

Diabetes & Obesity

RESEARCH REVIEW™

Making Education Easy

Issue 197 – 2025

In this issue:

- Comorbidities and mortality across adult-onset diabetes subgroups
- CV outcomes of semaglutide and tirzepatide for type 2 diabetes
- Screening and assessment of type 2 diabetes risk factors among Māori/Pacific youth
- Comparative GI safety of GLP-1 agonists and tirzepatide in type 2 diabetes
- Association of age at type 2 diabetes onset with progression
- Infection-related hospitalisation risk with SGLT-2 inhibitors
- Global burden of early-onset type 2 diabetes
- Achieving glycaemic, BP and lipid targets in type 2 diabetes
- Acute pancreatitis and biliary disease risk after incretin initiation
- Combining SGLT-2 inhibitors with GLP-1 agonists for type 2 diabetes

Abbreviations used in this issue

BP = blood pressure
CV = cardiovascular
DALY = disability-adjusted life-year
DPP = dipeptidyl peptidase
GI = gastrointestinal
GLP = glucagon-like peptide
HbA_{1c} = glycated haemoglobin
HDL/LDL = high-/low-density lipoprotein
HR = hazard ratio
RCT = randomised controlled trial
SGLT = sodium glucose cotransporter

KINDLY SUPPORTED BY:

New Zealand Society
NZSSD
for the Study of Diabetes

**NZMedJobs
& NZLocums**

**Hauora
Taiwhenua**
Rural Health
Network

Welcome to issue 197 of Diabetes and Obesity Research Review.

Our last issue for 2025 begins with a paper describing long-term outcomes and mortality across the different forms of adult-onset diabetes. NZ research is included in the form of an exploration of type 2 diabetes awareness, knowledge, attitudes and risk factors among youth of Pacific and Māori descent in Auckland. A few papers deal with tolerability of medications we use for treating diabetes, including GI events with GLP-1 receptor agonists and tirzepatide, infections associated with SGLT-2 inhibitor and DPP-4 inhibitor use, and the risks of acute pancreatitis and biliary disease across a range of incretin-based agents. We conclude the year with research reporting on combining SGLT-2 inhibitors with GLP-1 receptor agonists for type 2 diabetes.

Whether you are working through or having a break, we wish you a safe and rewarding holiday season, and remember, we are still happy to receive your comments and feedback during this time.

Kind regards,

Professor Jeremy Krebs

jeremykrebs@researchreview.co.nz

Comorbidities and mortality in subgroups of adults with diabetes with up to 14 years follow-up

Authors: Asplund O et al.

Summary: Long-term outcomes and mortality were reported for different types of adult-onset diabetes for 19,076 individuals. The severe autoimmune diabetes and severe insulin-deficient diabetes subgroups had the highest HbA_{1c} levels, both at diagnosis and over time, as well as the greatest risks of retinopathy and neuropathy, whereas the severe insulin-resistant diabetes subgroup had the greatest prevalences of hypertension, dyslipidaemia, kidney disease, CV disease and steatotic liver disease at diabetes diagnosis. Severe insulin-deficient and -resistant diabetes were associated with an increased risk of incident kidney disease despite differences in HbA_{1c} levels. The greatest atrial fibrillation risk was seen with severe insulin-resistant diabetes and mild obesity-related diabetes, whereas the stroke risk was increased only in severe insulin-deficient diabetes. The steatotic liver disease and heart failure risks were increased with severe insulin-resistant diabetes. Mortality risk was increased in the severe insulin-deficient and -resistant diabetes and mild obesity-related diabetes subgroups, largely due to CV-related mortality.

