

Diabetes & Obesity

RESEARCH REVIEW™

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150th
ISSUE

Making Education Easy

Issue 150 – 2021

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Welcome to issue 150 of Diabetes and Obesity Research Review.

This issue begins with research reporting that RYGB for obesity appears to provide greater weight loss, better diabetes control and lower risks of major adverse CV events and nephropathy than NZ's preferred bariatric surgery of sleeve gastrectomy. After this, there is research comparing real-world persistence of GLP-1 receptor agonists with SGLT-2 inhibitors in patients with type 2 diabetes, and a network meta-analysis of RCT data comparing these two drug classes and DPP-4 inhibitors for their CV outcomes. Another selected research paper reports that the prevalences of psychiatric illness, illicit substance use and social disadvantage are high in adults with type 1 diabetes admitted to hospitals for DKA, particularly those who present multiple times. A number of other research papers in this issue highlight how important it is for our patients with diabetes and obese individuals to be vaccinated against COVID-19, with haste, if they haven't already done so.

We hope you enjoy this update in diabetes and obesity research, and we look forward to your comments and feedback.

Best regards,

Professor Jeremy Krebs

jeremykreb@researchreview.co.nz

Cardiovascular outcomes in patients with type 2 diabetes and obesity: comparison of gastric bypass, sleeve gastrectomy, and usual care

Authors: Aminian A et al.

Summary: Major adverse CV events were compared between 1362 obese patients with type 2 diabetes who had undergone RYGB and 693 who had undergone sleeve gastrectomy (there were also 11,435 controls who had not undergone bariatric surgery included in the study). Compared with patients who had undergone sleeve gastrectomy, those who had undergone RYGB had a lower 5-year cumulative incidence of a primary endpoint event (coronary artery event, cerebrovascular event, HF, nephropathy, AF or death from any cause; 13.7% vs. 24.7%; adjusted HR 0.77 [95% CI 0.60, 0.98]), largely driven by a lower 5-year cumulative incidence of nephropathy (2.8% vs. 8.3%; 0.47 [0.28, 0.79]). Patients who had undergone RYGB also had greater reductions in bodyweight, HbA_{1c} level and use of medications for diabetes and CV disease than those who had undergone sleeve gastrectomy, but they were more likely to require upper endoscopy and abdominal surgical procedures within 5 years (45.8% vs. 35.6% and 10.8% vs. 5.4%, respectively [p<0.001]).

Comment: Sleeve gastrectomy has become the de rigueur bariatric procedure in NZ, but I have been somewhat sceptical about whether this is the best procedure for long-term outcomes in people with type 2 diabetes. The Swedish Obesity Study has given us excellent long-term outcome data that show durability of weight loss, metabolic and CV benefits for RYGB, but we are yet to see similar data for sleeve gastrectomy. This paper would suggest that my scepticism may be well founded, with clear benefits for RYGB versus sleeve gastrectomy for weight loss, diabetes control and CV disease and renal outcomes at 5 years. There was a trade-off of more endoscopy and abdominal surgery over that time after RYGB, which must be considered. However, these data call in to question the national policy of sleeve gastrectomy as the chosen procedure for publicly funded bariatric surgery.

Reference: *Diabetes Care* 2021;44:2552–63

[Abstract](#)

Abbreviations used in this issue

BMI = body mass index
CV = cardiovascular
DKA = diabetic ketoacidosis
DPP = dipeptidyl peptidase
GLP = glucagon-like peptide

HbA_{1c} = glycosylated haemoglobin
HF = heart failure
HR = hazard ratio
OR = odds ratio

RCT = randomised controlled trial
RR = risk ratio
RYGB = Roux-en-Y gastric bypass
SGLT = sodium glucose cotransporter



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References: 1. Contrave Data Sheet. 2. Billes SK et al. *Pharmacol Res* 2014;84:1-11. 3. Greenway FL et al. *Lancet* 2010;376(9741):595-605. 4. Hollander P et al. *Diabetes Care* 2013;36(12):4022-9.

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Comparing medication persistence among patients with type 2 diabetes using sodium-glucose cotransporter 2 inhibitors or glucagon-like peptide-1 receptor agonists in real-world setting

Authors: Rea F et al.

