Diabetes & Obesity
RESEARCH REVIEW™

Making Education Easy

Issue 152 – 2021

In this issue:

Abbreviations used in this issue
ACE = angiotensin converting enzyme
ARB = angiotensin-II receptor blocker
BP = blood pressure
CKD = chronic kidney disease
CV = cardiovascular
GFR = glomerular filtration rate
HbA_{1c} = glycosylated haemoglobin
HR = hazard ratio
OGTT = oral glucose tolerance test
RCT = randomised controlled trial
SGLT = sodium glucose cotransporter

Welcome to issue 152 of Diabetes and Obesity Research Review.

This issue includes research from the US reporting on the impact that neighbourhood food environments have on type 2 diabetes risk across a variety of community types, and we also have a systematic review of evidence for the impact that colour-coded labels and warnings can have on consumers' food purchase choices. The issue also includes two papers from our trans-Tasman neighbours, both of which have a particular focus on Aboriginal peoples and provide us with lessons that can be translated to our shores: one reported on the prevalence and severity of diabetic retinopathy and presenting vision level, and the other, which concludes our diabetes and obesity research for the year, evaluated the feasibility of routine HbA_{1c} level screening for hyperglycaemia in pregnancy.

We look forward to receiving your comments any time, even over the holiday season, as we will be back with our next issue in January.

Best regards,

Professor Jeremy Krebs
jeremykrebs@researchreview.co.nz

Association of bariatric surgery with major adverse liver and cardiovascular outcomes in patients with biopsy-proven nonalcoholic steatohepatitis

Authors: Aminian A et al.

Summary: The SPLENDOR study examined long-term relationships between Roux-en-Y gastric bypass or sleeve gastrectomy (n=650) versus nonsurgical care (n=508) and incident major adverse liver outcomes and major adverse CV events in obese individuals with fibrotic noncirrhotic nonalcoholic steatohepatitis. Over a median 7 years of follow-up, five bariatric surgery patients and 40 nonsurgical patients experienced major adverse liver outcomes, while 39 and 60 patients experienced major adverse CV events. The 10-year cumulative incidence of major adverse liver outcomes was lower in the bariatric surgery versus nonsurgical group (2.3% vs. 9.6%; adjusted HR 0.12 [95% CI 0.02, 0.63]), as was the 10-year cumulative incidence of major adverse CV events (8.5% vs. 15.7%; 0.30 [0.12, 0.72]). In the first year after surgery, four patients died from surgical complications, including two from gastrointestinal leak and two from respiratory failure.

Comment: Fatty liver disease is one of the important but rather silent and insidious complications of obesity – until it's too late and cirrhosis and liver failure have ensued. Other than weight loss, to date there have been no effective drug treatments to reverse or delay the progression of fatty liver disease. This paper reported the outcomes for both liver and CV endpoints in a group of people with obesity who underwent bariatric surgery, and compared them with a matched control group who did not have surgery. It is important to note that this was not an RCT. The outcomes are very dramatic, with important differences in the incidences of both end-stage liver disease and CV disease between groups. Historically there has been caution in selection of patients with liver disease for surgery, but this paper supports a surgical approach in reducing morbidity and mortality in those with fatty liver disease.

Reference: JAMA 2021;326:2031–42
Abstract

MERRY CHRISTMAS & A HEALTHY, HAPPY 2022!
FROM THE TEAM AT RESEARCH REVIEW

Longitudinal analysis of neighborhood food environment and diabetes risk in the Veterans Administration Diabetes Risk Cohort

Authors: Kanchi R et al.

Summary: The association between neighbourhood food environment and incident type 2 diabetes risk was explored for high-density urban, low-density urban, suburban and rural communities in this research of over 4 million US veterans without type 2 diabetes at baseline. Positive but modest associations were evident between the relative density of fast-food restaurants and increased type 2 diabetes risk across all community types (adjusted HRs 1.01 [95% CI 1.00, 1.02], 1.01 [1.01, 1.01], 1.02 [1.01, 1.03] and 1.01 [1.01, 1.02] for high-density urban, low-density urban, suburban and rural communities, respectively). There were also associations between relative density of supermarkets and decreased type 2 diabetes risk in suburban and rural communities (respective adjusted HRs 0.97 [95% CI 0.96, 0.99] and 0.99 [0.98, 0.99]).