Comment: As we know, type 2 diabetes is really a heterogeneous group of conditions with a common theme of hyperglycaemia. However, there are important, yet subtle, differences in the underlying pathophysiology that result in the common glucose phenotype, but different comorbidities and different risks for complications. This paper reported a prospective longitudinal cohort of people with type 2 diabetes grouped into broad subgroups, which have previously been defined, based largely on levels of β -cell function and insulin sensitivity. What is observed mirrors what I see in practice, in that the people who seem to have the highest rates of complications are those who are very insulin-resistant. This is of course usually associated with obesity, which may be the driving causative factor. It is commonly what is driving the diabetes in younger adults with type 2 diabetes, and likely also explains why that group often do so poorly. **Take home: beware the very insulin-resistant person with type 2 diabetes – they are likely to be at greater risk of complications and premature mortality.**

Reference: *Lancet Diabetes Endocrinol* 2025;14:29–40

[Abstract](#)

Earn CPD Points

RACP MyCPD Program participants can claim the time spent reading and evaluating research reviews as CPD in the online **MyCPD program**.

Please contact MyCPD@racp.edu.au for any assistance.

MERRY CHRISTMAS & A HEALTHY, HAPPY 2026!

FROM THE TEAM AT

RESEARCH REVIEW™
Making Education Easy – Since 2006



Cardiovascular outcomes of semaglutide and tirzepatide for patients with type 2 diabetes in clinical practice

Authors: Krüger N et al.

Summary: The effectiveness of tirzepatide and semaglutide was explored across five cohorts of patients with elevated CV risk. Two CV outcome trials, SUSTAIN-6 (semaglutide versus sitagliptin as placebo proxy) and SURPASS-CVOT (tirzepatide versus dulaglutide), were emulated to benchmark and critically evaluate the design, data and analytic framework of the study, each drug was then evaluated in expanded populations that reflected routine clinical practice patients, and finally tirzepatide was compared with semaglutide. Benchmarking revealed good agreement between the reference trials and their emulations for each component of the composite primary endpoint (myocardial infarction, stroke and all-cause mortality), with the exception of all-cause mortality in SUSTAIN-6. When semaglutide was compared with sitagliptin in expanded populations, the risk of myocardial infarction or stroke was reduced (HR 0.82 [95% CI 0.74, 0.91]), as was the risk of the composite outcome, including mortality, when tirzepatide was compared with dulaglutide (0.87 [0.75, 1.01]), but not in the head-to-head comparison of tirzepatide versus semaglutide (1.06 [0.95, 1.18]).

Comment: We await the arrival of tirzepatide in NZ, which will hopefully be in 2026. As previously included in Diabetes and Obesity Research Review, the evidence for the weight loss benefits of tirzepatide is very clear, both in people with and without type 2 diabetes. However, across the incretin class of medications, we see that the degree of weight loss in those with type 2 diabetes is a quantum less than in those without. Whatever is driving that may also impact on the CV benefits of these drugs. Unfortunately, it is uncommon for large CV outcome trials to be conducted that compare agents in a head-to-head fashion, largely because it isn't in the interest of the pharmaceutical companies, who generally fund such expensive trials. This study reported data from real-world patients using a strategy to mimic an RCT in order to compare outcomes from people prescribed semaglutide versus tirzepatide. **Take home: the bottom line is that in the absence of a true RCT, real-world data suggest that semaglutide and tirzepatide confer similar CV benefits in people with type 2 diabetes.**

Reference: *Nat Med*; Online Nov 9, 2025
Abstract

JARDIANCE® for T2D: Jardiance® (empagliflozin)
More Than Glucose Control – A Proven Reduction in Cardiovascular Death^{1,2*}

[^]In adult patients with T2D and established CV disease (CAD, PAD, MI or stroke)^{1,2*}