Summary: These researchers reported on drug therapy persistence in Italy between patients aged ≥ 40 years with type 2 diabetes who had started GLP-1 receptor agonists versus those who had started SGLT-2 inhibitor therapy while on metformin. A final matched cohort for analysis consisted of 1276 GLP-1 receptor agonist-SGLT-2 inhibitor pairs, among whom around 24% and 29% discontinued these respective treatments. Compared with the SGLT-2 inhibitor group, GLP-1 receptor agonist recipients had a 15% lower likelihood of discontinuing their treatment of interest and a 45% lower risk of discontinuing any antidiabetic pharmacotherapy; once-weekly GLP-1 receptor agonist recipients had better treatment persistence.

Comment: This paper caught my eye, but I'm not sure it answers the real question. My suspicion is that SGLT-2 inhibitors are associated with more side effects in real-world clinical practice than were reported in the clinical trials. Whilst I think they are great drugs with clear benefits for CV and renal outcomes, they do have some tricky side effects that make them a more difficult class of drug to use than the DPP-4 inhibitors, for example. We are just beginning to see the real-world experience of GLP-1 agonists in NZ, so this paper, which explored the persistence with treatment of these classes in an Italian population, is of interest. It shows two useful outcomes. The first is that overall approximately 25% of people come off either agent. The second is that less people stop a GLP-1 agonist than stop an SGLT-2 inhibitor. Unfortunately, these data do not give us an explanation of why or what factors determine cessation of therapy. Nevertheless, these are useful data as we learn how best to use these drugs in NZ.

Reference: *Diabetes Res Clin Pract* 2021;180:109035
[Abstract](#)

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[†]38% RRR in CV death in patients with established CV disease (CAD, PAD, MI or stroke) and T2D (HR=0.62; p<0.001).^{‡2}
*JARDIANCE is a funded medicine. Restrictions apply: Pharmaceutical Schedule, Hospital Medicines List. [†]In adult patients with insufficiently controlled type 2 diabetes and CAD, PAD, or a history of MI or stroke. [‡]The absolute risk for CV death was reduced from 5.9% in patients receiving standard of care plus placebo to 3.7% in patients receiving standard of care plus JARDIANCE® (p<0.001).^{1,2}

1. JARDIANCE® Data Sheet 2019 2. Zinman B et al. N Engl J Med. 2015;373(22):2117-2128

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The efficacy and safety of novel classes of glucose-lowering drugs for cardiovascular outcomes

Authors: Lin DS-H et al.

Summary: This was a network meta-analysis of 21 RCTs (n=170,930) comparing SGLT-2 inhibitors, GLP-1 receptor agonists or DPP-4 inhibitors with placebo, other controls or each other, and reporting CV or renal outcomes. GLP-1 receptor agonists and SGLT-2 inhibitors were both associated with lower risks of a composite primary outcome of CV death, nonfatal myocardial infarction and nonfatal ischaemic stroke when compared with placebo (respective RRs 0.89 [0.84, 0.94] and 0.88 [0.83, 0.94]) and when compared with DPP-4 inhibitors (0.89 [0.82, 0.98] and 0.89 [0.81, 0.97]), with no significant difference between each other (0.99 [0.91, 1.08]). The risk of stroke was lower with GLP-1 receptor agonists versus placebo (RR 0.85 [0.76, 0.94]), whereas SGLT-2 inhibitors were better than GLP-1 receptor agonists for reducing hospitalisations for HF (0.76 [0.68, 0.84]) and adverse renal outcomes (0.78 [0.65, 0.93]). The benefits of SGLT-2 inhibitors and GLP-1 receptor agonists were best in elderly patients, white and Asian patients, those with established atherosclerotic CV disease, those with longer diabetes duration and those with worse glycaemic control.

