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SGLT-2 inhibitors for people with type 2 diabetes

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15% with SGLT2i will be very small in absolute terms when the starting risk is already low. The second is that this starting risk might have already been lowered by the implementation of other recommended interventions, such as statins or aspirin. Since most patients with type 2 diabetes are at low cardiovascular risk, the opportunity cost of acting in accordance to this conclusion might threaten the viability of using these drugs in patients at high risk, to whom most of their benefit can accrue. The larger investments demanded for these expensive drugs might threaten the viability of other programmes, including some with a larger health impact. In low-resource settings, the consequences might not only be adverse but also unethical.

We declare no competing interests.

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Sodium-glucose co-transporter-2 inhibitors (SGLT2i) seem promising for the prevention and treatment of cardiovascular disease, as shown in a study by Zelniker and colleagues.¹ They are now suggested as second-line therapy for most patients with type 2 diabetes.² However, important questions remain open for an important patient group, older patients (particularly those older than 80 years).

There is strong evidence that SGLT2i can prevent heart failure, both

incident and worsening. Heart failure is progressively a geriatric syndrome, with an estimated 60% increase in individuals older than 80 years until 2030;³ however, octogenarians have not been adequately represented in SGLT2i trials. SGLT2i also appear to be beneficial for patients with poor renal function, which might be reassuring because for many drug treatments you are as old as your kidneys.⁴ However, it is still not clear how safe SGLT2i actually are in older patients, particularly those with frailty, multimorbidity, volume depletion, hypotension, and weight reduction, in addition to kidney dysfunction.⁵

Another important question is whether SGLT2i can prevent both systolic (reduced ejection fraction) and diastolic (preserved ejection fraction; especially prevalent in older patients) heart failure. So far, the two types have not been differentiated in large SGLT2i trials.⁵

It is possible that SGLT2i will be of major interest also in geriatric patients at risk of heart failure, with and without type 2 diabetes. At the moment, systematic expansion of the study and evaluation of SGLT2i in all age groups, including older people, is needed. Specifically, aiming to study older people with multimorbidity, frailty, and polypharmacy will close the knowledge gaps, which will ultimately enable personalised medicine approaches.

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Authors' reply

German Malaga and Eloy F Ruiz suggest that some patients might perceive that the cost and side-effects of sodium-glucose co-transporter-2 inhibitors (SGLT2i) could outweigh the benefit in terms of reduction in cardiovascular and renal events.¹ It should go without saying that shared decision making between the doctor and patient is always prudent.

At the public health level, cost is an important factor, and allocation of limited resources can be challenging for payers and prescribing doctors. To that end, cost-effectiveness analyses might be helpful. However, it is important to note that glycaemic control is fundamental to the treatment of patients with diabetes, and thus the issue is not whether to treat with a glucose-lowering drug, but with which one.

In addition to reducing the risk of major adverse cardiovascular events in patients with atherosclerotic cardiovascular disease, SGLT2i lower the risk of hospitalisation for heart failure and progression of kidney disease across broad subgroups, including patients in primary prevention. This advantage contrasts with several classes of glucose-lowering drugs in frequent use that do not have such clinical benefits. Although, as always, the absolute benefit depends on the baseline risk and tends to be greatest in patients at