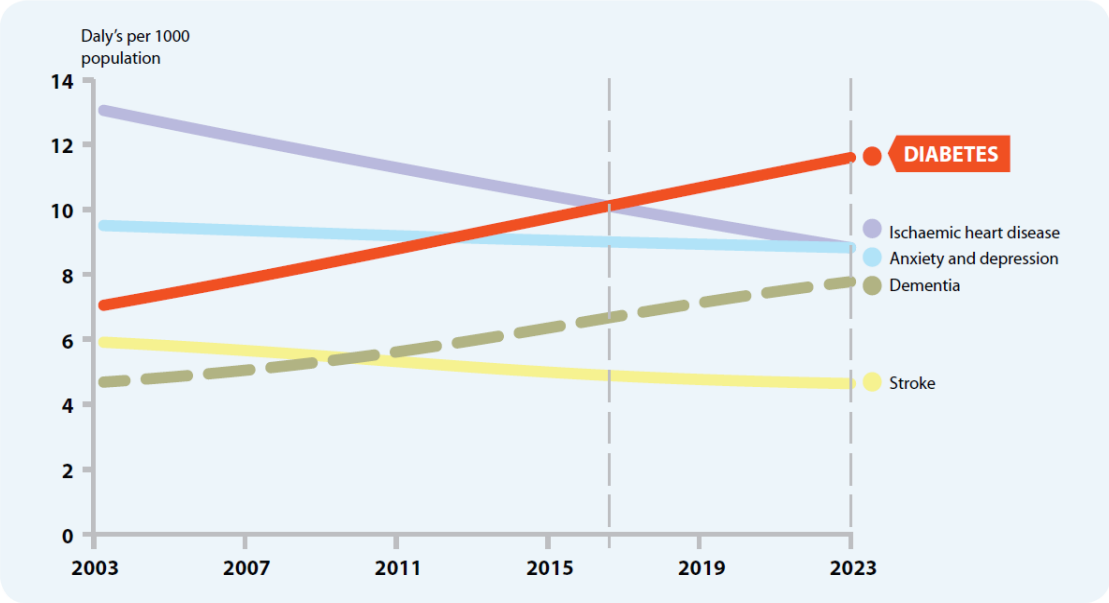


Figure 1 *shows trends in leading causes of burden of disease in Australia.[9] The upward trend in diabetes accompanies a lack of both national and state-wide strategies for diabetes in contrast with other leading illnesses.*

Diabetes and its complications which affect the feet, eyes, kidneys, and cardiovascular health are not only costly to society and healthcare systems but to the individual, their family and community.

Diabetes is the leading cause of non-injury related lower limb amputation. In 2012-13, there were 4,190 lower limb amputations provided in hospital to admitted patients with a diagnosis of either diabetes or peripheral vascular disease. The majority of these amputations (3,570 or 85%) were provided for patients with diabetes.[10] Diabetic eye disease is a leading cause of irreversible blindness in Australian adults. Almost all those with type 1 diabetes and more than 60% of those with type 2 diabetes will develop diabetic eye disease within 20 years of diagnosis. 98% of diabetes induced blindness is preventable.[11]

Cardiovascular disease (CVD) is the primary cause of death in people with diabetes, with around 65% of all CVD deaths in Australia occurring in people with diabetes or pre-diabetes.[12] Poor psychological well-being is also a factor with anxiety, stress and depression reported by 41% of people with diabetes in this country.[13]

Type 1 diabetes

The prevalence of type 1 diabetes incidence varies greatly between countries and is increasing worldwide. There are currently no national data that capture the prevalence of type 1 diabetes at all ages.[14]

According to the National Diabetes Service Scheme Diabetes Map, there are currently 118,723 children, young adults and adults living with type 1 diabetes.[15] It was estimated that in 2015, there over 6,000 children aged 0-14 had type 1 diabetes.[14]

There were 2,600 new cases (incidence) of type 1 diabetes in Australia in 2015, equating to 12 cases per 100,000 population.[15] Rates also vary across states in Australia and across different ethnic groups.[1]

Type 2 diabetes

In Australia the prevalence of diabetes has more than doubled since 1989. The AusDiab Study released in April 2001, showed that 1 in 4 Australians had a problem with glucose metabolism. The study identified that 3.8% of adults (25 years plus) had diagnosed diabetes, 3.8% had undiagnosed diabetes and 16.3% had either impaired glucose tolerance or impaired fasting glucose (pre diabetes).[16] The prevalence of diabetes rises sharply with age.