Comment: Now that we have access to funded agents within all classes of DPP-4 inhibitors, SGLT-2 inhibitors and GLP-1 agonists, it is useful to have a review of the relative efficacies and variations in outcomes between these agents to help guide treatment. This systematic review and meta-analysis provides this update of the clinical trial evidence up to the end of 2020, as it relates to CV and renal outcomes. This is not considering glycaemic lowering *per se* and not taking into account side effects or patient preferences for oral versus injectable therapies. The message is very clear. SGLT-2 inhibitors and GLP-1 agonists are superior to placebo/control and to DPP-4 inhibitors with respect to CV outcomes. There is no overall difference between them, with the exception that GLP-1 agonists appear to have a greater benefit in lowering the risk of stroke. SGLT-2 inhibitors have greater benefit for reducing HF and renal outcomes. This confirms the interpretation we have had from individual outcome trials at a meta-analysis level. This can be added to the discussion we have when individualising treatments.

Reference: *Diabetologia*; Published online Sept 18, 2021

[Abstract](#)

Identifying adults at high-risk for change in weight and BMI in England

Authors: Katsoulis M et al.

Summary: Electronic health records of > 9 million BMI measurements for 2,092,260 adults attending 400 primary-care practices in England were reviewed to identify high-risk groups for changes in weight and BMI in this population-based cohort study. The strongest risk factor for weight gain at 1, 5 and 10 years of follow-up was young adult age; for example, those aged 18–24 years had an OR of 4.22 (95% CI 3.86, 4.62) for transitioning from normal weight to overweight or obesity at 10 years compared with those aged 65–74 years. Similarly, adults from the youngest age group who were overweight or obese at baseline were at increased risk of transitioning from overweight to class 1 or 2 obesity (OR 4.60 [95% CI 4.06, 5.22]) and from class 1 or 2 to class 3 obesity (OR 5.87 [5.23, 6.59]). Associations of other demographic factors with transitioning from normal weight to overweight or obesity were consistently less strong, but there were significant associations for individuals living in the most versus least deprived areas (OR 1.23 [95% CI 1.18, 1.27]), men versus women (1.12 [1.08, 1.16]) and Black versus White individuals (1.13 [1.04, 1.24]).

Comment: This is a very interesting paper looking at predictors of weight gain in adulthood using real-world primary-care population data from the UK. There are many factors that you might expect would predict weight gain based on associations with prevalent obesity, such as ethnicity, deprivation, family history, etc. However, this study clearly shows that age is the overwhelming predictor of future weight gain over a 10-year period and importantly progression to morbid obesity. Whilst the other factors were relevant, those with the highest risk of progression overall were the youngest cohort of 18–24 years. Whether this would be the same in the NZ population is not known, particularly with respect to Māori and Pacific peoples who are not represented in the UK data. It is hard to imagine that it would be completely different, and possibly even enhance the age effect. We need policies that reflect this and a focus on prevention that is tailored and, dare I say it, developed by young people.

Reference: *Lancet Diabetes Endocrinol*; Published online Sept 2, 2021;

[Abstract](#)

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Association between characteristics of behavioural weight loss programmes and weight change after programme end

Authors: Hartmann-Boyce J et al.

Summary: This systematic review and meta-analysis included data from 249 trials (n=59,081) of behavioural weight loss programmes in overweight or obese adults; the risk of bias was low in 52 trials, high in 57 and unclear in 140. Compared with controls, weight loss interventions were associated with more rapid weight regain (0.12–0.32 kg/year), with each kilogram lost at programme end associated with weight regain of 0.13–0.19 kg/year, the between-group differences maintained for ≥5 years, and financial incentives for weight loss increasing the regain rate to 1–1.5 kg/year. Programmes that included partial meal replacements were associated with faster weight regain, but not after adjustment for weight loss during the programme. Weight regain was slower when the programme could be accessed outside of the study, and when programmes with gradual reductions in the intensity of the intervention were used (although the point estimate suggested a small association). Heterogeneity in weight regain could not be explained by any of the other characteristics considered.

Comment: Finding effective sustained dietary weight loss programmes may be the holy grail of obesity research. There are many different ways to facilitate weight loss through manipulation of diet and behavioural patterns. These differ in dietary prescription and in the type and intensity of support or incentives. Unfortunately, weight regain after a period of weight loss is common – if not universal. This systematic review and meta-analysis explored factors related to the weight loss programme that influence the rate of weight regain after an intervention. Notably, the greater the weight loss, the more rapid the weight regain. However, importantly, because of the greater initial weight loss there was still a longer period of reduced weight after the programme. Features of the programme that reflect less personal control or 'retraining' of food choices, such as meal replacements or financial incentives, were more likely to result in faster weight regain, whereas a slower transition or ongoing availability of support was beneficial. These are useful observations when planning a weight loss programme for translation to the real world.