Not an actual patient

INDICATION

ADDITIONAL BENEFITS

38% RRR
IN CV DEATH^{1,2*}

HR=0.62
95% CI: 0.49, 0.77;
p<0.001.^{1,2}

35% RRR
IN HOSPITALISATION FOR HEART FAILURE^{1,2*}

HR=0.65
95% CI: 0.50, 0.85;
p<0.002.^{1,2}

39% RRR
IN NEW OR WORSENING NEPHROPATHY^{1,3}**

HR=0.61
95% CI: 0.53, 0.70;
p<0.001.³

32% RRR
IN ALL CAUSE MORTALITY^{1,2}**

HR=0.68
95% CI: 0.57, 0.82;
p<0.001.^{1,2}

*Versus placebo on top of standard of care. Standard of care included antihypertensives, lipid-lowering agents, anticoagulants and glucose-lowering therapies. †Secondary endpoint. See full Data Sheet for further details. 2 CAD, coronary artery disease; CKD, chronic kidney disease; CI, confidence interval; CV, cardiovascular; HF, heart failure; HHF, hospitalisation for heart failure; HR, hazard ratio; MI, myocardial infarction; PAD, peripheral artery disease; RRR, relative risk reduction; T2D, type 2 diabetes.

References: 1. Zinman et al. *N Engl J Med* 2015;373:2117-28. 2. JARDIANCE Data Sheet. 3. Wanner C et al. *N Engl J Med* 2016;375:323-34.

JARDIANCE® empagliflozin 10mg, 25mg film coated tablets. Before prescribing, please review full Data Sheet which is available on request from Boehringer Ingelheim or from <http://www.medsafe.govt.nz/profs/datasheet/dsform.asp>

Indication: *Glycaemic control:* Treatment of type 2 diabetes mellitus (T2DM) to improve glycaemic control in adults and children aged 10 years and above as: *Monotherapy* - When diet and exercise alone do not provide adequate glycaemic control in patients for whom use of metformin is considered inappropriate due to intolerance; *Add-on combination therapy* - With other glucose-lowering medicinal products including insulin, when these, together with diet and exercise, do not provide adequate glycaemic control. *Prevention of cardiovascular (CV) events:* In adult patients with T2DM and established CV disease to reduce the risk of CV death. To prevent CV deaths, Jardiance should be used in conjunction with other measures to reduce CV risk in line with the current standard of care. **Dosage and Administration:** Recommended starting dose is 10mg once daily taken with or without food. Patients tolerating 10mg once daily and requiring additional glycaemic control, increase dose to 25mg once daily. No dose adjustment is recommended based on age, patients with eGFR ≥30mL/min/1.73m² or hepatic impairment. No data is available for children with eGFR <60 mL/min/1.73 m² and children below 10 years of age. When Jardiance is used in combination with a sulfonylurea (SU) or with insulin, a lower dose of the sulfonylurea or insulin may be considered. **Contraindications:** Hypersensitivity to empagliflozin or any of the excipients. **Warnings and Precautions:** Patients with type 1 diabetes; diabetic ketoacidosis; necrotising fasciitis of the perineum (Fournier's gangrene); not recommended to initiate in patients on dialysis; assess renal function before treatment and regularly thereafter; patients for whom a drop in BP could pose a risk (e.g. those with known CV disease, on anti-hypertensive therapy with a history of hypotension, or aged ≥75 years); urinary tract infections (UTIs); rare hereditary conditions of galactose intolerance, e.g. galactosaemia; pregnancy; lactation; children (<10 years). **Interactions:** Diuretics; insulin and SU; interference with 15-anhydroglucitol assay. Interaction studies have only been performed in adults. **Adverse Reactions:** *Very common:* hypoglycaemia (when used in combination with SU or insulin). *Common:* hypoglycaemia (combination with metformin; pioglitazone with or without metformin; metformin and linagliptin – patients aged ≥18 years); vaginal moniliasis, vulvovaginitis, balanitis and other genital infections; UTIs (including pyelonephritis and urosepsis); pruritus (patients aged ≥18 years); allergic skin reactions (e.g. rash, urticaria); increased urination; thirst; serum lipids increased; volume depletion (patients aged ≥75 years); constipation (patients aged ≥18 years). For other adverse reactions, see full Data Sheet. **Actions:** Empagliflozin is a reversible competitive inhibitor of sodium-glucose co-transporter 2 (SGLT2), which is responsible for glucose absorption in the kidney. It improves glycaemic control in patients with type 2 diabetes by reducing renal glucose reabsorption. Through inhibition of SGLT2, excessive glucose is excreted in the urine.

