Type 2 diabetes in adults: management

NICE guideline
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Your responsibility

The recommendations in this guideline represent the view of NICE, arrived at after careful consideration of the evidence available. When exercising their judgement, professionals and practitioners are expected to take this guideline fully into account, alongside the individual needs, preferences and values of their patients or the people using their service. It is not mandatory to apply the recommendations, and the guideline does not override the responsibility to make decisions appropriate to the circumstances of the individual, in consultation with them and their families and carers or guardian.

Local commissioners and providers of healthcare have a responsibility to enable the guideline to be applied when individual professionals and people using services wish to use it. They should do so in the context of local and national priorities for funding and developing services, and in light of their duties to have due regard to the need to eliminate unlawful discrimination, to advance equality of opportunity and to reduce health inequalities. Nothing in this guideline should be interpreted in a way that would be inconsistent with complying with those duties.

Commissioners and providers have a responsibility to promote an environmentally sustainable health and care system and should assess and reduce the environmental impact of implementing NICE recommendations wherever possible.
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Overview

This guideline covers care and management for adults (aged 18 and over) with type 2 diabetes. It focuses on patient education, dietary advice, managing cardiovascular risk, managing blood glucose levels, and identifying and managing long-term complications.

Who is it for?

- Healthcare professionals that care for adults with diabetes
- Commissioners and providers of diabetes services
- Adults with type 2 diabetes, and their families and carers.
Introduction

Type 2 diabetes is a chronic metabolic condition characterised by insulin resistance (that is, the body's inability to effectively use insulin) and insufficient pancreatic insulin production, resulting in high blood glucose levels (hyperglycaemia). Type 2 diabetes is commonly associated with obesity, physical inactivity, raised blood pressure, disturbed blood lipid levels and a tendency to develop thrombosis, and therefore is recognised to have an increased cardiovascular risk. It is associated with long-term microvascular and macrovascular complications, together with reduced quality of life and life expectancy.

In 2013, over 3.2 million adults were diagnosed with diabetes, with prevalence rates of 6% and 6.7% in England and Wales respectively. It is estimated that about 90% of adults currently diagnosed with diabetes have type 2 diabetes. Type 2 diabetes is more common in people of African, African-Caribbean and South Asian family origin. It can occur in all age groups and is increasingly being diagnosed in children.

Multiple vascular risk factors and wide-ranging complications make diabetes care complex and time-consuming, and many areas of healthcare services must be involved for optimal management. Necessary lifestyle changes, the complexities and possible side effects of therapy make patient education and self-management important aspects of diabetes care. Diabetes care is estimated to account for at least 5% of UK healthcare expenditure, and up to 10% of NHS expenditure.

This guideline contains recommendations for managing type 2 diabetes in adults, and focuses on patient education, dietary advice, managing cardiovascular risk, managing blood glucose levels, and identifying and managing long-term complications. The guideline does not cover diagnosis, secondary diabetes, type 1 diabetes in adults, diabetes in pregnancy and diabetes in children and young people.
Recommendations

People have the right to be involved in discussions and make informed decisions about their care, as described in NICE’s information on making decisions about your care.

Making decisions using NICE guidelines explains how we use words to show the strength (or certainty) of our recommendations, and has information about prescribing medicines (including off-label use), professional guidelines, standards and laws (including on consent and mental capacity), and safeguarding.

1.1 Individualised care

1.1.1 Adopt an individualised approach to diabetes care that is tailored to the needs and circumstances of adults with type 2 diabetes, taking into account their personal preferences, comorbidities, risks from polypharmacy, and their ability to benefit from long-term interventions because of reduced life expectancy. Such an approach is especially important in the context of multimorbidity. Reassess the person's needs and circumstances at each review and think about whether to stop any medicines that are not effective. [2015]

1.1.2 Take into account any disabilities, including visual impairment, when planning and delivering care for adults with type 2 diabetes. [2015]

1.2 Patient education

1.2.1 Offer structured education to adults with type 2 diabetes and/or their family members or carers (as appropriate) at and around the time of diagnosis, with annual reinforcement and review. Explain to people and their carers that structured education is an integral part of diabetes care. [2009]

1.2.2 Ensure that any structured education programme for adults with type 2 diabetes includes the following components:

- It is evidence-based, and suits the needs of the person.
• It has specific aims and learning objectives, and supports the person and their family members and carers in developing attitudes, beliefs, knowledge and skills to self-manage diabetes.

• It has a structured curriculum that is theory-driven, evidence-based and resource-effective, has supporting materials, and is written down.

• It is delivered by trained educators who have an understanding of educational theory appropriate to the age and needs of the person, and who are trained and competent to deliver the principles and content of the programme.

• It is quality assured, and reviewed by trained, competent, independent assessors who measure it against criteria that ensure consistency.