Reference: *BMJ* 2021;374:n1840

[Abstract](#)

Long-term complications in youth-onset type 2 diabetes

Authors: TODAY Study Group

Summary: These authors reported on participants with youth-onset type 2 diabetes from a 2004–2011 study of metformin, metformin plus rosiglitazone or metformin plus an intensive lifestyle intervention, who were transitioned to metformin with or without insulin in a two-phase observational follow-up study (evaluable n=500) conducted during 2011–2020. At the end of the second phase, after a mean time since diabetes diagnosis of 13.3 years, the respective incidences of hypertension, dyslipidaemia, diabetic kidney disease and neuronal disease were 67.5%, 51.6%, 54.8% and 32.4%. The respective prevalences of retinal disease (including more advanced stages) during the 2010–2011 and 2017–2018 periods were 13.7% and 51.0%. There was ≥1 complication recorded for 60.1% of the participants, with 28.4% having ≥2. Factors associated with the development of complications included minority race/ethnicity, hyperglycaemia, hypertension and dyslipidaemia. There were no adverse events recorded during follow-up.

Comment: This is a very revealing eyeopener to the problems we face with the obesity epidemic and increasing incidence of type 2 diabetes in young people. This study reported the long-term follow up of a cohort of youths diagnosed with type 2 diabetes (mean age of 13 years) who took part in an intervention trial, and were then followed in an observational study out to a mean follow up of 13 years, or 26 years of age. The rates of microvascular complications and of elevated CV risk factors is alarming. Sixty percent had at least one complication and almost a third had two. This highlights what we observe clinically that young people struggle with a diagnosis of diabetes, and those with type 2 diabetes seem to be at particularly high risk. If ever there were data to support more intensive preventative strategies, these are them.

Reference: *N Engl J Med* 2021;385:416–26

[Abstract](#)

Effects of the Norfolk diabetes prevention lifestyle intervention (NDPS) on glycaemic control in screen-detected type 2 diabetes

Authors: Sampson M et al., on behalf of the NDPS group

Summary: Patients with type 2 diabetes were randomised to a group-based lifestyle intervention of six core and ≤15 maintenance sessions with (n=141) or without (n=142) additional support from volunteers with type 2 diabetes trained in codelivery of the intervention, or a control group (n=149). Compared with controls, participants assigned to the lifestyle intervention plus additional support arm, but not the lifestyle intervention-only arm, had achieved a significantly lower mean HbA_{1c} level at 12 months (45.6 and 46.5, respectively, vs. 48.5 mmol/mol [p values 0.007 and 0.07]). The effect size was significantly greater for intervention participants aged <65 vs. ≥65 years (mean difference compared with controls, −4.76 vs. −0.46 mmol/mol [p=0.02 for interaction]), particularly for the group who received the additional support (−6.01 vs. −0.22 mmol/mol [p=0.007 for interaction]). Oral hypoglycaemic medication use was associated with a significantly lower mean HbA_{1c} level in the intervention plus support arm compared with the control arm (−7.0 mmol/mol [p=0.003]).

Comment: Lifestyle change is a bit like level 4 lockdown – it works but it's really hard to sustain! This paper reported the outcomes of an RCT of an intensive lifestyle intervention delivered in two different ways, compared with a control, on glycaemic control in people identified with new type 2 diabetes on screening. The use of volunteer peer support made a positive difference to the reduction in HbA_{1c} level, which was most evident in those under 65 years and when oral hypoglycaemics were prescribed. Sadly, this benefit was lost by 2 years. It is unlikely that we will find a one-size-fits-all approach. These types of studies simply remind us how difficult sustained changes to engrained lifestyle behaviours are. We mustn't give up, but we need to find ways to individualise interventions, and to be flexible in approach and change when things are not working.

