# Updates from the ADA conference, the NHS RightCare diabetes pathway and more

**Stay abreast of the latest news that could influence diabetes care. Pam Brown, Editor-in-Chief of *Diabetes & Primary Care*, rounds up the latest national and international news and clinical research stories.**

## ADA in brief

A number of important cardiovascular outcome trials were presented in June at the American Diabetes Association (ADA) 77th Scientific Sessions. More in-depth discussion and a greater range of topics are presented in the PCDS meeting report on page 108 of the Journal; however, a summary of the findings from three of the highest-profile studies are provided below.

### CANVAS/CANVAS-R: Canagliflozin cardiovascular safety results

Results of the CANVAS (Canagliflozin Cardiovascular Assessment Study) programme were presented at ADA and published simultaneously in the *New England Journal of Medicine* (Neal et al, 2017). Data were pooled from two trials, CANVAS and CANVAS-Renal (CANVAS-R), and showed that, compared with placebo, the sodium–glucose cotransporter 2 (SGLT2) inhibitor reduced the risk of major cardiac events (a composite outcome of death from cardiovascular disease [CVD], non-fatal myocardial infarction or non-fatal stroke) by 14% and heart failure by 33% in people with type 2 diabetes at high risk of CVD. Progression of albuminuria was also reduced by 27%, and the composite renal endpoint of a sustained 40% reduction in eGFR, need for dialysis or renal death was reduced by 40%.

The results suggest that the CV benefits seen with empagliflozin in 2015 (Zinman et al, 2015) could be a class-wide effect. However, the CV benefits of canagliflozin were accompanied by an increased risk of toe amputations and fracture. In addition to the expected adverse events of genitourinary infections, lower limb amputations (71% of which were at the toe or metatarsal) occurred at a rate of 6.3 per 1000 person-years, compared with a rate of 3.4 per 1000 person-years in placebo recipients (hazard ratio [HR], 1.97). Fracture risk was increased by 26% only in CANVAS, not CANVAS-R, with no explanation found.

### DEVOTE: Cardiovascular safety study of insulin degludec vs insulin glargine

The results of DEVOTE, a double-blind, treat-to-target, event-driven CV outcome trial of the ultra-long-acting, once-daily basal insulin degludec were presented at ADA and published in the *New England Journal of Medicine* (Marso et al, 2017). A total of 7637 people were randomised to degludec or insulin glargine 100 units/mL. The majority of participants had established CVD, chronic kidney disease or both.

Degludec was found to be non-inferior and did not increase CV risk compared with glargine in people with type 2 diabetes. However, in addition to the finding of CV non-inferiority, degludec significantly reduced rates of severe hypoglycaemia (a pre-specified, adjudicated secondary endpoint) by 40% and nocturnal severe hypoglycaemia by 53% compared with glargine.

Overall, 40 people would need to be treated with degludec rather than glargine to prevent one severe hypoglycaemic event.

### CVD-REAL: Real-world study of SGLT2 inhibitors in people with and without cardiovascular disease

Further interesting data on the effects of SGLT2 inhibitors were presented from the CVD-REAL (Comparative Effectiveness of Cardiovascular Outcomes) study, a real-world, observational registry study conducted in five countries, including the UK. A total of 154 528 people with type 2 diabetes who had been initiated on an SGLT2 inhibitor (mainly dapagliflozin or canagliflozin) were compared with the same number of propensity score-matched people initiated on other oral antidiabetes drugs.

Over the ensuing 8 months, SGLT2 inhibitor treatment was associated with significant reductions in the risk of death (HR, 0.49) and heart failure/hospitalisation for heart failure (HR, 0.61; Kosiborod et al, 2017).

Only 13% of SGLT2 inhibitor recipients had established CVD, and the number needed to treat was lower in this subgroup. However, the results were significant both in people with and without established CVD. Given this and the fact that and there was no evidence of heterogeneity between the different drugs, Matthew Cavender, who presented the data on behalf of the study group, said: "These data suggest that a broad group of patients with type 2 diabetes, with and without CVD, may benefit from treatment with this class of drugs."

## Ertugliflozin efficacy confirmed

Data from two phase III studies of the investigational SGLT2 inhibitor ertugliflozin were presented at the ADA conference. In VERTIS MET, ertugliflozin 5 mg and 15 mg, in combination with metformin, resulted in significant reductions in $HbA_{1c}$ of 8 and 10 mmol/mol

(0.7% and 0.9%), respectively, compared with placebo. In VERTIS SITA, both doses of ertugliflozin, in combination with sitagliptin, reduced $HbA_{1c}$ by 13 mmol/mol (1.2%) compared with placebo. Reductions in body weight, fasting plasma glucose and blood pressure were also observed.

