



Diabetes & Obesity Research Review™

Making Education Easy

Issue 89 – 2014

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Abbreviations used in this issue

- BP** = blood pressure
HbA_{1c} = glycosylated haemoglobin
HR = hazard ratio
RCT = randomised controlled trial

Welcome to issue 89 of Diabetes and Obesity Research Review.

The final issue for 2014 includes a useful report from the UK NHS (National Health Service) on costs associated with providing footcare to patients with diabetes. Spanish research has identified a possible link between type 1 diabetes and reduced fertility, particularly in women. US researchers' attempts at improving the diets of schoolchildren by providing a healthy corner store intervention were, unfortunately, unsuccessful. On a brighter note to end the year, encouraging results were seen when pharmacists led an intervention to help manage type 2 diabetes in the community.

I look forward to bringing you our next issue of Diabetes Research Review in 2015.

Best wishes for happy and safe holidays,

Dr Jeremy Krebs

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Glycemic control and excess mortality in type 1 diabetes

Authors: Lind M et al.

Summary: This research included 33,915 Swedish registry patients with type 1 diabetes each matched to five controls from the general population. During mean follow-up periods of 8.0 and 8.3 years, respectively, the mortality rate was greater in the diabetes group than the control group (8.0% vs. 2.9%; adjusted HR 3.52 [95% CI 3.06, 4.04]), including a higher cardiovascular-related mortality rate (2.7% vs. 0.9%; 4.60 [3.47, 6.10]). Multivariable analyses revealed increasing respective all-cause and cardiovascular-related mortality risks as HbA_{1c} level increased among diabetics versus controls (adjusted HRs 2.36 and 2.92 for HbA_{1c} level ≤52 mmol/mol [≤6.9%], 2.38 and 3.39 for 53–62 mmol/mol [7.0–7.8%], 3.11 and 4.44 for 63–72 mmol/mol [7.9–8.7%], 3.65 and 5.35 for 73–82 mmol/mol [8.8–9.6%] and 8.51 and 10.46 for ≥83 mmol/mol [≥9.7%]).

Comment: This study is somewhat sobering for December. We have quoted DCCT to our patients with type 1 diabetes as evidence that achieving tight glycaemic control is important for reducing the risk of microvascular complications. Even to say that if the HbA_{1c} level is less than 53mmol/mol, such risk is minimal. This may be true, but unfortunately this large registry study from Sweden showed that achieving tight control did not protect completely from excess macrovascular disease. It must be noted that poor glycaemic control conferred significantly greater risk, and is therefore still supportive evidence for aiming for tight control.

Reference: *N Engl J Med* 2014;371(21):1972–82

[Abstract](#)



Independent commentary by Dr Jeremy Krebs,

Endocrinologist & Clinical Leader at Wellington Hospital. He is also a Senior Clinical Lecturer with the University of Otago, and Director of the Clinical Research Diploma at Victoria University.

For full bio [CLICK HERE](#).



Merry Christmas and a healthy, happy 2015!

FROM THE TEAM AT

RESEARCH REVIEW





A cascade of care for diabetes in the United States: visualizing the gaps

Authors: Ali MK et al.

Summary: These researchers developed a 'cascade of care' concept for diabetes in adults using data from the US NHANES. They estimated 28.4 million adults had diabetes in 2012, 72.2% of whom were aware of their diagnosis. Of those diagnosed, 95.3% had a usual care provider to whom 91.7% had made ≥ 2 or more visits in the preceding year. Among undiagnosed adults, 84.5% had a usual care provider to whom 66.5% reported ≥ 2 visits in the preceding year. Respective individualised goals for HbA_{1c}, BP (<140/80mm Hg), lipid (LDL [low-density lipoprotein] cholesterol <2.6 mmol/L [<100 mg/dL]) and nonsmoking were met by 63.7%, 65.5%, 56.6% and 80.6% of diagnosed patients and by 77.0%, 57.9%, 36.0% and 77.9% of undiagnosed adults. A combined HbA_{1c}, BP and LDL cholesterol target was met by 26.7% and 22.1% of diagnosed and undiagnosed adults, respectively, and a combination target of all four goals (i.e. including nonsmoking) was met by 21.3% and 18.8%, respectively.

