Diabetes & Obesity
RESEARCH REVIEW™

Making Education Easy

Issue 142 – 2021

In this issue:

Abbreviations used in this issue
CGM = continuous glucose monitoring
CV = cardiovascular
DPP = dipeptidyl peptidase
GLP = glucagon-like peptide
HbA$_{1c}$ = glycosylated haemoglobin
HR = hazard ratio
QOL = quality of life
RYGB = Roux-en-Y gastric bypass
SGLT = sodium glucose cotransporter

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Welcome to issue 142 of Diabetes and Obesity Research Review.

This month's issue includes two systematic reviews with meta-analyses published in the BMJ: one provides a comparative analysis of SGLT-2 inhibitors and GLP-1 receptor agonists for reducing CV and renal outcomes in patients with type 2 diabetes, while the other reports on the impact of low- and very low-carbohydrate diets for inducing diabetes remission. Local research is also included reporting that our Māori, Pasifika and younger patients with type 1 diabetes are over-represented in the statistics on cessation of continuous subcutaneous insulin infusions. Other included research has confirmed that as well as the known benefits of bariatric surgery in terms of bodyweight and CV outcomes, diabetes-related microvascular complications are also reduced. This issue concludes with a report from Scotland on the increased risks of a severe or fatal outcome among patients with diabetes who develop COVID-19.

We hope you enjoy this issue, which includes a few extra research papers than usual, and we look forward to your comments and feedback.

Best regards,

Professor Jeremy Krebs
jeremykrebs@researchreview.co.nz

Sodium-glucose cotransporter protein-2 (SGLT-2) inhibitors and glucagon-like peptide-1 (GLP-1) receptor agonists for type 2 diabetes

Authors: Palmer SC et al.

Summary: This systematic review with network meta-analysis included 764 RCTs (n=421,346) that compared SGLT-2 inhibitors or GLP-1 receptor agonists (added to existing treatments) with placebo, standard care or other glucose lowering treatment in adults with type 2 diabetes with follow-up of ≥24 weeks. The results showed with high certainty that all-cause mortality, CV mortality, nonfatal myocardial infarction and kidney failure were all reduced by both SLGT-2 inhibitors and GLP-1 agonists, with SGLT-2 inhibitors more effective for reducing mortality and admission to hospital for heart failure and GLP-1 agonists better for reducing nonfatal stroke compared with each other. SGLT-2 inhibitors were associated with increased genital infections, whereas GLP-1 receptor agonists were associated with more gastrointestinal events. There was low certainty evidence that SGLT-2 inhibitors and GLP-1 receptor agonists were associated with reductions in bodyweight, and there was little or no evidence for either class for effects on limb amputations, blindness, eye disease, neuropathic pain or health-related QOL. The absolute benefits of SGLT-2 inhibitors and GLP-1 agonists varied among patients from low to very high risk of CV and renal outcomes.

Comment: Now that we are finally here in NZ with funded access to an SGLT-2 inhibitor and eagerly awaiting the imminent availability of a GLP-1 agonist, it is timely to again review the state of the evidence for them. Over the last year I have included numerous trials and reviews of these agents, and the messages have been consistent with respect to reduced CV and renal risk. This meta-analysis somewhat adds to this story by trying to also take into account the magnitude of this risk reduction depending on baseline risk. This is highly relevant for both funders and prescribers of these medications. The message is clear and not surprising, that the greater the background risk, the greater the benefit. This is how the PHARMAC criteria have been shaped and these data would support that. Once again, I can't stress enough that now the challenge is to ensure that we get these agents to **all** those who are eligible.

Reference: BMJ 2021;372:m4573
Abstract

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Youth and non-European ethnicity are associated with increased loss of publicly funded insulin pump access in New Zealand people with type 1 diabetes

Authors: Hennessy LD et al.

Summary: The loss of access to publicly funded continuous subcutaneous insulin infusions was investigated using nationally held data including the New Zealand Virtual Diabetes Register. Cessation rates for publicly funded insulin pumps were approximately 4% per year, with youth aged 10–29 years and Māori and Pasifika patients being over-represented. These same patient groups were also less likely to gain initial access to public funding for continuous insulin infusions.