• The outcomes are audited regularly. [2015]

1.2.3 Ensure the patient-education programme provides the necessary resources to support the educators, and that educators are properly trained and given time to develop and maintain their skills. [2009]

1.2.4 Offer group education programmes as the preferred option. Provide an alternative of equal standard for a person unable or unwilling to participate in group education. [2009]

1.2.5 Ensure that the patient-education programmes available meet the cultural, linguistic, cognitive and literacy needs within the local area. [2009]

1.2.6 Ensure that all members of the diabetes healthcare team are familiar with the patient-education programmes available locally, that these programmes are integrated with the rest of the care pathway, and that adults with type 2 diabetes and their family members or carers (as appropriate) have the opportunity to contribute to the design and provision of local programmes. [2009]

1.3 Dietary advice and bariatric surgery

1.3.1 Provide individualised and ongoing nutritional advice from a healthcare professional with specific expertise and competencies in nutrition. [2009]

1.3.2 Provide dietary advice in a form sensitive to the person's needs, culture and
beliefs, being sensitive to their willingness to change and the effects on their quality of life. [2009]

1.3.3 Emphasise advice on healthy balanced eating that is applicable to the general population when providing advice to adults with type 2 diabetes. Encourage high-fibre, low-glycaemic-index sources of carbohydrate in the diet, such as fruit, vegetables, wholegrains and pulses; include low-fat dairy products and oily fish; and control the intake of foods containing saturated and trans fatty acids. [2009]

1.3.4 Integrate dietary advice with a personalised diabetes management plan, including other aspects of lifestyle modification, such as increasing physical activity and losing weight. [2009]

1.3.5 For adults with type 2 diabetes who are overweight, set an initial body weight loss target of 5% to 10%. Remember that lesser degrees of weight loss may still be of benefit, and that larger degrees of weight loss in the longer term will have advantageous metabolic impact. [2009]

1.3.6 Individualise recommendations for carbohydrate and alcohol intake, and meal patterns. Reducing the risk of hypoglycaemia should be a particular aim for a person using insulin or an insulin secretagogue. [2009]

1.3.7 Advise adults with type 2 diabetes that limited substitution of sucrose-containing foods for other carbohydrate in the meal plan is allowable, but that they should take care to avoid excess energy intake. [2009]

1.3.8 Discourage the use of foods marketed specifically for people with diabetes. [2009]

1.3.9 When adults with type 2 diabetes are admitted to hospital as inpatients or to any other care setting, implement a meal planning system that provides consistency in the carbohydrate content of meals and snacks. [2009]

1.3.10 For recommendations on lifestyle advice, see the NICE guidelines on preventing excess weight gain, weight management, obesity, physical activity, stop smoking interventions and services, smoking: harm reduction, and smoking: acute, maternity and mental health services. [2015]
1.3.11 For recommendations on bariatric surgery for people with recent-onset type 2 diabetes, see the section on bariatric surgery for people with recent-onset type 2 diabetes in the NICE guideline on obesity.

1.4 Diagnosing and managing hypertension

The recommendations on diagnosing and managing hypertension have been removed. For recommendations on hypertension in people with type 2 diabetes, see the NICE guideline on hypertension in adults. Diagnosis, treatment and monitoring of hypertension is broadly the same for people with type 2 diabetes as for other people. When a different approach is needed for people with type 2 diabetes, this is specified in the hypertension guideline.

1.5 Antiplatelet therapy

1.5.1 Do not offer antiplatelet therapy (aspirin or clopidogrel) for adults with type 2 diabetes without cardiovascular disease. [2015]

1.5.2 For guidance on the primary and secondary prevention of cardiovascular disease in adults with type 2 diabetes, see the NICE guidelines on cardiovascular disease and acute coronary syndromes. [2015]

1.6 Blood glucose management

HbA1c measurement and targets

Measurement

1.6.1 In adults with type 2 diabetes, measure HbA1c levels at:

- 3 to 6-monthly intervals (tailored to individual needs), until the HbA1c is stable on unchanging therapy
- 6-monthly intervals once the HbA1c level and blood glucose lowering therapy are stable. [2015]

1.6.2 Use methods to measure HbA1c that have been calibrated according to International Federation of Clinical Chemistry (IFCC) standardisation. [2015]

1.6.3 If HbA1c monitoring is invalid because of disturbed erythrocyte turnover or
abnormal haemoglobin type, estimate trends in blood glucose control using one of the following:

- quality-controlled plasma glucose profiles
- total glycated haemoglobin estimation (if abnormal haemoglobins)
- fructosamine estimation. [2015]

1.6.4 Investigate unexplained discrepancies between HbA1c and other glucose measurements. Seek advice from a team with specialist expertise in diabetes or clinical biochemistry. [2015]

Targets

1.6.5 Involve adults with type 2 diabetes in decisions about their individual HbA1c target. Encourage them to achieve the target and maintain it unless any resulting adverse effects (including hypoglycaemia), or their efforts to achieve their target, impair their quality of life. [2015]

1.6.6 Offer lifestyle advice and drug treatment to support adults with type 2 diabetes to achieve and maintain their HbA1c target (see the section on dietary advice and bariatric surgery). For more information about supporting adherence, see the NICE guideline on medicines adherence. [2015]

1.6.7 For adults with type 2 diabetes managed either by lifestyle and diet, or by lifestyle and diet combined with a single drug not associated with hypoglycaemia, support the person to aim for an HbA1c level of 48 mmol/mol (6.5%). For adults on a drug associated with hypoglycaemia, support the person to aim for an HbA1c level of 53 mmol/mol (7.0%). [2015]

1.6.8 In adults with type 2 diabetes, if HbA1c levels are not adequately controlled by a single drug and rise to 58 mmol/mol (7.5%) or higher:

- reinforce advice about diet, lifestyle and adherence to drug treatment and
- support the person to aim for an HbA1c level of 53 mmol/mol (7.0%) and
- intensify drug treatment. [2015]

1.6.9 Consider relaxing the target HbA1c level (see recommendations 1.6.7 and 1.6.8)
on a case-by-case basis, with particular consideration for people who are older or frail, for adults with type 2 diabetes:

