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Welcome to issue 101 of Diabetes and Obesity Research Review, the final issue for 2015. Authors from the Clinical Network for Children with Diabetes in New Zealand report widespread under-resourcing of DHB secondary-care diabetes clinics for children and adolescents with type 1 diabetes. Other NZ research highlights differences between patients with a high BMI compared with normal BMI patients at Christchurch Hospital. The year ends with two systematic reviews and meta-analyses. The first one, which involves data from nearly 6 million individuals, reports incident type 2 diabetes risks associated with various smoking statuses. The other attempts to compare the effects of low-fat diets versus a variety of other diets on bodyweight loss.

I hope your year has been enjoyable and productive, and I look forward to returning with our next issue in January.

Best regards,

Associate Professor Jeremy Krebs
jeremykrebs@researchreview.co.nz

Development and validation of risk prediction equations to estimate future risk of blindness and lower limb amputation in patients with diabetes

Authors: Hippisley-Cox J & Coupland C

Summary: This prospective cohort study used data from 454,575 patients with diabetes from 763 general practices in England to develop risk prediction equations to quantify the absolute risks of blindness and amputations. During follow-up, 4822 new cases of lower-limb amputation and 8063 new cases of blindness developed in this derivation cohort. The algorithms, which are based on variables likely to be known by the patients or recorded in the general practice computer systems, identify patients at high risk for prevention or further assessment. Two validation cohorts (142,419 patients from 254 practices and 206,050 from 357 practices) confirmed good calibration of the equations, and good discrimination was demonstrated for both men and women in the latter cohort for amputation and blindness.

Comment: Retinopathy leading to blindness and peripheral neuropathy with or without peripheral vascular disease leading to lower-limb amputation are two of the major microvascular complications of diabetes. Identifying those who are at greatest risk of these would allow targeted and more aggressive intervention to reduce this risk. Just as we have risk prediction equations for macrovascular disease derived from ‘real-world’ population data, this study reports the derivation of a similar prediction equation for the risks of blindness and amputation. The final models for blindness in men and women included age, cholesterol/HDL cholesterol ratio, systolic blood pressure, HbA1c level, deprivation, duration of diabetes, type of diabetes, chronic renal disease and existing proliferative retinopathy or maculopathy. The final model for lower-limb amputation had similar factors, with some additional components. In women it included age, systolic blood pressure, HbA1c level, deprivation, duration of diabetes, smoking status, ethnicity, rheumatoid arthritis, congestive cardiac failure, peripheral vascular disease and chronic renal disease. The final model in men also included type of diabetes and atrial fibrillation. These models could be incorporated into practice management systems. However, it cannot be assumed that they will have the same predictive precision in an NZ population as they did in the UK. Validation would be worthwhile.

Reference: BMJ 2015;351:h5441

Merry Christmas and a healthy, happy 2016!

FROM THE TEAM AT RESEARCH REVIEW

Independent commentary by Associate Professor Jeremy Krebs, an endocrinologist with a particular interest in obesity and diabetes. He is an Associate 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.
Care for children and adolescents with diabetes in New Zealand District Health Boards: is the clinical resourcing ready for the challenge?

Authors: Jefferies C et al., for the Clinical Network for Children with Diabetes in New Zealand, on behalf of the Paediatric Society of New Zealand diabetes clinical network

Summary: This NZ research sought to determine the clinical resources available to manage children and adolescents with diabetes. Survey data regarding specialist services provided in 2012 were compiled by all the 21 DHB secondary-care sites approached. Among the 1587 patients aged ≤18 years with diabetes managed by these DHBs, >95% had type 1 diabetes, including 16% who were on insulin-pump therapy. Many of the centres did not have data available on clinic HbA1C levels. The median staffing for specialists such as general paediatricians or paediatric endocrinologists was 0.2 per 100 patients, whereas for diabetes nurses it was 0.7 per 100 patients. Only three of the centres provided psychology services and social workers.

Comment: The results of this study will probably not come as any surprise to many of you. The support and care of children and adolescents with diabetes and their families is time-consuming and often very intensive. This is particularly the case at the time of diagnosis and in those diagnosed at very young ages. This study highlights that in NZ there is significant variability across the country in the resourcing of services to meet the needs of this group of patients. Access to psychological expertise is perhaps the most scarce, which can be a major challenge for adolescents. With an increasing focus on primary-care based management of type 2 diabetes, it is very important that funders do not lose sight of the importance of specialist teams in the care of those with type 1 diabetes across all age ranges.


