Implications of prescribing SGLT2 inhibitors to a wider population

I was recently asked to give an update on SGLT2 inhibitors to prescribing colleagues in my practice, I suspect prompted by the realisation that many more individuals with diabetes will be eligible for an SGLT2 inhibitor within the updated NICE guidance on the management of type 2 diabetes in adults (NG28; NICE, 2022). Additionally, we are seeing regular licence extensions for several SGLT2 inhibitors to include indications for heart failure and chronic kidney disease both in those with and without diabetes.

In individuals with type 2 diabetes, I do not think there will be many for whom we do not at least consider an SGLT2 inhibitor. This is likely to have a significant impact on our workload and at a time when many practices are still struggling to re-establish routine diabetes services and address the backlog due to the COVID-19 pandemic. A planned approach is needed, rather like the way we tackled the backlog, which prioritises those with the most to gain.

We are fortunate within primary care to be able to access a wealth of data on our clinical systems. Almost everything we do is linked to a code and, while at times it can feel like an endless box-ticking exercise, the data recorded allows us to perform searches relatively easily. We can identify and prioritise groups of patients into manageable cohorts for review. I think this is something we could consider as part of a more proactive approach to implementing the new NICE recommendations.

In NG28, early combination therapy with metformin and an SGLT2 inhibitor with proven cardiovascular benefit is recommended for those with chronic heart failure or established atherosclerotic cardiovascular disease (e.g. coronary heart disease, cerebrovascular disease and peripheral arterial disease). Individuals within this group can be easily identified within searches and, where possible, should be prioritised.

In those with type 2 diabetes and a urinary albumin–creatinine ratio (ACR) ≥3 mg/mmol, we are reminded to offer an ACE inhibitor or ARB, titrate to the maximal tolerated dose and, additionally, offer an SGLT2 inhibitor (according to licence criteria) where urinary ACR is ≥30 mg/mmol and consider an SGLT2 inhibitor if urinary ACR is 3–30 mg/mmol.

SGLT2 inhibitors have been available for several years now and many patients will already be prescribed them. There are others who may have been prescribed an SGLT2 inhibitor in the past and for whom a reason for stopping (such as failure to reach the agreed HbA_{1c} target for that individual) will hopefully have been documented and can be explored, as there may be other reasons (such as cardiorenal benefit) for using an SGLT2 inhibitor, rather than purely for glycaemic control. For others, their SGLT2 inhibitor may have been stopped due to a fall in eGFR – we would have typically stopped these agents in those with an eGFR persistently <45 mL/min/1.73 m^2 (not due to safety concerns, but because of reduced glucose-lowering effects). Additionally, these agents were only licensed for initiation if the eGFR was ≥60 mL/min/1.73 m^2, so there are likely to be patients who were not considered in the past for this reason.

Trying to remember which agents have a licence for which indication (be it insufficiently controlled type 2 diabetes, diabetic/chronic kidney disease and/or heart failure [with reduced or preserved ejection fraction]) is a real challenge, because it changes. The other difficulty is that the doses and eGFR thresholds for initiating and then stopping vary between agents and according to the primary indication for using the agent. Pam Brown developed an invaluable crib sheet for our *Need to know* series. Look out for an updated version, with most recent licence changes, which will appear in the journal soon.

NG28 also recommends early combination therapy with metformin and an SGLT2 inhibitor with proven cardiovascular benefit for those at

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"We have a duty of care to ensure that our patients are aware of any material risks involved in any recommended treatment, and of any reasonable alternative treatment options."

high risk of cardiovascular disease. It defines this as a QRISK2 score ≥10% in those ≥40 years, or an elevated lifetime cardiovascular risk in those aged <40 years (defined as the presence of ≥1 cardiovascular risk factor, such as hypertension, dyslipidaemia, smoking, obesity and family history [in a first-degree relative] of premature cardiovascular disease). There are likely to be significant numbers of people within this category and, given the current workload pressures, I think it will be more realistic to identify them and perhaps add a reminder/alert to their records, but discuss the addition of an SGLT2 inhibitor at their next routine review.

SGLT2 inhibitors are being recommended in a far wider population. We are likely to be counselling individuals on the benefits and risks of these agents on a daily basis. I have wondered, at times, how much information I need to give a person on potential adverse effects, particularly the very rare ones such as Fournier's gangrene and diabetic ketoacidosis. These may be rare but they are serious and potentially life-threatening, so it is important a person knows how to reduce the risk, recognise the signs and seek urgent medical advice, if needed. I guess the worry is that, in doing so, the person may be completely put off the idea of taking the medication.

I recently chaired the *22nd Annual Abracadabra Nursing Conference*, and this dilemma was beautifully addressed by Bev Bostock (Advanced Nurse Practitioner and Lead Nurse) in her session on *Clinical Conversations: Medicolegal considerations in diabetes care: advice from an expert witness*, which is available on demand. In her presentation she discusses a Supreme Court case which, with its judgment in *Montgomery v. Lanarkshire Health Board* [2015], revolutionised the legal landscape regarding informed consent.