Comment: Insulin pump therapy in type 1 diabetes has the potential to improve glycaemic control and reduce complications when used appropriately. It is not a panacea for solving all the difficulties that people with type 1 diabetes face in achieving good control. This study reports on the very relevant and important issue of loss of funded access to insulin pump therapy in NZ, highlighting that youth and Māori or Pacific ethnicity are both over-represented. However, I am sure that if you did a similar analysis of glycaemic control and diabetes complications across those with type 1 diabetes using multiple daily subcutaneous injections, you would find a very similar result. As the authors conclude, the major issue and priority here is understanding and then addressing the factors that are driving these disparities. In my opinion that is the relevant question, and if solved, the disparities in pump access will disappear.

Reference: Diabet Med 2021;38:e14450
Abstract

Impact of age at type 2 diabetes mellitus diagnosis on mortality and vascular complications

Authors: Nanayakkara N et al.

Summary: This was a systematic review with meta-analyses of 26 observational studies that included 1,325,493 adults with type 2 diabetes from 30 countries and investigated the impact that age at diabetes diagnosis had on macrovascular and microvascular diabetes complications. Each 1-year increase in age at diabetes diagnosis was associated with 4%, 3% and 5% decreases in the risks of all-cause mortality, macrovascular disease and microvascular disease, respectively, with the effects consistent for the individual components of composite outcomes.

Comment: The epidemiology of type 2 diabetes in NZ and worldwide over the last 20 years has been a progressive reduction in the age of onset. This has of course paralleled the obesity epidemic. Those working in primary care will have observed this trend and will also have observed the greater challenges in managing younger people with type 2 diabetes. This meta-analysis of observational studies across many different countries, and therefore ethnicities and health systems, identified that younger age at diagnosis is associated with more complications and risk of premature mortality. This confirms our clinical observations, and once again highlights the need to address the risk factors for developing type 2 diabetes in individuals at risk and across the population.

Reference: Diabetologia 2021;64:275–87
Abstract

Efficacy and safety of low and very low carbohydrate diets for type 2 diabetes remission

Authors: Goldenberg JZ et al.

Summary: This was a systematic review and meta-analysis of 23 trials (n=1357; low risk of bias for 40.6% of outcomes) assessing the effects of low- and very low-carbohydrate diets for ≥12 weeks in adults with type 2 diabetes. Data from eight trials showed that compared with control diets, low-carbohydrate diets were associated with a higher 6-month diabetes remission rate defined as HbA_{1c} level <6.5% (57% vs. 31%; risk difference 0.32 [95% CI 0.17, 0.47]); the effect size was smaller and nonsignificant when no medication use was added to the definition for diabetes remission, and diabetes remission with low-carbohydrate diets was markedly reduced in studies that included insulin recipients. Data on 12-month remission were sparse. There were also large clinically important improvements in weight loss, triglyceride levels and insulin sensitivity at 6 months, but these had diminished by 12 months. Very low-carbohydrate diets were found to be less effective than less restrictive low-carbohydrate diets for weight loss at 6 months, but this effect was explained by diet adherence. There was no significant difference in QOL at 6 months, but clinically important statistically nonsignificant worsening of QOL and LDL cholesterol levels was seen at 12 months; no other significant or clinically important between-group differences were seen for adverse events or blood lipid levels at 6 or 12 months.

Comment: Could there be a more controversial topic in nutrition circles than the efficacy and safety of ketogenic diets in cardiometabolic health? Everyone has an opinion on this, whether they be nutrition professors, celebrity dieters, news media or the general public. So much of the debate is clouded by the murkiness of the definition of reduced-, low- or very low-carbohydrate diet, and by the composition of the remaining diet with respect to quantity and quality of fat and protein. It is further muddied by whether outcomes considered relate only to weight loss or whether they also consider metabolic and CV disease risk. Furthermore, there are the considerations of duration of dietary exposure and adherence. Not surprisingly whichever side of the debate that you sit on, you can find evidence to support your argument. Therefore I simply let this meta-analysis speak for itself. Keep an open mind. Horses for courses.

Reference: BMJ 2021;372:m4743
Abstract

Metabolic surgery versus conventional medical therapy in patients with type 2 diabetes

Authors: Mingrone G et al.

Summary: Ten-year outcomes were reported for 57 of 60 participants with type 2 diabetes from a trial that had randomised them to receive medical therapy, RYGB or biliopancreatic diversion. The respective 10-year diabetes remission rates in the medical therapy, RYGB and biliopancreatic diversion arms were 5.5%, 25.0% and 50.0% (p=0.0082), with hyperglycaemia relapse rates among those achieving remission at 2 years (the trial's primary endpoint) of 66.7% and 52.6% in the RYGB and biliopancreatic diversion arms, respectively; however, all participants who relapsed maintained adequate glycaemic control at 10 years. Compared with medical therapy, both surgeries were associated with fewer diabetes-related complications (relative risk 0.07 [95% CI 0.01, 0.48] for each), while biliopancreatic diversion but not RYGB was associated with a greater likelihood of serious adverse events (respective odds ratios 2.7 [1.3, 5.6] and 0.7 [0.3, 1.9]).

