Diabetes & Obesity
RESEARCH REVIEW™

Making Education Easy

Issue 146 – 2021

In this issue:

Abbreviations used in this issue
BP = blood pressure
CV = cardiovascular
HbA_{1c} = glycosylated haemoglobin
LDL = low-density lipoprotein
OR = odds ratio

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Welcome to issue 146 of Diabetes and Obesity Research Review.

This issue begins with an article published in the Lancet reporting that patients with pre-existing diabetes derived a greater survival/life-expectancy benefit from metabolic-bariatric surgery than obese nondiabetics, although both groups benefited from surgery compared with usual care. There are also two trials of interventions for type 2 diabetes management that seem like they should work, but didn't work very well: one looked at an intervention of information and communications technology and contact with nonphysician personnel, and the other trialled a 'game' that assigned participants points and levels for achieving step goals and bodyweight loss targets. Other included research explored the expectations of parents of children with type 1 diabetes regarding perceived barriers to and benefits of monthly video consultations combined with regular outpatient care.

We hope you find this research update stimulating and informative. As always, we appreciate your comments and suggestions.

Best regards,

Professor Jeremy Krebs
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Association of metabolic-bariatric surgery with long-term survival in adults with and without diabetes

Authors: Syn NL et al.

Summary: This was a one-stage meta-analysis of 16 matched cohort studies and one prospective controlled study (n=174,772) reporting on all-cause mortality after metabolic-bariatric surgery versus nonsurgical management in obese individuals. There were 7712 deaths recorded over 1.2 million patient-years of follow-up. Metabolic-bariatric surgery was found to be associated with a reduced hazard rate of death (49.2% [95% CI 46.3, 51.9]), with an increase in median life expectancy of 6.1 years, compared with usual care. All-cause mortality was reduced in patients with and without diabetes at baseline (respective hazard ratios 0.409 [0.370, 0.453] and 0.704 [0.588, 0.843]), with a greater treatment effect seen in those with diabetes (I^2 95.7% [p<0.0001]); the respective numbers needed to treat to prevent one additional death over 10 years were 8.4 and 29.8, respectively. There was no evidence of differential treatment effects according to bariatric surgery type. It was estimated that every 1.0% increase in metabolic-bariatric surgery utilisation rate would yield 5.1 million and 6.6 million potential life-years for patients with and without diabetes, respectively.

Comment: Whilst bariatric surgery is not appropriate for everyone with type 2 diabetes, there has been ample evidence published to date that it is a very effective treatment for weight management and improved glycaemic control, and often facilitates resolution of diabetes. There have been some studies reporting the effect of bariatric surgery on mortality in obesity, and this meta-analysis adds further to that. Although it includes both matched cohort studies and prospective controlled trials, its strength is in the large number of included participants. There is a clear reduction in all-cause premature mortality with bariatric surgery compared with those not undergoing surgery. However, the most interesting finding from this study is the greater benefit observed in those with diabetes, where the increase in life expectancy is almost double that of those without diabetes. This is very useful and compelling evidence for advocating for funding for more public bariatric surgery.

Reference: Lancet 2021;397:1830–41
Abstract

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Temporal variations in maternal treatment requirements and early neonatal outcomes in patients with gestational diabetes

Authors: Fox RA et al.

Summary: These researchers sought evidence of temporal variation in maternal treatment requirements and early neonatal outcomes for 791 women with gestational diabetes and a singleton infant from a UK tertiary obstetric centre. They found that the likelihood of requiring insulin was significantly highest in November, while the average total daily insulin dose peaked in January compared with the average of 19 U/day (p<0.05). Neonatal hypoglycaemia rates were highest in December at 40% above average (p<0.05), but there was no evidence of temporal variation in NICU admission rates or neonatal capillary blood glucose levels.

Comment: I include this one for quirky interest. Women with gestational diabetes are more likely to need insulin and higher doses of it if they are diagnosed during winter than summer. This study from the UK shows the seasonal variation in insulin requirements. The most obvious conclusion as to why relates to lifestyle factors, with women less likely to be active during winter and perhaps preferring different types of food. How this translates to tropical NZ is unknown.

Reference: Diabet Med; Published online May 8, 2021
Abstract

Association of lactation with maternal risk of type 2 diabetes

Authors: Pinho-Gomes A-C et al.