Comment: These data from the US are not dissimilar to those taken from our 'Get Checked' data. A combined achieved target of less than 25% of people meeting glucose, lipid and BP goals is appalling. In many cases though, this is not through lack of effort on behalf of clinicians or patients. In addition the acceptance of more individualised targets makes it harder to interpret these data. However, clinical inertia has been shown in other studies to be a major contributor. Of more concern are the group of patients who do not engage with primary care. They are hard to reach and even harder to motivate to engage. These data call for increased efforts to systematically standardise care, actively review practice data down to an individual patient level and proactively reach out to those not achieving targets, rather than depend on more patient-driven encounters. This is a real challenge that many primary-care systems are grappling with.

Reference: *Ann Intern Med* 2014;161(10):681–9

[Abstract](#)

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Disclaimer: This publication is not intended as a replacement for regular medical education but to assist in the process. The reviews are a summarised interpretation of the published study and reflect the opinion of the writer rather than those of the research group or scientific journal. It is suggested readers review the full trial data before forming a final conclusion on its merits.

Research Review publications are intended for New Zealand health professionals.

Incidence of remission in adults with type 2 diabetes

Authors: Karter AJ et al.

Summary: The incidence of diabetes remission was examined in 122,781 adults with type 2 diabetes in the Diabetes and Aging study; remission was defined as absence of ongoing antidiabetic therapy and an HbA_{1c} level of 39–46 mmol/mol (5.7–6.4%) for ≥ 1 year (partial remission) or an HbA_{1c} level <39 mmol/mol (<5.7%) for ≥ 1 year (complete remission) or ≥ 5 years (prolonged remission). The respective partial, complete or prolonged remission incidence densities were 2.8, 0.24 and 0.04 per 1000 person-years and the 7-year cumulative incidences were 1.47%, 0.14% and 0.007%. The 7-year cumulative incidence of any remission was 1.60% overall and 4.6% in those with a recent diabetes diagnosis (<2 years). Age >65 years, <2 years since diagnosis, baseline HbA_{1c} level <39 mmol/mol (<5.7%) and no diabetes medication at baseline were among the correlates for remission after adjustments.

Comment: When discussing treatment options with people with type 2 diabetes who are obese, it is not infrequent to be asked if people can reverse their diabetes. This is commonly in the context of a discussion about potential benefits of bariatric surgery versus escalation of drug treatment. This study provides useful real-world data to show just how rarely people do reverse diabetes without surgery. This does not mean that significant improvements in control and delays in progression to insulin therapy can't be achieved with weight loss through diet and lifestyle changes, but so-called 'remission' is rare.

Reference: *Diabetes Care* 2014;37(12):3188–95

[Abstract](#)

Cost of diabetic foot disease to the National Health Service in England

Authors: Kerr M et al.

Summary: Using national datasets and economic modelling, these authors estimated that diabetic footcare cost the UK NHS £580 million in 2010–2011, which was ~0.6% of the NHS's total expenditure in England. They estimated that £307 million was spent on ulcer care in primary and community settings. Hospital records showed that 8.8% of diabetes admissions included ulcer care or amputation. A regression analysis suggested that foot disease increased length of stay by a factor of ~2.5. The respective estimated costs of inpatient ulcer care and amputation were £219 million and £55 million.

Comment: I include this paper not because it is brilliant science, but because it addresses an important issue that is highly relevant to NZ. The paper reports on cost to the health system of diabetes-related footcare in the UK, and estimates this to be 0.6% of the total NHS budget. There are two important observations. The first was that half of this was for ulceration in a primary-care setting, and the second was the increased length of stay during hospital admissions. In NZ there are new guidelines and pathway for footcare in diabetes that should go a long way to prevent ulceration and amputation in diabetes. What is critically important is that these guidelines are implemented across the DHBs and that podiatry services are adequately staffed and resourced to manage the workload. Unfortunately, at present neither are the case. Note to planners and funders for 2015 – must try harder.

Reference: *Diabet Med* 2014;31(12):1498–504

[Abstract](#)



Socio-economic status and incident diabetes mellitus among employees in Denmark

Authors: Cleal B et al.

Summary: This prospective analysis of Danish registry data from 1005,572 men and 951,039 women aged 20–59 years explored the relationship between socioeconomic status and incident diabetes. There were 43,439 cases of incident diabetes recorded during 9533,199 person-years at risk among men and 29,266 cases among 9163,405 person-years among women. Compared with a 'professionals' socio-occupational reference group, other groups had an increased risk of developing diabetes, and excess fractions were 0.342 (95% CI 0.329, 0.354) and 0.359 (0.349, 0.369) for men and women, respectively.

