Diabetes & Obesity RESEARCH REVIEW™

Making Education Easy

Issue 157 – 2022

In this issue:

Abbreviations used in this issue

CGM = continuous glucose monitoring
CSII = continuous subcutaneous insulin infusion
HbA_{1c} = glycosylated haemoglobin
HR = hazard ratio
RCT = randomised controlled trial

Welcome to issue 157 of Diabetes and Obesity Research Review.

This month's issue begins with research estimating how much a person's life expectancy could be increased if they were to adopt a healthier diet. This is followed by research investigating the impact that restricting advertisements for foods high in salt, sugar or fat across the public transport network in London had on consumers' purchases of these and healthier products. There is also similar research from the UK investigating the impact of interventions instigated by major UK grocery stores to promote selection of healthier products by their shoppers. Local research is represented by a survey of NZ CSII prescribers on whether they think the special authority criteria required by PHARMAC for CSII use in this country are fit for purpose.

Thank you for the comments and feedback you have sent us – we look forward to receiving more.

Best regards,

Professor Jeremy Krebs
jeremykrebs@researchreview.co.nz

Estimating impact of food choices on life expectancy

Authors: Fadnes LT et al.

Summary: Life expectancy changes according to diet were estimated in this modelling study from the US that used data from the 2019 Global Burden of Disease study. It was estimated that a sustained change from a typical Western diet to an optimal diet of increased intake of whole grains, legumes, fish, fruits, vegetables and nuts and decreased red and processed meat, sugar-sweetened beverage and refined grain intake from age 20 years would increase life expectancy by 10.7 years for women and 13.0 years for men. The largest gains were seen for increased legume, whole grain and nut consumption and reductions in red and processed meat consumption. Switching to an optimised diet at age 60 years was estimated to increase life expectancy for women and men by 8.0 and 8.8 years, respectively, and the estimated increase of switching at age 80 years was 3.4 years (both sexes). Switching from a typical diet to a feasible-approach diet (midway between a typical Western and an optimal diet) at age 20 years was estimated to increase life expectancy by 6.2 years for women and by 7.3 years for men.

Comment: As these authors point out, interpreting, integrating and really using the incredible wealth of data from nutritional research is extremely difficult. Nutrition research is very complex with many inter-related variables, outcomes of interest, populations studied and study designs making comparison of studies difficult and synthesising outcomes almost impossible. This study takes an interesting approach by using data from the 2019 Global Burden of Disease study and modelling life expectancy for men and women across age brackets if they were to adopt and sustain a dietary pattern, for which general agreement represents an optimised diet. This is a pattern rich in wholegrains, legumes, fish and fruit and vegetables with minimal refined carbohydrate, red meat and processed meat. A common criticism of promoting such a diet is the sustainability or adherence over the long term, in part because the changes required for many are quite extreme, so the authors have also modelled a 'feasible diet' with intakes between ideal and typical Western diets. The findings are dramatic with major increases in life expectancy across the board, which not surprisingly are greater if adopted at a younger age.

Reference: PLoS Med 2022;19:e1003889
Abstract

Changes in household food and drink purchases following restrictions on the advertisement of high fat, salt, and sugar products across the Transport for London network

Authors: Yau A et al.

Summary: This controlled interrupted time-series analysis of >5 million take-home food and drink purchases recorded by 977 randomly selected households in London (intervention) and 933 from the North of England (control) estimated average weekly household purchases of energy and nutrients from products high in fat, salt and sugar during the postintervention period (44 weeks) versus a counterfactual derived from the control group and pre-intervention (36 weeks) period; the intervention was restriction on advertising products high in fat, salt and sugar implemented in Feb 2019. Compared with the counterfactual, intervention households purchased 6.7% less energy from products high in fat, salt and sugar, including a 19.4% reduction in energy from chocolate and confectionery purchases.

Comment: There have been calls for restrictions to advertising of unhealthy foods as a high-level intervention to reduce rates of obesity for well over a decade now. It has been hard to get action on this at a political level, in part because of strong food industry lobbying, which often relates to difficulties in defining healthy and unhealthy foods, and in part because of limited evidence for efficacy of such an approach. This study provides some support for restriction on advertising of products with high fat, salt and sugar. In a population case-control study in the UK, average weekly household purchasing of high fat, salt and sugar products was compared between an area with restricted outdoor advertising and a control population. Although there are a number of limitations to the design as acknowledged by the authors, there was compelling evidence of a beneficial effect of the restriction on advertising. Let's face it, why would the food industry waste money on advertising if it didn't increase sales!

Reference: PLoS Med 2022;19:e1003915
Abstract

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Diabetes & Obesity Research Review

Progression to diabetes among older adults with hemoglobin A_{1c}-defined prediabetes in the US

Authors: Koyama AK et al.

