Prioritising prevention: focusing on reducing complications, not just progression

I am so pleased to share with everyone that Jane Diggle has agreed to join me as Joint Editor-in-Chief of *Diabetes & Primary Care*. Jane has played a significant role in developing the electronic journal, our "How to" series and the "At a Glance" factsheets, as well as writing regularly for the Journal. Following Jane's contributions to our work on education around remote diabetes consultations and prioritising diabetes services to help teams meet the challenges of COVID-19, and in recognition of her expertise, creativity and dedicated effort, it feels timely to invite Jane to share the editorial leadership of the Journal going forward. I look forward to continuing to work closely with Jane, our editorial board and our in-house team to bring you more practical tools and pragmatic educational content as we rebuild our diabetes services over the months ahead.

Undiagnosed type 2 diabetes

Just as we begin to catch up with our backlog of diabetes reviews and settle back into the luxury of face-to-face consultations, albeit with askmyGP or similar email and virtual consultations running in parallel, a study from Manchester reminds us of the potential burden of undiagnosed type 2 diabetes due to the impact of COVID-19 (Carr et al, 2021). Reviewing data from 25 million people included in the Clinical Practice Research Datalink databases, the authors demonstrated a significant reduction in new diagnoses of type 2 diabetes in April 2020, compared to the 10-year historical trend. Rates were comparable in England and the other UK nations, and lower rates of diagnosis were supported by a reduction in new metformin prescriptions. Although the diagnosis rates slowly recovered from May to December, they remained below historical levels. Extrapolating from these data, along with data from the Office for National Statistics, and assuming that rates of new type 2 diabetes remained constant, the Manchester team estimated that there were around 60 000 missed or delayed diagnoses of type 2 diabetes across the UK from March to December 2020 due to interruptions to routine care. However, as we have seen from our reviews of those with existing type 2 diabetes, HbA_{1c} has tended to increase rather than reduce, and weight gain has been the norm, suggesting these figures may be an underestimate. The benefits of early diagnosis and prompt treatment mean we need to diagnose and manage these people as soon as possible.

Rates of HbA_{1c} testing amongst those with type 2 diabetes were also reduced across the UK during 2020, with the largest reductions not surprisingly being in older people and those in areas of high deprivation. Delays in HbA_{1c} testing are likely to translate into delayed intensification of management, further impacting pre-existing clinical inertia.

So, where should we look for these people with new type 2 diabetes? Some will appear without any preceding fanfare, without any symptoms or pre-existing pre-diabetes/non-diabetic hyperglycaemia (NDH), and will be discovered incidentally. We need to ensure initial results are repeated, if appropriate, type 2 diabetes is coded, and that these people are seen and have their new diagnosis discussed promptly and are not lost to follow-up. Others will already be on our radar, previously diagnosed and coded with NDH, and awaiting their annual test. In England, hopefully this latter group will have been referred or have self-referred into Healthier You, the NHS Diabetes Prevention Programme, for remote group support or are undertaking the digital option, as discussed in Chirag Bakhai's comment piece in this issue.

Recent type 2 diabetes reviews demonstrate that the majority of HbA_{1c} values have risen significantly since the previous review. The oft-repeated explanation (or justification) is that this is due to lack of activity owing to COVID restrictions, boredom due to home working and lockdown, and the proximity of the fridge and

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edible goodies making snacking an inevitable part of daily life. This is likely to have also affected those with NDH, where only small rises in HbA_{1c} could push people across the threshold into type 2 diabetes.

Diabetes prevention

Considering the Manchester study and talking with colleagues about diabetes prevention last week has prompted thoughts about how we might kick-start our practice prevention efforts. In Wales, there is not yet a national prevention programme so, with over 400 diagnosed with NDH in our practice (and likely many more not yet identified), prior to the pandemic we had begun piloting group education sessions, and participating in a cluster project auditing our data and delivering brief one-to-one lifestyle counselling. Throughout the pandemic, our proactive healthcare assistant has been opportunistically delivering brief lifestyle counselling during blood pressure checks and other data collection visits, including to people with NDH. Re-running previous audits has, as expected, demonstrated significant unmet need and raised challenging questions.

Can we justify prioritising NDH work over our final backlog of type 2 diabetes reviews? If we decide to focus on prevention, what does the literature tell us about how to prioritise? Should we start with those most overdue their annual HbA_{1c} and work through by date? Should we prioritise those with highest HbA_{1c} values who are potentially at highest risk of progression to type 2 diabetes, as recommended by NICE in its PH38 guideline (NICE, 2017), when resources are scarce? When prioritising type 2 diabetes reviews, we consider glycaemic control and risk from comorbidities. Should we do the same with people with NDH? What does the evidence tell us?

