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# A summary of the National Institute for Health and Clinical Excellence (NICE) Clinical Guideline 66: the management of type 2 diabetes

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## PERSPECTIVE

We are currently in the midst of a global epidemic of diabetes, driven by the rapidly increasing prevalence of obesity. Over 240 million people have diabetes worldwide, with the total number of cases predicted to increase to over 360 million by 2030.[1] In the UK, about 1.9 million individuals are living with diabetes, with a further half-a-million cases undiagnosed.[2] Type 2 diabetes is by far the most common form of diabetes, accounting for about 85% of all diagnoses.[2]

Type 2 diabetes is associated with increased cardiovascular risk, such that the risk of a cardiovascular event in a diabetic patient is as high as in a non-diabetic who has already had a cardiovascular event.[3] In addition, type 2 diabetes is associated with a range of microvascular complications, which can lead to eye, kidney and nerve damage, adding to the morbidity burden of the disease. The prevalence of these complications is also on the increase, paralleling the increase in type 2 diabetes seen in recent years. As a consequence, type 2 diabetes and its complications exact a huge economic and socioeconomic burden, while in clinical terms, their individual management is often complex, time-consuming and resource intensive.

### The new NICE Guideline[4]

In May 2008, NICE issued a new guideline on the management of type 2 diabetes which updates and replaces the suite of guidelines for the management of the condition published in 2002. This update encompasses new evidence that has emerged since these earlier recommendations were published, and will act as a single point of reference for healthcare professionals from a range of disciplines tasked with diabetes care. Given the complexity of diabetes management and the need for significant lifestyle modification and long-term adherence to a range of drug therapies, this guideline places patient education and information at the centre of its recommendations.

This article provides an overview of some of the key recommendations in the new guideline, and highlights some of the challenges that will face us when implementing the guidance it contains in routine clinical practice.

## THE NICE RECOMMENDATIONS

The NICE recommendations encompass the following areas of type 2 diabetes management: patient education; lifestyle management; blood

glucose targets; self-monitoring; oral glucose control therapy; insulin therapy; control of blood pressure; cardiovascular risk estimation; control of blood lipids; antithrombotic therapy; management of microvascular complications. NICE have distilled their main recommendations into a series of key priorities for implementation, which are summarised in Box 1.

## Patient education

Patients should receive structured and ongoing education, preferably in a group setting, from initial diagnosis onwards in order to help them understand and manage their condition. Educational programmes should be reviewed and reinforced annually.

## Lifestyle management

A trial of lifestyle intervention with ongoing education is recommended before a patient is initiated on drug therapy. However, time and resource constraints in primary care may limit the success of any lifestyle programmes that can be offered in this setting.

Individualised and ongoing nutritional advice should be given to all patients with type 2 diabetes, and should be similar in nature to the nutritional advice offered to the general population. Delivery of this advice should take place through a professional with specific expertise in nutrition.

NICE recommend initial body weight loss of 5–10% in overweight patients with type 2 diabetes. It should be emphasised to the patient that even modest amounts of weight loss will still be of benefit to health, while more profound weight loss over the longer term will provide even greater metabolic benefits.

## Blood glucose targets

NICE continue to highlight the importance of tight glucose control. Nevertheless, $HbA_{1C}$ targets remain similar to those issued in the earlier guidance, with the ideal target set at 6.5%. However, this NICE guideline acknowledges that a single $HbA_{1C}$ target is unhelpful, and recommend that healthcare professionals should agree with patients individual targets and how best to achieve them through ongoing lifestyle changes and drug therapy. $HbA_{1C}$ levels should be checked every 2–6 months to ensure that glycaemic control is maintained.

**Box 1.** Key priorities for implementation. Abridged from NICE clinical guideline 66: management of type 2 diabetes. $HbA_{1C}$, glycated haemoglobin.

- Offer structured education; review and reinforce annually.
- Provide ongoing individualised dietary advice.
- When setting a target $HbA_{1C}$[a]: involve the individual patient in decision making; encourage the individual to maintain target; offer therapy to achieve target; emphasise that any reduction in $HbA_{1C}$ towards target is beneficial; avoid highly intensive management to targets below 6.5%.
- Offer glucose self-monitoring to a newly diagnosed patient only as part of self-management and education.
- When initiating insulin therapy, employ a structured programme encompassing: education; telephone support; self-monitoring; dose titration to target; diet; management of hypoglycaemia; management of acute changes in plasma glucose; support from trained healthcare professionals.