Summary: This research estimated annual progression rates of prediabetes (defined as HbA_{1c} level 5.7–6.4%) to diabetes using electronic health record data for 50,152 outpatients aged ≥65 years from the longitudinal US LEADR study. Over a median 2.3 years of follow-up, the crude incidence of diabetes was 53 per 1000 person-years, for an annual progression rate of 5.3%. Patient groups defined by age, sex, race/ethnicity, family history of diabetes, hypertension diagnosis, social vulnerability index, BMI and HbA_{1c} level all had annual progression to diabetes rates of ≥5.0% except for groups represented by the lowest social vulnerability index, BMI <30 kg/m² or a baseline HbA_{1c} level of 5.7–5.9%. The annual progression of diabetes rate among participants with a BMI of 18.5–24.9 kg/m² was 3.5%, compared with 7.6% for those with a BMI of ≥40 kg/m², and for participants with HbA_{1c} levels of 5.7–5.9% it was 2.8%, compared with 8.2% for those with an HbA_{1c} level in the 6.0–6.4% range.

Comment: The relevance and importance of prediabetes continues to be debated. Since moving to HbA_{1c} level as the screening tool for diagnosis of diabetes, and therefore prediabetes, there has been great uncertainty about the real risk of prediabetes as we define it in NZ. Older data, based on oral glucose tolerance tests, have suggested a significant lifetime risk of progression to diabetes and cardiovascular disease, but contemporary data from those defined by HbA_{1c} level are largely lacking. What we do have from NZ primary care data suggests that the risk of progression is not as high as previously thought. This current study adds to this discussion, albeit that the data are from the US, where prediabetes is defined at a lower HbA_{1c} level threshold, and of course the population is not representative of NZ. Nevertheless, these are useful additional data for the ongoing discussion of who we should be targeting for intervention.

Reference: JAMA Netw Open 2022;5:e228158
Abstract

Calorie restriction with or without time-restricted eating in weight loss

Authors: Liu D et al.

Summary: Obese individuals were randomised to calorie restriction (1500–1800 kcal/day for men; 1200–1500 kcal/day for women) with or without time-restricted eating (i.e. eating only between 8:00AM and 4:00PM) for 12 months; 118 of the 139 randomised participants completed their 12-month follow-up visit. Mean weight losses from baseline at 12 months (primary outcome) in the time restriction and control (calorie restriction-only) groups were 8.0 and 6.3kg, respectively (p=0.11), with similar outcomes seen for change in waist circumference, BMI, bodyfat, body lean mass, blood pressure and metabolic risk factors, and no substantial between-group differences for adverse events.

Comment: The concept of intermittent fasting has become popular in recent years as a strategy to facilitate weight loss and/or improve metabolism. Intermittent fasting may be achieved by either restricting eating to within a set number of hours during the day, or by selecting one or more days of the week to restrict energy intake (commonly the 5:2 diet). This RCT explored whether a time-restricted eating pattern in addition to overall calorie restriction promotes greater weight loss than calorie restriction alone after 12 months. Although the time-restricted group had a mean of 1.8kg greater weight loss, this was not statistically significant, and there was quite a large range of responses in both groups. As is so often the case in RCTs of weight loss, some of the really interesting data can be lost in the group mean changes. What I take from this study is that we do not have evidence to say that time-restricted eating is the best approach to achieve calorie restriction for everyone, but we can say that it is a very good approach for some people. What we would like to know is how to pick those people for whom this would be the best approach!

Reference: N Engl J Med 2022;386:1495–504
Abstract

Insulin pump special eligibility criteria in New Zealand

Authors: Groves M et al.

Summary: These researchers from NZ surveyed prescribers of CSII regarding PHARMAC's current special authority criteria. A substantial majority (88%) of the 94 respondents felt that the special authority criteria for CSII needed updating; however, 75% maintained that CSII funding by PHARMAC should remain under updated special authority criteria. Sixty percent of the respondents indicated that they thought the current criteria did not promote health equity for Māori and Pasifika. Only a third of the respondents reported strict adherence to the criteria. Thematic analyses of free text revealed that the respondents did not believe that the current special authority criteria for CSII reflected quality of life benefits, changes in life course, clinician or patient autonomy or beneficence of CSII.

Comment: We are all familiar with the model of funding for pharmaceuticals in NZ, with the availability and funding being controlled by PHARMAC. This was extended to some medical devices, which included insulin pumps and glucose monitoring devices. We have now had access to funded insulin pumps and associated consumables for people with type 2 diabetes for over a decade, and this paper reports on the views of the health professionals responsible for prescribing these tools. The overwhelming conclusion from this survey is that the current special authority criteria for pumps are no longer fit for purpose. Interestingly, 75% agreed that special authority provisions should remain, but since only 33% strictly adhered to the current ones, it is very clear that they need to be revised to meet the needs of patients and represent the current state of evidence. This must include an incorporation of funding for CGM to enable the optimal use of pump technology, or else we will only see increasing inequity.