Reference: *BMC Med* 2021;19:183

[Abstract](#)

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References: 1. A rising tide of type 2 diabetes in younger people: what can primary care do? BPAC. [Online]. Accessed: https://bpac.org.nz/2018/docs/diabetes.pdf. 2. Leon M. Primary care-led weight management for remission of type 2 diabetes (DIRECT): an open-label, cluster-randomised trial 2017. [http://dx.doi.org/10.1016/S0140-6736\(17\)33102-1](http://dx.doi.org/10.1016/S0140-6736(17)33102-1). **DUROMINE™** IS A CS CONTROLLED DRUG. **DUROMINE™** IS AN UNFUNDING MEDICINE - A PRESCRIPTION CHARGE WILL APPLY. PLEASE REVIEW FULL DATA SHEET BEFORE PRESCRIBING AVAILABLE AT WWW.MEDSAFE.GOV.NZ OR PHONE 0800 5098 375394. Minimum Data Sheet Information (phenentermine). **DUROMINE™** Indications: For the management of obesity as a short-term adjunct in a medically monitored weight loss programme based on exercise, diet and behaviour modification in obese patients with a body mass index (BMI) of 30 kg/m² or greater. **DUROMINE™** may appropriately be initiated in overweight patients with a lower BMI when risk of morbidity from other medical conditions is increased. **Dosage and Administration:** The usual starting dose in adults and children over 12 years is 30 mg once daily at breakfast. Continuous or inter-mittent maintenance dose is 15 mg to 30 mg once daily depending on responsiveness. Patients require medical review after a defined course of treatment, which should not exceed three months. Available in 15 mg and 30 mg capsules. **Contraindications:** Pulmonary artery hypertension, heart valve abnormalities, heart murmurs, moderate to severe hypertension, cerebrovascular disease, severe cardiac disease including arrhythmias, advanced arteriosclerosis, hypersensitivity to sympathomimetic drugs, hyperthyroidism, psychiatric illnesses, glaucoma, drug/alcohol abuse or dependence, concomitant MAOIs or within 14 days of MAOI use. **Precautions:** Short term monotherapy only. Co-administration of drug products for weight loss is not recommended. There have been no reported cases of valvular heart disease occurring with phenentermine alone. Use with caution in mild hypertension, established coronary artery disease, epilepsy, and in those receiving insulin, oral hypoglycaemic agents or psychotropic agents. **Adverse Effects:** The most common are palpitations, tachycardia, elevation of blood pressure and pre-dawn pain. Others included restlessness, insomnia, nausea, and dry mouth. Psychotic episodes, hallucinations and serious cardiovascular events are rare. Full Data Sheet and Consumer Medicine Information is available from Medsafe at www.medsafe.govt.nz. (Inova Pharmaceuticals (Australia) Pty Limited, Level 10, 12 Help Street, Chatswood NSW 2067, Australia. Distributed in New Zealand by Radiant Health Ltd, c/o Supply Chain Solutions, 74 Westney Road, Airport Oaks, Auckland. For all product enquiries: New Zealand Toll Free: 0508 375 394. TAPS NA 12719. NZ-2021-02-0010. February 2021.



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Abbreviation: GLP-1 RA, Glucagon-like peptide-1 receptor agonist.

References: 1. Trulicity Data Sheet August 2021. 2. Pharmaceutical Schedule. Available at: <https://schedule.pharmac.govt.nz/ScheduleOnline.php>. Last Accessed September 2021. 3. Trulicity Product Detail. Medsafe. Available at: <https://www.medsafe.govt.nz/regulatory/ProductDetail.asp?ID=21737>. Last accessed September 2021.

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Date of preparation: September 2021.



Clinical, psychological and demographic factors in a contemporary adult cohort with diabetic ketoacidosis and type 1 diabetes

Authors: Hare MJL et al.