Diagnosed	3.8%
Undiagnosed	3.8%
IGT of IFG	16.3%
Total	**23.9%**

Clinical presentation

The symptoms of diabetes vary from individual to individual and in relation to the level of hyperglycaemia. Some people with type 2 diabetes may also be asymptomatic. Symptoms are similar in each type of diabetes, however, intensity and onset varies.

The following terms describe associated symptoms of **hyperglycaemia.**

Glycosuria – the presence of glucose in the urine. When blood glucose concentration exceeds the renal threshold of approximately 10mmol/L in a young person (in older people it can be higher) glucose is excreted in the urine and is detected with a reagent testing strip.

Polyuria – excessive urination. Glucose is osmotically active and requires water for excretion. In uncontrolled diabetes, the filtered glucose `pulls' large quantities of water with it which leads to increased urine production.

Polydipsia – excessive drinking. Polyuria causes loss of water, resulting in dehydration. Dehydration triggers thirst in the person in an effort to replace lost water.

Polyphagia – excessive eating of food. Without insulin, glucose is unavailable to the cells for energy. The body perceives a state of `starvation' and the appetite is increased in an effort to gain enough food for energy. The body also loses nutrients through the urine (glycosuria, ketonuria).

Weight loss – in type 1 diabetes, protein and fat stores are broken down to be used for energy. Ketones are produced and excreted in the urine.

Ketotosis – in type 1 diabetes there may be the presence of ketones in the urine or blood. When there is not enough insulin to utilise the glucose, fat stores are broken down for energy, ketones are produced. Moderate to large ketones found in urine or blood may indicate ketoacidosis, a life-threatening emergency situation.

Tiredness – caused by the inability to utilise glucose, resulting in insufficient energy supply.

Skin and genital infections – hyperglycaemia results in a lowered resistance to infection, glycosuria results in thrush (monilia / candida infection), pruritus vulvae or balanitis.

Blurred vision – due to changes in the shape of the lens of the eye because of hyperglycaemia. Occasionally this is the main symptom and may last several weeks while blood glucose is being stabilised.

Diagnosis and management

Type 1 diabetes

Diagnosis

In the months or years before clinical presentation of type 1 diabetes, one or more autoantibodies can be detected as markers of β-cell autoimmunity. These include insulin autoantibodies (IAA), glutamic acid decarboxylase (GAD), the insulinoma-associated 2 molecule (IA-2) and zinc transporter 8 (ZnT-8).

Type 1 diabetes can be diagnosed if the characteristic symptoms and signs are present and the fasting venous plasma glucose concentration is greater than or equal to 7.0mmol/L, and/or the random venous plasma glucose concentration taken at least 2 hours after eating is greater than 11.1mmol/L.

However, clinical presentation at diagnosis can vary widely in people with type 1 diabetes. There may be those who present with severe diabetic ketoacidosis who require hospitalisation, intensive rehydration and intravenous insulin infusion. For more information, refer to the Evidence Summary - '*Unstable diabetes'*.

Alternatively, there may be persons without symptoms of hyperglycaemia, who may be detected incidentally. These milder degrees of metabolic decompensation make it more difficult to differentiate type 1 diabetes from type 2 and other forms of diabetes. In such cases, the absence or presence of signs of insulin resistance (eg.acanthosis nigrans, overweight or obesity) and investigations for the detection of islet antibodies including anti-GAD, IAA, ICA, and ZnT-8 will help to clarify the diagnosis.

An oral glucose tolerance test (OGTT) is rarely indicated in diagnosis of type 1 diabetes in childhood and adolescence.[1] A child or adolescent may present with diabetic ketoacidosis.

Ongoing management principles

- Children and young people with type 1 diabetes should have access to care by a multidisciplinary team trained in childhood diabetes.
- The family and/or carer should be recognised as being part of the management team.
- Education from a credentialled diabetes educator should be part of the management of type 1 diabetes.

