

Diabetes & Obesity

RESEARCH REVIEW™

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Issue 143 – 2021

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Abbreviations used in this issue

BMI = body mass index
BP = blood pressure
CV = cardiovascular
DPP = dipeptidyl peptidase
HbA_{1c} = glycosylated haemoglobin
OR = odds ratio
SGLT = sodium glucose cotransporter

Welcome to issue 143 of Diabetes and Obesity Research Review.

This issue includes two NZ papers, one of which reports that our clinical workforce for managing patients with type 1 diabetes when they transition from paediatric to adult services is under-resourced. The second reports encouraging results from a programme in which youth from two distinctive Pasifika communities were trained to lead a small-scale, community-based intervention programme targeted at overweight/obese adults. A study from our neighbours across the Tasman confirms the value of integrated community-based care of complex type 2 diabetes. There is also a systematic review with meta-analysis describing the efficacy and safety of add-on SGLT-2 inhibitor therapy for type 2 diabetes inadequately controlled on metformin and a DPP-4 inhibitor, which provides useful information as we navigate our way with using SGLT-2 inhibitors now they are funded here in NZ.

We hope you enjoy the research selected, and we welcome your comments and suggestions.

Best regards,

Professor Jeremy Krebs

jeremykrebs@researchreview.co.nz

Lifestyle intervention with or without lay volunteers to prevent type 2 diabetes in people with impaired fasting glucose and/or nondiabetic hyperglycemia

Authors: Sampson M et al., for the Norfolk Diabetes Prevention Study (NDPS) Group

Summary: The Norfolk Diabetes Prevention Study randomised individuals at high risk of developing type 2 diabetes to usual care (n=178) or a theory-based lifestyle intervention of six core and up to 15 maintenance sessions with (n=426) or without (n=424) support from volunteer diabetes prevention mentors. Compared with usual care, the intervention either with or without mentorship was associated with lower rates of progression to type 2 diabetes (15.0% and 13.7%, respectively, vs. 22.8%; respective ORs 0.61 [95% CI 0.39, 0.96] and 0.54 [0.34, 0.85]).

Comment: The prevalence of type 2 diabetes continues to rise, and we define a state of prediabetes for which we believe there is a high risk of progression to full diabetes. However, there is still uncertainty around rates of progression, especially where prediabetes is defined by HbA_{1c} level. Furthermore, we know that lifestyle interventions can reduce the progression of prediabetes to diabetes, but real-world translation of clinical trial interventions has not been forthcoming. This may be because interventions in clinical trials are intensive and people-resource dependent. This study sought to establish whether utilising trained volunteers with diabetes to help support people with prediabetes in their effort to change their lifestyle would improve their chance of success. Two interesting findings were that over a mean of 2 years, 22% of those in the control arm progressed to diabetes. The second interesting finding was that the intervention did reduce this by about half. The volunteer support did not make any additional benefit. So, rates of progression are high and can be reduced.

Reference: *JAMA Intern Med* 2021;181:168–78

[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. Lean 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 C5 CONTROLLED DRUG. **DUROMINE™** IS AN UNFUNDED MEDICINE - A PRESCRIPTION CHARGE WILL APPLY. PLEASE REVIEW FULL DATA SHEET BEFORE PRESCRIBING AVAILABLE AT WWW.MEDSAFE.GOV.NZ OR PHONE Freephone 0508 375394. Minimum Data Sheet Information (phentermine). **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 intermittent 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 phentermine 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 precordial pain. Others included restlessness, insomnia, nausea, and dry mouth. Psychotic episodes, hallucinations and serious cardiovascular or cerebrovascular events are rare. Full Data Sheet and Consumer Medicine Information is available from Medsafe at www.medsafe.govt.nz. (Novo 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. NZ2021-02-0010. February 2021.



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References: 1. Caterson ID, et al. *Diabetes Obes Metab* 2019; 21(8): 1914-24. 2. Saxenda® Data Sheet. 3. Pi-Sunyer X, et al. *N Engl J Med* 2015; 373(1):11-22, and supplementary appendix. 4. le Roux CW, et al *Lancet* 2017; 389: 1399-409. 5. Fujioka K, et al. *Obesity (Silver Spring)* 2016; 24(11): 2278-88.



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The clinical workforce caring for emerging adults with diabetes in New Zealand is under resourced

Authors: Paul R & Corbett C

Summary: These NZ researchers surveyed lead clinicians and representatives of the New Zealand Diabetes Young People Special Interest Group from each of the 20 DHBs on staffing for the care of emerging adults with diabetes; responses were received from all DHBs, which together provide care for ~2300 emerging adults with diabetes. The results showed that the median age of transfer from paediatric services to adult services was 16 years, but all DHBs offered flexibility in transition according to clinical circumstances. Care for emerging adults with diabetes was provided by multidisciplinary teams, general adult diabetes services, general medicine and primary care in twelve, five, two and one DHB, respectively.