Comment: Diet and associated quality and quantity of food is an important modifiable risk factor for type 2 diabetes. In general, fast food has a higher energy density, and previous research has shown associations between energy density of food and obesity and type 2 diabetes. What this study examined is the association between neighbourhood food environment and the incidence of type 2 diabetes in the US. There was a small effect seen when food environment was measured by counts of fast-food outlets. However, the association is likely more nuanced than is immediately obvious from these data. In NZ, deprivation is a very strong risk factor for type 2 diabetes and interacts with ethnicity. Poorer neighbourhoods often have more fast-food outlets and fewer supermarkets. It is therefore very likely that a count of fast-food outlets is a surrogate, and probably very crude, marker of deprivation. Achieving equitable access to nutritious food is really what we need to aim for.

Reference: JAMA Netw Open 2021;4:e2130789
Abstract

CLICK HERE
to read previous issues of
Diabetes & Obesity Research Review

Deintensification of treatment with sulfonylurea and insulin after severe hypoglycemia among older adults with diabetes

Authors: Alexopoulos A-S et al.

Summary: These researchers evaluated sulfonylurea and insulin deintensification following an emergency department visit or hospitalisation for hypoglycaemia in a retrospective cohort of 76,278 US Medicare beneficiaries aged ≥65 years. There were 32,074 such emergency department visits or hospitalisations among sulfonylurea only recipients, 60,350 among insulin only recipients, and 13,869 among those receiving both a sulfonylurea and insulin, for whom the respective deintensification rates were 44.2%, 24.0% and 48.1%, respectively. There were also significant trends for treatment deintensification rates to increase between 2007 and 2017 for all three groups. Deintensification was less likely for patients of lower socioeconomic status, irrespective of hypoglycaemic regimen, whereas frailty, CKD, history of falls and depression were each significantly associated with an increased likelihood of deintensification.

Comment: Although our treatment guidelines strongly advocate for individualisation of therapy, which includes a consideration for risk of hypoglycaemia, there is also strong underlying pressure for achieving tight glycaemic control. As a result, people with type 2 diabetes often end up on multiple drugs, including insulin. Prior to the availability of the newer agents this year, most people would be prescribed a sulfonylurea as second line and then insulin. Often these are combined, which increases the risk of hypoglycaemia. Sometimes it is easy to forget that the evidence for tight control relates to the long-term micro- and macrovascular risk, which becomes less relevant in the elderly, particularly when other comorbidities mean that life expectancy is relatively short. Then the greater risk is of falls and/or the cognitive effects of hypoglycaemia. This paper reports on deintensification of therapy in this group in the US, and concludes that there is room for improvement. It would be very good to know how well we are doing in NZ. I suspect we would find similar results.

Reference: JAMA Netw Open 2021;4:e2132215
Abstract

Blood pressure lowering and risk of new-onset type 2 diabetes

Authors: Nazarzadeh M et al., on behalf of the Blood Pressure Lowering Treatment Trialists' Collaboration

Summary: The role of BP lowering in the prevention of diabetes was explored in a one-stage meta-analysis of individual participant data from 19 RCTs (n=145,939) and an individual participant data network meta-analysis of 22 trials. There were 9883 study participants diagnosed with new-onset type 2 diabetes over a median 4.5 years of follow-up. Across all trials, each 5mm Hg reduction in systolic BP was associated with a reduced risk of type 2 diabetes (HR 0.89 [95% CI 0.84, 0.95]). Analyses of the five major antihypertensive drug classes revealed that compared with placebo, the risk of type 2 diabetes was reduced by ACE inhibitors and ARBs (respective relative risks 0.84 [95% 0.76, 0.93] and 0.84 [0.76, 0.92]), whereas calcium channel blockers had no significant impact (1.02 [0.92, 1.13]) and β-blocker and thiazide diuretic use both increased the risk (1.48 [1.27, 1.72] and 1.20 [1.07, 1.35]).