[a]An individual's target $HbA_{1C}$ may be above the 6.5% target set for most patients with type 2 diabetes.

## Self-monitoring

Self-monitoring is recommended for a newly diagnosed patient only as part of self-management education. Patients should receive assistance in understanding how to interpret results, and its purpose and utility should be reviewed annually.

## Oral glucose control therapy

Response to oral glucose control therapy should be assessed by measuring $HbA_{1C}$. As endogenous insulin production declines as type 2 diabetes progresses, higher doses of oral therapy and the addition of other agents will need to be considered during ongoing disease management. The following treatments (and their relative position in the treatment algorithm) are recommended in the NICE guideline.

*Metformin*: use first-line when $HbA_{1C}$ is not controlled to target, unless contraindicated.

*Sulphonlyureas:* use second-line, or first-line where metformin is contraindicated or the patient is not overweight.

*Thiazolidinediones*: use as a second- or third-line therapy for patients in whom insulin is contraindicated and who are not at risk of heart failure or bone fracture. The choice of thiazolidinedione should reflect current advice from regulatory authorities, cost and safety.

*Exenatide*: a 12-month trial of exenatide is recommended only as a third-line option for obese patients with type 2 diabetes (BMI >35), whose $HbA_{1c}$ is ≥7.5% despite conventional oral treatment, and who may otherwise require high-cost medication, such as a thiazolidinedione or insulin.

*Acarbose:* consider for patients who are unable to use other medications.

*New therapies:* the lengthy process of guideline development has precluded the inclusion of some recently available therapies, such as the dipeptidyl peptidase-4 (DPP4) inhibitors. Presumably, NICE will assess the utility of these agents for blood glucose control through its technology appraisal process in due course.

## Insulin therapy

When $HbA_{1C}$ rises above 7.5% despite other measures, insulin therapy should be considered. The benefits and risks of insulin therapy should be discussed with the patient. Treatment should normally be started with human NPH insulin, although long-acting insulin analogues (e.g. insulin glargine) and insulin pre-mixes can be considered in certain circumstances. A structured programme should be used when initiating insulin therapy (see Box 1).

## Control of blood pressure

Blood pressure should be monitored at least annually in patients with type 2 diabetes, and more frequently in cases where blood pressure has previously been above target. If patients are receiving antihypertensive drugs at the time of a diagnosis, changes to the regimen should only be made in cases where there is poor blood pressure control.

Two blood pressure targets have been set for patients with type 2 diabetes in this new guideline: <140/80 mmHg in uncomplicated type 2 diabetes and <130/80 mmHg in cases where kidney, eye or cerebrovascular damage is evident. Lifestyle advice is recommended as the first-line intervention to achieve these targets. If blood pressure targets are not achieved, blood pressure-lowering drugs should be considered. The treatment algorithm for the stepwise addition of blood pressure-lowering drugs and combination therapy reflects the established 'ACD' algorithm published in previous NICE guidance on the management of hypertension,

which has been endorsed by the British Hypertension Society (BHS).[5]

## Cardiovascular risk estimation

Formal cardiovascular risk estimation is not normally necessary for patients with type 2 diabetes given that the condition is considered a cardiovascular risk equivalent.[3] However, in those not deemed as being at high cardiovascular risk by virtue of meeting a range of criteria (normal weight, non-smoker, normotensive, with normal lipids, no microalbuminuria, and no personal or family history of cardiovascular disease), cardiovascular risk should be estimated annually.

## Control of blood lipids

NICE have established the following targets for blood lipid control in patients with type 2 diabetes:

- total cholesterol below 4.0 mmol/L
- LDL cholesterol below 2.0 mmol/L.

NICE recommends that generic simvastatin (40 mg/day) is initiated in the majority of patients with type 2 diabetes aged 40 years or older and in younger patients with additional cardiovascular risk factors. If the cholesterol targets are not achieved, consideration should be given to increasing the dose of simvastatin to 80 mg/day or intensifying therapy with a more potent statin or adding ezetimibe (in cases of new or existing cardiovascular disease or increased albumin excretion rate). In patients with high serum triglycerides (>4.5 mmol/L), fenofibrate can be considered after assessment of secondary causes of hypertriglyceridaemia. Fibrates may also be considered in patients with triglyceride levels in the range of 2.3–4.5 mmol/L despite statin therapy. The lipid profile should be assessed every 1–3 months after initiating treatment.

