Type 1 diabetes in adults: new NICE guidance on diagnosis and management

There have been many changes in the management of type 1 diabetes since the last NICE guidelines in 2004. These have included the development of a wider range of analogue insulins, improvements in technology for blood glucose monitoring and insulin delivery, and interest in therapies other than insulin for treatment. Despite these new developments, people with type 1 diabetes still have a reduced life expectancy of 11–13 years. New NICE guidance (NG17) published in August sets out to change our practice, with evidence-based practice to improve glycaemic control and reduce the complications of diabetes while working in a cost effective way.

So what’s new?
Many of the new recommendations are uncontroversial and reflect changes in clinical practice over the last decade. Structured education is now recommended for all patients, either in a group format or on an individual basis. Guidelines for continuous subcutaneous insulin infusion therapy and referral for pancreas or islet-cell transplantation have been incorporated. Checking thyroid function is now recommended annually. Use of blood ketone testing is now recommended both as part of the ‘sick day rules’ and for monitoring ketoacidosis in hospital.

Some recommendations may be more controversial. The guideline suggests a much tighter target for HbA1c of 48 mmol/mol or lower. This is equivalent to 6.5%, significantly lower than the 7.5% target in 2004. Targets for fasting glucose levels have increased from 4–7 mmol/L to 5–7 mmol/L. Targets before other meals remain at 4–7 mmol/L with postprandial results of 5–9 mmol/L, now specified at least 90 minutes after eating.

The evidence for the benefits of tight glycaemic control is strong. The Diabetes Control and Complications Trial (DCCT) compared intensive glycaemic control aiming for an HbA1c of 6% against usual care in 1441 people with type 1 diabetes over 6.5 years. For patients without retinopathy, nephropathy or neuropathy at baseline, the development of these complications was reduced by 34–76%. For patients who already had microvascular complications, progression was reduced by 26–63%. Follow up of 1394 of these patients over a further 11 years as part of the Epidemiology of Diabetes Interventions and Complications (EDIC) study showed that prior intensive control was associated with a 57% reduction in first episode of non-fatal myocardial infarct, stroke or death from cardiovascular disease. Benefits of tight control have been confirmed by the Swedish National Diabetes Register where patients with an HbA1c of 5–7.9% had a 41% reduction in fatal and non-fatal coronary heart disease and a 37% reduction in stroke over five years compared with those whose HbA1c was 8% or more.

The incidence of severe hypoglycaemia in the DCCT was three times higher in the intensively controlled group and this has led to caution in aiming for very tight control. The previous HbA1c target of 7.5% corresponded to the crossover between the benefits of improved control and the risk of significant hypoglycaemia. However, more recent studies suggest that tight glycaemic control can be achieved without significant increases in hypoglycaemia, particularly after training on carbohydrate counting and insulin dose adjustment.

In order to achieve tight glycaemic control, the recommendations for frequency of blood glucose testing have been increased. Routine testing is now recommended at least four times per day for all patients, with testing 4–10 times per day where HbA1c target is not achieved, hypoglycaemia becomes more frequent or for other indications such as before driving and during sport, illness or pregnancy. There are many cross-sectional studies that show increased frequency of self-testing is associated with lower HbA1c and with lower incidence of complications. However, in cross-sectional studies, it is acknowledged that the monitoring of glucose alone is not the cause of the better glycaemic control. Blood glucose information must be used effectively. Frequent testing is a behaviour related to good glycaemic control but not directly causal.

No randomised controlled trials were found to support testing more frequently than four times per day. The guideline recommendations are based on an economic analysis using an internet-based model (IMS CORE Diabetes Model) with data taken from a cross-sectional study of 20 555 patients with type 1 diabetes. This model ranked testing eight times per day as the most cost-effective strategy. Quality of life was included only as measured by complication-free survival. For some patients, this increased expectation for testing may be seen more of a burden in the short term than the perceived long-term benefits. This is particularly true as alternate site testing is still not recommended.

The guidelines state that diabetes services should document the proportion of adults with type 1 diabetes in the service who achieve an HbA1c of 58 mmol/mol or lower. There is no guidance on how this should be recorded. Choosing the most recent HbA1c for each patient on a given day may give a proportion of patients different from that when taking the lowest recorded HbA1c in the last year. In DCCT, although 44% of the intensively treated group...
reached the target HbA1c at least once during the study, only 5% were able to sustain it.3

The final area of possible controversy is around the choice of insulin. It is recommended that all patients are offered basal-bolus rather than twice-daily mixed insulins and that newly-diagnosed patients are not offered any choice other than basal-bolus. Rapid-acting analogues are now the choice for meal times. The only recommended basal insulin is now twice-daily insulin detemir. The evidence for this is weak.

There are few direct comparisons of glargine against detemir. In a 52-week randomised but non-blinded trial in 443 patients with type 1 diabetes, there were no significant differences in HbA1c or hypoglycaemia between patients randomised to glargine or detemir. Of the 263 patients randomised to detemir, 173 changed from once-daily to twice-daily dosing based on failure to control afternoon glucose levels.12 In a 32-week crossover trial in 88 patients with type 1 diabetes, there were no significant differences in glucose variability nor adverse events between the glargine required twice-daily dosing.13 Given the lack of randomised controlled trials, the authors performed a network meta-analysis which compared glargine, detemir (once or twice daily), degludec and NPH insulin (once or twice daily). This found that only twice-daily detemir was significantly more effective at reducing HbA1c than twice-daily NPH insulin. This was based on a mean decrease from baseline HbA1c of 0.39 for twice-daily NPH, 0.42 for once-daily glargine, 0.40 for once-daily detemir, and 0.48 for twice-daily detemir. Hazard ratios for major hypoglycaemic events compared to twice-daily NPH insulin were 1.03 for once-daily glargine, 1.31 for once-daily detemir, and 0.96 for twice-daily detemir. It is not clear whether these statistically significant differences in HbA1c and hypoglycaemia have enough clinical significance compared to the daily quality of life to justify the recommend use of twice-daily basal insulin.

**Summary**

The new guidelines may aid motivated patients who want to test more frequently in order to aim for very tight glycaemic control. For newly-diagnosed patients expected to inject five times per day and for those patients with suboptimal control who may now be criticised for not doing up to 10 blood tests per day, the short-term quality of life may make it difficult to see the long-term health gains. Diabetologists must respect the choices of individual patients and use their judgement in applying some of the recommendations.

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**References**