- Education should be adapted to each individual's age, maturity, stage of diabetes, lifestyle and culture.
- After the initial period of diagnosis and education (when frequent contact may be required), the child or young person should be regularly reviewed throughout the year. This should be no less than 3-4 times per year), including one major annual review (paying particular attention to growth, development, nutrition, physical activity, co-morbidities, acute and chronic diabetes related complications) with the multidisciplinary team.
- In rural and remote areas, children and young people with diabetes may be successfully cared for by a local paediatrician/physician with training and experience in paediatric diabetes, access to resources, support and advice from a specialised diabetes team.
- The transition from a paediatric to an adult service for the young person with diabetes is often difficult. Transfer to an adult service should be comprehensive and include a preparation phase and evaluation phase.[1]

Principles of medical management

- People with type 1 diabetes are dependent on insulin for survival.
- Insulin **must not** be stopped under any circumstances.
- Insulin is not normally used in combination with any other hypoglycaemic agents, however, metformin is sometimes used for people with type 1 diabetes who have insulin resistance but the evidence for its effectiveness is limited.[1]

Type 2 diabetes

Risk factors and screening

Patients should be screened for diabetes risk every three years from 40 years of age. Aboriginal and Torres Strait Islander peoples should be screened from 18 years of age.

Testing for undiagnosed type 2 diabetes is recommended for the following high risk individuals.[2]

- People of any age with impaired glucose tolerance (IGT) or impaired fasting glucose (IFG)*.
- All patients with a history of a cardiovascular event (eg acute myocardial infarction, angina, peripheral vascular disease or stroke).
- People aged ≥35 years originating from the Pacific Islands, Indian subcontinent or China.
- People aged ≥40 years with body mass index (BMI) ≥30 kg/m2 or hypertension.
- Women with a history of gestational diabetes mellitus.
- Women with polycystic ovary syndrome.
- Patients taking antipsychotic medication.

*Annual fasting blood glucose (FBG) or HbA1c is reserved for those people identified with IGT test or IFG (not limited by age) people with impaired glucose tolerance or impaired glucose tolerance or impaired fasting glucose.

The Australian Type 2 Diabetes Risk Assessment Tool (AUSDRISK) is recommended for screening.

Those with an AUSRISK risk score of 12 or more should have a blood examination for fasting blood glucose (FBG) or HbA1c.[2]

Diagnosis

Diagnosis is based on plasma glucose measurements in conjunction with clinical assessment.[2]

In the presence of symptoms suggestive of hyperglycaemia or a clear clinical diagnosis (eg a patient presenting with extreme hyperglycaemia, a single elevated FBG ≥7.0 mmol/L or a random blood glucose ≥11.1 mmol/L), this is confirmatory of a diagnosis of diabetes. A second laboratory test is not required to confirm the diagnosis.

In those patients who are asymptomatic, diagnosis of diabetes involves one of these three types of biochemical analyses:

- Fasting blood glucose (FBG) ≥7.0 mmol/L or random blood glucose ≥11.1 mmol/L confirmed by a second abnormal FBG on a separate day.
- Glycated haemoglobin (HbA1c) ≥48 mmol/mol (6.5%; on two separate occasions).
- Oral glucose tolerance test (OGTT) before (fasting) and two hours after an oral 75 g glucose load is taken. Blood glucose is measured. Diabetes is diagnosed as FBG ≥7.0 mmol/L or two-hour blood glucose is ≥11.1 mmol/L.[2]

A second laboratory result is required for confirmation of the diagnosis of diabetes in asymptomatic patients. It is recommended that the same laboratory result be repeated without delay using a new blood sample for confirmation because there will be a greater likelihood of concurrence.