Comment: This is a really important issue and reaching a crisis point. In Wellington, as I am sure you are around the country, we are seeing the rise in numbers of young adults with diabetes, and the increasing complexity of trying to help them manage themselves. As well as all of the usual challenges of the teenage years that are hard enough without diabetes, we are seeing a very disturbing rise in mental health issues, which when combined with diabetes create major risk. This paper highlights the lack of resourcing for the extended young adult team, which is generating a lot of stress, particularly for the nursing team. A big part of that is the inability to access acute mental health services in a timely and responsive way. Young adults with diabetes turn to the people they know they can trust, and this places an inappropriate burden on the nursing team. This is a system under stress that is ultimately under-resourced.

Reference: *N Z Med J* 2021;134(1529):80-5

[Abstract](#)

Maternal dietary quality, inflammatory potential and childhood adiposity

Authors: Chen L-W et al.

Summary: Using data from 16,295 mother-child pairs from seven European birth cohorts in the ALPHABET consortium, these researchers investigated the impact of maternal whole diet quality and inflammatory potential on childhood adiposity; the mothers in the study had a mean BMI of 23.4 kg/m². Each standard deviation increase in a pro-inflammatory diet score before pregnancy was associated with a higher odds of overweight or obesity in later childhood (OR 1.09 [95% CI 1.00, 1.19]), and an inverse association was seen for late-pregnancy pro-inflammatory diet score and overweight or obesity in early childhood (0.91 [0.83, 1.00]). Each standard deviation increase in dietary quality score during the entire pregnancy was associated with a lower likelihood of overweight or obesity in late childhood (OR 0.92 [95% CI 0.87, 0.98]). In two cohorts with available data, lower dietary quality and higher dietary proinflammatory scores during the entire pregnancy were associated with a lower late childhood fat-free mass index in males and a higher mid-childhood free mass index in females (p<0.10 for interactions).

Comment: The role of maternal diet during pregnancy on later health outcomes in children is a controversial and sensitive issue. Mothers worldwide are desperate to do everything they can to do the best for their children. This extends to wanting to eat the best diet they can during pregnancy, but the evidence for exactly what that should be is lacking. When looking at most outcomes, and childhood obesity is a good example, the interaction between maternal genetics and lifestyle factors is very difficult to separate. This study is interesting because the mean BMI of the women included was only 23 kg/m². That reduces the confounding of maternal obesity on risk for childhood obesity. The study found that a diet lower in proinflammatory components is associated with lower risk of childhood obesity. These are useful supportive data to help inform pregnant mothers.

Reference: *BMC Med* 2021;19:33

[Abstract](#)

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Pasifika Prediabetes Youth Empowerment Programme

Authors: Firestone R et al.

Summary: These NZ researchers reported learnings from a group of 25 individuals aged 15–24 years from two distinctive Pasifika communities in NZ who were trained to lead a small-scale, community-based intervention programme, delivered to 29 participants over 8 weeks. The intervention targeted overweight or obese individuals aged 25–44 years, and used an empowerment-based programme and a codesign approach to motivate participants to engage in physical activity. The intervention participants' physical activity levels improved, and they had significant reductions in their total bodyweight and waist circumference.

Comment: Obesity in youth continues to increase, and is a major risk factor for the development of type 2 diabetes. This is particularly common in young Pacific people. Unfortunately, young people with type 2 diabetes do not do well. They tend to have higher HbA_{1c} levels and are more resistant to the lifestyle changes necessary to help them manage their diabetes. Therefore there is an urgent need to find effective ways to prevent the development of diabetes in young people. This study reports on a very positive approach that has been successful in engaging young Pacific people and in helping them to achieve positive health outcomes. The approach, which is heavily dependent on codesign, could be effective on a larger scale and warrants further development and implementation.

Reference: *N Z Med J* 2021;134(1530):57–68
[Abstract](#)

Less sedentary time is associated with a more favourable glucose-insulin axis in obese pregnant women

Authors: Dieberger AM et al.

Summary: Longitudinal associations of physical activity and sedentary time with the glucose-insulin axis in 232 obese pregnant women at <20 weeks' gestation at enrolment were explored in this secondary analysis of the DALI study. Greater sedentary time was associated with significantly higher fasting glucose level, fasting insulin level, homeostatic model assessment of insulin resistance and first-phase and second-phase insulin release, whereas greater moderate-to-vigorous physical activity was associated with significantly lower first-phase and second-phase insulin release. An increase in sedentary time during gestation was associated with significantly increased first-phase and second-phase insulin release.