- who are unlikely to achieve longer-term risk-reduction benefits, for example, people with a reduced life expectancy
- for whom tight blood glucose control poses a high risk of the consequences of hypoglycaemia, for example, people who are at risk of falling, people who have impaired awareness of hypoglycaemia, and people who drive or operate machinery as part of their job
- for whom intensive management would not be appropriate, for example, people with significant comorbidities. [2015]

1.6.10 If adults with type 2 diabetes achieve an HbA1c level that is lower than their target and they are not experiencing hypoglycaemia, encourage them to maintain it. Be aware that there are other possible reasons for a low HbA1c level, for example, deteriorating renal function or sudden weight loss. [2015]

1.6.11 For guidance on HbA1c targets for women with type 2 diabetes who are pregnant or planning to become pregnant, see the NICE guideline on diabetes in pregnancy. [2015]

Self-monitoring of blood glucose

1.6.12 Take the Driver and Vehicle Licensing Agency (DVLA)'s Assessing fitness to drive: a guide for medical professionals into account when offering self-monitoring of blood glucose levels for adults with type 2 diabetes. [2015]

1.6.13 Do not routinely offer self-monitoring of blood glucose levels for adults with type 2 diabetes unless:

- the person is on insulin or
- there is evidence of hypoglycaemic episodes or
- the person is on oral medication that may increase their risk of hypoglycaemia while driving or operating machinery or
The person is pregnant, or is planning to become pregnant. For more information, see the NICE guideline on diabetes in pregnancy. [2015]

1.6.14 Consider short-term self-monitoring of blood glucose levels in adults with type 2 diabetes (and review treatment as necessary):

- when starting treatment with oral or intravenous corticosteroids or

- to confirm suspected hypoglycaemia. [2015]

1.6.15 Be aware that adults with type 2 diabetes who have acute intercurrent illness are at risk of worsening hyperglycaemia. Review treatment as necessary. [2015]

1.6.16 If adults with type 2 diabetes are self-monitoring their blood glucose levels, carry out a structured assessment at least annually. The assessment should include:

- the person's self-monitoring skills

- the quality and frequency of testing

- checking that the person knows how to interpret the blood glucose results and what action to take

- the impact on the person's quality of life

- the continued benefit to the person

- the equipment used. [2015]

Drug treatment

Recommendations in this section that cover dipeptidyl peptidase-4 (DPP-4) inhibitors, glucagon-like peptide-1 (GLP-1) mimetics and sulfonylureas refer to each of these groups of drugs at a class level.

1.6.17 For adults with type 2 diabetes, discuss the benefits and risks of drug treatment, and the options available. Base the choice of drug treatment(s) on:

- the effectiveness of the drug treatment(s) in terms of metabolic response
• safety (see Medicines and Healthcare products Regulatory Agency guidance) and tolerability of the drug treatment(s)

• the person's individual clinical circumstances, for example, comorbidities, risks from polypharmacy

• the person's individual preferences and needs

• the licensed indications or combinations available

• cost (if 2 drugs in the same class are appropriate, choose the option with the lowest acquisition cost). [2015]

Rescue therapy at any phase of treatment

1.6.18 If an adult with type 2 diabetes is symptomatically hyperglycaemic, consider insulin (see recommendations 1.6.32 to 1.6.34) or a sulfonylurea, and review treatment when blood glucose control has been achieved. [2015]

Initial drug treatment

1.6.19 Offer standard-release metformin as the initial drug treatment for adults with type 2 diabetes. [2015]

1.6.20 Gradually increase the dose of standard-release metformin over several weeks to minimise the risk of gastrointestinal side effects in adults with type 2 diabetes. [2015]

1.6.21 If an adult with type 2 diabetes experiences gastrointestinal side effects with standard-release metformin, consider a trial of modified-release metformin. [2015]

Algorithm for blood glucose lowering therapy in adults with type 2 diabetes

To download the pdf, see the tools and resources.
There is MHRA safety advice on the following drugs:

- **Pioglitazone**: exercise particular caution if the person is at high risk of the adverse effects of the drug. Pioglitazone is associated with an increased risk of heart failure, bladder cancer and bone fracture. Known risk factors for these conditions, including increased age, should be carefully evaluated before treatment: see the manufacturers’ summaries of product characteristics for details. Follow the MHRA guidance on the risk of bladder cancer with pioglitazone.

- **SGLT2 inhibitors**: follow the MHRA safety advice on the increased risk of lower-limb amputation with SGLT2 inhibitors.

- **SGLT2 inhibitors**: follow the MHRA safety advice on the increased risk of diabetic ketoacidosis with SGLT2 inhibitors.

1.6.22 In adults with type 2 diabetes, review the dose of metformin if the estimated glomerular filtration rate (eGFR) is below 45 ml/minute/1.73m².
- Stop metformin if the eGFR is below 30 ml/minute/1.73m$^2$.

- Prescribe metformin with caution for those at risk of a sudden deterioration in kidney function and those at risk of eGFR falling below 45 ml/minute/1.73m$^2$. [2015]

1.6.23 In adults with type 2 diabetes, if metformin is contraindicated or not tolerated, consider initial drug treatment with:

- a dipeptidyl peptidase-4 (DPP-4) inhibitor or
- pioglitazone or
- a sulfonylurea. [2015]

Be aware that, if metformin is contraindicated or not tolerated, repaglinide is both clinically effective and cost effective in adults with type 2 diabetes. However, discuss with any person for whom repaglinide is being considered, that there is no licensed non-metformin-based combination containing repaglinide that can be offered at first intensification.

