Journal club: My patient is on a statin. Why are they not also on an SGLT2 inhibitor?

The International Diabetes Federation (IDF, 2021) estimates that there are 537 million people living with diabetes on Planet Earth. This is set to increase by a further 50% over the next 25 years to over 800 million. With the US spending almost a trillion dollars per year on diabetes care, countries need to focus on prevention of type 2 diabetes and its associated complications, as these form the bulk of the expenses associated with this condition. Preventing obesity, optimising physical activity and having balanced diets that meet the needs of the body (especially plant-based) are all important societal and individual considerations to prevent type 2 diabetes or induce remission (Rosenfeld et al, 2022).

In the first study reviewed in this journal club, out of 27 255 patients reviewed, 16 148 complication episodes occurred in 7895 people (Sund et al, 2022). These comprised the vast majority of the overall spending in people with diabetes. Among new complication episodes (in people with no prior complications), the highest costs were for foot disorders (€16 843), nephropathy (€15 264) and cardiovascular disease (€13 121). The number of treatment days in hospital was the most significant driver of costs. This demonstrates the critical importance of preventing complications for healthcare systems.

Although this commentary focuses on glycaemic control and glucose-lowering agents, the triple National Diabetes Audit target of HbA_{1c} ≤58 mmol/mol, blood pressure ≤140/80 mmHg and total cholesterol <5 mmol/L (or an appropriate statin for primary and secondary prevention of cardiovascular disease), individualised to the patient, will always apply. With respect to glycaemic control, Whyte et al (2022), reviewing a cohort of 26 180 people with type 2 diabetes, revealed that early achievement of glycaemic control in the first year after diagnosis improved all the major cardiovascular outcomes. It was failure to attain and then maintain good glycaemic control that led to an increased risk of cardiovascular events.

These data were from the era before widespread use of new agents such as SGLT2 inhibitors and GLP-1 receptor agonists (only 5% of the cohort was on these agents). The study by Peng et al (2022) adds to the evidence that use of an SGLT2 inhibitor would be a far more cost-effective approach to achieving fewer cardiovascular and renal complications. The study was a direct cost-efficiency analysis of SGLT2 inhibitors versus DPP-4 inhibitors, and further confirms that DPP-4 inhibitors should be ranked below SGLT2 inhibitors because of the latter's propensity to reduce complications. The specific agent chosen (canagliflozin, dapagliflozin, empagliflozin or ertugliflozin) would need to be based on the specific patient clinical phenotype: whether low cardiovascular risk, high risk, chronic kidney disease, heart failure or manifest atherosclerotic cardiovascular disease (Varadhan et al, 2022).

In a *post hoc* analysis of the DAPA-CKD trial, patients were grouped into modified KDIGO risk categories (Waijer et al, 2022). The proportion of participants in each risk category was as follows: moderately high risk, 14.4%; high risk, 31.3%; and very high risk, 54.3%. Although SGLT2 inhibitors may be less effective at lowering blood glucose as renal function declines, this study shows that the risk of the composite primary outcome (a sustained 50% decline in eGFR, end-stage renal disease, or renal or cardiovascular death) was reduced across all these risk categories.

The updated NICE (2015) NG28 guideline and accumulating evidence from clinical trials and subsequent analyses have firmly cemented the use of SGLT2 inhibitors in preventing diabetes complications. NICE advocates the use of these agents in people with type 2 diabetes who are at high cardiovascular risk (10-year QRISK2 ≥10%). These patients should already be on statins. We therefore must ask ourselves the question: **If a patient is on a statin, why are they not also on an SGLT2 inhibitor?** ■

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