PRESCRIPTION MEDICINE. JARDIANCE is a funded medicine – Restrictions apply: Pharmaceutical Schedule, Special Authority



BOEHRINGER INGELHEIM (NZ) Ltd. PO Box 76216 Manukau City, Auckland 2241.
JARDIANCE® is a registered trademark of Boehringer Ingelheim. Copyright ©2025.
PC-NZ-100553. TAPS MR12444. Prepared Sep 2025.

For more information, please go to www.medsafe.govt.nz

Earn CPD when you read or watch Research Review publications or videos.

Find out more [HERE](#)



Screening and assessment of type 2 diabetes risk factors among Pacific youth attending community health events in Auckland

Authors: Shannon II FQ et al.

Summary: These NZ researchers explored type 2 diabetes awareness, knowledge, attitudes and risk factors for a convenience sample of 135 individuals aged 16–25 years, and an additional three opportunistically assessed participants aged 26–31 years, of Pacific and Māori descent from South, Central and East Auckland; 51.9% of the participants were classified as obese, and there was one new case of diabetes diagnosed during the study period (May 25 to Jul 31, 2024). Structured survey responses showed that type 2 diabetes awareness was reported by ~60% of participants, of whom 40% were made aware mainly via familial sources. There was also a high level of sugary drink consumption reported. Nondietary risk factors for type 2 diabetes included a family history in a first-degree relative (36%), smoking (39%) and alcohol consumption (45%). Engagement in regular physical activity was reported by 41% of males and 59% of females. A multifaceted, youth-focussed care model of primarily lifestyle management for preventing and managing type 2 diabetes was suggested by the participants.

Comment: It is well reported that obesity is common in Pacific communities in NZ, and that there are increasing rates of type 2 diabetes in younger Pacific people. This study provides some further insight into this. It reported an opportunistic screening approach to testing in young adults from community events. Therefore, there are selection biases at play that need to be taken into account. Nevertheless, there were several stand out results. Firstly, the rate of obesity was approximately 50%. Secondly, the rate of undiagnosed diabetes was only <1%, which surprised me and may indicate selection bias, or may be that the rate of undiagnosed diabetes in this age group is not as high as we might imagine. The third observation that I found disturbing was the rate of smoking was 39%. Take note Minister Brown. **Take home: rates of adverse health parameters such as obesity and smoking are high in young Pacific people in NZ, and as the authors identified, a multifaceted approach to addressing this and reducing risk of diabetes and CV disease is needed.**

Reference: *N Z Med J* 2025;138(1625):20–34

[Abstract](#)

Comparative gastrointestinal safety of dulaglutide, semaglutide, and tirzepatide in adults with type 2 diabetes

Authors: Crisafulli S et al.

Summary: These researchers compared severe GI adverse event risk for dulaglutide, subcutaneous semaglutide and tirzepatide in routine clinical practice adult patients with type 2 diabetes. Three cohorts of pairwise comparisons were analysed, with 65,238 matched pairs for semaglutide versus dulaglutide, 20,893 for tirzepatide versus dulaglutide, and 46,620 for tirzepatide versus semaglutide. There was no significant difference in GI event risk for any of the comparisons (respective HRs for semaglutide versus dulaglutide, tirzepatide versus dulaglutide and tirzepatide versus semaglutide, 0.96 [95% CI 0.87, 1.06], 0.96 [0.77, 1.20] and 1.07 [0.90, 1.26]).

