In this issue:

- Physical and social environments affect incident type 2 diabetes
- Hypothyroidism increases diabetes risk
- Ethnicity and lower limb amputations in type 2 diabetes
- NZ-specific diabetes self-management education programme
- Fatty acid intake and risks of mortality, CV disease and type 2 diabetes
- Retrospective device data review in type 1 diabetes
- Type 1 diabetes and fracture risk
- Sugar intake increases progression to type 1 diabetes
- High-protein breakfast prevents bodyfat gain in adolescents
- Premeal water preloading helps with weight loss

Abbreviations used in this issue

CHD = coronary heart disease
CV = cardiovascular
HR = hazard ratio
RR = relative risk

Welcome to issue 98 of Diabetes and Obesity Research Review.

Among the research selected for this month’s issue, I have included two papers specific to NZ. One of these found that relative to European patients with type 2 diabetes, our Māori patients are more likely, and our Asian patients less likely, to require lower limb amputations. The second described good efficacy for an NZ type 2 diabetes self-management education programme. This is followed by a large meta-analysis in the BMJ on the highly topical subject of the impact of fatty acid intake on diabetes, CV diseases and mortality. It appears we may need to add fractures to our list of diabetes-related complications. We conclude this issue with two strategies for facilitating weight loss, namely high-protein breakfasts and preloading with water before a main meal.

I hope you find the research selected for this month interesting. I enjoy receiving your feedback, questions and suggestions, so please keep them coming.

Best regards,

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Longitudinal associations between neighborhood physical and social environments and incident type 2 diabetes mellitus

Authors: Christine PJ et al.

Summary: These researchers used data from 5124 participants without type 2 diabetes at baseline from the population-based MESA (Multi-Ethnic Study of Atherosclerosis) cohort study to explore the relationships between neighborhood physical and social environments and incident type 2 diabetes; 610 participants (12%) developed type 2 diabetes over 37,394 person-years of follow-up. The risk of developing type 2 diabetes was lowered by greater cumulative exposure to indicators of neighborhood healthy food (adjusted HR per interquartile range increase in summary score 0.88 [95% CI 0.79, 0.98]) and physical activity resources (0.79 [0.71, 0.88]), but not social environment (0.96 [0.88, 1.07]).

Comment: Diet and lifestyle factors are known important components to the risk of developing obesity and diabetes. Understanding the complexities of the determinants of healthy or unhealthy factors would help plan interventions to be tested to reduce risk. The built environment is often cited as one of the modifiable variables contributing to obesity, and this is one of the features of neighbourhoods. This study has taken complex data from a population cohort study and examined the association between characteristics of neighbourhoods and risk of incident diabetes. The results support the notion that environments with greater access to physical activity and healthier diets have lower risk of developing diabetes. This adds further support to the multifaceted approach to tackling obesity. What a great opportunity for Christchurch.

Abstract

Hypothyroidism is a risk factor for new-onset diabetes

Authors: Gronich N et al.

Summary: In the first phase of this study, biomedical data were subjected to high-throughput in silico processing to identify risk factors for the development of statin-associated diabetes, and in the second phase, the most prominent risk factor identified was confirmed in an observational cohort study. Statin nonusers (n=39,263) and propensity matched, highly compliant statin initiators in 2004–2005 (n=20,334) were followed until the end of 2010. The risk of developing diabetes was increased in the entire cohort by hypothyroidism and subclinical hypothyroidism, with hypothyroidism a risk factor for both statin users and nonusers (respective RRs 2.06 [95% CI 1.42, 2.99] and 1.20 [1.05, 2.64]), whereas subclinical hypothyroidism was a risk factor for only statin users (1.94 [1.13, 3.34] and 1.20 [0.62, 2.73]). Hypothyroidism was not a risk factor for diabetes in patients receiving thyroid hormone replacement therapy.

Comment: Autoimmune hypothyroidism is associated with type 1 diabetes through a shared propensity to autoimmunity. However, this study now also suggests that untreated hypothyroidism is also a risk factor for type 2 diabetes. Here, in a study designed to study the effect of statin use on risk of diabetes in a large cohort over a 5-year period, hypothyroidism doubled the incidence of diabetes. Those with subclinical hypothyroidism were also at increased risk, although only in those also taking a statin. This finding raises more questions than it answers, especially about potential mechanisms and interactions with statins. It may also reopen the debate about the need to treat subclinical hypothyroidism.