Summary: This was a systematic review of 17 cohort and five cross-sectional observational studies (mostly of modest quality) reporting on the association between lactation and maternal type 2 diabetes risk, 16 of which were included in a meta-analysis. Conflicting results were seen across studies investigating the relationship between lactation and type 2 diabetes risk in the first months after birth in women with gestational diabetes: those with longer follow-up indicated a graded protective association for lactation on type 2 diabetes risk, with a potentially greater protective effect in women with versus without gestational diabetes. Overall, the type 2 diabetes risk was lower for ever versus never lactation (relative risk 0.73 [95% CI 0.65, 0.83]), with each additional month of lactation lowering the risk (0.99 [0.98, 0.99]).

Comment: Breastfeeding has many benefits for women and babies alike. Most women would probably prefer to breastfeed if they are able to (says a man). This systematic review and meta-analysis adds further support to that. Although the overall quality of the studies was modest, the overall message is clear. Breastfeeding is associated with less risk of type 2 diabetes for women who are able to, by almost a third. This effect is further enhanced by duration of lactation. There are many possible reasons for this, including the effect on maternal weight. This message is clear and suggests promoting and facilitating breastfeeding for women with gestational diabetes.

Reference: Diabetes Obes Metab; Published online April 28, 2021
Abstract

Development and validation of a machine learning model using administrative health data to predict onset of type 2 diabetes

Authors: Ravaut M et al.

Summary: A decision analytical model using linked administrative health data for 1,657,395 patients from Ontario, Canada, was used to develop a population-level machine learning model for predicting type 2 diabetes 5 years prior to onset. The model, which was also validated in 243,442 patients and tested in 236,506, had a test area under the curve value of 80.26, showed good calibration and was robust to sex, immigration status, area-level marginalisation with respect to material deprivation and race/ethnicity, and low contact with the healthcare system.

Comment: The relevance of a diagnosis of prediabetes is a controversial topic. I have included papers on this topic previously, highlighting the uncertainty of the rate of progression to type 2 diabetes and the risk of CV disease when prediabetes is defined by HbA_{1c} level rather than older definitions based on the glucose tolerance test. When it is estimated that 25% of the adult population may have prediabetes, this is a very relevant question. If it were possible to simply predict who will develop diabetes and more importantly who might develop complications of diabetes, then this would enable a more targeted and cost-effective intervention to prevent this. This paper set in Canada used a machine learning approach to develop an algorithm to do just that, with inputs from a range of domains of readily available patient data. Whilst this couldn't be directly translated to the NZ population, a similar approach could be taken here, particularly since we have a well-connected data infrastructure.

Reference: JAMA Netw Open 2021;4:e2111315
Abstract

Effects of a technology-assisted integrated diabetes care program on cardiometabolic risk factors among patients with type 2 diabetes in the Asia-Pacific region

Authors: Lim L-L et al., for the Asia-Pacific JADE Study Group

Summary: The 12-month open-label JADE Program trial randomised patients with type 2 diabetes from eight Asia-Pacific countries to an intervention of technology-guided structured evaluation, automated personalised reports to encourage patient empowerment and ≥2 telephone or face-to-face contacts by nurses to increase patient engagement (phase 1, n=3732; phase 2, n=6645) or a control group of technology-guided structured evaluation with (phase 1, n=3805) or without (phase 2, n=6652) automated personalised reports. Compared with the control groups, similar proportions of the intervention groups experienced a primary outcome (CV disease, chronic kidney disease, visual impairment or eye surgery, lower-extremity amputation or foot ulcers requiring hospitalisation, any-site cancer or death; respective ORs for phases 1 and 2, 0.94 [95% CI 0.74, 1.21] and 1.02 [0.83, 1.25]), but greater proportions of the intervention groups attained ≥2 diabetes-associated targets (HbA_{1c} level <7.0%, BP <130/80mm Hg and LDL cholesterol level <100 mg/dL; 1.34 [1.21, 1.49] and 1.25 [1.14, 1.37]) and ≥2 key performance indices (reductions in HbA_{1c} level of ≥0.5%, systolic BP of ≥5mm Hg, LDL cholesterol level of ≥19 mg/dL and bodyweight of ≥3.0%; 1.18 [1.04, 1.34] and 1.50 [1.33, 1.68]). For attainment of ≥2 primary diabetes-associated targets, participants from low- and middle-income countries had greater effects than those from high-income countries (OR 1.50 vs. 1.20 [p=0.04]).

