## In this issue:

**Abbreviations used in this issue**
**BMI** = body mass index
**CV** = cardiovascular
**HbA1c** = glycosylated haemoglobin
**MI** = myocardial infarction
**QALY** = quality-adjusted life-years
**RCT** = randomised controlled trial

# Welcome to issue 82 of Diabetes and Obesity Research Review.

NZ research is represented in this issue, with a paper describing a rather disappointing degree of management of bodyweight gain during pregnancy by midwives, despite good knowledge of the issues. ADVANCE trial data support U-shaped relationships between alcohol consumption and CV outcomes and mortality among patients with type 2 diabetes. Retrospective research from France suggests metformin recipients sleep better than those not treated with the agent, while UK researchers analysed food diaries to investigate the effects of dairy dietary intake on the development of type 2 diabetes.

I hope you enjoy the selection for this issue, and I am looking forward to receiving your comments, feedback and suggestions.

Best regards,

**Dr Jeremy Krebs**
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## A gender-sensitised weight loss and healthy living programme for overweight and obese men delivered by Scottish Premier League football clubs (FFIT)

**Authors**: Hunt K et al.

**Summary**: Male football fans aged 35–65 years from Scotland with BMI ≥28 kg/m² were randomised to a bodyweight loss programme delivered by community coaching staff in 12 sessions held every week (evaluable n=333) or a 12-month waiting list (evaluable n=355) in this pragmatic RCT. The intervention was associated with greater baseline-adjusted bodyweight loss at 12 months (mean difference 4.94kg; 4.36% [p<0.0001]). Two of the five serious adverse events reported in the intervention group (gallbladder removal and ruptured Achilles tendon) were attributed to participation in the programme.

**Comment**: Achieving uptake and success of weight loss programmes in overweight and obese men is a universal challenge. In NZ, this is even greater in Māori and Pacific Islanders who have higher rates of obesity and its health consequences than Europeans. This study is therefore of great interest, as it demonstrated the ability to engage men in weight loss programmes through a common passion of sport. The modest weight loss achieved is still clinically meaningful, particularly if these men had prediabetes or early type 2 diabetes. Given the NZ male obsession for rugby and/or league, this may be an equally effective strategy here and warrants testing.

*Reference: Lancet 2014;383(9924):1211–21*
Abstract

## Changes in diabetes-related complications in the United States, 1990–2010

**Authors**: Gregg EW et al.

**Summary**: This analysis of US health data investigated changes in the incidences of diabetes-related complications over the period 1990–2010. Declines were seen over this period for the rates of acute MI (–67.8%; 95.6 fewer cases per 10,000 persons), death from hyperglycaemic crisis (–64.4%), stroke (–52.7%), amputations (–51.4%) and end-stage renal disease (–28.3%). The reductions were greatest among adults with diabetes compared with those without diabetes. When expressed as rates for the overall population, declines were seen for acute MI and death from hyperglycaemic crisis (2.7 and 0.1 fewer cases per 10,000, respectively), but not amputation, stroke or end-stage renal disease.

**Comment**: It's good to know we are getting something right. This study reported rates of both microvascular and macrovascular complications in the US population with diabetes over a 20-year period from 1990. There has been an impressive reduction in complications, particularly MI, over this time. There are many potential contributors to this, and it is likely to be a multifactorial effect, perhaps the most overwhelming of which will be the increased use of statin therapy over that time. Additionally, the impact of landmark trials such as UKPDS demonstrating the importance of both glycaemic control and BP management is also important. However, as the authors pointed out, the overall burden to the health system is not reducing because the incidence of diabetes continues to increase. The test of our success over the next 20 years will surely be whether we can actually reverse this tide.