Reference: Diabetes Care 2015;38(9):1657–64
Abstract
Ethnicity and risk of lower limb amputation in people with type 2 diabetes

Authors: Robinson TE et al.

Summary: Primary-care and linked hospital record data for a cohort of 62,002 NZ patients with type 2 diabetes were prospectively analysed to explore the relationship between ethnicity and lower-limb amputation. During median follow-up of 7.14 years, 892 lower-limb amputations were undertaken (2.11 per 1000 person-years). Compared with Europeans, the risk of amputation was higher among Māori (adjusted HR 1.84 [95% CI 1.54, 2.19]) and lower among East and South Asians (0.18 [0.08, 0.44] and 0.39 [0.22, 0.67], respectively); these differences remained significant and substantial after further adjustments for available clinical variables.

Comment: Peripheral neuropathy and peripheral vascular disease are important complications of diabetes and increase the risk of ulceration and ultimately amputation. This study reported the rates of amputation in NZ and assessed the risk factors for this. Whilst amputation is an important and largely avoidable endpoint, the overall rates in NZ are actually quite low. However, what this study demonstrates is a large variation between ethnicities, highlighting a need to identify the determinants of this and work to address the factors creating these disparities. It is notable that similar patterns between ethnicities were evident across the range of diabetes complications, and therefore it is likely that there are common determinants. With our Pacific community having the highest relative rates of diabetes, details of the relative rates of complications for Pacific people would also be very helpful.

Reference: Diabet Med; Published online Jul 16, 2015

Abstract

Development of a structured diabetes self-management education program specific to the cultural and ethnic population of New Zealand

Authors: Gamble E et al.

Summary: These researchers developed and piloted a self-management education programme specifically for NZ patients with type 2 diabetes. The development of the programme involved a literature review, consultation with end-user groups and drafting the content, and used concepts and content from similar international programmes. Extensive testing of the content and concept was undertaken in discussion groups of 71 individuals with type 2 diabetes and practice nurses with the aim of ensuring the unique cultural needs of NZ patients were met. The programme was piloted in 27 patients with type 2 diabetes, of whom attended four of the six sessions. The final programme (which now requires a longitudinal trial) incorporated feedback from the participants, observing nurses and facilitators.

Comment: Enhancing self-management has been identified as an important component of effective care of all chronic diseases. There have been many studies demonstrating efficacy of self-management programmes internationally, with a range of designs and level of healthcare professional involvement. However, it cannot be assumed that these programmes can be directly translated to the NZ context, as our population is unique and our societal structure and healthcare system are different than the populations in which the original studies were conducted. This manuscript describes the process of translating this international evidence into a programme for self-management specific to NZ. It would be good to think that we can use this experience across the country, as it does not make sense to reinvent the wheel in every DHB. That is not to say that one size does or should fit all, but rather an attempt to reduce wasted effort and money through unnecessary duplication.

Reference: Nutr Diet; Published online Feb 6, 2015

Abstract
**Intake of saturated and trans unsaturated fatty acids and risk of all cause mortality, cardiovascular disease, and type 2 diabetes**

*Authors: de Souza RJ et al.*

**Summary:** This was a systematic review and meta-analysis of prospective cohort studies reporting relevant data on associations between dietary saturated and trans unsaturated fat intake and mortality, CV diseases and type 2 diabetes. Significant associations were seen between total trans fat intake (2–7 comparisons for 12,942–230,135 participants) and all-cause mortality (HR 1.21 [95% CI 1.10, 1.33]), CHD mortality (1.28 [1.09, 1.50]) and total CHD (1.10 [0.95, 1.27]), but not ischaemic stroke (1.07 [0.88, 1.28]) or type 2 diabetes (1.10 [0.95, 1.27]). Moreover, the higher risks of CHD and CHD mortality were present for industrial but not ruminant trans fats (HRs 1.42 vs. 0.93 and 1.18 vs. 1.01, respectively). An inverse association was seen between ruminant trans-palmitoleic acid intake and type 2 diabetes (HR 0.58 [95% CI 0.46, 0.74]). Certainties for the associations were ‘very low’ for saturated fats and all outcomes, ‘moderate’ for trans and total CHD, and ‘high’ for trans-palmitoleic acid intake and type 2 diabetes.

