Reducing the type 2 diabetes epidemic: Where can we make most impact?

asked recently with talking about diabetes epidemiology in Kuwait, where 1 in 8 adults have diabetes and the tsunami of obesity continues to engulf all ages, the statistics made for a potentially very gloomy teaching session. Rather than dwelling on the bad news, we did some blue-sky thinking around where and how we might make the most impact on type 2 diabetes in our own diabetes services.

We discussed what works in preventing and managing childhood obesity (including sugar taxes); managing youth-onset type 2 diabetes meticulously (a condition that is increasing rapidly in the Middle East, and is often diagnosed late and managed poorly, leading to rapid progression); and encouraging women to lose weight before and between pregnancies (to reduce the intergenerational impact of hyperglycaemia in pregnancy). There was discussion about identifying high-risk groups and the role of metformin, as well as lifestyle, in type 2 diabetes prevention (since lifestyle changes are challenging and there is no prevention programme); how to find the missing millions with undiagnosed type 2 diabetes; and what tight, early control of glycaemia and cardiovascular disease (CVD) risk factors could achieve.

Building on the results of the DiRECT clinical trials, we explored how we might motivate people to achieve sufficient weight loss for diabetes remission, or at least improved control. And, finally, how we might use simple audits in a high workload environment to help us tackle clinical inertia (identifying both undertreatment and over-treatment, particularly in older people at risk of hypoglycaemia) and ensure evidence-based management of complications. Quite an agenda and it made for a lively discussion.

A few core themes and questions emerged. Weight loss of 5–15 kg can impact each of these scenarios, so how can we best help people achieve this? How can we make this the

accepted first step when handed a new diagnosis? What services could we signpost locally to aid weight loss, both in the health and commercial sectors? Could occupational health services assist with the working-age population and, with Ramadan approaching, how can we build on the impact that fasting may have on weight loss? The majority of people prefer medication to lifestyle change, so how can we challenge and work with this? For example, we might focus on assisting people to choose behaviour change, or elect to use SGLT2 inhibitors or GLP-1 receptor agonists earlier to achieve weight reduction that could change the course of the condition. To make a major impact on the escalating epidemic of type 2 diabetes, we brainstormed how to tackle the intergenerational effect of obesity and hyperglycaemia in pregnancy, allowing us to impact on the health of two generations. The evidence-base in this area is developing fast, so I will share some of the literature and our discussions in my next editorial.

We all left the session filled with enthusiasm, and with ideas and plans to better tackle these areas in our practices. Deciding how to use our limited resources to achieve the biggest "bang for our buck" was the discussion topic for the remainder of the meeting, and conversations continue with practice colleagues. In the UK, with the latest data collated by Diabetes UK demonstrating that there is an average of one new case of diabetes diagnosed every 3 minutes and around 1 million people with undiagnosed type 2 diabetes, I would suggest these are all areas that we might explore and re-evaluate in order to increase our personal impact.

DiRECT and durability of remission

Important new information from the DiRECT study about the durability of remission with the use of a primary care-led, low-calorie liquid diet was presented recently at the Diabetes UK Professional Conference. At 2 years, 70% of



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"We must code remission correctly to ensure these people to not get lost in our electronic systems, and that they continue to receive regular reviews and retinal screening." those who were in remission at 1 year remained in remission (36% of the original 149 in the intervention group), with 64% of those who lost at least 10 kg remaining in remission (Lean et al, 2019). Additionally, 5 control group participants (2%) were also in remission. Of course, benefit was also seen in those in the treatment group who did not achieve remission, with the average HbA_{1c} reducing from 60 mmol/mol at the start of the trial to 54 mmol/mol at 2 years, with no significant change in average HbA_{1c} in the control group.

Those in the intervention group continued to receive monthly 30-minute appointments with the practice nurse or dietitian using a structured workbook approach, so there was significant ongoing input. Weight gain of >2 kg prompted an offer of 2-4 weeks' "rescue", with partial meal replacements, while a gain of >4 kg prompted 4 weeks of total meal replacement and 4 weeks of food reintroduction. Around half of the intervention group availed themselves of these rescue measures at some point following food reintroduction. control group continued with their normal care and medication, and had data collection visits at baseline, 1 year and 2 years. Following the success of the 2-year programme, DiRECT is now being rolled out to 5000 people with early type 2 diabetes across the UK.

If we are not fortunate enough to participate in the roll-out, what can we offer? Other organisations offer face-to-face support and very-low-calorie diet (VLCD) meal replacement programmes similar to those used in DiRECT; some patients will choose to self-fund such programmes. We will have a role in monitoring blood pressure and ensuring appropriate medication changes to avoid hypotension and hypoglycaemia.

In Scotland, practice nurses have been trained to deliver the Counterweight programme and some deliver Counterweight-Plus, as used in DiRECT. It is important to find some way to gather real-world data on outcomes in people with type 2 diabetes undertaking commercial programmes outside DiRECT. How can this best be achieved?

Remission in DiRECT is defined as having HbA_{1c} <48 mmol/mol off all type 2 diabetes medication. The Primary Care Diabetes Society and Association of British Clinical Diabetologists have launched a joint statement discussing all aspects of diabetes remission, including a plea to make sure that we code remission correctly to ensure these people do not get lost in our electronic systems, and that they continue to receive regular reviews and retinal screening.