Comment: This is a great example of why clinical trials are so important. On the surface of it, it is a no-brainer that a programme set up to empower patients through individualised reports and regular contact with a nurse would improve care and outcomes. Indeed, the intervention did improve care and improved a range of cardiometabolic risk factors. Had this been the primary outcome, as so many studies are, then we would have concluded that this intervention was highly effective. However, the primary outcome was actual clinical events, which of course is far more important. Unfortunately, and somewhat surprisingly, the intervention did not reduce these. Whether this is due to other confounding factors that overwhelmed the benefit of reduction in measured risk factors or some other reason is not clear. However, we must conclude that this intervention is not effective.

Reference: JAMA Netw Open 2021;4:e217557
Abstract

Effect of behaviorally designed gamification with social incentives on lifestyle modification among adults with uncontrolled diabetes

Authors: Patel MS et al.

Summary: Adults with type 2 diabetes (HbA_{1c} level ≥8%) and BMI ≥25 kg/m² were equipped with a wearable device and smart weight scale, and were randomised to an additional 1-year game that assigned points and levels for achieving step goals and weight loss targets, with support and intervention (n=92), with collaboration (n=95) or with competition (n=87) or a control group (device feedback only; n=87). Compared with controls, participants assigned to gamification with support and with competition, but not with collaboration, had significant increases from baseline in mean daily steps (respective adjusted differences, 503 steps [p=0.01], 606 steps [p=0.003] and 280 steps [p=0.16]). Significant reductions from baseline were seen for bodyweight and HbA_{1c} level in all four trial arms, but no significant differences were seen between any of the intervention arms and the control arm.

Comment: Gamification – is that really a word? Anyway, this is sadly another example of a great idea that you could imagine might work, but didn't. Sustained lifestyle change of the magnitude required to influence diabetes parameters is really hard. No kidding Sherlock, I hear you say! That is why ideas like this one of harnessing tools such as wearable devices and remote data collection and feedback to help motivate people, added to an incentive based on healthy competition, all make sense. They should work, so why don't they? That's the real question to come out of this research. We are complex fickle beasts.

Reference: JAMA Netw Open 2021;4:e2110255
Abstract

Achieving a useful and person-centred diabetes consultation is a shared responsibility between diabetologists and people with diabetes

Authors: Schultz AA et al.

Summary: The perceptions regarding the usefulness of routine type 1 diabetes consultations with diabetologists were evaluated in this Danish qualitative study, which acquired data for analysis from semistructured interviews completed by 33 patients with the condition. It was perceived by the respondents that achieving a useful consultation was a shared responsibility between patients with diabetes and diabetologists. However, there was variability expressed regarding what constitutes a useful consultation, and also with respect to expectations for both consultation and diabetologist in relation to: i) the interaction between the patients and the diabetologist (including preparedness, honesty, rapport and preferring a partnership with the diabetologist versus 'keeping it clinical'); and ii) the diabetologist's approach to diabetes care (including the provision of up-to-date knowledge, listening and showing understanding).

Comment: Sometimes you know you've got it right and sometimes you know it could have gone better! We can all reflect on our interactions with our patients and reach these conclusions. This qualitative study addresses the question of what factors are important in achieving an effective consultation for people with type 1 diabetes in specialist clinics. There are some interesting themes arising from this work. Apart from what is surely evident to any clinician, that we need to individualise our approach, is the message that it is important to identify and be clear about the expectations of the consultation for both parties. The suggestion to use tools to prepare for a consultation with this in mind is a good one and warrants further exploration.

Reference: Diabet Med 2021;38:e14382
Abstract

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CONGRATULATIONS TO

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and **Peter Shapkov** (Breast Surgeon at Waitemata DHB)

who were winners in our prize draw by taking part in our recent Research Review Annual Subscriber Update.

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Parental expectations before and after 12-month experience with video consultations combined with regular outpatient care for children with type 1 diabetes

Authors: von Sengbusch S et al.

Summary: Expectations regarding perceived barriers to and benefits of 1 year of monthly video consultations combined with regular outpatient care of children with type 1 diabetes were explored in this analysis of 54 qualitative interviews with parents. While it was thought that video consultations offered a greater frequency of contact for optimised insulin dosing (including increased confidence) and saving time compared with standard care, difficulties with internet connections were identified as the principle barrier. Other perceived improvements were digital prescriptions and being able to meet with the same diabetologist in both outpatient and telemedical care. Most interviewees indicated that they preferred intervals of 4–6 weeks between video consultations.