Comment: This is a very interesting paper. We know how important BP is as a risk factor for CV and microvascular complications of diabetes and this drives targets for lower BP than we might accept in people without diabetes. However, this paper raises the intriguing possibility that BP itself is a risk for diabetes; or is it that specific antihypertensive agents have additional non-BP-related effects on glucose metabolism? The association between β-blockers and thiazide diuretics use and incident type 2 diabetes has been around for a while. However, what is striking from this paper is the contrast with ACE inhibitors and ARBs. Here, the overall finding was a reduction in risk of diabetes with reduction in BP, but in fact this was all driven by ACE inhibitors and ARBs when β-blockers and thiazide diuretics were again shown to increase the risk. This has important implications for hypertension management, particularly in those with prediabetes.

Reference: Lancet 2021;398:1803–10
Abstract

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

Prevalence of diabetic retinopathy and reduced vision among Indigenous Australians in the nurse-led iDEES study in a regional primary care clinic

Authors: Atkinson-Briggs S et al., on behalf of the Centre of Research Excellence in Diabetic Retinopathy Study Group

Summary: These researchers reported on the prevalence and severity of diabetic retinopathy and presenting vision level for a cohort of 135 Indigenous Australian adults attending an Indigenous primary care clinic; 130 had type 2 diabetes and 132 had gradable retinal images. The respective prevalences of mild nonproliferative, moderate-to-severe and sight-threatening retinopathy were 25%, 2.5% and 1.5%, and a third of the patients had subnormal presenting vision.

Comment: I include this paper to illustrate the value of thinking a bit outside of the traditional model of care. Although conducted in Australia, there are similarities between the rates of diabetes and outcomes between the indigenous populations of both Australia and NZ. This is particularly true when considering accessing care, where we know that there are many factors, both system and individual, that create barriers. Importantly, when these barriers are overcome we have data to confirm that outcomes are as good for Māori as non-Māori. This paper shows that a model that utilises nurse-led community-based outreach clinics with a comprehensive package of care was able to engage indigenous Australians. As we look to reshape our health system, these are the types of initiatives that are likely to be effective in NZ and should be explored and codeveloped with the communities they serve. It is essential that we make sure that such an approach is nationwide and does not further increase inequities by post code or other demographic.

Reference: Intern Med J; Published online Nov 15, 2021
Abstract

RACP MyCPD Program participants can claim **one credit per hour** (maximum of 60 credits per year in Category One – Educational Activities) **for reading and evaluating Research Reviews.**
Please CLICK HERE to download CPD Information

Impact of color-coded and warning nutrition labelling schemes

Authors: Song J et al.

Summary: This systematic review of 101 RCTs and 55 non-RCTs with a network meta-analysis of data from 134 of the studies found that a traffic light food labelling system, nutrient warnings and health warnings all increased the likelihood that consumers would select more healthy products (respective odds ratios 1.5 [95% CI 1.2, 1.87], 3.61 [2.82, 4.63] and 1.65 [1.32, 2.06]), and Nutri-Scores, nutrient warnings and health warnings also appeared to reduce selection of less healthy products (0.66 [0.53, 0.82], 0.65 [0.54, 0.77] and 0.64 [0.53, 0.76]). Nutri-Scores and nutrient warnings were also associated with increased overall healthfulness, and traffic light labelling, Nutri-Scores and nutrient warnings were associated with reductions in the contents of energy, sodium and overall and saturated fat in purchased products.