Comment: For a long time, RCTs were absent from the bariatric surgery literature. However, over recent years we have had a number of trials comparing surgery with medical therapy, with endpoints of weight loss and more importantly cardiometabolic outcomes. Perhaps not surprisingly, the studies reporting 2-year and 5-year outcomes show significantly greater weight loss with surgery and greater rates of diabetes resolution. Previous long-term observational studies have shown robust persistent benefits for weight, diabetes and CV events. Therefore I was a little surprised that the 10-year outcomes in this study were not as impressive. Yes the rates of diabetes resolution remain considerably higher after surgery than medical therapy, but only 25% of those who had RYGB remained free of diabetes at 10 years. This shows the progressive nature of type 2 diabetes and specifically the inexorable decline in β-cell function. I still firmly believe that there is an important place for bariatric surgery in the management of obesity and diabetes, but these data provide important cautions that need to be communicated with patients.

Reference: Lancet 2021;397:293–304
Abstract

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A comparison of two hybrid closed-loop systems in adolescents and young adults with type 1 diabetes (FLAIR)

Authors: Bergenstal RM et al., for the FLAIR Study Group

Summary: Patients aged 14–29 years with type 1 diabetes treated with an insulin pump or multiple daily insulin injections (HbA_{1c} level 53–97 mmol/mol; n=113) used a MiniMed 670G hybrid closed-loop system or an advanced Medtronic hybrid closed-loop system each for 12 weeks in a randomised crossover manner with no washout. Compared with the MiniMed 670G hybrid closed-loop system, the advanced Medtronic hybrid closed-loop system was associated with a lower mean proportion of time with daytime glucose levels >10.0 mmol/L (34% vs. 37% [p<0.0001]) with the mean 24-hour proportions of time with glucose levels <3.0 mmol/L meeting the noninferiority criterion (0.46% vs. 0.50% [p<0.0001]). There was one severe hypoglycaemic event in the advanced Medtronic hybrid closed-loop system group, which was not considered to be treatment related, and none in the MiniMed 670G hybrid closed-loop system.

Comment: Why does it feel like we are frustratingly close, but not quite there yet with closed-loop technology? The promise of a commercially available real-time, functional closed-loop insulin pump/CGM has been tantalisingly on the horizon now for a few years. So why does this study feel like incrementalism rather than a quantum leap? With the new advanced system, patients glucose levels were still above 10 mmol/L for 34% of the day in the young adult cohort. The real advance of these systems has been the protection against hypoglycaemia, and we see that again here. Sadly, it just goes to show how damn clever and sophisticated our normal physiology is. We are getting there, but still frustratingly slowly if you are a young person with type 1 diabetes.

Reference: Lancet 2021;397:208–19
Abstract

The impact of bariatric surgery on incident microvascular complications in patients with type 2 diabetes

Authors: Singh P et al.

Summary: The impact of bariatric surgery on the incidences of microvascular complications was explored for a retrospective cohort of 1126 obese adults with type 2 diabetes who had undergone bariatric surgery (22.1%, 22.7%, 52.2% and 1.1% gastric band, sleeve gastrectomy, RYGB and duodenal switch, respectively) versus a matched cohort of 2219 who had not undergone bariatric surgery. Median follow-up was 3.9 years. Compared with controls, bariatric surgery recipients had lower likelihoods of combined microvascular complications (adjusted HR 0.53 [95% CI 0.43, 0.66]), diabetes-related foot disease (0.61 [0.50, 0.75]), sight-threatening diabetic retinopathy (0.66 [0.44, 1.00]) and chronic kidney disease (0.63 [0.51, 0.78]). Although RYGB recipients had the greatest reduction for the composite of microvascular complications, all types of surgery had a favourable impact.

Comment: There is often focus on the benefits of bariatric surgery on weight and CV risk factors or events. However, for people with type 2 diabetes, whilst these benefits are very important, so too is the issue of microvascular complications. I am often asked whether a person who has type 2 diabetes and goes into remission after bariatric surgery still requires microvascular complication screening. This study used a case-control design with retrospective matching to look at the effect of surgery on rates of microvascular complications. It is clear that bariatric surgery reduces these risks compared with medical management, and that RYGB seems to be the most effective procedure. This is great news and supports the use of surgery in appropriate people. However, the rate of microvascular complications is not zero, and that reinforces the need to continue to monitor for these complications, even in those who go into remission after surgery.