Comment: With the increasing use of the GLP-1 receptor agonist class of medications both for weight loss and for diabetes management, it is important to continually review the safety profile of each agent, and the class as a whole, when being prescribed in the real world and not in the selected patients enrolled in clinical trials. The most common side effect is GI upset and constipation. However, there have continued to be concerns about pancreatitis and biliary disease. This real-world population cohort study compared the rates of acute pancreatitis, biliary disease, bowel obstruction, gastroparesis and severe constipation in adults with diabetes prescribed dulaglutide, semaglutide or tirzepatide. There was no evidence to suggest any important difference in the rates of these side effects among the three agents. **Take home: rates of GI side effects appear to be similar across agents in the GLP-1 receptor agonist class.**

Reference: *Ann Intern Med*; Online Nov 4, 2025

[Abstract](#)

Association of the age at type 2 diabetes onset with diabetes progression

Authors: Sajjadi SF et al.

Summary: Using data from the Indian Kerala Diabetes Prevention Program and the US Diabetes Prevention Program (146 and 802 participants, respectively), these researchers examined the impact that age at type 2 diabetes onset has on disease progression. BMI was higher both at diagnosis and at follow-up in individuals who were diagnosed at younger ages; the BMI change over time was relatively small in the US cohort. There was no significant association of fasting plasma glucose or HbA_{1c} level at diabetes onset with age at onset, but these parameters increased faster in those diagnosed at a younger age, although not to a statistically significant level for the Indian cohort. There were also associations of younger onset age with higher estimated glomerular filtration rate and lower HDL-cholesterol levels and systolic BP in both cohorts, although the association with HDL-cholesterol level did not reach statistical significance in the Indian cohort. There were slight decreases in systolic BP over time among participants from the US cohort diagnosed at older ages, but not among those diagnosed at younger ages.

Comment: The theme of this month might be that all type 2 diabetes is not the same. As discussed with other papers, the common denominator is hyperglycaemia, but the underlying pathophysiology varies widely. With the emerging evidence that type 2 diabetes is increasing in younger age groups, it is important that we understand the implications of this. This paper reported longitudinal data from two prospective studies of diabetes prevention interventions, and reported on the characteristics of those who did develop diabetes over the mean 7- to 8-year follow-up. From these data, we see that individuals diagnosed at a younger age had higher rates of obesity and lower HDL cholesterol levels, in keeping with a more insulin-resistant profile. The finding of lower BP and better renal function in this group is not surprising, as these factors are highly influenced by age independently of diabetes. **Take home: this study provides more evidence for the concerning adverse features of people diagnosed with type 2 diabetes at a young age, and further supports the need to address the antecedent factors – primarily obesity.**

Reference: *Diabetes Care* 2025;dc251811

[Abstract](#)

Earn CPD Points

GPs

Research Review publications, videos and e-Learning modules have been endorsed by The Royal New Zealand College of General Practitioners (RNZCGP) and have been approved for up to **2 CME credits** per learning hour for Continuing Professional Development (CPD) purposes.

Please CLICK HERE to download RNZCGP Dashboard.



Nurses

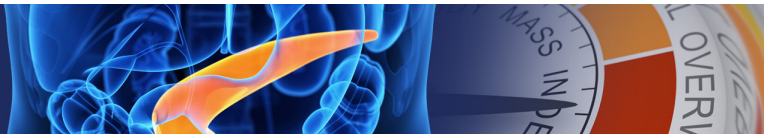
Time spent reading this publication has been approved for CNE by The College of Nurses Aotearoa (NZ) for RNs and NPs.

For more information on how to claim CNE hours CLICK HERE.



Journal reading (including Research Reviews) may be considered a professional development activity by The Nursing Council of New Zealand. Nurses can record your professional development via **MyNC** on the “Continuing Competence” tab.

For more information CLICK HERE.



Initiation of sodium-glucose cotransporter-2 inhibitors and the risk of infection-related hospitalisations

Authors: Alfonso Arvez MJ et al.

