ADA/EASD type 2 diabetes consensus 2022: News from the 58th EASD Annual Meeting

Update to the ADA/EASD Consensus Report, a new GIP/GLP-1/glucagon receptor agonist and UKPDS 44 years on. Highlights from the European Association for the Study of Diabetes (EASD) Annual Meeting, held in Stockholm and online from 20 to 23 September 2022.

ADA/EASD Consensus Report: 2022 update launched

The EASD and the American Diabetes Association (ADA) together launched their updated Consensus Report on the Management of Hyperglycaemia in Type 2 Diabetes. A draft version had previously been presented at the ADA conference in June, and the final version has incorporated feedback from the diabetes healthcare community, to include a greater focus on person-centred care, equity of care and managing weight loss.

The update provides guidance on improving equity of care and also on how the social determinants of health (SDOH) impact on effective management of hyperglycaemia. It also focuses on the importance of weight loss, placing it on equal footing with glycaemic-lowering, and including advice on using medications (both glucose-lowering and weight-specific).

Greater attention has been given to the person's involvement in their own diabetes care, including their home and economic circumstances, how they feel about the side effects of different possible medications and helping choose their medication, and playing a full part in forming a care management plan with their healthcare professional that is regularly monitored and updated. Early aggressive care is encouraged, including combination therapy from the time of diagnosis, along with ensuring regular reviews and avoiding therapeutic inertia.

Various recommendations on physical activity are included, including light exercise or resistance training every 30 minutes while sitting; an extra 500 steps per day; 150 minutes of moderate-to-vigorous physical activity every week; strength training two or three times per week; and finally daily sleep of between 6 and 9 hours' duration. A new infographic (*Figure 1*) provides a concise summary.

Advice on glucose-lowering therapies, including a revised treatment algorithm, has been updated, to include recommendations on oral GLP-1 RAs, higher doses of dulaglutide and semaglutide, the GIP/GLP-1 RA class, and combination of GLP-1 RAs and insulin. Specific information on comorbid conditions is included, including atherosclerotic cardiovascular disease, heart failure and chronic kidney disease.

The Consensus was simultaneously published in *Diabetes Care* and *Diabetologia*. Click here to view it in full.

Click here to read Pam Brown's summary of the changes since the 2018/2019 versions.

Novel triple-acting agent shows promising effects on glycaemia and weight

Many of the newer glucose-lowering therapies have centred around the incretin hormones glucagon-like peptide-1 (GLP-1) and gastric inhibitory peptide (GIP), with DPP-4 inhibitors, GLP-1 RAs and the dual GIP/GLP-1 receptor agonist tirzepatide all in production.

Development is ongoing, and results of a Phase 1 study of LY3437943, a novel agent targeting the GIP, GLP-1 and glucagon receptors, were presented at the EASD Meeting. Seventy-two people with

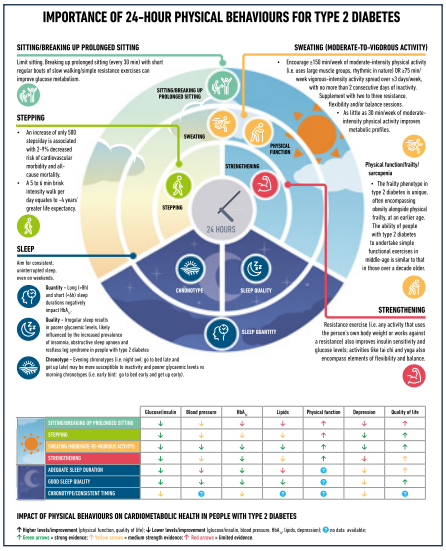

Figure 1. The importance of 24-hour physical behaviours for type 2 diabetes.
Image courtesy of *Diabetologia*. Click on the figure to access.

type 2 diabetes were randomised to varying doses of the study drug, or to dulaglutide or placebo, for up to 12 weeks.

By week 12, mean HbA_{1c} decreased in all groups, with higher doses of LY3437943 showing significant placebo-adjusted reductions of up to 17.1 mmol/mol. Dose-dependent reductions in body weight, up to 8.96 kg greater than placebo, were observed with the new agent. Although the authors cautioned against using cross-study comparisons, it appears that the reductions in HbA_{1c} and body weight were greater even than those achieved with tirzepatide in its Phase 3 trials. Significant reductions in blood pressure were also seen in the LY3437943 groups.

As with the GLP-1 RA class, the most common treatment-emergent adverse events

were gastrointestinal in nature and mostly mild in severity. However, some concern was expressed over increases in heart rate, with increases of 10 beats/min from baseline seen with the highest dose, roughly double that seen with tirzepatide and semaglutide in the SURPASS-2 study.

UKPDS at 44 years: Legacy effect persists

Analysis of the UK Prospective Diabetes Study (UKPDS) is ongoing and shows that, 44 years on, the legacy effects of implementing intensive blood glucose control straight after type 2 diabetes diagnosis continue to persist.

Starting in 1977, the UKPDS randomly allocated people with newly diagnosed type 2 diabetes to an intensive blood glucose control strategy with sulfonylureas, insulin or metformin, or to a conventional blood glucose control strategy, primarily with diet. The 20-year trial results, published in 1998, showed that good blood glucose control reduced the risk of diabetes complications. The results led to international guidelines recommending intensive blood glucose control for everyone with type 2 diabetes. This meant that, post-study, the therapies and blood glucose levels in the two UKPDS groups rapidly became similar. Despite this convergence, the 10-year post-study follow-up analysis, published in 2008, showed that the reduction in the risk of diabetes complications continued for up to 30 years – the so-called legacy effect of early intensive blood glucose control.

In this latest analysis, the legacy effect was shown to persist at 44 years' follow-up, with early intensive control with insulin or sulfonylureas resulting in 11% fewer deaths and 26% fewer diabetes complications such as kidney failure and retinopathy, compared with conventional treatment. Early intensive control with metformin led to 31% fewer heart attacks and 25% fewer deaths. ■

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