Comment: There has been a lot of talk about the need for public health measures to be combined with individual interventions to address the obesity epidemic. Some of these public health measures could include interventions that require legislation, such as sugar taxes or food labelling. It feels like we have been talking about these for 20 years or more and still there is no action. I don't think anyone believes that any one single action will be the magic bullet, but doing nothing certainly won't. This paper highlights the benefit of front-of-label food information to influence consumers. The challenges have always been definition of 'healthy' and the power of the food industry lobby to derail the process of getting agreement on that. However, I include this paper to again raise the issue for discussion and promotion.

Reference: PLoS Med 2021;18:e1003765
Abstract

Glucose Awareness to Motivate and Enable Solutions (GAMES) in diabetes mellitus using flash glucose monitoring

Authors: Yeoh E et al.

Summary: The short and medium-term effects of intermittent flash glucose monitoring on HbA_{1c} level, glycaemic variability and lifestyle changes were reported for 42 patients with type 1 diabetes and 120 with type 2 diabetes participating in a global observational clinical programme, which provided the participants with two first-generation Libre® flash glucose monitoring sensors 3–4 months apart. After receiving the first sensor, mean HbA_{1c} level did not change significantly at 3–4 months in the type 1 diabetes group, but there was a significant reduction of 4 mmol/mol in the type 2 diabetes group (p=0.008), even though there were no significant changes in carbohydrate intake and exercise frequency or duration. HbA_{1c} level reductions were greatest in participants with baseline levels >86 mmol/mol (–12 and –11 mmol/mol for the type 1 and type 2 diabetes groups, respectively), and both groups also had improvements in Glucose Management Indicator score and percentage time-above-range when the first and second weeks of use of the same sensor were compared. Glycaemic parameters and certain measures of glycaemic variability were better with higher scan frequencies. While 85% of the participants felt that the device was useful, only 60% indicated a desire to use it for daily monitoring.

Comment: The development of flash-glucose monitoring has provided a continuous glucose monitoring device that becomes more cost accessible for people with diabetes than previous technology. Although not funded (and they should be for some people – just saying), many people with type 1 or type 2 diabetes are paying for them themselves. Primary- and secondary-care services are also using them in a variety of ways to try to improve patient care and outcomes. This paper is a real-world observational study of the impact of intermittent use of a flash monitor on lifestyle behaviours, diet composition and glycaemic control. It shows utility of this for people with type 2 diabetes, particularly those with higher baseline HbA_{1c} levels. It was interesting that the vast majority of people saw benefit, but fewer were keen to use it regularly. These findings are consistent with my anecdotal observations in people with type 2 diabetes.

Reference: Diabet Med; Published online Oct 26, 2021
Abstract

Effect of dapagliflozin on the rate of decline in kidney function in patients with chronic kidney disease with and without type 2 diabetes

Authors: Heerspink HJL et al., for the DAPA-CKD Trial Committees and Investigators

Summary: The DAPA-CKD trial investigated the long-term efficacy and safety of the SGLT-2 inhibitor dapagliflozin in patients with CKD, with or without type 2 diabetes. This secondary analysis of the trial investigated the effect of dapagliflozin on the rate of decline in kidney function in patients with CKD. It found that the effect of dapagliflozin on estimated GFR slope was more pronounced in those with diabetes (difference versus placebo, 1.18 mL/min/1.73m^2 per year [95% CI 0.79, 1.56]) than those without diabetes (0.46 mL/min/1.73m^2 per year [–0.10, 1.03]; p=0.04 for interaction). It also showed that the moderating effect of dapagliflozin on estimated GFR slope was positively correlated with baseline HbA_{1c} level and urinary albumin-to-creatinine ratio.

Reference: Lancet Diabetes Endocrinol 2021;9:743–54
Abstract

Effect of dapagliflozin on urinary albumin excretion in patients with chronic kidney disease with and without type 2 diabetes

Authors: Jongs N et al., for the DAPA-CKD Trial Committees and Investigators

Summary: This secondary analysis of the DAPA-CKD trial assessed the effects of dapagliflozin on albuminuria in patients with CKD with and without type 2 diabetes. Relative to placebo, treatment with dapagliflozin resulted in a geometric mean percentage change in urinary albumin-to-creatinine ratio during follow-up of –35.1 percentage points in patients with type 2 diabetes and –14.8 percentage points in patients without type 2 diabetes (p<0.0001 for interaction). Larger reductions in urinary albumin-to-creatinine ratio at day 14 with dapagliflozin were significantly associated with attenuated estimated GFR decline during subsequent follow-up.