Abstract

Differences in acute general surgical admissions between obese or overweight patients compared to normal-sized patients

Author: Flint R

Summary: This prospective observational study from Christchurch Hospital compared patterns of acute general surgical admissions between patients with a BMI >25 kg/m² (n=2676) versus a normal BMI. Compared with patients with a normal BMI, those in the high BMI group were younger (48.3 vs. 50.5 years [p=0.0001]), had a shorter hospital stay (2.9 vs. 3.2 days [p=0.14]), and were more likely to need a theatre visit (34% vs. 29%; p=0.0001), had access to psychological expertise (13% vs. 8%; p=0.015) or financial assistance (1.84 [1.60, 2.10]), and have biliary conditions (13% vs. 8%; p=0.015) or pancreatitis (6% vs. 4%; p=0.015) or gastrointestinal bleeding (4% vs. 6%; p=0.015). With a normal BMI, those in the high BMI group were younger (48.3 vs. 50.5 years [p<0.0001]), had a shorter hospital stay (2.9 vs. 3.2 days [p=0.14]), and were more likely to need a theatre visit (34% vs. 29%; p=0.0001), had access to psychological expertise (13% vs. 8%; p=0.015) or financial assistance (1.84 [1.60, 2.10]), and have biliary conditions (13% vs. 8%; p=0.015) or pancreatitis (6% vs. 4%; p=0.015) or gastrointestinal bleeding (4% vs. 6%; p=0.015). With a normal BMI, those in the high BMI group were younger (48.3 vs. 50.5 years [p<0.0001]), had a shorter hospital stay (2.9 vs. 3.2 days [p=0.14]), and were more likely to need a theatre visit (34% vs. 29%; p=0.0001), had access to psychological expertise (13% vs. 8%; p=0.015) or financial assistance (1.84 [1.60, 2.10]), and have biliary conditions (13% vs. 8%; p=0.015) or pancreatitis (6% vs. 4%; p=0.015) or gastrointestinal bleeding (4% vs. 6%; p=0.015).

Comment: Obesity is changing the pattern of modern health and illness. As highlighted in this study, obese individuals admitted to acute surgical services in a tertiary hospital were younger than normal weight individuals and more likely to have gallstone-related disease. Somewhat surprisingly they had a shorter length of stay. Other evidence has suggested the opposite with a longer length of stay, delays in time to diagnosis and greater difficulty with diagnosis due to difficulty with procedures. Furthermore obese individuals have higher rates of postoperative complications. These are some of the less well-publicised consequences of obesity that should be taken into consideration in government policy and action to fight obesity.


Prescribing practices and clinical predictors of glucose-lowering therapy within the first year in people with newly diagnosed type 2 diabetes

Authors: Mol A et al.

Summary: These researchers followed 1158 enrollees in a Danish type 2 diabetes cohort, who were from outpatient hospital clinics and general practices, to investigate prescribing practices and predictors of glucose-lowering therapy during the first year of a type 2 diabetes diagnosis. Glucose-lowering therapy was prescribed to 26% of the patients within their first year, 62% received monotherapy, among whom 95% received metformin, and 12% received >1 drug. Predictors of receiving any versus no therapy and combination versus monotherapy were age <40 years (relative risk ratios 1.29 [95% CI 1.16, 1.44] and 3.60 [2.36, 5.50]), high Charlon Comorbidity Index (1.20 [1.05, 1.38] and 2.08 [1.16, 3.72]), central obesity (1.23 [1.04, 1.44] and 1.93 [0.76, 4.94]), fasting blood glucose level ≥7.5 mmol/L (1.25 [1.10, 1.42] and 1.94 [1.02, 3.71]) and HbA1C level ≥8% (1.25 [1.10, 1.42] and 2.86 [1.97, 4.14]). Therapy was also predicted by bodyweight gain of ≥30kg since the age of 20 years, lack of physical exercise and C-peptide level <30 pmol/L.

Comment: I am often asked whether we should be commencing everyone on medical therapy at the time of initial diagnosis of type 2 diabetes. Of course the answer is that we should be individualising treatment, and not everyone needs drugs immediately, but equally some need multiple therapy from the start. This study describes some of the clinical predictors at the time of diagnosis that may identify those who will be on drug treatments within the first year. As expected, worse glycaemic control at baseline is a strong predictor. Of interest younger age was also predictive. From this study it is not possible to determine whether this is reflective of worse control, or of practice differences amongst clinicians identifying younger patients at greater risk of future complications and therefore having a lower threshold for intervention. Whilst interesting, this does not change our practice, which remains an individualised assessment, including but not exclusive to the factors identified here.


Abstract

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Routine use of continuous glucose monitoring in 10 501 people with diabetes mellitus

Authors: Battelino T et al.