Comment: The utility of virtual consultations, or telemedicine, has come under the spotlight in the last 12 months with the impact of COVID-19. This study reports on the experiences of parents of children with type 1 diabetes, where regular clinic visits were enhanced with additional monthly virtual appointments. The benefits of the extra video contact was in confidence and optimising insulin therapy, as well as time saving by not needing to attend a clinic. As we have all seen over the last 12 months, a significant barrier was internet connectivity. What is not explored here is the additional time commitment placed on the health professional. I would be surprised if any patient or parent wouldn't prefer more frequent contact, either in person or virtual, but this is not necessarily realistic in a time-pressured and cost-restrained public health system. In our adult clinic, we are seeing less people now preferring a virtual consult than we would have expected 12 months ago. We need more work to establish the optimal use of this tool.

Reference: Diabet Med 2021;38:e14410
Abstract

Dose-dependent associations of dietary glycemic index, glycemic load, and fiber with 3-year weight loss maintenance and glycemic status in a high-risk population

Authors: Zhu R et al.

Summary: This secondary analysis of data from the PREVIEW diabetes prevention study explored longitudinal and dose-dependent associations of dietary glycaemic index, glycaemic load and fibre intake with bodyweight and glycaemic status over 3 years of weight loss maintenance in 1279 adults at high risk of type 2 diabetes. Each 10-unit increment in glycaemic index and each 20-unit increment in glycaemic load were associated with bodyweight regains of 0.46 and 0.49 kg/year, respectively ($p<0.001$ for both) with 10-unit increment in glycaemic index also associated with an increase in HbA_{1c} level. Associations of glycaemic index and glycaemic load with HbA_{1c} level were independent of weight change. Patients in the highest versus lowest glycaemic index and glycaemic load tertiles had significantly greater weight regain and HbA_{1c} level increases. An inverse association was seen between fibre intake and increased waist circumference; associations with weight regain and glycaemic status were not robust across analyses.

Comment: This secondary analysis of the PREVIEW study provides an interesting perspective on the difference between a 'dietary prescription' and the actual nutritional composition consumed when prescribed a specific diet. In the PREVIEW study, people with prediabetes were randomised to either a high-protein, low-glycaemic index or a moderate protein, moderate-glycaemic index diet, with additional randomisation to two physical activity interventions. What this secondary analysis has done is to pool all participants regardless of group and then reanalyse the outcomes based on reported food intake. Three important observations come from this. The first is that high glycaemic index or load is associated with worsening HbA_{1c} level independent of weight. Second, that high glycaemic index or glycaemic load are also associated with weight regain. Third, that surprisingly, fibre intake was not definitively protective against weight regain or glycaemia, as we might expect from other literature. The evidence supports policies to reduce glycaemic load in our diet, regardless of the specific 'dietary prescription'.

Reference: Diabetes Care; Published online May 27, 2021
Abstract

Cognitive performance declines in older adults with type 1 diabetes

Authors: Jacobson AM et al., the DCCT/EDIC Research Group

Summary: Participants with type 1 diabetes from the DCCT and EDIC study (n=1051) were evaluated for independent risk factors for cognitive decline over 32 years of follow-up. Substantive declines in memory and psychomotor and mental efficiency were seen, with declines in psychomotor and mental efficiency five times greater between 18 and 32 years of follow-up when compared with up to 18 years. Significant independent predictors of greater decrements in psychomotor and mental efficiency at year 32 were exposure to higher HbA_{1c} levels, more severe hypoglycaemic episodes and elevated systolic BP ($p<0.0001$), with the effect of all three combined being equivalent to an additional 9.4 years of age.

Comment: We tend to think of complications of diabetes as the classical microvascular complications of retinopathy, nephropathy and neuropathy, and the macrovascular complications of ischaemic heart disease, stroke and peripheral vascular disease. However, we have all seen the cognitive issues associated with frequent hypoglycaemia. This study used the DCCT and EDIC study participants with type 1 diabetes and very long-term outcome data over 30 years to determine factors associated with cognitive decline. The factors identified are those we might predict of glycaemic control, hypertension and hypoglycaemia frequency, all of which are modifiable. This evidence gives another angle in discussion with patients over the benefits of attention to tight but safe control of glucose level and BP.

Reference: Lancet Diabetes Endocrinol 2021;9:436–45
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. **FOR FULL BIO CLICK HERE.**