Figure 2a. Screening and diagnosis algorithm – Fasting blood glucose

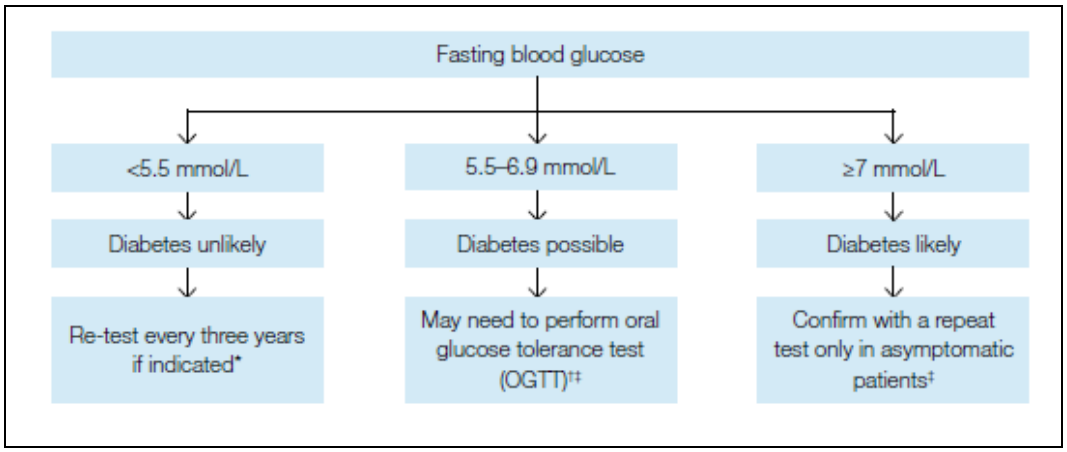


Figure 2b. Screening and diagnosis algorithm – Glycated haemoglobin (HbA1c)

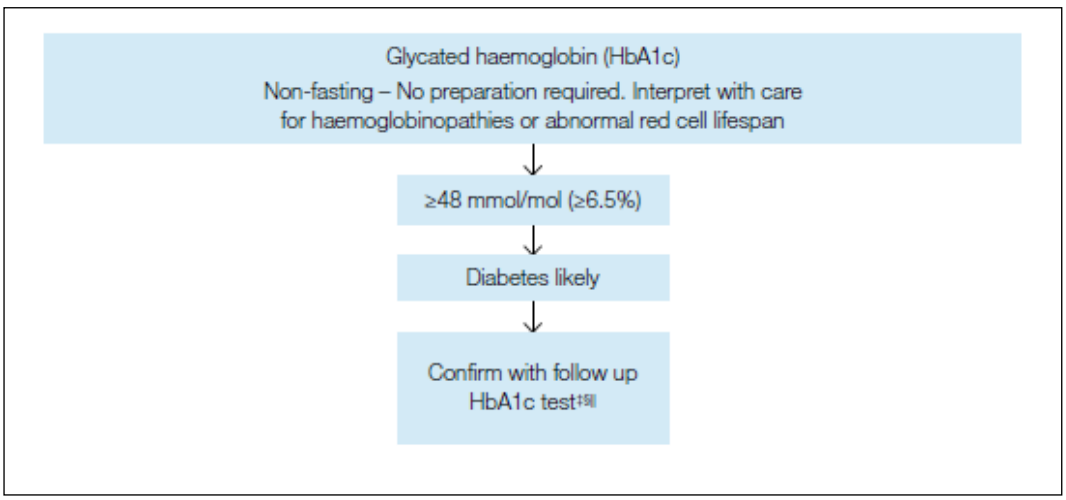
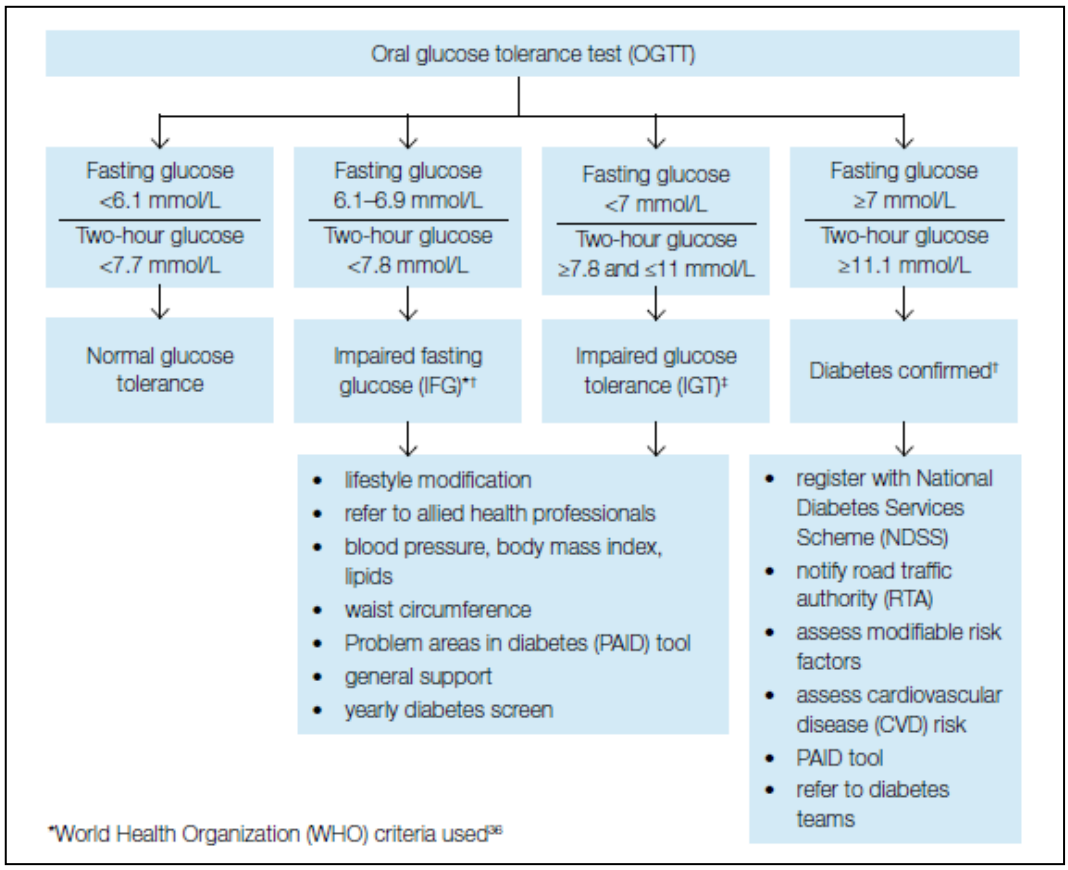


