cardiovascular disease (CVD), but only 3% had a history of chronic kidney disease (CKD). Total follow-up for the SGLT2 inhibitors was 42,632 years (mean 1.4 years) and for DPP-4 inhibitors 58,473 years (mean 1.7 years).

The primary endpoint of serious renal events was a composite of renal replacement therapy i.e. dialysis or transplant, death from renal causes and hospital admission for renal events.

After adjusting for confounding variables such as BMI, blood pressure (BP) and smoking status, the use of SGLT2 inhibitors compared with DPP-4 inhibitors was associated with a 58% reduced risk of serious renal events (2.6 events per 1,000 person years vs 6.2 events per 1,000 person years); hazard ratio 0.42 (95% CI: 0.34-0.53). The difference was mainly driven by lower rates of renal replacement therapy and hospital admissions with use of SGLT2 inhibitors. No significant differences were seen in death rates from renal causes between the groups.

The SGLT2 inhibitors are the most recent class of hypoglycaemic drugs introduced for type 2 diabetes. They work by reducing glucose/sodium exchange in the proximal tubule and increasing urinary loss of glucose. From first licensing, they have been subject to outcome studies. Not only have they been shown to result in weight reduction, BP lowering and improved HbA_{1c} levels, but outcome studies suggest a real reduction in cardiovascular deaths on these drugs.

The study authors conclude: 'Complementing data from clinical trials, this study provides further support for the use of SGLT2 inhibitors in a broad range of patients with type 2 diabetes.'

An accompanying editorial in the *BMJ* states that although there is no evidence of a protective effect against renal disease by DPP-4 inhibitors, they do not worsen renal outcomes.[1] The author of the editorial concludes that SGLT2 inhibitors seem preferable to DPP-4 inhibitors in diabetes patients who may be more at risk of renal disease.

In the UK, SGLT2 inhibitors are not recommended to be initiated in patients with an eGFR below 60 ml/min/1.73m^2, or continued in patients with an eGFR below 45 ml/min/1.73m^2.

The findings of this study are encouraging. The realisation of the role of lifestyle in preventing and treating type 2 diabetes, combined with new classes of drugs that assist weight loss and improve outcomes give grounds for cautious optimism about the future for diabetes management.

DR MATTHEW LOCKYER

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Addiction

Increased risk of fatal overdose or suicide associated with stopping opioids

Ceasing treatment with opioids is associated with an increased risk of death from overdose and suicide, an observational study from the United States has found.

A total of 1,394,102 patients, mean age 60 years, in the Veterans Health Administration system who had received outpatient prescriptions for an opioid medication during the 2013 fiscal year were included in the study. Data on death rates up to the end of the fiscal year 2014 were analysed. The vast majority of participants were men (92%). Just over half the patients had three or more medical diagnoses. Alcohol use disorders were diagnosed in about 10% of patients and the most common mental health conditions were depressive disorders and post-traumatic stress disorder.

There were 2,887 deaths from overdose or suicide (1,851 overdoses and 1,249 suicides, these figures were not mutually exclusive). Just over half of patients (57.4%) stopped opioid treatment during the study period.

Patients had been prescribed opioids for variable periods, and the longest period identified, longer than 400 days, accounted for 37% of patients. Around a third (32%) of patients were prescribed opioids for up to 30 days, 9% for 31-90 days and 23% for 91-400 days.

The hazard ratios (HR) for death by overdose or suicide for patients who stopped opioid treatment were:

- HR 1.67 for ≤ 30 days' opioid treatment
- HR 2.80 for 31-90 days' opioid treatment
- HR 3.95 for 91-400 days' opioid treatment
- HR 6.77 for > 400 days' opioid treatment

Other factors that were independently associated with a greater risk of death from overdose or suicide were: prescriptions for long- or short-acting opioids as opposed to tramadol; log maximum daily morphine mg equivalents; the number of medical diagnoses; and having a mental health or substance use disorder. Older age, female gender, and being married were independently associated with a lower risk of death from overdose or suicide.

Concerns about recent rapid increases in the prescribing of opioid medication, particularly for chronic non-cancer pain, and associated risks such as overdose and dependence, has led to a range of initiatives to support clinicians in reducing and stopping prescribing opioids when appropriate.

The authors conclude that: 'Patient-centred efforts to mitigate the risk of death from overdose or suicide in patients prescribed opioids need to look at a broad array of risk factors for patients rather than focus solely on long-term prescription management. Our findings suggest close monitoring for at least three months for any patient stopping treatment with opioids but especially in those on long-term treatment or those with other risk factors (e.g. mental health and substance use disorders)'.

DR JEZ THOMPSON

Oliva EM, Bowe T, Manhapra A et al. Associations between stopping prescriptions for opioids, length of opioid treatment, and overdose or suicide deaths in US veterans: observational evaluation. *BMJ* 2020;368:m283

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