Summary: This research explored glucose sensor use in 10,501 patients with type 1 and type 2 diabetes among whom 7916 had used glucose sensors for ≥15 days over a 6-month period during the 2-year observation period. Compared with patients with nil or <25% sensor use, those with ≥75% use had significantly lower mean and standard deviation of blood glucose level, were more likely to achieve a mean blood glucose level of <8.6 mmol/L (OR 1.5 [95% CI 1.3, 1.7]) and had 50% fewer hypoglycaemic episodes. Among new glucose sensor users, predictors of early discontinuation included use during the first month of therapy and lack of full reimbursement, whereas glycaemic control measures predicted discontinuation during long-term treatment.

Comment: Currently in NZ we do not have funded access to CGM for routine care of patients with diabetes. This present study and others have demonstrated that use of CGM can help facilitate better glycaemic control and reduce rates of hypoglycaemia. However, even when funded CGM is available, there is often an attrition rate in usage of the device. This study identified use during the first month as a strong predictor of continued use in those combining it with pump therapy. One of the factors that contribute to reduced usage/ adherence is the physical and psychological burden of being attached to a device(s). However, in the subset of patients who have frequent hypoglycaemia, the benefits of a reduction in the frequency of these may well offset this burden. There is certainly a place for the use of CGM in modern diabetes management, with or without insulin pump therapy.


Marijuana use and risk of prediabetes and diabetes by middle adulthood

Authors: Bancks MP et al.

Summary: Using data from CARDIA (Coronary Artery Risk Development in Young Adults) study participants, these researchers explored cross-sectional and longitudinal associations between self-reported marijuana use and both prediabetes and diabetes. Self-reported current marijuana use decreased over the study’s follow-up period. Analyses of prediabetes and diabetes prevalences in 3034 participants found that compared with marijuana never-users, participants reporting current marijuana use and lifetime use of ≥100 times had higher likelihoods of prediabetes (respective adjusted ORs 1.65 [95% CI 1.15, 2.38] and 1.49 [1.06, 2.11]), but not diabetes, at CARDIA examination year 25. Similarly over 18 years of follow-up (n=3151), participants reporting lifetime marijuana use of ≥100 times were at greater risk of prediabetes than never-users (hazard ratio 1.39 [95% CI 1.13, 1.71]), but not diabetes.

Comment: Marijuana use in young adults is relatively common, although for many this is for a brief period of time and at low levels of exposure. However, some continue to use it for many years. This study explored the relationship between chronic marijuana use and risk of developing metabolic dysfunction. Marijuana use was associated with a greater risk of prediabetes by middle adulthood. This did not extend to diabetes, which raises doubt over the biological link. However, low absolute rates of diabetes in this age group are likely to be a factor in this lack of association. Whether there is a direct biological mechanism or whether marijuana use is a marker of other important lifestyle factors, such as poor diet or sedentary behaviour, is not possible to determine from this study. However, these data support the stance of not legalising marijuana and continuing to discourage its use.


Abstract

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Low-density-lipoprotein cholesterol concentrations and risk of incident diabetes

Authors: Andersson C et al.

Summary: These authors sought to relate blood LDL cholesterol levels and genetic risk score for LDL cholesterol to incident diabetes risk in 8011 Framingham Heart Study participants (14,120 person-observations) who did not receive lipid-modifying or antihypertensive medications and were cardiovascular disease-free at baseline; incident diabetes developed in 312 participants during mean 4.5 years follow-up. A significant association was seen between genetic risk score and LDL cholesterol level (adjusted estimated influence 0.24 [p<0.0001]). Multivariable models revealed that each standard deviation increase in LDL cholesterol level and in genetic risk score was associated with lower risks of incident diabetes (respective ORs 0.81 [95% CI 0.70, 0.93] and 0.85 [0.76, 0.96]).

Comment: It is now well established that although statins have a major beneficial role in reducing the risk of cardiovascular disease, in those without existing diabetes, they increase the risk of developing type 2 diabetes by a small amount. The mechanism for this is not understood. The present study adds an interesting perspective to this issue. In the Framingham offspring study, those who were not taking statins and did not have diabetes were assessed for incident diabetes based on LDL cholesterol level. A low LDL cholesterol level increased the risk of developing diabetes over time. This may suggest that the observations with statin therapy are due to the reduction in LDL cholesterol level rather than any other specific statin effect. This is of course speculation, but does warrant further study.


Abstract

Clinical review: insulin pump-associated adverse events in adults and children

Authors: Ross PL et al.

Summary: The current and past literature on adverse effects of insulin pumps was discussed in this paper. Potential metabolic and nonmetabolic adverse events were covered, particularly pump malfunction, infusion set/site issues and cutaneous problems. Adverse events occurred in >40% of users each year. A minority of these required hospitalisation, although children were particularly at risk. Hyperglycaemia and ketosis were the most common consequences with current pumps, usually required hospitalisation, although children were particularly at risk. Hyperglycaemia and ketosis were the most common consequences with current pumps, usually associated with infusion set failure; infections at infusion sites were the most common problem with older technologies.