*Reference: N Engl J Med 2014;370(16):1514–23*
Abstract

**Independent commentary by Dr Jeremy Krebs,** Endocrinologist & Clinical Leader at Wellington Hospital. **For full bio CLICK HERE.**

# Management of excess weight in pregnancy in Otago: a qualitative study with lead maternity carers

**Authors**: Fieldwick D et al.

**Summary**: These researchers conducted three semistructured focus groups and an in-depth interview with 12 NZ midwives providing lead maternity care, including one student midwife, to determine their knowledge regarding gestational weight gain. The themes discussed at the focus groups included knowledge of gestational weight gain, methods for identifying BMI and weight gain during pregnancy, current management, barriers to management and the tools used to overcome these barriers. Knowledge of the risks associated with excess gestational weight gain was considered satisfactory, but adherence to the NZ guidelines and awareness of international guidelines were limited. Gestational weight gain management varied and it was uncommon to weigh pregnant women. One major barrier to weight management was sensitivity.

**Comment**: The potential impact of weight gain in pregnancy on both maternal and foetal health, both during and after the pregnancy, makes this an important area to research. In NZ, the majority of pregnancies are managed in the community by midwives. This qualitative study assessed knowledge and practices of midwives around weight gain during pregnancy. The striking finding was that whilst knowledge of the risks of excessive weight gain was known, action to manage this was not so good. The sensitivity of the issue was seen as a barrier; however, it is concerning that simply weighing women was not even commonly done, making any management of this virtually impossible. This would seem like a very good and simple place to start.

*Reference: NZ Med J 2014;127(1392):27–37*
Abstract

# Effects of moderate-to-vigorous intensity physical activity on overnight and next-day hypoglycemia in active adolescents with type 1 diabetes

**Authors**: Metcalf KM et al.

**Summary**: Nineteen patients aged 14–20 years of average fitness and adiposity with type 1 diabetes wore an accelerometer continuously for 3–5 days to estimate physical activity. The US guideline of accumulating 60 min/day of moderate-to-vigorous intensity physical activity was met by 63.2% of participants. Participants who accumulated 30 min/day more moderate-to-vigorous physical activity in the previous afternoon were 31% more likely to experience hypoglycaemia (assessed using continuous glucose monitoring) than those who accumulated less activity ($p=0.017$).

**Comment**: There really aren't any surprises from this research, but it is a nicely done piece of work to demonstrate what we see clinically. Promoting good levels of physical activity is important for all people with diabetes, types 1 and 2 alike. However, understanding the impact of exercise on glycaemic levels and medication adjustments is essential. It doesn't take too many episodes of significant hypoglycaemia to put people off trying to get good levels of intense exercise. The risk for this is of course greater in those with type 1 diabetes, and equipping individuals with skills to understand the likely effects of different types and durations of exercise and strategies to modify their insulin regimen appropriately is necessary.

*Reference: Diabetes Care 2014;37(5):1272–8*
Abstract

# Second-line agents for glycemic control for type 2 diabetes: are newer agents better?

**Authors**: Zhang Y et al.

**Summary**: These researchers developed and validated a new Markov model to simulate natural variation in HbA1c progression. They calibrated the model using a US dataset of privately insured individuals with type 2 diabetes, and compared treatment intensification of metformin monotherapy with sulfonylurea, dipeptidyl peptidase-4 inhibitor, glucagon-like peptide-1 receptor agonist or insulin therapy. The model showed that the regimens resulted in similar life-years and QALYs irrespective of glycaemic control goal, but sulfonylureas were associated with a significantly lower cost per QALY and the longest time to insulin dependence. Compared with 64 mmol/mol (8%), an HbA1c target of 53 mmol/mol (7%) was associated with higher QALYs for all regimens.

**Comment**: It continues to be one of the great debates in the management of diabetes; what is the most appropriate second-line agent after metformin? There are many factors to consider, such as effectiveness in glucose control, side effects, quality of life and cost. Whilst it is tempting to believe that newer agents with specific actions and profiles should intuitively be better at achieving control and minimising side effects, the field is littered with examples of drugs that have shown us that we can't make these assumptions. The glitazones are the most recent examples. It is also tempting to believe that with a greater range of agents, we can tailor our regimen to the specific phenotype of an individual patient. The reality, as demonstrated by this study, is that we aren't really in that space at this time.