## Antithrombotic therapy

Aspirin (75 mg/day) should be offered to patients aged over 50 years and to younger individuals with additional cardiovascular risk factors. Clopidogrel can be considered in patients intolerant of aspirin.

## Management of microvascular complications

### *Kidney damage*

An albumin:creatinine ratio (ACR) on a first-pass morning urine sample should be estimated annually. Suspected microalbuminuria (i.e. an abnormal ACR of >2.5 mg/mmol for men and >3.5 mg/mmol for women) should be confirmed over two repeat tests within 3–4 months if at least one out of these additional tests is abnormal. Estimate glomerular filtration rate annually. Exclude the possibility of non-diabetic renal disease through further investigations. Once diabetic nephropathy has been confirmed, discuss the significance with the patient and offer an ACE inhibitor dose titrated to maximum dose (or an angiotensin receptor antagonist if not tolerated) to maintain blood pressure below 130/80 mmHg.

### *Eye damage*

Eye screening should be performed at the time of diagnosis and repeated annually. The patient should be educated as to the reasons for eye screening and its importance. When photographing the retina, mydriasis with tropicamide should be used after appropriate discussion with the patient regarding the advantages and disadvantages of this approach, including precautions for driving. Digital retinal photography should be delivered by staff with appropriate expertise. Visual acuity tests should also be conducted as a component of eye screening. Emergency review by an ophthalmologist should be arranged in cases of sudden loss of vision, rubeosis iridis, pre-retinal or vitreous haemorrhage or retinal damage, and

rapid review in cases of new vessel formation. In addition, routine referral to an ophthalmologist should take place in cases of maculopathy, pre-proliferative retinopathy or any unexplained decline in visual acuity.

### *Nerve damage*

*Neuropathic pain:* Clinicians should enquire annually about the development of neuropathic symptoms which are causing distress to the patient, and should explain their cause, prognosis and possible treatment options. Where standard analgesia fails, a trial of a tricyclic drug should be used to manage any neuropathic discomfort that is present; this should be given before the time of day when symptoms are normally troublesome. Duloxetine, gabapentin or pregabalin may be used where tricyclic drugs have proved ineffective. Where severe pain persists despite these measures, consider trialling opioid analgesia or refer the patient to a pain management service.

*Gastroparesis*: consider a diagnosis of gastroparesis in cases of erratic glycaemic control or where unexplained gastric symptoms such as bloating or vomiting occur; if gastroparesis is confirmed, consider a trial of metoclopramide, domperidone or erythromycin.

*Erectile dysfunction*: review erectile function annually in men with type 2 diabetes and offer a phosphodiesterase type-5 (PDE-5) inhibitor where erectile dysfunction is present; if PDE-5 inhibitors are ineffective, discuss other management options such as other medical treatments, surgery or psychological support.

*Foot problems:* the management of foot problems associated with type 2 diabetes is considered in a separate NICE guideline.[6]

*Other signs of autonomic neuropathy:* consider the possibility of sympathetic nervous system damage in patients who have lost the warning signs of hypoglycaemia; unexplained diarrhoea (particularly at night) and bladder-emptying difficulties may also relate to autonomic neuropathy.

## CONCLUSION

As we seek to improve the care of patients with type 2 diabetes and as the range of treatment options increases and becomes more complex, it is vital that management guidelines remain up-to-date, enshrined in the evidence and able to be implemented in practice. Moreover, it is important that guidelines remain in line with other policy initiatives such as the quality and outcomes framework (QOF) of the General Medical Services contract. Furthermore, sufficient resources should be made available to ensure that key recommendations are embraced in routine clinical practice. This will involve training of staff tasked with the management of type 2 diabetes in both primary and secondary care.

In this context, this new NICE guideline for the management of type 2 diabetes should be welcomed, but the challenges involved in implementing it should not be underestimated. The individual challenges of guideline implementation with respect to the management of blood pressure, lipids and excess weight will be addressed in future articles in this series from experts in their respective fields.

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