Summary: Infection-related hospitalisations were compared between SGLT-2 inhibitor new users and DPP-4 inhibitor new users over 2 years after discharge from all hospitals in Victoria, Australia. Compared with DPP-4 inhibitor new users, SGLT-2 inhibitor new users had a lower overall infection-related hospitalisation rate (weighted incidence rate ratio 0.74 [95% CI 0.71, 0.77]), with significantly lower hospitalisation rates for sepsis, pneumonia, GI infections, urinary and respiratory tract infections, influenza and kidney infections, but not cellulitis. In contrast, SGLT-2 inhibitor new users had higher hospitalisation rates for osteomyelitis, foot infections and genital mycotic infections than DPP-4 inhibitor new users.

Comment: We have known about the increase in risk for genital fungal infections with SGLT-2 inhibitors since the initial clinical trials. This paper reviewed the risk of hospitalisation for a range of infections in users of SGLT-2 inhibitors in an Australian population. The overall risk was lower when compared with those using DPP-4 inhibitors. This included urinary tract and kidney infections. However, there were more genital fungal infections as expected, and concerning more osteomyelitis and foot infections, with SGLT-2 inhibitors. This reminds me of the early concerns about canagliflozin and amputations. This hasn't been observed with other SGLT-2 inhibitors as far as I am aware. However, the findings in this study perhaps need to be considered in that context. **Take home: SGLT-2 inhibitors are associated with an overall lower rate of hospitalisations for infection than DPP-4 inhibitors. Genital fungal infections remain an issue, and there is some concern around foot infections, which may be more relevant for those with existing foot disease.**

Reference: *Diabetes Obes Metab*; Online Nov 12, 2025
[Abstract](#)

The global burden of early-onset type 2 diabetes (1990–2050)

Authors: Yu W et al.

Summary: This was an age-period cohort analysis of data from the Global Burden of Disease Study 2021 exploring the incidence, disparities and projections for type 2 diabetes diagnosed between the ages of 15 and 39 years (early-onset). Prevalent cases of early-onset type 2 diabetes increased globally by 222.32% over the 1990–2021 period, with significant increases in the age-standardised incidence rate, the age-standardised prevalence rate and age-standardised DALYs, for which the respective estimated annual percentage changes were 2.45, 2.85 and 2.10. The greatest burden was evident in middle sociodemographic index regions and South/East Asia, whereas the highest age-standardised rates were seen in Oceania. The age group most affected was the 35- to 39-year group, and men were more affected than women. There was also a 35% increase in mortality, with disparity affecting low-income populations. The main drivers of increased incidence and DALYs were epidemiological changes, and 44.7–69.2% of attributable DALYs were due to high BMI. It was projected that the age-standardised incidence rate will continue to increase, reaching 529.52 per 100,000 by 2050 (i.e. 17.14 million new cases).

Comment: Continuing the theme of this review is a report of the global burden of diabetes. The predictions of increasing incidence of diabetes over the last couple of decades appears to be panning out globally. What is even more concerning is that the acceleration in rate seems to be greatest in younger adults – highest in men aged 35–39 years. Furthermore, some of the other concerning features we have seen, such as socioeconomic deprivation and obesity, appear to be driving factors. **Take home: these findings echo the observations in other papers included this month, and again highlight how important it is that we think very hard about how to turn this trend around. We must find a way to address obesity in young people.**

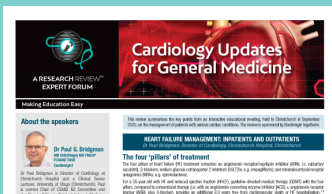
Reference: *Diabetes Obes Metab*; Online Nov 10, 2025
[Abstract](#)

YOU MAY BE INTERESTED IN OUR LATEST EXPERT FORUM

Cardiology Updates for General Medicine

This review summarises the key points from an interactive educational meeting held in Christchurch in September 2025. Cardiologist Paul Bridgman and cardiac electrophysiologist Ross Downey spoke about the management of patients with various cardiac conditions. The meeting concluded with case presentations and discussion.