1.6.24 In adults with type 2 diabetes, do not offer or continue pioglitazone if they have any of the following:

- heart failure or history of heart failure
- hepatic impairment
- diabetic ketoacidosis
- current, or a history of, bladder cancer
- uninvestigated macroscopic haematuria. [2015]

Treatment with sodium–glucose cotransporter 2 (SGLT2) inhibitors may be appropriate for some adults with type 2 diabetes if metformin is contraindicated or not tolerated (see NICE’s guidance on canagliflozin, dapagliflozin and empagliflozin as monotherapies for treating type 2 diabetes).

See the section on chronic kidney disease for guidance on SGLT2 inhibitors for people with type 2 diabetes and chronic kidney disease.
First intensification of drug treatment

There is MHRA safety advice on the following drugs:

- Pioglitazone: exercise particular caution if the person is at high risk of the adverse effects of the drug. Pioglitazone is associated with an increased risk of heart failure, bladder cancer and bone fracture. Known risk factors for these conditions, including increased age, should be carefully evaluated before treatment: see the manufacturers' summaries of product characteristics for details. Follow the MHRA guidance on the risk of bladder cancer with pioglitazone.

- SGLT2 inhibitors: follow the MHRA safety advice on the increased risk of lower-limb amputation with SGLT2 inhibitors.

- SGLT2 inhibitors: follow the MHRA safety advice on the increased risk of diabetic ketoacidosis with SGLT2 inhibitors.

1.6.25 In adults with type 2 diabetes, if initial drug treatment with metformin has not continued to control HbA1c to below the person's individually agreed threshold for intensification, consider dual therapy with:

- metformin and a DPP-4 inhibitor or
- metformin and pioglitazone or
- metformin and a sulfonylurea. [2015]

1.6.26 In adults with type 2 diabetes, if metformin is contraindicated or not tolerated and initial drug treatment has not continued to control HbA1c to below the person's individually agreed threshold for intensification, consider dual therapy with:

- a DPP-4 inhibitor and pioglitazone or
- a DPP-4 inhibitor and a sulfonylurea or
• pioglitazone and a sulfonylurea.

Be aware that the drugs in dual therapy should be introduced in a stepwise manner, checking for tolerability and effectiveness of each drug. [2015]

Treatment with combinations of medicines including SGLT2 inhibitors may be appropriate for some people with type 2 diabetes; see the NICE guidance on canagliflozin in combination therapy for treating type 2 diabetes, dapagliflozin in combination therapy for treating type 2 diabetes and empagliflozin in combination therapy for treating type 2 diabetes.

See the section on chronic kidney disease for guidance on SGLT2 inhibitors for people with type 2 diabetes and chronic kidney disease.

NICE has also produced a patient decision aid and user guide about taking a second medicine to control blood glucose in adults with type 2 diabetes.

**Second intensification of drug treatment**

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<th>There is MHRA safety advice on the following drugs:</th>
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<td>• Pioglitazone: exercise particular caution if the person is at high risk of the adverse effects of the drug. Pioglitazone is associated with an increased risk of heart failure, bladder cancer and bone fracture. Known risk factors for these conditions, including increased age, should be carefully evaluated before treatment: see the manufacturers’ summaries of product characteristics for details. Follow the MHRA guidance on the risk of bladder cancer with pioglitazone.</td>
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1.6.27 In adults with type 2 diabetes, if dual therapy with metformin and another oral drug (see recommendation 1.6.25) has not continued to control HbA1c to below the person’s individually agreed threshold for intensification, consider either:
• triple therapy with:
  - metformin, a DPP-4 inhibitor and a sulfonylurea or
  - metformin, pioglitazone and a sulfonylurea or

• starting insulin-based treatment (see recommendations 1.6.32 to 1.6.34). [2015]

1.6.28 If triple therapy with metformin and 2 other oral drugs (see recommendation 1.6.27) is not effective, not tolerated or contraindicated, consider combination therapy with metformin, a sulfonylurea and a glucagon-like peptide-1 (GLP-1) mimetic for adults with type 2 diabetes who:

• have a body mass index (BMI) of 35 kg/m² or higher (adjust accordingly for people from black, Asian and other minority ethnic groups) and specific psychological or other medical problems associated with obesity or

• have a BMI lower than 35 kg/m² and:
  - for whom insulin therapy would have significant occupational implications or
  - weight loss would benefit other significant obesity-related comorbidities. [2015]

1.6.29 Only continue GLP-1 mimetic therapy if the person with type 2 diabetes has had a beneficial metabolic response (a reduction of at least 11 mmol/mol [1.0%] in HbA1c and a weight loss of at least 3% of initial body weight in 6 months). [2015]

1.6.30 In adults with type 2 diabetes, if metformin is contraindicated or not tolerated, and if dual therapy with 2 oral drugs (see recommendation 1.6.26) has not continued to control HbA1c to below the person’s individually agreed threshold for intensification, consider insulin-based treatment (see recommendations 1.6.32 to 1.6.34). [2015]

1.6.31 In adults with type 2 diabetes, only offer a GLP-1 mimetic in combination with insulin with specialist care advice and ongoing support from a consultant-led multidisciplinary team. [2015]

Treatment with combinations of medicines including SGLT2 inhibitors may be appropriate for some people with type 2 diabetes; see the NICE guidance on canagliflozin in combination therapy for treating type 2 diabetes, dapagliflozin in combination therapy for treating type 2 diabetes.
dapagliflozin in triple therapy for treating type 2 diabetes and empagliflozin in combination therapy for treating type 2 diabetes.