Comment: Being more physically active is well known to be an independent factor in reducing the risk of diabetes across the population. Furthermore, less sedentary time is also independent of total physical activity time. In other words, getting off your bum and doing something, anything, is more important than the duration and intensity of the activity. That observation is confirmed and extended in this study looking at activity during pregnancy and risk of gestational diabetes. As pregnancy progresses, because of the physiological and physical changes, women are often less active. What this study shows is that this has a very negative effect on glucose metabolism and increases the risk of gestational diabetes mellitus. Therefore encouraging and facilitating women to remain active throughout pregnancy is important.

Reference: *Int J Obes* 2021;45:296–307
[Abstract](#)

[†]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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Acute and chronic improvement in postprandial glucose metabolism by a diet resembling the traditional Mediterranean dietary pattern: can SCFAs play a role?

Authors: Vitale M et al.

Summary: Overweight/obese individuals aged 20–60 years were randomly assigned to a Mediterranean diet (n=16) or a control diet (n=13) in this study. Compared with the control diet, the Mediterranean diet was associated with significant reductions in glucose and insulin responses after a test meal at baseline, and the effects increased over 8 weeks ($p<0.05$) along with an improvement in oral glucose insulin sensitivity. The Mediterranean diet was also associated with a significant increase in postprandial plasma butyric acid incremental area under the curve at the end of the intervention, which was inversely, significantly correlated with plasma insulin incremental area under the curve and directly with oral glucose insulin sensitivity. These metabolic changes were accompanied by significant changes in gut microbiota (e.g. increases in the relative abundances of *Intestinimonas butyriciproducens* and *Akkermansia muciniphila*) in the Mediterranean diet group.

Comment: The Mediterranean dietary pattern has been shown to reduce the risk of cardiometabolic disease and is thus promoted as a healthy diet to follow. This small controlled dietary intervention study in overweight adults aimed to examine potential mechanisms for the beneficial effects of a Mediterranean diet. It was only over 8 weeks, but none the less serves to confirm the potential benefits on glucose metabolism. What is novel is the finding that these benefits may be mediated by changes in the gut microbiota and associated short-chain fatty-acid profile. Such short-term studies are useful to explore mechanisms, but of course what really counts is whether people are able to sustain the dietary change and make it their habitual diet. It would be very interesting to know whether the observed changes in gut microbiota persist over time.

Reference: *Clin Nutr* 2021;40:428–37

[Abstract](#)

Inverse association of total polyphenols and flavonoids intake and the intake from fruits with the risk of gestational diabetes mellitus

Authors: Gao Q et al.

Summary: These researchers explored relationships between polyphenol and flavonoid intake and gestational diabetes mellitus risk in a prospective cohort of 2231 pregnant women, 185 of whom were positive for gestational diabetes at 24- to 28-week screening. Comparing the highest with the lowest quartiles, the risk of developing gestational diabetes was reduced for total polyphenol intake (adjusted OR 0.55 [95% CI 0.30, 0.99]), total flavonoid intake (0.57 [0.32, 0.99]), polyphenol intake from fruits (0.51 [0.30, 0.87]), flavonoid intake from fruits (0.58 [0.34, 0.99]) and anthocyanidin intake from fruits (0.62 [0.38, 1.00]). In addition, each 100mg increase in total polyphenols and of polyphenols from fruits was associated with a decrease in 2-hour post-load blood glucose level (respective adjusted ORs 0.054 [95% CI 0.008, 0.096] and 0.061 [0.012, 0.109]). Total polyphenol intake from vegetables was not significantly associated with gestational diabetes risk.

Comment: There is a good reason that we promote the intake of fruit and vegetables as part of a healthy diet. Although most fruit has a relatively high sugar content, it is the other micronutrients they contain that confer health benefits. There is a wide range of polyphenols in fruit and vegetables that have attracted interest from a health perspective. This study specifically looked at the intake of fruit and vegetables and the associated intake of polyphenols in the setting of pregnancy. Women who had diets higher in fruit and vegetables had higher polyphenol intake and lower rates of gestational diabetes. This is a simple message and further evidence to support the general health claims.

Reference: *Clin Nutr* 2021;40:550–9

[Abstract](#)

Association of oily and nonoily fish consumption and fish oil supplements with incident type 2 diabetes

Authors: Chen G-C et al.

Summary: The associations of consumption of oily and nonoily fish and fish oil supplements with incident type 2 diabetes were explored in a large prospective population-based study of 392,287 middle-aged and older participants from the UK Biobank without diabetes, major CV disease or cancer at baseline. During a median of 10.1 years of follow-up, there were 7262 incident cases of type 2 diabetes recorded. Compared with oily fish never consumption, consumption of <1, 1 and ≥ 2 servings per week was associated with lower likelihoods of developing type 2 diabetes (respective adjusted hazard ratios 0.84 [95% CI 0.78, 0.91], 0.78 [0.72, 0.85] and 0.78 [0.71, 0.86]); $p<0.001$ for trend). There was no significant association between nonoily fish consumption and type 2 diabetes risk. Compared with individuals who did not consume fish oil, the risk of developing type 2 diabetes was reduced by 9% (95% CI 4%, 14%) for those who reported regular consumption at baseline, and by 18% (8%, 27%) for those who regularly consumed it at baseline and also reported consumption at ≥ 1 of 24-hour dietary recalls.