Summary: Clinical, psychological and demographic factors, and their associations with recurrent admission, were investigated across 154 admissions for DKA in 128 adults with type 1 diabetes (13% with multiple DKA admissions). A history of depression was recorded for 32% of the patients. Factors that most frequently contributed to presentation with DKA included insulin omission (54%), infection (31%), alcohol excess (26%) and a new diagnosis of diabetes (16%). Compared with patients with a single admission for DKA, those with recurrent admissions were more likely to smoke (69% vs. 27% [$p=0.003$]), be unemployed (31% vs. 11% [$p=0.04$]) or partake in illicit drug use (44% vs. 17% [$p=0.02$]).

Comment: There is nothing particularly new in this paper, but it does serve to remind us of the issues associated with ketoacidosis in people with type 1 diabetes. This retrospective audit of a tertiary hospital in Australia shows that the majority of admissions with DKA are a result of insulin omission. Many of these are simply errors of judgement or simply forgetting, but some of these may be intentional. It also highlights that those with recurrent admissions have higher rates of depression and deprivation and illicit drug use – all factors that have been previously demonstrated. Although almost 50% of admissions were related to infection or a new diagnosis of type 1 diabetes, the majority were associated with modifiable triggers that can and should be addressed during the admission or in a follow-up clinic visit soon after.

Reference: *Intern Med J* 2021;51:1292–9

[Abstract](#)

Glucose control in diabetes during home confinement for the first pandemic wave of COVID-19

Authors: Silverii GA et al.

Summary: This was a meta-analysis of data from observational studies reporting glucose control and variability measures before, during and/or after periods of COVID-19-associated confinement. Twenty-seven studies in individuals with type 1 diabetes reported that HbA_{1c} levels did not change significantly after entering lockdown (weighted mean difference, -1.474 mmol/mol), but time in range for glucose level significantly increased both during and after lockdown (2.73% and 3.73%, respectively). Nine studies in patients with type 2 diabetes revealed no significant variation in HbA_{1c} level due to entering lockdown (weighted mean difference, -1.257 mmol/mol). A more favourable trend regarding HbA_{1c} level was evident in studies performed in Asia than in those from Europe ($p=0.022$).

Comment: The effect of lockdown for COVID on all manner of health risks and outcomes has been the topic of many observational studies over the last 18 months. This paper reports a meta-analysis of studies reporting the impact of lockdown on glycaemic control in people with both type 1 and type 2 diabetes. It must be remembered that the shape of lockdown and the level of restrictions varied considerably around the world. NZ has had some of the strictest restrictions, which have impacted on food availability, particularly takeaways, and on exercise options. In this paper, there are more reports in type 1 diabetes than type 2, but there was no significant detrimental effect of lockdown on glycaemic control identified in either patient group. This is reassuring, particularly since earlier reports identified poor glycaemic control as a risk factor for hospitalisation and for death.

Reference: *Acta Diabetol* 2021;58:1603–11

[Abstract](#)



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Intensive care unit admission, mechanical ventilation, and mortality among patients with type 1 diabetes hospitalized for COVID-19 in the U.S.

Authors: Barrett CE et al.

Summary: Using a US database of COVID-19 hospitalisations (n=269,674), these researchers compared the risks of severe COVID-19 outcomes for patients with type 1 versus type 2 diabetes. Patients with type 1 diabetes had higher risks of requiring ICU admission or invasive mechanical ventilation and death than nondiabetics (respective adjusted RRs 1.49 [95% CI 1.43, 1.56] and 1.40 [1.24, 1.57]), and they also had a higher risk of needing ICU admission or invasive mechanical ventilation, but not death, compared with patients with type 2 diabetes (1.17 [1.12, 1.22] and 1.00 [0.89, 1.13]). However, after adjustment for DKA occurring before or at COVID-19 diagnosis, there was no significant difference between patients with type 1 versus type 2 diabetes for ICU/mechanical ventilation requirement (risk difference, 0.01 [95% CI -0.01, 0.03]) and the mortality risk was significantly lower for patients with type 1 diabetes (-0.03 [-0.05, -0.01]).