*Reference: Diabetes Care 2014;37(5):1338–45*
Abstract

# The relationship between alcohol consumption and vascular complications and mortality in individuals with type 2 diabetes

**Authors**: Blomster JI et al.

**Summary**: The relationship between alcohol consumption and vascular outcomes was explored using data from ADVANCE (Action in Diabetes and Vascular Disease: Preterax and Diamicron Modified-Release Controlled Evaluation) trial participants. During follow-up of median 5 years, the respective mortality, CV event and microvascular complication rates were 9%, 10% and 10%. Compared with no alcohol consumption, moderate consumption was associated with fewer CV events, microvascular complications and deaths (respective adjusted hazard ratios 0.83 [95% CI 0.72, 0.95; p=0.008], 0.85 [0.73, 0.99; p=0.03] and 0.87 [0.75, 1.00; p=0.05]), particularly CV events and death from any cause among those who drank predominantly wine (0.78 [0.63, 0.95; p=0.01] and 0.77 [0.62, 0.95; p=0.02]). Heavy alcohol consumption was associated with dose-dependent increased risks of CV events and all-cause mortality compared with no alcohol consumption.

**Comment**: Interpret with caution. The question of whether moderate alcohol consumption is beneficial to health has been explored in many epidemiological studies. The general observation is a U-shaped curve, with the lowest risk of CV disease in those with a moderate intake, particularly red wine. The present report is from the ADVANCE study, which was an RCT of intensive versus standard glycaemic control in patients with type 2 diabetes at high risk of CV events. It was not an RCT of alcohol intake versus abstinence. Therefore the report is simply an observational study within this trial population. The findings are of interest, and broadly in agreement with similar studies in populations without diabetes, but should not be used to promote alcohol use for health benefit. I will still be having my glass of wine with dinner tonight though.

*Reference: Diabetes Care 2014;37(5):1353–9*
Abstract

# Increased intestinal permeability to oral chromium ($^{51}$Cr)-EDTA in human type 2 diabetes

**Authors**: Horton F et al.

**Summary**: This research examined intestinal permeability using $^{51}$Cr-EDTA urinary recovery in 20 men with well-controlled type 2 diabetes and matched controls. Compared with controls, the men with diabetes had significantly increased intestinal permeability (p=0.002), which correlated with increased systemic levels of high-sensitivity C-reactive protein (r=0.694 [p=0.001]), interleukin-6 (r=0.548 [p=0.012]) and tumour necrosis factor-$\alpha$ (r=0.564 [p=0.010]).

**Comment**: There has been a lot of interest over the last decade on the association between low-grade systemic inflammation and type 2 diabetes. It is often somewhat of a chicken and egg discussion with regard to its causal direction. This study addressed this question. The notion being that increased gut permeability allows the passage of bacterial endotoxins promoting a systemic inflammatory response. Utilising labelled chromium as a marker of this, the study demonstrated significantly greater gut permeability in those with diabetes compared with matched controls. This is a very interesting finding and supports the hypothesis, although still doesn't definitively explain whether this increased permeability is an early feature of diabetes or whether it is a feature that develops as a later complication.

*Reference: Diabet Med 2014;31(5):559–63*
Abstract

# The relationship between metformin therapy and sleep quantity and quality in patients with type 2 diabetes referred for potential sleep disorders

**Authors**: Kajbaf F et al.

**Summary**: Metformin-treated patients with potential sleeping disorders (n=314) and those not treated with metformin (n=73) were retrospectively compared in this observational study. Compared with metformin nonusers, metformin users had significantly longer total sleep time (399 vs. 363 min [p=0.002]) and better sleep efficiency (77.9% vs. 71.5% [p=0.003]), differences that persisted after adjustment for covariates, including BMI, which was significantly higher among metformin users (median 37.5 vs. 34.8 kg/m$^2$ [p=0.045]).