See the section on chronic kidney disease for guidance on SGLT2 inhibitors for people with type 2 diabetes and chronic kidney disease.

**Insulin-based treatments**

There is MHRA safety advice on the following drugs:


1.6.32 When starting insulin therapy in adults with type 2 diabetes, use a structured programme employing active insulin dose titration that encompasses:

- injection technique, including rotating injection sites and avoiding repeated injections at the same point within sites

- continuing telephone support

- self-monitoring

- dose titration to target levels

- dietary understanding

- the [DVLA's Assessing fitness to drive: a guide for medical professionals](https://www.gov.uk/government/publications/dvla%E2%80%99s-assessing-fitness-to-drive-a-guide-for-medical-professionals)

- management of hypoglycaemia

- management of acute changes in plasma glucose control

- support from an appropriately trained and experienced healthcare professional. [2015]
1.6.33  When starting insulin therapy in adults with type 2 diabetes, continue to offer metformin for people without contraindications or intolerance. Review the continued need for other blood glucose lowering therapies. [2015]

1.6.34  Start insulin therapy for adults with type 2 diabetes from a choice of a number of insulin types and regimens:

- Offer NPH insulin injected once or twice daily according to need.

- Consider starting both NPH and short-acting insulin (particularly if the person's HbA1c is 75 mmol/mol [9.0%] or higher), administered either:
  - separately or
  - as a pre-mixed (biphasic) human insulin preparation.

- Consider, as an alternative to NPH insulin, using insulin detemir or insulin glargine if:
  - the person needs assistance from a carer or healthcare professional to inject insulin, and use of insulin detemir or insulin glargine would reduce the frequency of injections from twice to once daily or
  - the person's lifestyle is restricted by recurrent symptomatic hypoglycaemic episodes or
  - the person would otherwise need twice-daily NPH insulin injections in combination with oral glucose-lowering drugs.

- Consider pre-mixed (biphasic) preparations that include short-acting insulin analogues, rather than pre-mixed (biphasic) preparations that include short-acting human insulin preparations, if:
  - a person prefers injecting insulin immediately before a meal or
  - hypoglycaemia is a problem or
  - blood glucose levels rise markedly after meals. [2015]

1.6.35  Consider switching to insulin detemir or insulin glargine from NPH insulin in adults with type 2 diabetes:

- who do not reach their target HbA1c because of significant hypoglycaemia or
- who experience significant hypoglycaemia on NPH insulin irrespective of the level of HbA1c reached or
- who cannot use the device needed to inject NPH insulin but who could administer their own insulin safely and accurately if a switch to one of the long-acting insulin analogues was made or
- who need help from a carer or healthcare professional to administer insulin injections and for whom switching to one of the long-acting insulin analogues would reduce the number of daily injections. [2015]

1.6.36 Monitor adults with type 2 diabetes who are on a basal insulin regimen (NPH insulin, insulin detemir or insulin glargine) for the need for short-acting insulin before meals (or a pre-mixed [biphasic] insulin preparation). [2015]

1.6.37 Monitor adults with type 2 diabetes who are on pre-mixed (biphasic) insulin for the need for a further injection of short-acting insulin before meals or for a change to a basal bolus regimen with NPH insulin or insulin detemir or insulin glargine, if blood glucose control remains inadequate. [2015]

Treatment with combinations of medicines including SGLT2 inhibitors may be appropriate for some people with type 2 diabetes; see the NICE guidance on canagliflozin in combination therapy for treating type 2 diabetes, dapagliflozin in combination therapy for treating type 2 diabetes and empagliflozin in combination therapy for treating type 2 diabetes.

See the section on chronic kidney disease for guidance on SGLT2 inhibitors for people with type 2 diabetes and chronic kidney disease.

**Insulin delivery**

1.6.38 For guidance on insulin delivery for adults with type 2 diabetes, see the section on insulin delivery in the NICE guideline on type 1 diabetes. [2015]
1.7 Managing complications

Gastroparesis

There is MHRA safety advice on the following drugs:

- Domperidone: follow the MHRA safety advice on the risk of cardiac side effects with domperidone.
- Metoclopramide: follow the MHRA safety advice on the risk of neurological adverse effects with metoclopramide.

In December 2015, the use of erythromycin in recommendations 1.7.2 and 1.7.3 was off label. See NICE’s information on prescribing medicines, NICE has published an evidence summary on oral erythromycin for gastroparesis in adults, including a version for the public.

1.7.1 Think about a diagnosis of gastroparesis in adults with type 2 diabetes with erratic blood glucose control or unexplained gastric bloating or vomiting, taking into account possible alternative diagnoses. [2009, amended 2015]

1.7.2 For adults with type 2 diabetes who have vomiting caused by gastroparesis, explain that:

- there is not strong evidence that any available antiemetic therapy is effective
- some people have had benefit with domperidone, erythromycin or metoclopramide.
- the strongest evidence for effectiveness is for domperidone, but prescribers must take into account its safety profile, in particular its cardiac risk and potential interactions with other medicines. [2015]

1.7.3 For treating vomiting caused by gastroparesis in adults with type 2 diabetes:

- consider alternating use of erythromycin and metoclopramide
- consider domperidone only in exceptional circumstances (if domperidone is the only effective treatment) and in accordance with MHRA guidance. [2015]

1.7.4 If gastroparesis is suspected, consider referral to specialist services if:
• the differential diagnosis is in doubt or