The US Diabetes Prevention Program (Knowler et al, 2002; Diabetes Prevention Program Research Group et al, 2009) and Finnish Diabetes Prevention Study (Lindström et al, 2006) recruited populations with mainly impaired glucose tolerance, whereas today we use HbA_{1c} to identify those at high risk. Although HbA_{1c} has been validated to identify those at higher risk of developing type 2 diabetes, those identified in this way are a different group, at possibly lower type 2 diabetes progression risk than those in early research studies. We should also be mindful that in the US and some other countries, prevention studies use the HbA_{1c} range 5.7–6.4% (i.e. 39–47 mmol/mol) rather than the 42–47 mmol/mol HbA_{1c} used in the UK, potentially including a population at lower risk of progression to type 2 diabetes.

Real-world studies seek to reassure us that prevention can be replicated, but often interventions are intensive. A recent systematic review and network meta-analysis of real-world/translational studies (Galaviz et al, 2018) demonstrated a 29% reduction in development of type 2 diabetes, with an absolute risk reduction of 3% in those receiving intervention programmes versus controls. When controlled and uncontrolled studies were combined, group education was associated with a 33% lower risk of type 2 diabetes than control interventions, reassuring us that real-world interventions can reduce or slow progression compared to normal care. Even small decreases in weight can reduce progression risk. For example, each additional 1 kg of weight loss was associated with 43% lower odds of type 2 diabetes.

The early findings from Healthier You (Valabhji et al, 2020) confirm that the programme has achieved comparable weight and HbA_{1c} reductions to other real-world studies, with 3.3-kg weight loss and HbA_{1c} reduction of just over 2 mmol/mol in completers (i.e. those who participated in at least 60% of sessions). Those leading the programme are confident this will translate into reductions in type 2 diabetes incidence and delayed progression to type 2 diabetes in future, although the impact of the pandemic is not yet clear.

A UK Biobank study (Honigberg et al, 2021) explored cardiovascular and kidney outcomes associated with a range of HbA_{1c}-measured glycaemia, including normoglycaemia, NDH (US criteria, 39–47 mmol/mol) and type 2 diabetes. Type 2 diabetes and NDH were both independently associated with significantly increased risk of atherosclerotic cardiovascular disease (ASCVD), chronic kidney disease (CKD), heart failure and all-cause mortality.

Having an HbA_{1c} of 39–47 mmol/mol, compared to HbA_{1c} <39 mmol/mol, was also associated with increased risks of ASCVD, CKD, heart failure and all-cause mortality. Increased risk of these comorbidities and mortality, even at the low HbA_{1c} values in this NDH population, suggest we should focus on identification and reduction of ASCVD, CKD, heart failure and mortality, rather than only focusing on progression to type 2 diabetes. This is supported by the fact that overall in this study only 14% with NDH progressed to type 2 diabetes over 11 years and, in many cases, progression to type 2 diabetes did not occur until after the ASCVD or CKD outcome. More than two thirds of those with NDH developing ASCVD or CKD did not progress to type 2 diabetes. The development of a first ASCVD or renal event substantially increased the risk of further events, even within 12 months, highlighting the importance of early identification and prompt primary and secondary prevention.

A *post-hoc* analysis explored whether it was possible to identify a high–risk pre-diabetes subgroup (Honigberg et al, 2021). The authors identified that current or previous smokers, and those in the top third of medication-adjusted systolic BP (≥133 mmHg on therapy), medication adjusted non-HDL cholesterol (≥3.34 mmol/L) and C-reactive protein (≥2.1 mg/L) could be defined as having "high-risk NDH". This identified 6% of the current cohort. Cumulative incidence of ASCVD and heart failure were similar in those with high-risk NDH compared with those with type 2 diabetes, validating action in this group. Those with "high-risk NDH", compared with those with other NDH, had nearly two-fold increased risk of ASCVD, CKD, heart failure or mortality overall, suggesting prioritisation in those with NDH at highest risk of complications may be possible.

These findings, including the nadir for risk of heart and kidney disease at HbA_{1c} around 5% or 31 mmol/mol, well below the diagnosis of NDH, suggest we may need to focus on different HbA_{1c} thresholds in future. The authors cautioned about study limitations. For example, the UK Biobank cohort may be healthier than the UK population generally and, although HbA_{1c} was measured at enrolment and new diagnoses of type 2 diabetes were identified, annual HbA_{1c} measurements were not available during the study to quantify regression.