The cost of delivering the clinical aspects of DiRECT, including healthcare professional training, the low-calorie formula diet, all review appointments, supporting resources and glucose-lowering and hypertension medications required (but excluding imaging and research studies designed to identify the mechanisms of remission), was £1223 per year (95% confidence interval, 1147-1294; Xin et al, 2019). Clinician visits were £447 and Counterweight-Plus meal sachets £708 per participant, representing a significant part of the cost. Allowing for savings on drug costs, the excess cost of delivering the programme in the first year was estimated at £1067 per participant in the intervention group. Factoring in the success rate of 46% in remission at 12 months, each remission would cost around £2564.

As a comparison, the most recent estimate of the cost of managing type 2 diabetes in the UK is from 2010/11, when it was £514 annually and £2560 when the costs of complications were included. With inflation, this is likely to be around £2801 per patient for 2016/17.

Preventing progression of diabetic kidney disease

In our news pages, we share the results of the CREDENCE trial (Perkovic et al, 2019), which demonstrates the first significant breakthrough in managing diabetic kidney disease (DKD) since studies confirmed the benefit of ACEIs and ARBs nearly 20 years ago. In a population with type 2 diabetes and albuminuria, canagliflozin produced a significant 30% relative risk reduction in progression of renal disease compared to placebo over the average

2.6 years of the study. These benefits occurred despite 99.5% of participants already receiving treatment with an ACEI or ARB. CREDENCE also confirmed it is possible to reduce the composite outcome of CVD death, non-fatal myocardial infarction or stroke (3-point MACE) and hospitalisations for heart failure in people with type 2 diabetes at high risk of CVD due to DKD. Importantly, there was no increased risk of lower-limb amputation or fracture in the canagliflozin-treated group.

what does mean our SGLT2 practice? inhibitors are not currently licensed for initiation in those eGFR <60 mL/min/1.73 m² and they need to be stopped if eGFR falls to <45 mL/min/1.73 m². This relates to their glucose-lowering development as and decreased efficacy at lower eGFR values. However, it is hoped that this study, demonstrating renal and CVD benefits in people with DKD and eGFR as low as 30 mL/min/1.73 m², will encourage licensing changes. The EMPA-KIDNEY and Dapa-CKD studies, exploring renal and CVD outcomes in people with DKD treated with empagliflozin and dapagliflozin respectively, are ongoing but not due to report for another 1-2 years. In the meantime, we can ensure that we are up to date with monitoring eGFR and ACR, so that those with DKD are identified. We can also make sure that everyone with DKD is correctly coded, is on an ACEI or ARB, has had smoking cessation advice, and has optimal blood pressure and glycaemic control to reduce renal progression and CVD.

In this issue

Ramadan begins shortly and, with around 16 hours of daylight at this time of year and warm weather on its way, fasting will be particularly challenging. It can be helpful to remind people with diabetes, particularly those on insulin and frail older people, that they can be exempt from fasting and can undertake alternative actions or fast at a less dangerous time of year. For those who choose to fast, we need to ensure that they understand any

alterations needed to their medication and that testing blood glucose during the day is not considered to be breaking their fast. Alia Gilani provides detailed guidance in *How to manage diabetes during Ramadan*, while patient information is available from <u>Diabetes UK</u> and The Muslim Council of Britain.

With the ADA/EASD consensus statement encouraging increased use of newer glucoselowering drugs, Nicki Milne shares guidance on How to use GLP-1 receptor agonist therapy safely. Tun Than shares his ideas on writing a compelling business case to secure funds for our diabetes services, while Prof Kamlesh Khunti and colleagues raise awareness of the importance of real-world data and their ERICAS database. Sian Bodman reflects on her learning from developing a team of diabetes specialist nurses to support practices in South Wales, and Danny Meetoo and Rebecca Rylance encourage us to think about how artificial intelligence can assist us to deliver diabetes care, both now and in the future. If you were unable to attend our National PCDS Conference, you can catch up with speakers' key messages in our conference report.

I am looking forward to the At the 4-Front: Leadership in Diabetes Nursing meeting and the Welsh Conference of the PCDS in May, where I hope to meet some of you. In the next issue, I will discuss more about hyperglycaemia in pregnancy and the evolving evidence of intergenerational impact. Until then, let's think about where we might use our available time and effort to make most impact. We would love to hear about your successes and how you and your team have been inspired to "make every contact count".

Lean M, Leslie W, Barnes A et al (2019) Durability of primary care-led weight management intervention for remission of type 2 diabetes: 2-year results of the DiRECT open-label, cluster-randomised trial. *Lancet Diabetes Endocrinol* **7**: 344–55

Perkovic V, Jardine M, Neal B et al (2019) Canagliflozin and renal outcomes in Type 2 diabetes and nephropathy. *N Engl J Med* 14 Apr [Epub ahead of print]

Xin Y, Davies A, McCombie L et al (2019) Within-trial cost and 1-year cost-effectiveness of the DiRECT/Counterweight-Plus weight-management programme to achieve remission of type 2 diabetes. Lancet Diabetes Endocrinol 7: 169–72 "For those who choose to fast for Ramadan, it can be helpful to remind people with diabetes, particularly those on insulin and frail older people, that they can be exempt from fasting."