Comment: Insulin pumps delivering continuous subcutaneous insulin as an infusion are increasingly being used in the management of type 1 diabetes. In NZ the proportion of those with type 1 diabetes using pumps has dramatically increased since the introduction of funding for pumps and consumables by PHARMAC. There is abundant evidence to support the use of pump therapy to facilitate better glycaemic control, particularly when there are frequent hypoglycaemic events despite the use of analogue insulins. However, pumps are not without their problems. This review paper highlighted the issues, reporting that 40% of pump users will have an adverse event per year of use. These are most commonly hyperglycaemia and/or ketoadisosis secondary to infusion set failure. However, with many pump users starting with this technology at a very young age, there are emerging issues with infusion-site changes, which can create issues with appropriate access. It will be interesting to observe whether this becomes a barrier to long-term pump use.


Abstract

Relation of active, passive, and quitting smoking with incident type 2 diabetes

Authors: Pan A et al.

Summary: This was a systematic review and meta-analysis of 88 prospective studies (n=5,988,795) reporting data on type 2 diabetes risk according to baseline smoking status; there were 295,446 incident cases of type 2 diabetes. Compared with never-smokers, current and former smokers had significantly increased risks of type 2 diabetes (respectively ORs 1.37 [95% CI 1.33, 1.42] and 1.14 [1.10, 1.18], as was the risk for never-smokers with versus without exposure to passive smoke (1.22 [1.10, 1.35]). Moreover, a dose-response relationship was seen between current smoking and diabetes risk, with respective ORs of 1.21, 1.34 and 1.57 for light, moderate and heavy smokers compared with never-smokers. Based on the assumption of a causal association, an estimated 11.7% of cases of type 2 diabetes in men and 2.4% in women were attributable to active smoking. There was also evidence of a reduction in risk of type 2 diabetes as duration since quitting smoking increased, with respective ORs of 1.54, 1.18 and 1.11 for former smokers who had quit for <5, 5–9 and ≥10 years.

Comment: There is unequivocal evidence that cigarette smoking is detrimental to health across a range of outcomes, including cancer, heart disease and metabolic disease. This meta-analysis of prospective observational studies examined the relationship between smoking and incident type 2 diabetes. It included an enormous number of individuals in total and was able to break down smoking into subgroups of current, former and never-smokers, as well as look at the impact of passive smoke and effect of quitting over time. What is very clear is that smoking is associated with an increased risk of diabetes. The authors estimated that 11.7% of cases of type 2 diabetes in men and 2.4% in women (i.e. about 27.8 million cases in total worldwide) were attributable to active smoking. This further reinforces the importance of public health measures to make NZ smoke-free.


Abstract

Effect of low-fat diet interventions versus other diet interventions on long-term weight change in adults

Authors: Tobias DK et al.

Summary: This systematic review and meta-analysis of 53 studies (n=68,128) reporting the effects over >1 year of low-fat and higher fat dietary interventions on weight loss, among 5,898,795 individuals: i) bodyweight loss was greater with a low-carbohydrate versus low-fat intervention (weighted mean difference 1.15kg [95% CI 0.52, 1.79]); ii) there was no difference in bodyweight change between low-fat versus higher fat interventions (0.3kg [−0.66, 1.37]); and iii) bodyweight decrease was greater with low-fat interventions versus usual diet (−5.41kg [−7.29, −3.54]). Among nonweight loss and weight maintenance trials, low-fat versus higher fat interventions had a similar effect on weight loss, and weight loss was greater with low-fat interventions versus usual diet; no low-carbohydrate comparisons were available. In weight loss trials comparing higher fat and low-fat interventions, significantly greater weight occurred when the groups differed by >5% of calories obtained from fat at follow-up (−0.66kg [0.50 to 2.25]).

Comment: This is perhaps one of the greatest contentious issues in the field of obesity management and nutrition. What is the best dietary macronutrient composition for achieving weight loss? The debate has raged for decades, but we seem no closer to a resolution! The literature is highly confounded by other dietary factors. Most importantly what degree of total calorie restriction is built in to the prescribed diet, but also other what is substituted for fat when this is restricted. Much attention was focused on protein, with equivocal evidence for greater weight loss. However, when fat is replaced by carbohydrate, the quality of the carbohydrate is critical. There is accumulating evidence that refined sugars are harmful, and this is often accompanied by limited fibre intake. Therefore whilst useful in some respects, large meta-analyses of dietary intervention studies, such as this one, can over simplify the debate. This is not equivalent to a drug trial where there is a one-dimensional intervention compared with an inactive placebo. If only it were that simple!

Reference: Lancet Diabetes Endocrinol 2015;3(12):968–79

Abstract