Reference: Lancet Diabetes Endocrinol 2021;9:755–66
Abstract

Comment: We are continuing to learn more about the role of the SGLT-2 inhibitors, particularly the impact on cardiorenal disease. Many studies have now been published to demonstrate the effectiveness of this class of drug on reduction in HbA_{1c} level, and in patients with established CV disease, a reduction in events and mortality, and dramatic benefits in heart failure particularly. Furthermore, in those with established diabetic nephropathy, SGLT-2 inhibitors have been shown to reduce albuminuria, progression to end-stage renal disease and need for dialysis. These studies have been very consistent across the various agents within this class, and underpin the place of SGLT-2 inhibitors as second-line agents after metformin in the management of type 2 diabetes for those with established, or high risk of CV disease or nephropathy. What is now beginning to emerge is that these cardiorenal benefits may be in part independent of the effects on glycaemic control. That raises the question whether they could be used in people with CV disease or renal disease who do not have type 2 diabetes. Evidence for this is accumulating for CV disease, especially for heart failure. The study reported in these two separate papers is of the effect of dapagliflozin on renal outcomes in those with and those without type 2 diabetes who have established CKD, including some degree of albuminuria. There was a clear overall benefit in all renal parameters. This benefit was greatest in those with type 2 diabetes, but the significant improvements in those without diabetes strongly support a nonglycaemic mechanism being involved. It is likely that over time we will see a broader use of SGLT-2 inhibitors than just limited to type 2 diabetes, which we have now.

New Zealand Research Review subscribers can claim CPD/CME points for time spent reading our reviews from a wide range of local medical and nursing colleges. Find out more on our **CPD page**.

This Research Review has been endorsed by The Royal New Zealand College of General Practitioners (RNZCGP) and has been approved for up to 1 CME credit for the General Practice Educational Programme (GPEP) and Continuing Professional Development (CPD) purposes. You can record your CME credits in your **RNZCGP Dashboard**

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 please **CLICK HERE**.

Association of dietary intake, physical activity, and sedentary behaviours with overweight and obesity among 282,213 adolescents in 89 low and middle income to high-income countries

Authors: Mahumud RA et al.

Summary: The prevalences of overweight and obesity and associated lifestyle risk factors were reported for 282,213 school-going adolescents from low- to middle- and high-income countries in this research. Overall, the respective prevalences of overweight and obesity were 10.12%, and 4.96%, with the prevalence of overweight ranging from 2.40% in Sri Lanka to 29.08% in Niue, and obesity ranging from 0.40% in Sri Lanka to 34.66% in the Cook Islands. Overweight and obesity were significantly associated with fast-food intake (respective adjusted relative risk ratios 1.09 [95% CI 1.05, 1.12] and 1.32 [1.26, 1.38]), high carbonated soft drink consumption (1.19 [1.12, 1.24] and 1.28 [1.18, 1.38]), low physical activity level (1.11 [1.06, 1.17] and 1.20 [1.12, 1.28]) and high sedentary behaviour level (1.33 [1.27, 1.39] and 1.73 [1.63, 1.84]). Vegetable consumption ≥2 times per day versus no regular daily consumption was associated with 22% and 17% lower risks of overweight and obesity, respectively.

