

Management & prevention of type 2 diabetes

EASD/ADA guideline: Managing hyperglycaemia in T2D



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The new American Diabetes Association (ADA) and European Association for the Study of Diabetes (EASD) glucose-lowering guideline, written by four experts from Europe and four experts from the US, and reviewed by a further 30 or so experts, was recently jointly published in *Diabetes Care* and

Diabetologia. It states that diet, exercise and education remain the foundation of any T2D treatment programme, and that, unless there are prevalent contraindications, metformin is the optimal first-line therapy for all people. Second to metformin, the choice of agent can be any one of the sulphonylureas, pioglitazone, dipeptidyl peptidase-4 inhibitors, glucagon-like peptide-1 (GLP-1) agonists or insulins (usually basal), depending on the individual. If two therapies together do not achieve agreed individualised goals, virtually any three-therapy combinations can be considered. It also states that if combination therapy that includes basal insulin has failed to achieve the agreed HbA_{1c} target, a more complex insulin strategy should be adopted, usually in combination with one or two non-insulin agents.

This approach, the authors say, reflects the limited data yielded from randomised controlled trials to guide decisions after metformin treatment. Different therapies work in different ways and one or more agents may be the appropriate choice for an individual based on

the risk of hypoglycaemia and adverse events, other comorbidities and disease duration.

The guideline mentions costs, labelling each treatment choice as being of low, moderate or high cost, but no cost-effectiveness calculations are quoted. If cost-effectiveness modelling is largely driven by HbA_{1c} reduction with much smaller contributions from weight change and hypoglycaemia, the therapy with very low acquisition cost is likely to be deemed most cost-effective. As glucose-lowering therapies in the UK can vary from £1–3 per month for generic metformin and sulphonylureas, and up to £80 per month for GLP-1 agonist therapy (BMJ Group and RPS Publishing, 2012), it is unlikely that NICE would ever recommend a “complete free for all” regarding medication after metformin, as is endorsed in this guideline.

The authors emphasise a patient-centred approach in that all treatment decisions, where possible, should be made in conjunction with the patient, focusing on their preferences, needs and values. However, it is noted that no patients were involved in writing the guideline! Furthermore, the guideline methodology is not as transparent as that of NICE guidelines and this, with the lack of cost-effectiveness information, means that in my opinion this guideline is unlikely to have much impact upon prescribing in the UK.

BMJ Group and RPS Publishing (2012) *British National Formulary 64*. BMJ Group and RPS Publishing, London

NEW ENGLAND JOURNAL OF MEDICINE

Bariatric surgery: Preventative effect on T2D in obese people

Readability	✓✓✓✓
Applicability to practice	✓✓✓✓✓
WOW! factor	✓✓✓✓

1 Weight loss may provide protection against T2D but research has shown that it is difficult to maintain with behavioural changes alone.

2 In this non-randomised prospective controlled study, the authors examined the effects of bariatric surgery on the prevention of T2D in 1658 people (compared with 1771 obese matched controls).

3 Participants in the bariatric-surgery cohort underwent vertical banded gastroplasty (69%), banding (19%) or gastric bypass (12%); non-randomised, matched, prospective controls received the usual care.

4 During the follow-up period of 15 years, T2D developed in 392 participants in the control group and 110 in the bariatric-surgery group, corresponding to incidence rates of 28.4 cases per 1000 person-years and 6.8 cases per 1000 person-years, respectively (adjusted hazard ratio with bariatric surgery, 0.17; 95% confidence interval, 0.13–0.21; $P < 0.001$).

5 The outcome of bariatric surgery was significantly affected by the presence or absence of impaired fasting glucose ($P = 0.002$ for the interaction) but not influenced by BMI ($P = 0.54$). Sensitivity analyses, including end-point imputations, did not affect the overall conclusions.

6 The authors concluded that bariatric surgery was markedly more efficient than usual care in the prevention of T2D in obese participants.

Carlsson LM, Peltonen M, Ahlin S et al (2012) Bariatric surgery and prevention of type 2 diabetes in Swedish obese subjects. *N Engl J Med* 23: 695–704

DIABETES CARE

Hyperglycaemia in T2D: A patient-centred approach

Readability	✓✓✓✓
Applicability to practice	✓✓✓✓✓
WOW! factor	✓✓✓

1 Glycaemic management in T2D has become increasingly complex with an array of pharmacological agents now available, as well as concerns regarding adverse effects and uncertainty surrounding the benefits of intensive glycaemic control on macrovascular complications.

2 The American Diabetes Association (ADA) and European Association for the Study of Diabetes (EASD) convened to examine the evidence and develop

recommendations for anti-hyperglycaemic therapy in non-pregnant adults with T2D.

3 The statement recommends a patient-centred approach, individualising treatment on the basis of the needs, preferences and tolerances of each patient.

4 The authors noted that diet, exercise and education should remain the foundation of any T2D treatment programme.

5 It was concluded that further comparative effectiveness research is needed, particularly on glycaemic control, costs and the outcomes that matter most to patients, including quality of life and the avoidance of diabetes complications such as cardiovascular disease.