[CLICK HERE TO READ](#)



To read previous issues of Diabetes & Obesity Research Review [CLICK HERE](#)



INDEPENDENT COMMENTARY BY
Professor Jeremy Krebs MBChB, FRACP, MD

Professor Krebs is an Endocrinologist with a particular interest in obesity and diabetes. He trained in Endocrinology at Wellington Hospital in New Zealand and then did his doctorate with the Medical Research Council - Human Nutrition Research unit in Cambridge, England. His thesis was on the impact of dietary factors on obesity and insulin resistance. Professor Krebs returned to New Zealand in 2002 to take up a consultant Endocrinology post at Wellington Hospital, where he was Clinical Leader of Endocrinology and Diabetes. He heads the research group and is Professor with the University of Otago, and former Director of the Clinical Research Diploma at Victoria University - which he established. **FOR FULL BIO** [CLICK HERE](#).

NZSSD 2026

May 6 – 8
Napier Conference Centre
Ahuriri, Napier

REGISTRATIONS FOR THE NZSSD 2026 ASM OPEN ON **DECEMBER 1, 2025**



Global guideline recommended target achievements in glycaemic, blood pressure, and lipid control in type 2 diabetes

Authors: Kacha G et al.

Summary: This updated meta-analysis included data from 1,618,972 participants from 63 observational studies reporting HbA_{1c} level, BP and LDL-cholesterol level target adherence and achievement of a combined target. HbA_{1c} level targets were achieved by 44% of participants, BP targets were achieved by 41%, and LDL-cholesterol level targets were achieved by 47%; however, all three targets were achieved simultaneously by only 12%. There was also no evidence of a significant improvement in achieving HbA_{1c} level targets between 1997 and 2023 in Europe or North America.

Comment: This paper is a bit depressing to include in the December issue, so I apologise. It is a systematic review and meta-analysis of observational studies assessing the achievement of targets for glucose level, BP and lipid levels in people with type 2 diabetes. The last decade has heralded major advances in medications for the management of type 2 diabetes. Therefore, we might feel hopeful that this would translate into improved attainment of guideline targets, in particular glycaemic control. However, that was not the case in 63 studies across the last 20 years. Less than half the individuals achieved HbA_{1c} level, BP and LDL-cholesterol level targets, with only 12% meeting all three. This is important to know when we assess our own data and helps put it into context. **Take home: globally, achievement of treatment targets in type 2 diabetes is disturbingly low. As the authors conclude, we need to find solutions to the barriers to this. We have plenty of tools.**

Reference: *Diabetes Res Clin Pract* 2025;230:113001

[Abstract](#)

Risk of acute pancreatitis and biliary events after initiation of incretin-based medications in patients with type 2 diabetes

Authors: Fang YE et al.

Summary: Associations of incretin medication use with acute pancreatitis and biliary disease risk were explored in three pairwise US cohorts each with >1.2 million adults with type 2 diabetes. After propensity weighting, the acute pancreatitis risk did not differ significantly for GLP-1 receptor agonist and DPP-4 inhibitor initiators when compared with SGLT-2 inhibitor initiators (respective HRs 1.01 [95% CI 0.90, 1.13] and 1.00 [0.85, 1.15]), but they did have small but significant increases in the risk of biliary disease (1.15 [1.05, 1.26] and 1.22 [1.03, 1.46]), equivalent to <1 additional event per 1000 person-years. GLP-1 receptor agonist initiators did not differ significantly from DPP-4 inhibitor initiators for the risk of acute pancreatitis (HR 1.08 [95% CI 0.95, 1.22]) or biliary disease (0.95 [0.86, 1.04]).