From the judgment, the test of materiality was born and essentially means that, as healthcare professionals, we have a duty of care to ensure that our patients are aware of any material risks involved in any recommended treatment, and of any reasonable alternative treatment options. The test of materiality can be described in terms of whether, in the circumstances of the particular case, a reasonable person in the patient's position would be likely to attach significance to the risk, or the healthcare professional is or should be aware that the particular patient would be likely to attach significance to it.

The principle of involving patients in their treatment and sharing information with them about risks has been in place for some time. In its guidance, *Decision Making and Consent*, the General Medical Council advises that doctors (though, arguably, this would apply to any healthcare professional) should try to find out what matters to patients, so they can share relevant information about the benefits and harms of proposed options and reasonable alternatives, including the option to take no action (GMC, 2020). They should tailor the discussion about potential benefits and harms to each individual, and be guided by what matters to them and share information in a way they can understand. They suggest the following information should be included when discussing benefit and harms:

- Recognised risks of harm that you believe anyone in the patient's position would want to know.
- The effect of the patient's individual clinical circumstances on the probability of a benefit or harm occurring.
- Risks of harm and potential benefits that the patient would consider significant for any reason (revealed during discussion with the patient about what matters to them).
- Any risk of serious harm, however unlikely it is to occur.
- Expected harms, including common side effects, and what to do if they occur.

These are important points to consider when discussing any treatment, and serve as useful reminders for those tempted not to worry a patient by telling them about the rarer side effects.

In this issue

Our coverage of the major diabetes conferences continues with a look at the *82nd American Diabetes Association Scientific Sessions*, which took place in New Orleans at the beginning of June 2022. Carefully selected for primary care, we present the most relevant news highlights in brief, while our conference "deep dive" focuses on some

of the key messages from the lifestyle and obesity sessions. You can find it all here.

Our *How to* guide for this issue provides really practical information from Nicola Milne on "How to prevent, identify and manage hypoglycaemia in adults with diabetes", while David Morris continues his popular interactive case study series with pre-pregnancy care in diabetes.

With such focus on the newer blood glucose-lowering agents, we decided it would be useful to re-visit the older agents that continue to be widely prescribed. This issue sees the launch of our brand new *Prescribing Pearls* series with "A guide to metformin".

Interestingly, on 20 June the Medicines and Healthcare products Regulatory Agency published new advice on monitoring vitamin B12 levels in patients taking metformin. Reduced vitamin B12 levels and vitamin B12 deficiency are now considered to be common side effects in patients on metformin treatment, particularly for those on a higher dose, treated for longer duration and where there are existing risk factors. The advice is to check vitamin B12 serum levels in patients being treated with metformin who have symptoms suggestive of vitamin B12 deficiency (e.g. presenting with megaloblastic anaemia or new-onset neuropathy). We should also consider periodic monitoring for patients with risk factors for vitamin B12 deficiency (e.g. low baseline level, conditions associated with reduced vitamin B12 absorption [such as elderly people, those with gastrointestinal disorders, inflammatory bowel disorder or autoimmune conditions] and diets with reduced sources of vitamin B12 [such as strict vegan and some vegetarian diets]).

Given the emphasis on cardiovascular risk assessment in NG28, I have developed an *At a glance* factsheet that highlights the risk factors considered in commonly used risk calculators, and circumstances where there may be an underestimation of cardiovascular risk. It summarises recommendations from NICE CG181 (2016), the more recently published *Summary of national guidance for lipid management* (NHS England, 2021), as well as the European Society of Cardiology (2021) cardiovascular disease prevention guidelines with respect to measuring lipids, calculating cardiovascular risk, and initiating statins and treatment targets. I hope you find this useful.

In *Diabetes Distilled*, Kevin Fernando reviews a study that found no short-term association between adverse outcomes and deintensification of diabetes medications in more vulnerable individuals with limited life expectancy. Pam Brown looks at data from the SURPASS-3 trial that position tirzepatide, a dual GIP/GLP-1 receptor agonist or "twincretin", as a promising future treatment for NAFLD. She also looks at the proposed changes to the ADA/EASD Consensus Report that would give a greater focus on person-centred care, weight loss and equity of care in the management of hyperglycaemia in type 2 diabetes.

Finally, we examine evidence that previous COVID-19 infection should be considered as a cardiovascular risk factor, and that missed routine diabetes care processes during the pandemic are associated with poorer diabetes outcomes.

Until next time – enjoy the summer! ■

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General Medical Council (2020) *Decision Making and Consent*. Available at: https://www.gmc-uk.org/ethical-guidance/ethical-guidance-for-doctors/decision-making-and-consent (accessed 07.07.22)

NHS England (2021) *Summary of National Guidance for Lipid Management for Primary and Secondary Prevention of cardiovascular disease*. Available at: www.england.nhs.uk/aac/publication/summary-of-national-guidance-for-lipid-management (accessed 07.07.22)

NICE (2016) *Cardiovascular disease: risk assessment and reduction, including lipid modification* (CG181). Available at: www.nice.org.uk/guidance/cg181 (accessed 07.07.22)

NICE (2022) *Type 2 diabetes in adults: management* (NG28). NICE, London. Available at: https://www.nice.org.uk/guidance/ng28 (accessed 07.07.22)

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