Comment: It has been well reported how rates of obesity are increasing worldwide, as have the well-established causal relationships between obesity and a range of comorbid disease. What has also been recognised is the concerning trend of increasing prevalence of obesity in adolescents and young adults. This left shift in population rates of obesity creates major public health challenges as we try to reduce the rates of diabetes and CV disease. This paper reports on the rates of overweight and obesity in adolescents across a range of countries with varying economic statuses. What struck me was the very wide range observed, particularly for obesity where it is as low as 0.4% in Sri Lanka but as high as 35% in the Cook Islands. It is notable that people from both of these countries have much higher rates of type 2 diabetes than Caucasians, indicating that whilst obesity is important, there are other factors at play.

Reference: Int J Obes 2021;45:2404–18
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. He is a 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.**

The effects of COVID-19 on self-management behaviours and service experiences in type 2 diabetes mellitus

Authors: Quirke-McFarlane S et al.

Summary: The impact COVID-19 had on adults with type 2 diabetes self-management behaviours and service experiences in the UK was evaluated with an 18-item cross-sectional survey. Of 150 respondents, 30% reported that they had changed their diabetes medication taking behaviour since the pandemic began, for a number of reasons. They also reported negative changes in physical activity levels and dietary behaviours. A high level of satisfaction was reported for telephone consultations, but a clear preference for face-to-face consultations was expressed.

Comment: COVID-19 is having dramatic effects on our health system in so many ways. Quite apart from the direct impact of those infected with COVID, there are the effects of disrupted services and changes in healthcare delivery. Furthermore, where there have been extended periods of lockdown and restrictions in access to sport and leisure facilities, there are the additional effects on lifestyle behaviours that further impact on disease risk factors or management. This survey from London highlights these issues. Although the response rate was rather low, it is probable that this would provide a more favourable impression, as nonresponders could be expected to have worse patterns. I was also struck by the preferences expressed for face-to-face consultations over virtual ones, which is what I have also observed here. Whilst it seems like a good idea and can be effective to use telephone or Zoom, many/most patients, and I suspect clinicians, prefer to be in person.

Reference: Pract Diabetes 2021;38:15–9b
Abstract

Real-world screening for diabetes in early pregnancy: improved screening uptake using universal glycated haemoglobin

Authors: Jamieson EL et al.

Summary: Early and routine OGTTs were compared with early HbA_{1c} level screening tests for diabetes in pregnancy in 600 women (233 Aboriginal) from 27 primary-care sites in rural or remote Western Australia; early HbA_{1c} tests were offered to all women presenting at <20 weeks' gestation, early OGTTs were requested on clinician discretion and routine OGTTs were offered at 24–28 weeks' gestation. The uptake rates for HbA_{1c} tests were 85.7% and 86.4% in Aboriginal and non-Aboriginal women, respectively, whereas completion rates for both early and routine OGTTs were lower in Aboriginal women compared with non-Aboriginal women (38.6% vs. 69.6% and 44.5% vs. 84.7%, respectively [p<0.001 for both]). Aboriginal women who completed both early tests completed their HbA_{1c} test significantly earlier in their pregnancy than their OGTT (9.6 vs. 12.5 weeks' gestation [p<0.001]).

Comment: In Australia, the Aboriginal indigenous population have a significantly higher rate of type 2 diabetes than other Australians. This is highly relevant for screening for diabetes during pregnancy – either undiagnosed type 2 diabetes or gestational diabetes. As in NZ, the standard screening is with an OGTT between 24–28 weeks' gestation; however, there are barriers to doing these and they are frequently not done. An alternative strategy is to screen with an HbA_{1c} level, which is a single test and does not require fasting. This study shows that uptake of HbA_{1c} level screening was better overall compared with OGTT, and especially for Aboriginal women. Similar issues exist in NZ for Māori and Pacific women, and we already have advice to use HbA_{1c} level in early pregnancy here for women at greater risk of diabetes. That approach is supported by these Australian data.

Reference: Prim Care Diabetes 2021;15:995–1001
Abstract

Kindly Supported by

PHARMACY GUILD OF NEW ZEALAND
NZMA New Zealand Medical Association
COLLEGE OF NURSES AOTEAROA NZ
diabetes new zealand
NEW ZEALAND RURAL GENERAL PRACTICE NETWORK