Inzucchi SE, Bergenstal RM, Buse JB et al (2012) Management of hyperglycaemia in type 2 diabetes: A patient centered approach. *Diabetes Care* 35: 1364–79

DIABETES CARE

Low HDL-C and risk of diabetic nephropathy

Readability	✓✓✓
Applicability to practice	✓✓✓
WOW! factor	✓✓

1 Although low high-density lipoprotein cholesterol (HDL-C) is a known risk factor for atherosclerosis, data on HDL-C and its association with the risk of microvascular disease are limited.

2 The authors tested the association between HDL-C and microvascular disease by assessing a cohort of 11 140 people with T2D and one additional vascular risk factor over a median period of 5 years.

3 Cox proportional hazards models were used to assess the association between baseline HDL-C and the development of new or worsening microvascular disease, defined as a composite of renal and retinal events.

4 The mean baseline HDL-C level was 1.3 mmol/L. During follow-up, 32% of participants developed new or worsening microvascular disease, with 28% experiencing a renal event and 6% a retinal event.

5 Compared with participants in the highest third of HDL-C levels, those in the lowest third had a 17% higher risk of microvascular disease (adjusted hazard ratio [HR], 1.17; 95% confidence interval [CI], 1.06–1.28; $P=0.001$), which was driven by a 19% higher risk of renal events (HR, 1.19; 95% CI, 1.08–1.32; $P=0.0005$). There was no association observed between HDL-C and retinal events (HR, 1.01; 95% CI, 0.82–1.25; $P=0.9$).

6 The HDL-C level was identified as an independent risk factor for the development of microvascular disease affecting the kidney but not the retina.

Morton J, Zoungas S, Li Q et al (2012) Low HDL cholesterol and the risk of diabetic nephropathy and retinopathy: Results of the ADVANCE study. *Diabetes Care* 13 Aug [Epub ahead of print]

DIABETOLOGIA

Physical activity: Reduced T2D risk across BMI levels

Readability	✓✓✓
Applicability to practice	✓✓✓✓
WOW! factor	✓✓✓

1 The authors set out to investigate the associations of physical activity and obesity with incident T2D in men and women.

2 The InterAct case-cohort study comprised 12 403 incident T2D cases and a randomly selected subcohort of 16 154 individuals, drawn

from a total cohort of 340 234 with 3.99 million person-years of follow-up.

3 Higher levels of physical activity were independently associated with a 13% and 7% relative reduction in the risk of T2D in men and women, respectively, whereas lower levels of physical activity were associated with a greater risk of T2D across all strata of BMI.

4 Physical activity was also associated with a reduction in the risk of developing T2D in abdominally lean and obese men and women.

InterAct Consortium (2012) Physical activity reduces the risk of incident type 2 diabetes in general and in abdominally lean and obese men and women: the EPIC-InterAct Study. *Diabetologia* 21 Apr [Epub ahead of print]

DIABETES, OBESITY AND METABOLISM

DPP-4 inhibitors: Reduced CV risk in people with T2D

Readability	✓✓✓
Applicability to practice	✓✓✓
WOW! factor	✓✓✓

1 Preliminary data from randomised trials have shown that treatment with dipeptidyl peptidase-4 (DPP-4) inhibitors could be associated

with a reduced incidence of major cardiovascular (CV) events.

2 The authors aimed to verify this protective effect, collecting all available data from a total of 70 randomised trials, enrolling 41 959 individuals with a mean follow-up of 44.1 weeks.

3 Treatment with DPP-4 inhibitors was verified to reduce the risk of CV events, particularly myocardial infarction, in people with T2D.

Monami M, Ahrén B, Dicembrini I, Mannucci E (2012) Dipeptidyl peptidase-4 inhibitors and cardiovascular risk: a meta-analysis of randomized clinical trials. *Diabetes Obes Metab* 23 Aug [Epub ahead of print]

DIABETES CARE

Longitudinal effects of medication non-adherence on costs

Readability	✓✓✓✓
Applicability to practice	✓✓✓✓
WOW! factor	✓✓✓✓

1 The authors examined the longitudinal effects of medication non-adherence (MNA) on costs, and estimated the potential savings from increased adherence using a new method that accounts for shared correlation among cost categories (pharmacy, inpatient and outpatient costs).

2 A total of 740 195 older people were followed from January 2002 until

death, loss to follow-up, or December 2006. At the end of follow-up, people were classified as “MNA” or “adherent”.

3 The authors demonstrated that the costs of MNA among people with diabetes are large and mostly driven by inpatient expenditures.

4 Between 2002 and 2006, MNA was associated with a 37% lower pharmacy cost, 7% lower outpatient cost, and 41% higher inpatient cost, relative to the adherent group.

5 The authors concluded that aggressive strategies and policies are required to achieve optimal medication adherence in diabetes.

Egede LE, Gebregziabher M, Dismuke CE et al (2012) Medication nonadherence in diabetes: Longitudinal effects on costs and potential cost savings from improvement. *Diabetes Care* 21 Aug [Epub ahead of print]

“The high-density lipoprotein cholesterol level was identified as an independent risk factor for the development of microvascular disease affecting the kidney but not the retina.”