Comment: From early development, the incretin based therapies have had some concerns around them for the increased risk of pancreatitis and biliary disease. These were initially raised from observations in studies in rats. However the actual risk in humans has been less clear. This real world study in a large cohort of patients in the US compared the rates of pancreatitis and biliary events in people with type 2 diabetes exposed to GLP-1 agonists, DPP-4 inhibitors or SGLT-2 inhibitors. From these data there does not appear to be any drug specific increased risk of pancreatitis, which is very reassuring. There was a very small increased risk of biliary events, but in absolute terms this is really not significant. **Take home: real-world data do not show an increased risk of pancreatitis with either DPP-4 inhibitor or GLP-1 agonist use in people with type 2 diabetes.**

Reference: *Diabetes Care* 2025;48:2127-37

[Abstract](#)

Effectiveness and safety of combining SGLT2 inhibitors and GLP-1 receptor agonists in individuals with type 2 diabetes

Authors: Colombijn JMT et al.

Summary: This was a systematic review with meta-analysis of data from 18 cohort studies in 1,164,774 participants with type 2 diabetes comparing combination SGLT-2 inhibitor and GLP-1 receptor agonist therapy with monotherapy from these medication classes. Compared with monotherapy (SGLT-2 inhibitor or GLP-1 receptor agonist), there was low-certainty evidence that the major adverse CV event risk was lower with combination therapy (risk ratio 0.56 [95% CI 0.43, 0.71]), as were the all-cause and CV-related mortality risks (0.50 [0.40, 0.63] and 0.26 [0.16, 0.43], respectively), and there was very low-certainty and moderate-certainty evidence that the respective risks of a kidney composite endpoint and hospitalisation for heart failure were also lower (0.48 [0.32, 0.73] and 0.67 [0.64, 0.71]). Lack of events precluded pooling safety data, but it did not appear that the risks of severe hypoglycaemia, diabetic ketoacidosis, genitourinary infection and GI side effects differed between combination and monotherapy.

Comment: Does 1+1=1, 2 or 3? There is overwhelming evidence to support both classes of drugs, the GLP-1 agonists and the SGLT-2 inhibitors, independently for reducing CV and renal events. Because they act in completely different ways and have different side-effect profiles, it is an obvious question to ask whether the major clinical benefits of each are additive or even synergistic? This paper reported a systematic review and meta-analysis of cohort studies where people had been exposed to each class individually or in combination. It includes 18 studies and over 1 million people. The results suggest an additive beneficial effect for all the major outcomes, including CV and renal events and mortality. However, to confirm this we really need an RCT. **Take home: consider the combined use of GLP-1 agonists and SGLT-2 inhibitors in the management of people with type 2 diabetes with a high risk of CV disease and renal events.**

Reference: *Diabetologia* 2026;69:36-49

[Abstract](#)

Pharmacy Council of New Zealand - Te Pou Whakamana Kaimatū o Aotearoa

Journal reading (including Pharmacy Research Review and other Research Reviews) and completing online activities may be considered a professional development activity as part of the 'Keeping up to Date Recertification Guidance'.

For more information go to

<https://pharmacycouncil.org.nz/pharmacist/recertification/>



REGISTER NOW TO SECURE YOUR SPOT!

10 - 13 April 2026 | Tākina Conference Centre | Wellington, New Zealand | www.ruralwonca2026.com

Independent Content: The selection of articles and writing of summaries and commentary in this publication is completely independent of the advertisers/sponsors and their products. **Privacy Policy:** Research Review will record your email details on a secure database and will not release them to anyone without your prior approval. Research Review and you have the right to inspect, update or delete your details at any time. **Disclaimer:** This publication is not intended as a replacement for regular medical education but to assist in the process. The reviews are a summarised interpretation of the published study and reflect the opinion of the writer rather than those of the research group or scientific journal. It is suggested readers review the full trial data before forming a final conclusion on its merits. **Research Review publications are intended for New Zealand health professionals.**