Comment: It has been recognised from early in the COVID-19 pandemic that people with diabetes are at greater risk of requiring hospitalisation or ICU admission and for death than the normal population. It has been less clear whether there are important differences between type 1 diabetes and type 2 diabetes. Early reports suggested that obesity, associated with type 2 diabetes, may have increased the risk for these people more than type 1 diabetes. This present study reports data from the US in mid-late 2020. These data show that type 1 diabetes confers greater risks than type 2 diabetes for ICU admission and mortality, but that is largely explained by additional ketoacidosis. Rates of ICU admission and death were strikingly higher than for those without diabetes. It is important to note that these data are from before the delta variant emerged and before vaccination. Both have transformed the landscape of COVID-19. However, these data can be used to strongly support the need to vaccinate anyone with diabetes – actually, everyone, full stop!

Reference: *Diabetes Care* 2021;44:1788–96

[Abstract](#)

Trends in glycaemic control and drug use in males and females with type 2 diabetes

Authors: Xiang AS et al.

Summary: Temporal changes in glycaemic control and antihyperglycaemic agent use for 11,930 patients with type 2 diabetes (44.9% female) were reported in this 2013–2019 Australian National Diabetes Audit. There was little change in mean HbA_{1c} level over the audit period or between the sexes (62–67 mmol/mol [$p>0.05$]), but the number of antihyperglycaemic agents used increased significantly over the audit period for both sexes, with significantly greater use by males ($p=0.014$), including increased use of DPP-4 inhibitors (11.7–25.7% [$p=0.045$] for females; 11.6–29.5% [$p=0.036$] for males) and GLP-1 receptor agonists (5.9–15.3% [$p=0.043$] for females; 4.9–11.1% [$p=0.043$] for males); SGLT-2 inhibitors were unavailable at the start of the audit, but their use increased substantially (4.9–26.3% [$p=0.013$] for females; 4.7–32.2% [$p=0.019$] for males).

Comment: The cynics amongst us might say that this paper shows what an expensive waste of time the newer diabetes agents are and that we are all being conned by the pharmaceutical companies. That would appear to be the case from the top line result and conclusions of this study. In Australia, between 2013 and 2019, there was more use of antihyperglycaemic drugs, particularly the newer (and more expensive) agents, but no corresponding improvement in overall glycaemic control. That is disappointing! What this doesn't examine is the changing demographic of diabetes, the adverse events of prescribed drugs, hospitalisations and, most importantly, hard clinical outcomes such as CV events, renal failure/dialysis and mortality. All of course are linked to HbA_{1c} level, but what we have learned about the SGLT-2 inhibitors and GLP-1 agonists particularly is their beneficial effects on these outcomes over and above HbA_{1c} level. So this is definitely an interesting paper and it would be good to see a similar analysis in NZ, but not all doom and gloom.

Reference: *Diabetes Obes Metab*; Published online Aug 2, 2021

[Abstract](#)

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Long-term population-based trends in the incidence of cardiovascular disease in individuals with type 1 diabetes from Finland

Authors: Harjutsalo V et al.

Summary: The cumulative incidence of CV disease was reported for a retrospective, Finnish population-based cohort of 11,766 registrants diagnosed with type 1 diabetes before the age of 15 years and followed for a median of 29.6 years (361,033 person-years). There were 2686 CV disease events affecting 1761 of the cohort, including 864 coronary artery disease events (663 acute myocardial infarctions), 497 strokes, 854 peripheral artery disease events (498 lower extremity amputations) and 471 HF events, and there were 1467 deaths recorded. Each incrementally later calendar year of diabetes diagnosis was associated with a lower risk of CV disease (HR 0.96 [95% CI 0.96, 0.97]). All 10-year age groups under 65 years showed decreases in the standardised incidence ratios for both coronary artery disease and stroke, with the exception of stroke in the oldest age group; however, for those diagnosed in the 1990s, the respective standardised incidence ratios for coronary artery disease and stroke were 8.9 (95% CI 3.9, 17.5) and 2.9 (1.3, 5.7). CV disease-related mortality declined consistently by diagnosis year.