**Comment:** There has been a long held belief that saturated fat is harmful, with respect to risk of both CV disease and type 2 diabetes. Together with evidence that high-fat diets contribute towards obesity, this has underpinned policy and dietary guidelines for the last 30 years. However, there have been claims that saturated fat is not as harmful as we have believed, and with growing focus on negative effects of high intakes of refined carbohydrate, the fat debate has been reignited. This meta-analysis of observational studies examining the associations between saturated or trans fats and CV disease and type 2 diabetes, puts further doubt on the long-held conclusions from this is poor. Evidence for harm is stronger for trans fats. I don’t believe that this study is reason to completely change our dietary advice, but it does strengthen the argument for a more flexible approach – an individualised dietary prescription taking into account the goals of that intervention, balanced against the existing risk factors and comorbidities.

Reference: BMJ 2015;351:h3978

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**A minority of patients with type 1 diabetes routinely downloads and retrospectively reviews device data**

*Authors: Wong JC et al.*

**Summary:** The proportion of patients with type 1 diabetes who regularly download and review their blood glucose and insulin dosing data was determined in this cross-sectional survey of 155 adults and 185 caregivers of children with the disease. The respective proportions of adults and caregivers reporting ever downloading data from >1 device were 31% and 56%, the proportions of routine downloaders (>4 times in the prior year) were 20% and 40% and the proportions of routine reviewers (reviewed ‘most’ of their downloaded data) were 12% and 27%. Routine review was associated with a lower mean HbA1c level in adults and children (7.2% vs. 8.1% [p=0.03] and 7.8% vs. 8.6% [p=0.001], respectively). Each 10-year increase in age among the adults was associated with a greater likelihood of being a a routine reviewer of >1 devices (adjusted odds ratio 1.5 [95% CI 1.1, 2.1]), as was each 10 years since diagnosis (1.7 [1.2, 2.4]).

**Comment:** I often say to people with diabetes, don’t prick your finger unless you are going to do something with the information. There seem to be many barriers for people to really get the best value out of self-monitoring of blood glucose. Whilst the modern meters are very quick to process the sample and give a result, time taken for the whole exercise is still often cited as a barrier. The discomfort of pricking a finger is also a barrier, particularly with very frequent testing. Fewer and fewer people appear to be prepared to use a record book on a regular basis, and even with phone apps available to futil function this, this is still infrequently utilised. The memory function of meters does enable downloaded data to be stored, and this can be very informative – so long as the date and time are correctly set! This study demonstrates this very nicely. Those who regularly downloaded and interrogated their meters had significantly better glycaemic control. We can’t conclude that this is the cause of the better control as it may simply be a marker of other factors, but it is suggestive.

Reference: Diabetes Technol Ther 2015;17(8):555–62

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**References:**

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Type 1 diabetes and risk of fracture

Authors: Shah VN et al.

Summary: This meta-analysis and systematic review of 14 studies reported that compared with nondiabetics (n=136,579), patients with type 1 diabetes (n=27,300) had significantly greater rates of fracture events overall (7.6% vs. 3.1%; RR 3.16 [95% CI 1.51, 6.63], with double the risk for men and a 4-fold increased risk for women, and for hip and spinal fractures separately (3.78 [2.05, 6.98] and 2.88 [1.71, 4.82], respectively).

Comment: As if all the other complications of diabetes were not enough, it now appears that people with type 1 diabetes are also at a greater risk of fractures. This meta-analysis of existing epidemiological data demonstrates a significantly greater rate of fractures in those with diabetes, and a gender difference with women having greater risk than men. The authors recognise that these findings require further confirmation in a well-conducted prospective study, but the findings are compelling and require further detailed study to determine the mechanisms at play. Ultimately it may also require a strategic plan for screening individuals for risk and interventions to reduce this.

Reference: Diabet Med 2015;32(9):1134-42

Sugar intake is associated with progression from islet autoimmunity to type 1 diabetes

Authors: Lamb MM et al.