• persistent or severe vomiting occurs. [2009]

**Painful diabetic neuropathy**

1.7.5 For guidance on managing painful diabetic peripheral neuropathy in adults with type 2 diabetes, see the NICE guideline on neuropathic pain in adults. [2015]

**Autonomic neuropathy**

1.7.6 Think about the possibility of contributory sympathetic nervous system damage for adults with type 2 diabetes who lose the warning signs of hypoglycaemia. [2009, amended 2015]

1.7.7 Think about the possibility of autonomic neuropathy affecting the gut in adults with type 2 diabetes who have unexplained diarrhoea that happens particularly at night. [2009, amended 2015]

1.7.8 When using tricyclic drugs and antihypertensive drug treatments in adults with type 2 diabetes who have autonomic neuropathy, be aware of the increased likelihood of side effects such as orthostatic hypotension. [2009]

1.7.9 Investigate the possibility of autonomic neuropathy affecting the bladder in adults with type 2 diabetes who have unexplained bladder-emptying problems. [2009]

1.7.10 In managing autonomic neuropathy symptoms, include specific interventions indicated by the manifestations (for example, for abnormal sweating or nocturnal diarrhoea). [2009]

**Diabetic foot problems**

1.7.11 For guidance on preventing and managing foot problems in adults with type 2 diabetes, see the NICE guideline on diabetic foot problems. [2015]
Chronic kidney disease

There is MHRA safety advice on the following drugs:

- SGLT2 inhibitors: follow the MHRA safety advice on the increased risk of lower-limb amputation with SGLT2 inhibitors.
- SGLT2 inhibitors: follow the MHRA safety advice on the increased risk of diabetic ketoacidosis with SGLT2 inhibitors.

1.7.12 For adults with chronic kidney disease and type 2 diabetes, offer an angiotensin receptor blocker (ARB) or an angiotensin-converting enzyme (ACE) inhibitor (titrated to the highest licensed dose that the person can tolerate) if albumin-to-creatinine ratio (ACR) is 3 mg/mmol or more, as recommended in the NICE guideline on chronic kidney disease. [2021]

1.7.13 For adults with type 2 diabetes and chronic kidney disease who are taking an ARB or an ACE inhibitor (titrated to the highest licensed dose that they can tolerate), offer an SGLT2 inhibitor (in addition to the ARB or ACE inhibitor) if:

- ACR is over 30 mg/mmol and
- they meet the criteria in the marketing authorisation (including relevant estimated glomerular filtration rate [eGFR] thresholds).

In November 2021, not all SGLT2 inhibitors were licensed for this indication. See NICE’s information on prescribing medicines. [2021]

1.7.14 For adults with type 2 diabetes and chronic kidney disease who are taking an ARB or an ACE inhibitor (titrated to the highest licensed dose that they can tolerate), consider an SGLT2 inhibitor (in addition to the ARB or ACE inhibitor) if:

- ACR is between 3 and 30 mg/mmol and
• they meet the criteria in the marketing authorisation (including relevant eGFR thresholds).

In November 2021, not all SGLT2 inhibitors were licensed for this indication. See NICE’s information on prescribing medicines. [2021]

1.7.15 For further guidance on managing kidney disease in adults with type 2 diabetes, see the NICE guideline on chronic kidney disease. [2015]

For a short explanation of why the committee made these recommendations and how they might affect practice, see the rationale and impact section on SGLT2 inhibitors for adults with type 2 diabetes and chronic kidney disease.

Full details of the evidence and the committee’s discussion are in evidence review A: SGLT2 inhibitors for people with chronic kidney disease and type 2 diabetes.

Erectile dysfunction

1.7.16 Offer men with type 2 diabetes the opportunity to discuss erectile dysfunction as part of their annual review. [2015]

1.7.17 Assess, educate and support men with type 2 diabetes who have problematic erectile dysfunction, addressing contributory factors such as cardiovascular disease as well as possible treatment options. [2015]

1.7.18 Consider a phosphodiesterase-5 inhibitor to treat problematic erectile dysfunction in men with type 2 diabetes, initially choosing the drug with the lowest acquisition cost and taking into account any contraindications. [2015]

1.7.19 Following discussion, refer men with type 2 diabetes to a service offering other medical, surgical or psychological management of erectile dysfunction if treatment (including a phosphodiesterase-5 inhibitor, as appropriate) has been unsuccessful. [2015]

Eye disease

1.7.20 When adults are diagnosed with type 2 diabetes, GPs should immediately refer them to the local eye screening service. [2009, amended 2020]
1.7.21 Encourage adults to attend eye screening, and explain that it will help them to keep their eyes healthy and help to prevent problems with their vision. Explain that the screening service is effective at identifying problems so that they can be treated early. [2009]

1.7.22 Arrange emergency review by an ophthalmologist for:

- sudden loss of vision
- rubeosis iridis
- pre-retinal or vitreous haemorrhage
- retinal detachment. [2009]

1.7.23 Refer to an ophthalmologist in accordance with the National Screening Committee criteria and timelines for any large sudden unexplained drop in visual acuity. [2009, amended 2020]

Terms used in this guideline

Consultant-led multidisciplinary team

A consultant-led multidisciplinary team may include a wide range of staff based in primary, secondary and community care.

Insulin glargine

The recommendations in this guideline also apply to any current and future biosimilar product(s) of insulin glargine that have an appropriate marketing authorisation that allows the use of the biosimilar(s) in the same indication.

Initial drug treatment

Treatment with a single non-insulin blood glucose lowering therapy (monotherapy).