Comment: It is not news that the main cause of premature mortality in people with diabetes is CV disease. Nor is it news that people with type 1 diabetes have a reduced life expectancy compared with the general population. What is news is that despite this knowledge, we are making little progress on reducing this gap. This study from Finland using retrospective registry population data shows a clear trend to reduced CV disease in people diagnosed with type 1 diabetes in childhood, but still a very significant excess. These data span the time when evidence for tight glycaemic control and blood pressure management have changed practice. It is also the period when statins have been introduced for CV disease risk reduction. However, population CV disease risk calculators do not take into account the overall effect of prolonged glycaemic burden from a very young age, and it remains unclear when aggressive CV disease risk reduction strategies should be implemented in type 1 diabetes. This is clearly an area for a large multicentre intervention study to give us more clarity on the best way to close the gap.

Reference: *Lancet Diabetes Endocrinol* 2021;9:575–85

[Abstract](#)



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Diabetes and Ramadan

Practical guidelines: pre-Ramadan assessment, medication adjustment during Ramadan and a post-Ramadan follow-up

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This module is based on the podcast by Sydney Endocrinologist and Clinical Lecturer, Dr Marwan Obaid, who provides overview of the importance of Ramadan to Muslims and practical guidance.

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Diabetes & Obesity

RESEARCH REVIEW™

BMI and pneumonia outcomes in critically ill COVID-19 patients

Authors: Chetboun M et al.

Summary: These researchers sought to clarify relationships between BMI and associated metabolic risk factors in 1461 patients (73.2% male; median BMI 28.1 kg/m²) who became critically ill after contracting COVID-19 in Europe, Israel or the US. Invasive mechanical ventilation was necessary for 73.9% of the patients, and the estimated 28-day mortality rate was 36.1%. A significant linear relationship was identified between BMI and need for invasive mechanical ventilation (OR for each 5 kg/m² increase, 1.27 [95% CI 1.12, 1.45]), and a significant association was also detected between obesity class III (≥ 40 kg/m²) and mortality (HR 1.68 [1.06, 2.64]).

Comment: This paper confirms previous evidence on the association between obesity and greater risk of adverse outcomes of COVID infection, and links well with the following paper. Aside from the population/environmental risk factors for COVID infection, there are several individual risk factors that are now pretty well defined that increase the risk of infection and/or hospitalisation and death. Some of these are inter-related, such as obesity, diabetes, hypertension and dyslipidaemia. This paper aimed to tease out the independent effect of obesity, and confirmed a linear increase in risk of needing ventilation with increasing BMI, and a threshold effect of a BMI ≥ 40 kg/m² for an independent risk of mortality. Once again, these data come from the pre-delta days of COVID, and this relationship may have changed. If anything, it is likely strengthened, and therefore highlights the critical importance of vaccination across the population, especially in those who are obese.

Reference: *Obesity* 2021;29:1477–86[Abstract](#)

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Research Review publications are intended for New Zealand health professionals.

COVID-19 vaccines are effective in people with obesity

Authors: Butsch WS et al.

Summary: This paper reported the position statement from the US Obesity Society on the efficacy of COVID-19 vaccines in obese individuals. It was concluded that current evidence suggests that COVID-19 vaccines are just as highly efficacious in obese individuals as they are in nonobese individuals, but there is no definitive way to determine which of the Pfizer-BioNTech, Moderna, and Johnson & Johnson vaccines is the 'best'. Regarding the Pfizer-BioNTech vaccine, the society recommends that all obese individuals aged ≥ 16 years receive this vaccination as soon as they are able.

Comment: In case any of the readers need more data or reassurance of the safety and efficacy of the vaccine for COVID, I include this statement from the Obesity Society. It is very clear that from the currently available evidence, people with obesity have the same benefits of vaccination as do those without obesity. The vaccination is highly effective in reducing hospitalisation and mortality. This is particularly important, as the evidence is clear that people with obesity are at greater risk of hospitalisation and death compared with nonobese individuals. This may be relevant data in our drive to convince the remaining small percentage of our country to get vaccinated.

Reference: *Obesity* 2021;29:1575–9[Abstract](#)

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. As well as clinical and teaching activities, Professor Krebs maintains active research interests in the area of obesity and diabetes, with a particular focus on the association between obesity and type 2 diabetes, both from an aetiology and management perspective, with a focus on nutritional aspects, bariatric surgery and diabetes service delivery.

SPECIAL REPORT ON THE 2021 NZSSD Type 2 Diabetes Management Guidelines

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