Figure 2c. Screening and diagnosis algorithm – Oral glucose tolerance test



The OGTT test is carried out after an overnight fast, following three days of adequate carbohydrate intake (greater than 150g per day). A 75g load of oral glucose is given and the diagnosis of diabetes can be made if venous plasma glucose level fasting is ≥7.0 mmol/L or 2 hour post glucose load is ≥11.1 mmol/L.

A person with type 2 diabetes may first present with long term complications - eg diabetic retinopathy, neuropathy, coronary artery disease, peripheral vascular disease and/or cataracts. For more information, refer to the Evidence Summary – *'Long term complications'*.

Routine examination may incidentally detect glycosuria and/or hyperglycaemia - eg during pregnancy or hospitalisation.

On-going management principles for people with type 2 diabetes

A team approach is essential for the successful management of diabetes, with the active participation of the person with diabetes and if appropriate including family members.

Ideal management involves:

> active involvement of the person with diabetes and their family members
> appropriate treatment plan
> appropriate nutrition and weight control
> appropriate physical activity
> advice for maintaining a healthy lifestyle eg stress management, reduce or quit smoking
> appropriate and safe use of pharmaceuticals as required (oral agent and/or injectable).

The aims of management are to:

- restore the altered metabolism of the person with diabetes and maintain blood glucose levels within the normal range
- identify and reduce risk factors of diabetes related complications
- prevent or delay progression of the short and long term complications
- empower the person to self-manage their own diabetes and restore the individual with diabetes to as independent a lifestyle as possible
- provide ongoing management, support and resources.

Principles of medical management:

- type 2 diabetes is a progressive disease which needs progressive increases in treatment to maintain target HbA1c levels
- people with type 2 diabetes usually progress from lifestyle recommendations, to oral medications and then onto injectables (including insulin)[17]
- oral medications can be combined with injectables.

For further information, refer to the Evidence Summary – '*Medication'* for medication pathway in type 2 diabetes.

Gestational diabetes

Risk factors and screening

The Australasian Diabetes in Pregnancy Society (ADIPS) recommends that all women should be screened for gestational diabetes (GDM). For further information, refer to the Evidence Summary – *'Pregnancy'*.

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