Comment: There is nothing particularly new here, but anything to do with fish oil always catches my eye after I used it as an anti-inflammatory dietary additive in my doctorate. There are plenty of epidemiological studies showing a reduced risk of CV disease and type 2 diabetes in those who regularly consume oily fish. This study is interesting because it used data from the UK Biobank and prospectively looked at incident diabetes. Individuals who consumed some oily fish per week were less likely to develop diabetes than those who had none. Of interest is that protection did not extend to nonoily fish but did to fish oil supplements, strongly suggesting a specific protective effect of the long-chain n-3 fatty acids. Throw a bit of salmon into the weekly food rotation as part of your Mediterranean dietary pattern and reap the benefits.

Reference: *Diabetes Care* 2021;44:672–80

[Abstract](#)

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Efficacy and safety of a sodium-glucose co-transporter-2 inhibitor versus placebo as an add-on therapy for people with type 2 diabetes inadequately treated with metformin and a dipeptidyl peptidase-4 inhibitor

Authors: De Builteir C et al.

Summary: This systematic review and meta-analysis included six randomised controlled trials (n=1661) comparing SGLT-2 inhibitors with placebo as add-on therapy after metformin and DPP-4 inhibitor therapy for managing type 2 diabetes. Compared with placebo, add-on SGLT-2 inhibitors significantly reduced HbA_{1c} level (mean difference -8 mmol/mol [p<0.00001]), fasting plasma glucose level (-1.70 mmol/L [p<0.00001]), bodyweight (-1.76kg [p<0.00001]) and systolic and diastolic BPs (-3.6 and -1.5mm Hg, respectively [p values <0.00001 and 0.002]). SGLT-2 inhibitors were also associated with an increased incidence of genital mycotic infections (OR 7.37 [95% CI 3.06, 17.76]) but not urinary tract infections (1.16 [0.63, 2.13]), hypoglycaemia (1.36 [0.61, 3.04]) or discontinuations due to adverse events (1.52 [0.78, 2.97]) compared with placebo.

Comment: We are all feeling our way with the use of the SGLT-2 inhibitors now that we have funded access and widespread use is possible. One question I am being asked from primary care is how effective they are when added in to existing combination therapy regimens. Since the funding of vildagliptin, more people are now on combination therapy with metformin and vildagliptin, but still not meeting target HbA_{1c} levels. Whilst we still have the option of sulfonylureas or insulin therapy, the added CV and renal benefits of an SGLT-2 inhibitor make them an attractive option to add in next. This meta-analysis clearly shows that this is effective for HbA_{1c} level and also for BP. There was the expected increase in fungal infections, but no increase in hypoglycaemia as none of the three agents stimulates insulin release dissociated from food intake. This is further supportive evidence for prescribing SGLT-2 inhibitors.

Reference: *Diabet Med* 2021;38:e14409

[Abstract](#)

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Community-based management of complex type 2 diabetes

Authors: Davis TME et al.

Summary: This article described an integrated model of complex type 2 diabetes care delivered in a community-based general practice by upskilled GPs co-located with an endocrinologist and diabetes nurse educator; 464 patients with type 2 diabetes (mean HbA_{1c} level 78 mmol/mol and mean BMI 33.7 kg/m²) were enrolled. An increase in the use of injectable blood glucose-lowering therapies between the initial and final visit was associated with a reduction in median HbA_{1c} level of 13 mmol/mol, which was sustained out to 12 months. Reductions in BP and serum low-density lipoprotein cholesterol and triglyceride levels were also recorded, as were improvements in patient satisfaction with current treatment, time for self-management, time spent in diabetes-related appointments and diabetes knowledge. The scheduled appointment nonattendance rate was <10%, and there were decreases in local hospital referrals and waiting lists over the study period.

Comment: The time of secondary care managing all people with diabetes, or even all those with complex diabetes and complications, has long gone. The scale of the diabetes epidemic has meant that the majority of people with diabetes are managed in primary care. Recent years have seen the upskilling of the whole primary care team, such that insulin initiation and titration are everyday skills. However, that is not to say that diabetes specialist teams are redundant! New models of care involving more integrated primary and secondary teams have emerged, and most of us now work in this way with variations on a theme. This study reports one such approach in Australia with good outcomes. As we have more tools to manage type 2 diabetes, it will become increasingly important to have integrated approaches to optimise care and maximise the benefits for patients.

Reference: *Intern Med J* 2021;51:62-8

[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. **FOR FULL BIO [CLICK HERE](#).**



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