Comment: This paper raises an interesting concept. In this very large Danish registry study, relative to professionals, other socio-occupational groups had an excess incidence of diabetes. Such studies always make big assumptions about those in occupational groups and are therefore open to major confounding. However, the authors raise a very interesting possibility that targeting individuals at risk in certain occupational settings could well be a very cost-effective strategy for preventing diabetes. Engaging with employers, particularly in larger workplaces, to work on weight management, food policies and activity opportunities could well yield results. Bus and taxi companies look ripe for the picking.

Reference: *Diabet Med* 2014;31(12):1559–62

[Abstract](#)

Impact of age, age at diagnosis and duration of diabetes on the risk of macrovascular and microvascular complications and death in type 2 diabetes

Authors: Zoungas S et al., for the ADVANCE Collaborative group

Summary: This was an analysis of data from 11,140 ADVANCE trial participants with type 2 diabetes who had been randomised to intensive or standard glucose control. Significant associations were seen between diabetes duration and risk of macrovascular events (adjusted HR 1.13 [95% CI 1.08, 1.17]), microvascular events (1.28 [1.23, 1.33]) and death (1.15 [1.10, 1.20]). Age (or age at diagnosis) was significantly associated with increased risks of macrovascular events (adjusted HR 1.33 [95% CI 1.27, 1.39]) and death (1.56 [1.48, 1.64]), but not microvascular events. No interactions were seen between diabetes duration, age and the risk of macrovascular events or death ($p > 0.4$ for both), but the effects of increasing diabetes duration on risk of microvascular events were greatest in younger versus older patients ($p = 0.002$).

Comment: Understanding risk for micro- and macrovascular complications for individuals with diabetes is an important part of our daily practice. This report from the ADVANCE dataset looked at the relationship between age and diabetes duration and complications. Although the number of participants in this trial was over 11,000, the results of this analysis must be interpreted with caution. Those enrolled were highly selected and are not representative of those seen most commonly in primary care. They were at high risk of a macrovascular event, either because they had already had one, or they had at least one risk factor and a duration of diabetes of at least 10 years. That said, the results align with what we might expect with diabetes duration being more important than age for microvascular disease, but both are important for macrovascular disease after adjustment for diabetes control.

Reference: *Diabetologia* 2014;57(12):2465–74

[Abstract](#)



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Fertility is reduced in women and in men with type 1 diabetes

Authors: Wiebe JC et al., on behalf of the T1DGC

Summary: This analysis of data from affected (n=3010) and unaffected (n=801) siblings aged ≥18 years from families included in the T1DGC (Type 1 Diabetes Genetics Consortium) explored the effect of type 1 diabetes on fertility. Unaffected individuals had more offspring than affected individuals, with the difference more pronounced in women than men. Sex and birth cohort significantly affected the between-group differences in a Poisson regression analysis. Among affected siblings, associations were seen between higher fertility and diabetes onset at age ≥18 years, female sex and older birth cohort.

Comment: This observational study assessed whether type 1 diabetes impacts on fertility. It used data from the genetics consortium, which includes siblings of those with diabetes, and compared the number of offspring between affected and unaffected siblings. Those with type 1 diabetes had fewer children and this was more pronounced in women. However, it isn't possible to determine from this study whether this is an infertility consequence of having diabetes or whether this may be personal choice and all the factors that may contribute to that. The observation that adult onset of disease was associated with a higher number of offspring might suggest that early onset of disease may have an effect on fertility, and this warrants further research.

Reference: *Diabetologia* 2014;57(12):2501–4

[Abstract](#)

Consumers believe nutrition facts labeling for added sugar will be more helpful than confusing

Authors: Kyle TK & Thomas DM

Summary: This paper reported responses of a voluntary online survey completed by 500 representative US adults. The respondents were asked how useful or confusing added sugar information on a nutrition facts panel would be and why. Most respondents (63%) reported that knowing the amount of sugar added to a food product would be helpful, while only 18% indicated they would find such information confusing. Being female significantly predicted the perceived helpfulness of the information on added sugar ($p < 0.03$).