Reference: Diabetes Care 2021;44:116–24
Abstract

Independent commentary by Professor Jeremy Krebs MBChB, FRACP, MD

Professor Krebs is an Endocrinologist with a particular interest in obesity and diabetes. He is a 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.

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Time in range in relation to all-cause and cardiovascular mortality in patients with type 2 diabetes

Authors: Lu J et al.

Summary: The association between time in glucose level range and mortality was explored in a prospective cohort of 6225 adults with type 2 diabetes from China followed for a median of 6.9 years. There were 838 deaths recorded in this cohort, with 287 due to CV disease. Compared with a reference time in glucose level range of >85%, times in range of 71–85%, 51–70% and ≤50% were associated with increasing likelihoods of death from any cause (respective adjusted HRs 1.23 [95% CI 0.98, 1.55], 1.30 [1.04, 1.63] and 1.83 [1.48, 2.28]; p<0.001 for trend) and of death from CV causes (1.35 [0.90, 2.04], 1.47 [0.99, 2.19] and 1.85 [1.25, 2.72]; p=0.015 for trend).

Comment: There has been an ongoing debate about whether glycaemic variability is as important as or independent of average glucose levels, measured by HbA_{1c} level, in terms of micro- and macrovascular outcomes in patients with diabetes. With the increasing use of CGM, we are getting considerably more data and the opportunity to review the 'time in range' that our patients achieve, which was not previously available with capillary glucose level monitoring. This study shows clearly that this metric does correlate with the hardest outcome of all – mortality! I think it is going to become an increasingly important metric for us to monitor with our patients in both type 1 and type 2 diabetes as CGM systems become more readily available.

Reference: Diabetes Care 2021;44:549–55
Abstract

The impact of physical activity on the prevention of type 2 diabetes

Authors: Kriska AM et al., and the DPP Research Group

Summary: These researchers analysed yearly self-reported physical activity, diabetes assessment and oral glucose tolerance test data from 3232 participants with one accelerometry assessment 11–13 years after randomisation in the long-standing Diabetes Prevention Program. Each metabolic equivalent hour per week increase in time-dependent physical activity was associated with a reduction in diabetes incidence for the entire cohort over an average of 12 years (adjusted HR 0.94 [95% CI 0.92, 0.96]), with a greater effect seen for those who were less active at baseline (<7.5 metabolic equivalent hours per week; 0.88 [0.83, 0.93]) and a stronger association seen in the lifestyle intervention arm. Compared with metformin and placebo, the lifestyle intervention was associated with significantly greater cumulative physical activity and more accelerometry total minutes per day during follow-up. Bodyweight had no significant impact on these associations.

Comment: It has been previously shown that sedentary behaviour is an important and independent risk factor for obesity and metabolic disease. Lifestyle interventions have compared increasing physical activity, dietary manipulation or combinations of both on a range of outcomes. Whilst increasing activity is generally less effective than energy intake restriction in terms of weight loss, it is very important in weight loss maintenance. In the Diabetes Prevention Program, the intensive lifestyle intervention included both energy restriction and physical activity in people with prediabetes defined by impaired glucose tolerance on an oral glucose tolerance test. This was more effective than standard care or indeed metformin in preventing the progression to type 2 diabetes. What this current study reports is the effect of physical activity across the whole study cohort, irrespective of allocated group and of dietary manipulation. It shows clearly that increasing physical activity even when weight loss is not achieved is still effective in reducing the incidence of diabetes.

Reference: Diabetes Care 2021;44:43–9
Abstract

Real-world use of cardioprotective glucose-lowering drugs in patients with type 2 diabetes and cardiovascular disease

Authors: Funck KL et al.

Summary: Temporal trends in time to starting SGLT-2 inhibitors and GLP-1 receptor agonists were reported for 41,733 patients newly diagnosed with type 2 diabetes and CV disease in Denmark between 2012 and 2018. The 1-year cumulative user proportion for cardioprotective glucose-lowering drugs increased from 4.0% in 2012 to 14.7% in 2018, and the 2-year cumulative user proportion increased from 5.5% in 2012 to 16.7% in 2017. Patients diagnosed with type 2 diabetes first and then with CV disease had higher 1-year cumulative user proportions than those diagnosed with CV disease first and then with type 2 diabetes in 2012 (7.0% vs. 1.4%) and also in 2018 (18.1% vs. 10.0%).