**Comment**: The area of sleep and metabolic risk is currently very active, with evidence that short sleep duration is associated with insulin resistance and type 2 diabetes. This is a retrospective analysis of people referred for sleep studies, comparing those taking metformin with those not. The observation that those on metformin had longer sleep duration, even after adjustment for age, BMI, neck circumference and other medication, is of great interest. However, the retrospective nature of the study and the small number of metformin nonusers make this difficult to interpret. The authors are well aware that to move this hypothesis forward, an RCT is required. Careful thought to the subject inclusion criteria would be required, particularly the diabetes status. Perhaps in the future metformin will become the sleeping tablet of choice!

*Reference: Diabet Med 2014;31(5):577–80*
Abstract

# Dietary dairy product intake and incident type 2 diabetes

**Authors**: O'Connor LM et al.

**Summary**: This was a prospective analysis of 7-day food diary data from a random subcohort (n=4000) and cases of incident diabetes (n=892, including 143 cases in the subcohort) within the EPIC-Norfolk Study followed for 11 years. No association was seen between the development of incident diabetes and dietary intake of total dairy, high-fat dairy, milk, cheese or high-fat fermented dairy products. Compared with the lowest tertiles, the highest tertiles of low-fat (<3.9%) dairy, low-fat fermented dairy and yoghurt intake were inversely associated with diabetes (respective adjusted hazard ratios 0.81 [95% CI 0.66, 0.98], 0.76 [0.60, 0.99; p=0.049 for trend] and 0.72 [0.55, 0.95; p=0.017 for trend]); the association with low-fat dairy was attenuated after further adjustments for anthropometric, dietary and diabetes risk factors.

**Comment**: Dairy products have had variable support as part of dietary recommendations. This study reported the associations between subgroups of dairy intake and incident diabetes over 11 years of a prospective cohort study. Overall, dairy consumption was not linked with the development of diabetes, and no subgroup was associated with an increased risk. However, low-fat dairy, most specifically yoghurt, appeared to be mildly protective. Whether this is due to specific positive components of these foods or negative effects of foods they may be substituting for cannot be answered by this study. However, it can be concluded that, with respect to metabolic risk, moderate consumption of low-fat dairy can be included as part of healthy dietary recommendations.

*Reference: Diabetologia 2014;57(5):909–17*
Abstract

# Using health primes to reduce unhealthy snack purchases among overweight consumers in a grocery store

**Authors**: Papies EK et al.

**Summary**: These researchers conducted a field experiment with a 2 (condition: health prime vs. control) × 2 (weight status: overweight vs. normal weight) between-participant design in which grocery store customers were given a recipe flyer that either contained a health and diet prime, or not. Questionnaire responses showed that overweight and obese participants who received the health prime purchased ~75% fewer snacks than control participants. While the prime was only effective when the participants paid initial attention to the flyer on which it was contained, conscious awareness of it during shopping was not necessary for its effects.

**Comment**: When considering the factors that influence obesity at an individual level, dietary choices are a major contributor. The foods that people choose are influenced by knowledge of nutrition and interpretation of package information, but there are so many other determinants, many outside the control of the individual. Most people get the majority of their food from supermarkets. Therefore, anything that can influence choice of foods purchased there is likely to have an impact on consumption. This study demonstrated a dramatic effect of a simple intervention at point of sale, which had a very positive effect on purchasing of snack foods. It is tempting to think that we should jump to roll out such an intervention, but this was a one-off shopping visit, and it is very likely that the impact would be attenuated over time. That is not to say that this may be usefully incorporated into other interventions, and it certainly warrants testing in a longitudinal study.

*Reference: Int J Obes 2014;38(4):597–602*
Abstract