HR 0.95 (95% CI: 0.84-1.07) respectively.

However, the excess risk of heart failure was substantially higher compared with controls, HR 1.45 (95% CI: 1.34-1.57)

There was a stepwise increase in the hazard ratios for each additional variable that did not meet the target range in patients with diabetes.

The strongest predictor for death was smoking and the strongest predictor for MI and stroke was raised HbA_{1c}.

Previous individual risk factor controlled trials have shown reductions in cardiovascular outcomes and deaths, and the Steno-2 study confirmed long-term reductions in mortality and morbidity from lifestyle and drug interventions.[1]

This study shows that effective control of risk factors can reduce the excess risk of cardiovascular events and death to that of individuals without diabetes.

An accompanying editorial comments that the results 'provide clear support for active management of risk factors.'[2] In my opinion, the results are further support for the intensive lifestyle interventions currently being considered with new onset diabetes, and vigorous treatment of risk factors in established cases. The low HbA_{1c} targets will add to the debate about hypoglycaemia risks.

DR MATTHEW LOCKYER

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Addiction

Tramadol associated with longer use of opioids after surgery

A study from the United States has found that patients prescribed tramadol for postoperative pain have a higher risk of prolonged opioid use relative to those given other short-acting opioids.

The authors undertook a retrospective observational study of opioid-naïve patients undergoing elective surgery between 2009 and 2018 using insurance claims data from a large private US health plan.

Overall 444,764 patients fulfilled the inclusion criteria of having at least 180 days of follow-up information. Of these, 357,884 filled a discharge prescription for one or more opioids following one of the 20 elective surgical operations identified in the study. These included a range of general surgical (for example, hernia repair and laparoscopic cholecystectomy), orthopaedic (including total knee replacement and carpal tunnel release), and colorectal, urological and thoracic procedures, in order to cover multiple specialties and a range of expected postoperative pain levels.

For analysis three commonly used definitions of prolonged opioid use were used:

- Additional opioid use post surgery (at least one opioid prescription filled 90-180 days after surgery)
- Persistent opioid use after surgery (any span of opioid use starting in the 180 days after surgery and lasting at least 90 days)
- The CONSORT definition of long-term opioid use (opioid use episode starting in the 180 days after surgery that spans at least 90 days and includes either ten or more opioid fills or 120 or more days' supply of opioids).

The most commonly prescribed opioid post-surgery was hydrocodone (53.0% of those prescribed a single opioid), followed by short-acting oxycodone (37.5%). Tramadol was relatively infrequently prescribed (4.0%).

The unadjusted risk of additional opioid use after surgery was 7.10% (n = 31,431); the figure for persistent opioid use was 1.0% (n = 4,457); and 0.5% of patients (n = 2,027) met the CONSORT definition of long-term opioid use.

Use of tramadol post surgery was associated with increased adjusted risk of all three definitions of prolonged opioid use, see table 1, below. Tramadol prescribing as a single opioid was associated with a 6% increase in the adjusted risk of additional opioid use relative to people receiving other short-acting opioids, a 47% increase in the adjusted risk of persistent opioid use and a 41% »

Table 1

Adjusted risk ratios for persistent opioid use (95% CI)

Opioid type	Additional opioid use after surgery	Persistent opioid use after surgery	CONSORT definition of opioid dependence
Other short acting	Reference	Reference	Reference
Tramadol only	1.06 (1.00-1.13); P = 0.049	1.47 (1.25-1.69); P < 0.001	1.41 (1.08-1.75); P = 0.013
Tramadol + short acting	1.05 (0.96-1.14); P = 0.261	1.04 (0.86-1.21); P = 0.685	1.40 (1.05-1.74); P = 0.022
Any long acting	0.95 (0.87-1.03); P = 0.218	1.18 (1.02-1.35); P = 0.029	1.69 (1.36-2.02); P < 0.001

increase in the adjusted risk of CONSORT-defined long-term opioid use.

The study authors conclude: 'We found that tramadol, a drug that is scheduled at a lower risk level than other common short-acting opioids has a similar or somewhat greater risk of prolonged opioid use after surgery.

They call for a rescheduling of tramadol 'to a level that better reflects its risk of prolonged use'.

In an accompanying editorial, a UK consultant in complex pain comments: 'Prescribing of any opioid should be in accordance with the evidence and with the effects and side effects reported by individual patients, as well as with the patient's and prescriber's full knowledge of the likelihood and risks of long-term use.'[1]

Opioid medications continue to have an important role in the management of severe acute pain. Ongoing prescribing following an acute painful event needs to be managed with care, and the potential for tramadol to be associated with longer-term use must not be underestimated.

DR JEZ THOMPSON

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