Comment: It is always interesting to compare our practice in NZ with other countries. Denmark has had access to SGLT-2 inhibitors and GLP-1 agonists for almost 10 years now. Over that time, the evidence base for the beneficial effects of these drugs on CV and renal outcomes has grown, and as we know, these agents are now seen as second-line therapy after metformin for anyone with elevated CV disease or renal risk. This study reports the use of these drugs in people with both diabetes and CV disease over the years between 2012 when evidence was still weak and 2018 when it was strong. Despite this, only 18% of those who would benefit were prescribed the drugs. Clinical inertia is a major problem in diabetes management. This study further reinforces my view that we need to systematically define and actively initiate therapy in patients who meet the PHARMAC criteria for these drugs now that we finally have access to them.

Reference: Diabetes Obes Metab 2021;23:520–9
Abstract

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Durability of triple combination therapy versus stepwise addition therapy in patients with new-onset T2DM

Authors: Abdul-Ghani M et al.

Summary: Three-year follow-up outcomes were reported for the EDICT trial, in which 318 untreated patients with new-onset type 2 diabetes were randomised to receive 3 years of combination therapy with metformin, pioglitazone and exenatide or the sequential addition of metformin followed by glipizide and insulin with the aim of maintaining an HbA_{1c} level of <48 mmol/mol (<6.5%). Compared with conventional sequential therapy, triple combination therapy was associated with a greater decrease in HbA_{1c} level at 6 months (difference, 0.30% [p=0.001]), and a lower HbA_{1c} level at 3 years (6.4% vs. 6.9% [p<0.0001]), despite antihyperglycaemic therapy intensification with sequential therapy. Triple therapy was also associated with a 3-fold increase in insulin sensitivity and a 30-fold increase in β-cell function, compared with no change and a 34% increase, respectively, with sequential therapy (p<0.0001 for both).

Comment: There has been interest in the idea of early intensive treatment of type 2 diabetes to lower glucose to normal or near normal levels for some time. The hypothesis being that early aggressive management may influence the longer-term trajectory of the disease by preserving β-cell function and/or impacting on insulin sensitivity. Trials that have addressed this are always hampered by the self-fulfilling prophecy that multiple drugs will always have a greater glucose level lowering effect than a single agent – insulin aside. This current study uses a triple therapy versus sequential addition of agents, with the conclusion that early triple therapy has a better effect on glycaemic control, insulin sensitivity and β-cell function. However, the major flaw of this study, whether intentional or accidental, is that the agents used in the two arms are very different in action, and therefore the conclusions are biased by this. A more appropriate test of the hypothesis would have been to sequentially add the same agents. I am not convinced by these data that early triple therapy with these agents is the way forward.

Reference: Diabetes Care 2021;44:433–9
Abstract

The impact of pharmacological and lifestyle interventions on body weight in people with type 1 diabetes

Authors: Tandon S et al.

Summary: This was a systematic review with meta-analysis of 33 RCTs (n=9344) that investigated pharmacological (GLP-1 receptor agonist, SGLT-2 inhibitor, DPP-4 inhibitor and metformin; 26 trials) and lifestyle interventions (seven trials) for adults with type 1 diabetes, and that reported bodyweight and HbA_{1c} level changes. Significant reductions in bodyweight were seen with liraglutide 0.6mg, 1.2mg and 1.8mg (respective mean differences –2.22, –3.74 and –4.85kg), empagliflozin 2.5mg, 10mg and 25mg (–1.47, –2.77 and –3.06kg) and sotagliflozin 200mg and 400mg (–2.40 and –3.23kg); significant bodyweight decreases were not seen for any DPP-4 inhibitors, other GLP-1-receptor agonists, metformin or lifestyle interventions.

Comment: Many people with type 1 diabetes struggle with their weight, just as those in the rest of the population do. Managing this is made more difficult by the need to use insulin therapy and the anabolic effects of this interacting with genetic and/or lifestyle factors. This meta-analysis reviews the evidence for the effect of lifestyle interventions or additional hypoglycaemic drugs on weight in people with type 1 diabetes. As seen in type 2 diabetes, these agents act independently of insulin to lower glucose levels and have additional effects that theoretically may be beneficial on weight. Notably, the GLP-1 agonist liraglutide, and the SGLT-2 inhibitor empagliflozin, show beneficial effects. On the back of the accumulating evidence for these classes on CV and renal outcomes in patients with type 2 diabetes, but also in those without diabetes, it raises the question whether they should also be funded for people with type 1 diabetes in NZ. SGLT-2 inhibitors are not without significant risk of ketoacidosis in type 1 diabetes, and the body of evidence remains small; however, the question needs to be asked.