Ertugliflozin is anticipated to be launched in the UK in 2018.

## Boys who lose excess weight in adolescence eliminate their increased risk of type 2 diabetes

Overweight boys who return to normal weight before young adulthood eliminate their increased risk of type 2 diabetes as adults. A Danish registry study, the results of which were presented at the ADA conference, looked at 62 565 males who had their weight and height measured at age 7 years and again at 17–26 years.

Being overweight as a child (5.4% of boys) or a young adult (8.4%) was associated with an increased risk of type 2 diabetes as adults (HR, 1.53 compared with normal-weight boys). However, this risk returned to the same as for men who had never been overweight if the children achieved normal weight by young adulthood. Men who remained overweight from childhood or became overweight as young adults were at three times the risk of type 2 diabetes as men who had never been overweight (HR, 2.88 and 2.95, respectively).

These findings highlight the need for efforts to be made to normalise weight in overweight children before they reach young adulthood and, according to study author Lise Bjerregaard, offer hope that the adverse metabolic health consequences of being overweight in childhood may be reversible.

## New NDA report: Annual NICE-recommended health checks linked to lower mortality

A new report from the National Diabetes Audit (NDA), published on 13 July, suggests that people with diabetes who receive their annual NICE-recommended health checks live longer and have fewer complications than those who do not.

Between 2006/07 and 2013/14, people who received all their blood glucose, blood pressure and serum cholesterol checks – a total of 21 checks over a 7-year period – were around half as likely to die as those who received 12 or fewer checks. The findings were consistent across all age groups. In addition, consistent healthcare attendance was associated with reduced progression to heart failure and reduced need for renal replacement therapy.

Although the report authors caution that the analysis cannot establish causality, they make the following recommendations:

- Healthcare professionals and people with diabetes should be aware of the correlation between regular review and good long-term health.
- Healthcare professionals should monitor poor attendance and make extra efforts to help people re-engage.
- The contributing factors to the high CV risk of all types of diabetes should be fully recognised and regularly assessed and managed.
- Healthcare professionals should ensure that CV risk reduction especially includes people of working age, as these people had the greatest relative risk.

## NHS England RightCare diabetes pathway launched

NHS England has published a new blueprint in a bid to improve and reduce variation in diabetes care. The pathway shows the core components of an optimal diabetes service, focusing on seven specific areas of intervention where the return on investment is likely to have the greatest outcomes and cost benefits.

The areas comprise type 2 diabetes risk detection, type 2 diabetes diagnosis, increasing referrals to structured education at diagnosis, improving completion rates of NICE care processes, developing specialist type 1 diabetes services, improving footcare services and improving safety in hospital inpatients.

In the next issue of *Diabetes & Primary Care*, Partha Kar, who has been instrumental in the development of the RightCare diabetes pathway, will discuss it and outline what it means for primary care.

## Bovine insulin to be discontinued

The only remaining manufacturer of bovine insulin has announced that, owing to global unavailability of the raw materials, the Hypurin® bovine insulin range is to be discontinued. Residual stocks will be carefully managed to ensure the product remains available for patients for as long as possible; however, current bovine insulin users need to switch treatment as soon as possible. Note that porcine insulin will continue to be manufactured.

## New NICE MIB published

NICE has published a Medtech Innovation Briefing (MIB) on the FreeStyle® Libre flash glucose monitoring system. The advice, which is designed to support NHS and social care commissioners and staff who are considering using new medical devices, features a summary of the technology, an evidence review and comments from four clinical experts (NICE, 2017).

The Libre is the second diabetes device to be reviewed in an MIB; advice on the MiniMed 640G system with SmartGuard was published last year (NICE, 2016). ■


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NICE (2016) *MiniMed 640G system with SmartGuard for managing blood glucose levels in people with type 1 diabetes* [MIB51]. NICE, London. Available at: www.nice.org.uk/advice/mib51 (accessed 17.07.17)

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Zinman B, Wanner C, Lachin JM et al (2015) Empagliflozin, cardiovascular outcomes, and mortality in type 2 diabetes. *N Engl J Med* **373**: 2117–28