First intensification of drug treatment

Treatment with 2 non-insulin blood glucose lowering therapies in combination (dual therapy).
Second intensification of drug treatment

Treatment with either 3 non-insulin blood glucose lowering therapies in combination (triple therapy) or any treatment combination containing insulin.
Recommendations for research

The 2015 Guideline Development Group made the following recommendations for research, based on its review of evidence, to improve NICE guidance and patient care in the future. The Guideline Development Group's full set of recommendations for research is detailed in the full guideline.

Key recommendations for research

The effects of stopping and/or switching drug treatments to control blood glucose levels

In adults with type 2 diabetes, what are the effects of stopping and/or switching drug treatments to control blood glucose levels, and what criteria should inform the decision?

Why this is important

There is a lack of evidence on the effects of stopping and/or switching drug treatments to control blood glucose levels. The current practice of 'stopping rules' is typically motivated by either inadequate blood glucose control (rising HbA1c levels) or intolerable side effects. There is limited understanding of the short- and long-term effects of stopping a therapy and switching to another in terms of diabetes control (HbA1c levels), hypoglycaemic risk, weight gain, and cardiovascular morbidity and mortality. In addition, there is limited understanding of how quickly consideration should be given to stopping and switching to another drug treatment and, if stopping and switching may be needed, what the optimal sequencing is of drug treatments. Randomised controlled trials examining these different issues would help to improve diabetes care.

Non-metformin-based drug treatment combinations to control blood glucose levels

In adults with type 2 diabetes, what treatment combinations (for example, glucagon-like peptide-1 [GLP-1] mimetics and insulin combination therapy with meglitinides) are most effective when initial drug treatment with non-metformin monotherapy fails to adequately control blood glucose levels?

Why this is important

Although it is recognised that metformin therapy is suitable for most adults with type 2 diabetes, its use is contraindicated or not tolerated in approximately 15% of individuals. To date, research
evidence has largely focused on metformin-based treatment combinations. Given the progressive nature of the condition, in which intensification of blood glucose lowering drug therapies are indicated over time, there is little evidence, for some adults, to guide management strategies on treatment combinations that do not include metformin. Randomised controlled trials are therefore needed to better understand the treatment choices that are available which improve blood glucose control and long-term risks of complications associated with diabetes.

Drug treatment (third intensification) for when blood glucose levels are inadequately controlled by 3 oral antidiabetic drugs and/or insulin combinations

When third intensification of treatment is indicated, which blood glucose lowering therapies should be used to control blood glucose levels?

Why this is important

As the incidence of type 2 diabetes increases in the younger population and as blood glucose control declines naturally over time, it is likely that further intensification of therapies would be needed. Currently, there is evidence up to second intensification of drug therapies, that is, when 2 or more non-insulin-based treatment combinations fail to adequately control blood glucose levels. Randomised controlled trials are needed to improve understanding of alternative treatment options for adults at second intensification whose blood glucose is inadequately controlled with insulin and/or triple non-insulin-based drug therapies.

Long-term outcomes associated with blood glucose lowering agents

In adults with type 2 diabetes, what are the long-term effects of blood glucose lowering therapies such as dipeptidyl peptidase-4 (DPP-4) inhibitors, sodium–glucose cotransporter-2 (SGLT2) inhibitors and meglitinides?

Why this is important

There is limited evidence in relation to the long-term effects (at least 5 years) of blood glucose lowering therapies, particularly newer agents in terms of efficacy and adverse events (for example, cardiovascular outcomes). Randomised controlled trials and prospective longitudinal studies are needed to better understand the long-term efficacy and safety issues surrounding these medicines.
Self-monitoring of blood glucose levels

What is the optimal frequency for self-monitoring of blood glucose in adults with type 2 diabetes?

Why this is important

It is widely recognised that self-monitoring of blood glucose is a multicomponent intervention. As well as being educated about how to use a self-monitoring device to assess blood glucose levels, adults with type 2 diabetes need to be able to understand their results and act on the observed readings.

In adults for whom self-monitoring is appropriate, there is limited evidence to guide clinical practice in prescribing self-monitoring regimens, in terms of frequency of testing and optimal blood glucose targets. Given the inconvenience and expense of self-monitoring, robust evidence from randomised controlled trials is needed to guide the optimal use of this intervention.

Other recommendations for research

The 2021 guideline committee has made the following recommendations for research.

1 Effectiveness of SGLT2 inhibitors for different ethnic groups

What is the clinical and cost effectiveness of SGLT2 inhibitors in adults with type 2 diabetes and chronic kidney disease, stratified across different ethnic groups?

For a short explanation of why the committee made this recommendation for research, see the rationale on SGLT2 inhibitors for adults with type 2 diabetes and chronic kidney disease.

Full details of the evidence and the committee's discussion are in evidence review A: SGLT2 inhibitors for people with chronic kidney disease and type 2 diabetes.

2 Effectiveness of SGLT2 inhibitors for adults with a urine ACR below 3 mg/mmol

What is the clinical and cost effectiveness of SGLT2 inhibitors in adults with type 2 diabetes, chronic kidney disease and a urine ACR of less than 3 mg/mmol?
For a short explanation of why the committee made this recommendation for research, see the rationale on SGLT2 inhibitors for adults with type 2 diabetes and chronic kidney disease.

Full details of the evidence and the committee's discussion are in evidence review A: SGLT2 inhibitors for people with chronic kidney disease and type 2 diabetes.
Rationale and impact

These sections briefly explain why the committee made the recommendations and how they might affect practice.