A recent evaluation of the Atherosclerosis Risk in Communities Study exploring progression from pre-diabetes (HbA_{1c} 39–47 mmol/mol, as this was a US study) to type 2 diabetes in older people, demonstrated that the likelihood of regression or death was much greater than risk of progression to type 2 diabetes (Rooney et al, 2021). In this community-based cohort (mean age 75.6 years at baseline), follow-up after 6.5 years demonstrated that, when using HbA_{1c} criteria for diagnosis, 9% had progressed to type 2 diabetes, 13% regressed to normoglycaemia and 19% had died whereas, when impaired fasting glycaemia at baseline was used, 9% progressed to type 2 diabetes and 44% regressed to normoglycaemia. When the population with HbA_{1c} levels <39 mmol/mol were examined, 17% progressed to pre-diabetes and 3% to type 2 diabetes. The authors concluded that within their study of older people, regression to normoglycaemia or death was more common than progression to type 2 diabetes, suggesting that the focus should be on preventing cardiovascular disease (CVD) and mortality in this age group, rather than focusing primarily on preventing progression to type 2 diabetes alone. A similar study (Shang et al, 2019) in Swedish adults >60 years demonstrated that, during 12 years of follow-up, most people with pre-diabetes remained in this category and more regressed than progressed.

The Norfolk Diabetes Prevention Study (Sampson et al, 2021), undertaken in primary and community care, randomised 1028 people of mean age 65.3 years with impaired fasting glycaemia or HbA_{1c} 42–47 mmol/mol and impaired fasting glycaemia to three groups: a control group receiving usual care; a group given theory-based lifestyle intervention (six core and up to 15 maintenance sessions); or the lifestyle intervention, with support from diabetes prevention mentors. Results published earlier this year, after a mean follow-up of 24.7 months, demonstrated that 22.8% of the control group had progressed, versus 13.7% receiving the

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lifestyle counselling, and 15% of those receiving lifestyle intervention and peer support (Sampson et al, 2021). This demonstrated that the lifestyle intervention programme was effective in reducing type 2 diabetes progression, but there was no additional benefit of adding peer support. The authors concluded that these results can inform current prevention efforts.

If you believe, as we do, that there is significant value in taking action to reduce CVD, CKD and type 2 diabetes progression risk amongst those with NDH, then we would do well to follow Nike's advice and "Just do it". We may have only a small window of opportunity to help protect this vulnerable group before further COVID-19-related workload overtakes us.

In this issue

As always, we have a brilliant group of contributors sharing their knowledge and ideas in this issue. Jen Bateman, clinical psychologist and member of our editorial board, shares practical guidance on "How to find the ideal words in consultations". Hyperglycaemia is particularly detrimental during pregnancy, and Helen Murphy provides a concise overview of its impact and how we might lessen it in her At a Glance factsheet, "Diabetes, before, during and after pregnancy". Sam Seidu, from Leicester, provides a valuable summary of what we need to know on "Early-onset and youth-onset type 2 diabetes" in his factsheet, while, as noted earlier, Chirag Bakhai provides a timely update on how the NHS Diabetes Prevention Programme has demonstrated its resilience during the pandemic.

I hope many of you were able to attend the virtual Diabetes UK Professional Conference 2021, to benefit first-hand from the science and practical guidance presented. For those of you unable to attend this year, George Posford, our in-house editor, and I share a two-part conference report highlighting news, views and reminders of good practice that we wanted to showcase. We hope these give you a flavour of the conference and inspire you to attend next year. If you were unable to attend the Welsh Conference of the PCDS this year, the sessions are now available on demand and our speakers will share their key messages in our conference report in the next issue.

In *Diabetes Distilled*, Kevin Fernando summarises a consensus document on diabetes and frailty, while I focus on the mortality benefits of metabolic–bariatric surgery, the surprisingly low BMIs associated with increased risk of type 2 diabetes in different ethnic groups and the updated *Management of Hyperglycaemia and Steroid (Glucocorticoid) Therapy* guidelines from the Joint British Diabetes Societies for Inpatient Care, which provide important guidance for steroid use in practice.

After a tough year, I know we are all ready for a break. Even if our travel plans remain on hold, I hope you all have the opportunity to rest, relax and recharge your batteries before we meet again in August. Until then, thank you so much for your support for the Journal. If you find it useful, please encourage colleagues to register to receive our fortnightly updates completely free of charge at DiabetesontheNet.com. ■

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