Comment: The impact of nutritional food labelling is very controversial. This simple online survey conducted in the US showed that consumers believe that food labelling for added sugars would be helpful in informing them when making food choices. However, the proof is in the (Christmas) pudding. There is a risk that the more complex food labels become, the less accessible they are for consumers, and even potentially misleading. So whilst I applaud a nice simple survey for identifying a potential target, what is required is an RCT to test the hypothesis. Does the addition of added sugars to a label change purchasing patterns? Ultimately even this is only an intermediate step in whether it reduces obesity.

Reference: *Obesity* 2014;22(12):2481–4

[Abstract](#)

A randomized controlled study of a healthy corner store initiative on the purchases of urban, low-income youth

Authors: Lent MR et al.

Summary: School students (n=767) from ten schools were randomised to a healthy corner store intervention or an assessment-only control, with food and beverage purchases assessed over a 2-year period. No significant difference was seen between intervention and control schools at years 1 and 2 for energy content derived from store purchases, students' body-mass index or obesity prevalence.

Comment: Have you seen what students buy and consume on the way to school? It astounds me how much rubbish I see being eaten for what I assume is breakfast. Most schools have a tuckshop or a dairy or fast-food shop very close by. Therefore if modifying the food sold in these could influence consumption, this may be a good target for combating childhood obesity. Sadly in this RCT there was no impact of such an intervention over 2 years. There were no differences between energy content of food purchased and therefore not surprisingly no difference in bodyweight. Pricing strategies may be a better way to influence this. When are hot chips ever the right answer for breakfast?

Reference: *Obesity* 2014;22(12):2494–500

[Abstract](#)

Cost-effectiveness of reducing glycaemic episodes through community pharmacy management of patients with type 2 diabetes mellitus

Authors: Hendrie D et al.

Summary: This Australian research compared a pharmacist-led diabetes education programme with standard care in patients with type 2 diabetes from Perth; eight community pharmacies were paired, with one randomised to deliver intervention with the other assigned as controls. The programme cost AU\$394 per patient to implement for the 6-month intervention period. Compared with controls, the intervention was associated with significantly greater reductions in the number of hyperglycaemic and hypoglycaemic episodes (respective odds ratios 0.34 [95% CI 0.22, 0.52; $p=0.001$] and 0.54 [0.34, 0.86; $p=0.009$]), with a net reduction in glycaemic episodes of 1.86 days per patient per month. Relative to standard pharmacy care, the cost-effectiveness of the programme was AU\$43 per day of glycaemic symptoms avoided. Furthermore, surveyed patients with type 2 diabetes indicated they were willing to pay an average of 1.9 times that amount to avoid 1 day of hypoglycaemia.

Comment: With increasing numbers of people with type 2 diabetes, it is important that we look for new opportunities to influence care, particularly in community and primary-care settings. Community pharmacies are increasingly being seen as a possible focus for long-term condition management. This RCT assessed whether a pharmacist-led education programme is cost effective for reducing symptomatic glycaemic excursions. The conclusion was that it is, and particularly when compared with what people with type 2 diabetes would be prepared to pay to avoid hypoglycaemia. It would have been useful to know whether this also impacts on HbA_{1c} level, and this should be an outcome tested in a longer RCT. However, these results are encouraging, that community pharmacists may have an important role to play.

Reference: *J Prim Prev* 2014;35(6):439–49

[Abstract](#)

Erratum

In the previous issue of Diabetes Research Review ([issue 88](#)), our summary of the study 'Metformin and low levels of thyroid-stimulating hormone in patients with type 2 diabetes mellitus' by Fournier J-P et al. incorrectly stated:

"Compared with sulphonylurea monotherapy, metformin monotherapy was associated with a significantly lower incidence rate of low TSH levels in patients with treated hypothyroidism (79.5 vs. 125.2 per 1000 person-years; adjusted HR 1.55 [95% CI 1.09, 2.20]), particularly 90–180 days after starting treatment (2.30 [1.00, 5.29]), but not in euthyroid patients (0.97 [0.69, 1.36])."

The correction for this sentence is as follows:

"Compared with sulphonylurea monotherapy, metformin monotherapy was associated with a significantly **higher** incidence rate of low TSH levels in patients with treated hypothyroidism (**125.2 vs. 79.5 per 1000 person-years**; adjusted HR 1.55 [95% CI 1.09, 2.20]), particularly 90–180 days after starting treatment (2.30 [1.00, 5.29]), but not in euthyroid patients (0.97 [0.69, 1.36])."