SGLT2 inhibitors for adults with type 2 diabetes and chronic kidney disease

Recommendations 1.7.12 to 1.17.14

Why the committee made the recommendations

Strong evidence from well-conducted randomised controlled trials showed that SGLT2 inhibitors reduced the risk of chronic kidney disease progression, mortality and cardiovascular events in adults with type 2 diabetes and chronic kidney disease.

Economic modelling for people with an ACR above 30 mg/mol at baseline showed that SGLT2 inhibitors were likely to be both more effective and cost saving in this group compared with standard treatment.

People with a baseline ACR of 3 to 30 mg/mmol will experience fewer cardiovascular events and events relating to chronic kidney disease progression than people with a higher ACR. Because of this, SGLT2 inhibitors would prevent fewer events for this group in absolute terms, even if the relative effect was the same. Economic modelling showed that SGLT2 inhibitors were still likely to be both more effective and cost saving in people with a baseline ACR of between 3 and 30 mg/mol compared with standard treatment. However, there was more uncertainty around the clinical and cost effectiveness in this group than in people with a baseline ACR over 30 mg/mmol. Because of this, SGLT2 inhibitors may not be suitable for everyone with a baseline ACR of between 3 mg/mmol and 30 mg/mmol, and the committee made a different recommendation for this group.

The committee made a recommendation for research on the effectiveness of SGLT2 inhibitors for people with a baseline ACR of less than 3 mg/mol, because there was no evidence looking specifically at this group.

The committee cautioned that SGLT2 inhibitors are not suitable for everyone and should only be used within their marketing authorisation.
Some ethnic groups have a higher risk of micro and macrovascular complications and so may benefit more from SGLT2 inhibitors. However, no evidence was found that stratified data by ethnicity. To address this gap, the committee made a recommendation for research on the effectiveness of SGLT2 inhibitors for different ethnic groups.

For an explanation of why the committee recommended ARBs and ACE inhibitors, see the rationale and impact section on pharmacotherapy for proteinuria and choice of antihypertensive agent in the NICE guideline on chronic kidney disease.

How the recommendations might affect practice

The recommendations will lead to a significant change in practice, since SGLT2 inhibitors will be prescribed more widely. This will result in a substantial cost impact. The committee noted, however, that there was likely to be a long-term cost saving from reduced downstream treatment costs, as SGLT2 inhibitors slow chronic kidney disease progression and reduce the number of cardiovascular and end-stage renal events.

Return to recommendations
Finding more information and committee details

You can see everything NICE says on this topic in the NICE Pathway on type 2 diabetes in adults.

To find NICE guidance on related topics, including guidance in development, see the NICE webpage on diabetes.

For full details of the evidence and the guideline committee's discussions, see the full guideline and evidence reviews. You can also find information about how the guideline was developed, including details of the committee.

NICE has produced tools and resources to help you put this guideline into practice. For general help and advice on putting our guidelines into practice, see resources to help you put NICE guidance into practice.
Update information

November 2021: We have reviewed the evidence and made new recommendations on SGLT2 inhibitors for adults with type 2 diabetes and chronic kidney disease. They are marked [2021].

December 2020: We have amended recommendations 1.7.20 and 1.7.23 to bring them in line with the diabetic eye screening programme. The evidence for these recommendations has not been reviewed, and they are marked [2009, amended 2020].

August 2019: The recommendations in section 1.4 on diagnosing and managing hypertension have been removed because diagnosis, treatment and monitoring of hypertension is broadly the same for people with type 2 diabetes as for other people (see the NICE guideline on hypertension in adults). When a different approach is needed for people with type 2 diabetes, this is specified in the hypertension guideline.

May 2017: Text on sodium–glucose cotransporter 2 (SGLT2) inhibitors was added to the section on initial drug treatment. The algorithm for blood glucose lowering therapy in adults with type 2 diabetes was also updated to revise footnote b with links to relevant NICE guidance on SGLT2 inhibitors, and new information on SGLT2 inhibitors was also added to the box on action to take if metformin is contraindicated or not tolerated.

December 2016: The text after recommendation 1.6.31 and the algorithm for blood glucose lowering therapy were updated to refer to NICE technology appraisal guidance on dapagliflozin in triple therapy for treating type 2 diabetes (TA418).

December 2015: We updated and replaced NICE guideline CG87 (published May 2009) and NICE technology appraisal guidance 203 and 248.

Recommendations are marked as [2015], [2009] or [2009, amended 2015]:

- [2015] indicates that the evidence has been reviewed.
- [2009] indicates that the evidence has not been reviewed since 2009.
• [2009, amended 2015] or [2009, amended 2016] indicates that the evidence has not been reviewed since 2009, but either changes have been made to the recommendation wording that change the meaning or NICE has made editorial changes to the original wording to clarify the action to be taken (see below).

We have made a change without an evidence review:

• The recommendation on the treatment of gastroparesis was replaced by recommendations from the NICE guideline on type 1 diabetes.

This change is labelled [2015].

Minor changes since publication

**December 2019:** Relationships to the NICE guideline on hypertension were clarified, and a link was added to the decision aid on choice of medicine to control blood glucose. We added a link to the patient decision aid and user guide about taking a second medicine to control blood glucose.

**June 2018:** Recommendation 1.3.11 was added to provide a link to NICE's advice on bariatric surgery.

**January 2018:** Notes were added with links to MHRA warnings about sodium–glucose cotransporter 2 (SGLT2) inhibitors.