Reference: Diabetes Obes Metab 2021;23:350–62
Abstract

The impact of maternal obesity and breast milk inflammation on developmental programming of infant growth

Authors: Enstad S et al.

Summary: The role of maternal BMI on breastmilk inflammatory and oxidative stress markers and the flow-on effects on infant growth were explored in a secondary analysis of 40 mother-infant dyads. Significant relationships were detected between greater maternal BMI and a higher omega-6:omega-3 polyunsaturated fatty acid ratio and leptin level in breastmilk. Infants exposed to a high breastmilk omega-6:omega-3 polyunsaturated fatty acid ratio had significantly greater BMI z-scores over time, while exposure to high leptin levels in breastmilk was associated with lower infant fat mass percentage at 4 months *post partum*. Infants exposed to high levels of IL-8, IL-6 or IL-1β in breastmilk had significantly higher bodyweight z-scores over time. Breastmilk malondialdehyde level had no significant impact on maternal BMI or infant growth.

Comment: Do we need to challenge the mantra that 'breast is best'? There have been many studies showing the benefits of breastfeeding compared with formula milk, ranging from immune effects, weight, skin conditions and others. This study challenges this somewhat, examining the effects of maternal obesity on the composition of breastmilk and weight trajectory in the infants. It makes some interesting observations that increasing maternal BMI is directly correlated with a more adverse profile of fatty acids and inflammatory cytokine levels in breastmilk, and with greater infant weight gain. Whilst interesting, this must be interpreted with caution. This is a secondary analysis of data that were observational and very open to confounding by other genetic and lifestyle factors. It raises very interesting questions to be explored, but should not change current recommendations to encourage breastfeeding where possible.

Reference: Eur J Clin Nutr 2021;75:180–8
Abstract

Risks of and risk factors for COVID-19 disease in people with diabetes

Authors: McGurnaghan SJ et al., the Public Health Scotland COVID-19 Health Protection Study Group & the Scottish Diabetes Research Network Epidemiology Group

Summary: These researchers investigated risk factors for fatal or critical care unit-treated COVID-19 for a cohort of 319,349 patients with diabetes from the entire population in Scotland (n=5,463,300, at March 1, 2020), and they also developed a cross-validated predictive model. Compared with individuals without diabetes, a greater proportion of those with diabetes had developed fatal or critical care unit-treated COVID-19 by July 31, 2020 (0.3% vs. 0.1%), with the risk increased both for those with type 1 and type 2 diabetes (respective adjusted odds ratios 2.396 [95% CI 1.815, 3.163] and 1.369 [1.276, 1.468]); 89.8% of the patients with diabetes who developed fatal or critical care unit-treated COVID-19 were aged ≥60 years. Among the individuals with diabetes, those who developed fatal or critical care unit-treated COVID-19 were significantly more likely to: i) be male; ii) live in residential care or a more deprived area; iii) have a pre-existing risk factor for COVID-19, retinopathy, reduced renal function or worse glycaemic control; iv) have a history of diabetic ketoacidosis or hypoglycaemia hospitalisation in the prior 5 years; v) be on medications for diabetes or other indications; or vi) have been a smoker. The C-statistic for the cross-validated predictive model developed for fatal or critical care unit-treated COVID-19 for diabetics was 0.85.

Comment: We have been so fortunate in NZ to be largely spared the impact of COVID-19 observed in so many other countries. However, it remains relevant to review the literature on the reciprocal effects of diabetes and COVID-19 and outcomes. Very early in the pandemic, reports were published showing that people with diabetes did not appear to be at greater risk of infection, but were at greater risk of severity of infection, hospitalisation and mortality. This study updates that early evidence, reporting data from Scotland with a population similar to NZ. These data confirm the early reports, with people with diabetes 40% more likely to develop fatal or critical-care treated COVID-19 than those without diabetes. Perhaps surprisingly, and counter to earlier studies, people with type 1 diabetes were at greater risk than those with type 2 diabetes. Once again, glycaemic control and comorbidities were important factors in this increased risk. Hopefully we can remain bystanders to this disease in NZ, and hopefully the vaccines will further reduce the risk and impact for people with diabetes.

Reference: Lancet Diabetes Endocrinol 2021;9:82–93
Abstract

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