Summary: These authors followed 1893 children at increased genetic risk for type 1 diabetes in DAISY (Diabetes Autoimmunity Study in the Young) for the development of autoantibodies to insulin, GAD or protein tyrosine phosphatase-like protein and progression to type 1 diabetes. They also reviewed questionnaire data on dietary intake of various types of sugars and beverages. The children’s mean age at last follow-up was 10.2 years. Islet autoimmunity developed in 142 children and 42 progressed to type 1 diabetes. Among children who developed islet autoimmunity, total sugar intake was associated with progression to type 1 diabetes (HR 1.75 [95% CI 1.07, 2.85]), and increased sugar-sweetened beverage intake was associated with progression to type 1 diabetes in children with a high-risk HLA (human leucocyte antigen) genotype (1.84 [1.25, 2.71]), but not those without genetic risk (p=0.02 for interaction). No associations were evident between sugar variables and islet autoimmunity risk.

Comment: Most of the recent focus on sugar and sugar-sweetened beverages has been on the association with obesity and type 2 diabetes. This study addressed whether there is a link between sugar intake and type 1 diabetes. By taking a group of children at known risk of type 1 diabetes by positivity of autoantibodies, the authors demonstrated that sugar intake was directly associated with increased progression to diabetes. At present we do not have any therapies with proven benefit to reduce the progression of those with positive antibodies to diabetes. This study suggests the need for a prospective intervention study to test whether reduction of sugar intake and/or avoidance of sugar-sweetened beverages in this group may have an important role in reducing this progression.

Reference: Diabetologia 2015;58(9):2027–34

A high-protein breakfast prevents body fat gain, through reductions in daily intake and hunger, in ‘breakfast skipping’ adolescents

Authors: Leidy HU et al.

Summary: These researchers randomised 57 overweight/obese adolescents to a 1464kJ breakfast with 13g (normal) or 35g (high) protein or to continue to skip breakfast in this 12-week trial. Fat mass increased by 1.6kg and 0.3kg in the no breakfast and normal-protein breakfast groups, respectively, but decreased by 0.4kg in the high-protein breakfast group. Similarly, daily intake increased by 1556kJ and 494kJ in the control and normal-protein groups, and decreased by 1724kJ in the high-protein group. The high-protein group also had a significant reduction in daily hunger compared with the control group (p<0.05). None of these outcomes differed significantly between the normal- and high-protein groups.

Comment: It is commonly stated that breakfast is the most important meal of the day. Many people struggle with having breakfast on a regular basis (something I cannot understand). There is evidence that missing breakfast is associated with obesity. There is also evidence that protein may have greater satiating properties than carbohydrate, and therefore a high-protein diet may have benefits in weight management. However randomised controlled trials have not been conclusive in demonstrating this. This small study in overweight adolescents who habitually skip breakfast has shown that the addition of a high-protein diet does result in reduced consumption of food later in the day and reduced bodyweight over 12 weeks. This is encouraging, but very short-term. Therefore a much longer trial needs to be done to confirm these findings and establish whether they are sustainable.

Reference: Obesity 2015;23(9):1761-4

Efficacy of water preloading before main meals as a strategy for weight loss in primary care patients with obesity

Authors: Parretti HM et al.

Summary: Obese adults received a 30-minute face-to-face bodyweight management consultation at baseline and were then randomised to drink 500mL of water 30 minutes before their main meals (n=41) or to an attention control group in which they were asked to imagine their stomach was full before meals (n=43); each participant also received a 10-minute follow-up telephone consultation at 2 weeks. Compared with the attention control group, participants who preloaded with water experienced a 1.2kg greater bodyweight loss at 12 weeks after adjusting for ethnicity, deprivation, age and gender (primary outcome; p=0.028).

Comment: Weight loss requires a deficit of energy intake compared with expenditure over a prolonged period of time. There is plenty of evidence that targeting energy intake is more likely to result in weight loss than targeting expenditure. Therefore anything that helps a sustained reduction of intake could be an effective strategy. By ‘preloading’ with water before the main meal of the day, thus increasing satiety and reducing the likelihood of overconsumption of intake at the meal, people may reduce their total daily energy intake. This small randomised controlled trial gives preliminary evidence that this might be a useful approach. The 12-week intervention did facilitate a modest additional weight loss compared with the control. A longer trial to demonstrate sustainability is required, but it is a simple, essentially free, easily translated intervention that could be promoted in public health messages.

Reference: Obesity 2015;23(9):1785–91

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