Hippocrates and diabetes prevention

"If we could give every individual the right amount of nourishment and exercise, not too little and not too much, we would have found the safest way to health."

Hippocrate

arch 2015 saw the launch of the NHS Diabetes Prevention Programme in England, which is based on recommendations in NICE public health guidance 38 (NICE, 2012). Seven demonstrator sites will pilot strategies which will hopefully reduce new diagnoses of type 2 diabetes (NHS England, 2015). However, with no definite plans for making such programmes available across the other nations, and the roll-out of the full programme not due to happen until 2017, many of us are exploring how we might help people with "pre-diabetes" in our own practices to reduce their risk.

In this issue of the journal, Nicola Milne and Abdullah Ali describe how they identified a rapid increase in IGR in their practice and their approach to managing those at high risk, and they present an audit of their outcomes (see page 121).

Without action, 5–10% of those with impaired fasting glycaemia (IFG) or impaired glucose tolerance (IGT) will develop type 2 diabetes annually, with around 70% progressing to the condition eventually (Tabak et al, 2012). Those with both IFG and IFT may develop the condition faster: around 15–19% progress per annum. While there is some overlap, the cohort of people with IFG or IGT is not the same as the cohort now diagnosed with IGR based on an HbA_{1c} of 42–47 mmol/mol (6.0–6.5%); however, it is believed that people with IGR will also progress at a rate of around 5–10% annually (Tabak et al, 2012).

The original diabetes prevention studies from the US (Diabetes Prevention Program [DPP] Research Group, 2002) and Finland (Tuomilehto et al, 2001) demonstrated a 58% relative reduction in progression to type 2 diabetes in those with IGT in the intensive lifestyle group versus those receiving normal care. Relative risk reductions of between 25% (acarbose; Chiasson et al, 2002) and 31% (metformin; DPP Research Group et al, 2009) have been achieved with drugs, but newer therapies for obesity or for diabetes (such as sodium—glucose cotransporter 2 inhibitors) have not yet been assessed.

There are some key messages from the original studies. The first is that the hugely resource-intensive intervention programmes resulted in relatively modest changes in behaviour and average weight loss of only 4.2–6.7 kg. In the DPP, there was a 16% relative reduction in diabetes risk per kilogram of weight loss (Hamman et al, 2006). Many of our patients manage to achieve similar lifestyle changes and weight loss, with or without our support.

The second key message is that the risk reduction observed in these high-risk groups correlates closely with weight loss, however this is achieved. This allows us to simplify our message – "lose weight and reduce your diabetes risk."

Thirdly, tackling IGR early in its course may have more of a bearing on outcomes than the precise strategy used. Those who regressed to normal glucose regulation at any point during the DPP, had a significantly lower risk of developing future diabetes (Perreault et al, 2012). This is likely to be easier to achieve in those with an HbA_{lc} of 42 mmol/mol (6.0%) than those with one of 47 mmol/mol (6.5%).

Over recent years, studies have sought to identify whether it is possible to achieve meaningful reductions in type 2 diabetes using less intensive, "real world" interventions. Interestingly, whether we get a positive or a negative response to this question depends on which review we consult.

Kahn and Davidson (2014) argue that delay in diabetes development of 4–5 years with lifestyle interventions, or around 2 years with drug therapy (DPP Research Group et al, 2009), may not translate into a meaningful impact on diabetes complications without sustained long-term weight loss. They concluded: "the absence of any persuasive evidence for the effectiveness of community programs calls into question whether the use of public funds or national prevention initiatives should be supported at this time."

In contrast, a UK systematic review and metaanalysis (Dunkley et al, 2014) of pragmatic lifestyle programmes for diabetes prevention concluded that, although the mean weight loss achieved was only 2.32 kg (one-third to half that in the original studies), the weight loss varied depending



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on adherence to guideline recommendations and a reduction in the rate of progression to diabetes was demonstrated.

So where should we target our efforts?

Having diagnosed IGR, we may have raised anxiety levels and need to manage expectations. How can we translate the evidence to our practice?

There is emerging clarity on pragmatic diet recommendations for diabetes prevention (Ley et al, 2014), with a Mediterranean diet having been demonstrated to deliver weight reduction in those with or without type 2 diabetes (Ajala et al, 2013), to reduce progression to type 2 diabetes in those at high risk (Martinez-Gonzalez et al, 2008), and to improve primary (Estruch et al, 2013) and secondary prevention (Kris-Etherton et al, 2001) of cardiovascular disease. The websites of Patient (www.patient.info; formerly Patient UK) and NHS Choices (www.nhs.uk) offer ready-made leaflets, allowing us to make recommendations with minimal effort. Coffee consumption, moderate alcohol intake and green leafy vegetables also reduce risk.

Carter and colleagues have reviewed the evidence supporting current dietary recommendations for diabetes prevention (Carter et al, 2012). They remind us that the evidence (often only from observational studies) demonstrates that fibre intake of >14 g/1000 kcal, lower fat intake, and "prudent dietary patterns" high in fruit, vegetables and whole grains and low in red meat (which includes a Mediterranean diet) have been shown to reduce type 2 diabetes and be healthy for all. This means we can recommend one eating pattern for everyone.

The recently published International Scientific Consensus Summit report on "Glycemic Index, Glycemic Load and Glycemic Response" (International Carbohydrate Quality Consortium et al, 2015) shares convincing evidence from a meta-analysis of cohort studies suggesting that diets with a low glycaemic index (GI) and a low glycaemic load (GL) reduce the risk of type 2 diabetes and that potential mechanisms include improved insulin sensitivity and beta-cell function. They remind us that acarbose's ability to reduce progression to type 2 diabetes in STOP-NIDDM (the Study to Prevent Non-Insulin-Dependent Diabetes Mellitus; Chiasson et al, 2002) is proof of the benefit of

slowing carbohydrate absorption, as also achieved by a low-GI and low-GL diet.

"Walking is man's best medicine" – Hippocrates

Although physical activity formed part of the intensive lifestyle programmes for diabetes prevention, a systematic review of the evidence for physical activity in the management of IGT concluded that the "contribution of physical activity independent of dietary or weight loss changes to the prevention of type 2 diabetes in people with prediabetes is equivocal" (Yates et al, 2007).

However, as part of the prevention package, increased activity needs to be encouraged, and, as Hippocrates previously identified, walking is a safe and sustainable way to achieve this. A small randomised trial, based on the PREPARE (Prediabetes Risk Education and Physical Activity Recommendation and Encouragement) programme, demonstrated that a single 3-hour education session to promote walking, combined with pedometer use, improved glucose tolerance in the absence of weight loss or reduction in waist circumference (Yates et al, 2009) and that effects were sustained at 2 years. However, without the pedometer, the programme did not achieve significant improvements. It is likely that feedback is required to motivate sustained increases in activity, so the use of pedometers and fitness trackers should be encouraged when we deliver advice. Resistance exercise is also likely to be beneficial in diabetes prevention and treatment (Strasser and Pesta, 2013).

Concluding thoughts

Over the next year, 10 000 people in the NHS Diabetes Prevention Programme will be offered help to reduce their risk of developing type 2 diabetes. I believe that we now have enough evidence to begin taking action to help prevent diabetes in our own high-risk patients. We have already identified many of those with IGR and can offer them evidence-based guidance on lifestyle to help them lose weight and reduce their risk of type 2 diabetes. We can learn about and recommend services available locally and encourage use of websites, apps and devices to provide support. If we collect and collate data, we will soon learn what works in our own setting. We, too, could make a real difference.

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