Reference: N Z Med J 2022;135(1552):82–8
Abstract

Testing availability, positioning, promotions, and signage of healthier food options and purchasing behaviour within major UK supermarkets

Authors: Piernas C et al.

Summary: This evaluation of six nonrandomised controlled retailer-led intervention studies and one pre/post within-store intervention found that compared with controls: i) stocking low-fat chips next to regular chips led to decreased sales of the latter; ii) increased availability of lower energy biscuits increased sales with reduced sales of regular biscuits, with the difference reaching significance in interrupted time-series models; iii) there was no evidence that placing higher fibre breakfast cereals at eye level increased sales or reduced sales of regular cereal; iv) price promotions on seasonal fruits and vegetables significantly increased sales in interrupted time-series models; v) use of Disney characters to promote nonsugar baked beans and selected fruits increased sales; and vi) there was no evidence of benefit for having labels highlighting lower sugar beverages at shelf level.

Comment: Could supermarkets become part of the solution rather than the problem? There has been a lot of attention on the duopoly we have in NZ with our supermarket chains controlling the food chain. Whilst there has been little political appetite to change this, could we use this situation to the advantage of the country if they are prepared to work together to influence the diets of the population towards a more healthy pattern? This study reports on some of the evidence for supermarket-based interventions. It is muddy to say the least! The absence of randomised trials hinders the interpretation of the data. However, what it does do is raise the possibility for change. What is needed is more community pressure to do so. Supermarkets already collect enormous amounts of data about our purchasing patterns and behaviours. They do this to increase profits. Imagine if they used their data to improve health and wellbeing. We might be a bit more forgiving of the ridiculous profits they make. What am I saying!

Reference: PLoS Med 2022;19:e1003952
Abstract

Artificial sweeteners and cancer risk

Authors: Debras C et al.

Summary: This population-based cohort study from France analysed 708,905 person-years of follow-up diet records from 102,865 adults (78.5% female) to assess cancer risk associated with artificial sweetener intake; aspartame was the most commonly consumed artificial sweetener (60% of intake), followed by acesulfame-K (29%) and sucralose (10%), which were consumed by 28%, 34% and 14% of participants, respectively. Soft drinks, table-top sweeteners and yoghurts were the most common source of artificial sweetener intake. A total of 3358 incident cancer cases were reported, predominantly obesity-related cancers (60%) with high rates of breast and prostate cancers. There was a 13% increased risk of cancer in high- versus non-artificial sweetener consumers (adjusted HR 1.13 [95% CI 1.03, 1.25]). When sweeteners were considered individually, both aspartame and acesulfame-K were associated with significantly increased risks of any cancer (respective HRs 1.15 and HR 1.13); aspartame also increased the risks of breast cancer and obesity-related cancer (1.22 and 1.13). These associations retained significance on sensitivity analyses.

Comment: The issue of whether artificial sweeteners have harmful health effects, and specifically risk for cancer, has been debated for as long as they have been used as sugar substitutes. The argument for using these agents is the reduction in calories from sugar and the direct metabolic effects of high sugar consumption. This epidemiological study has shown an approximately 15% increased risk of cancer generally, and breast and obesity-related cancers specifically, in higher consumers of artificial sweeteners. This is after adjusting for many variables known to increase cancer risk, including obesity. This is not insignificant and raises the question again whether we should be promoting the substitution of these agents for sugar. It certainly suggests that we should promote water over any sweetened beverage.

Reference: PLoS Med 2022;19:e1003950
Abstract

Effectiveness of adding alarms to flash glucose monitoring in adults with type 1 diabetes under routine care

Authors: Boscari F et al.

Summary: This research assessed switching from 4 weeks using a standard flash glucose monitoring system to 8 weeks using a system with alarms for hypo- and hyperglycaemia in 38 adults with type 1 diabetes who had >4% of time in hypoglycaemia or >40% of time in hyperglycaemia recorded. During the first 4 weeks of use with the alarm-equipped system, time in target glucose level range increased significantly from 52.8% to 57.0%, and time below range fell significantly from 6.2% to 3.4%, as did time with a level <54 mg/dL (from 1.4% to 0.3%) and the coefficient of variation (from 39.6% to 36.1%); similar changes were confirmed 8 weeks after switching systems. There were also improvements recorded for treatment satisfaction and fear of hypoglycaemia. The greatest benefits in glucose level control and treatment satisfaction were noted in participants who had >4% of time in hypoglycaemia at baseline.

Comment: This is a really nice real-world study of great relevance to practice in NZ. Flash glucose monitoring systems have become popular amongst our patients with type 1 diabetes, and until PHARMAC get around to funding them, they remain the most cost-effective subcutaneous glucose monitoring system. The Libre device we currently have is limited by the lack of 'bluetoothing' to a phone or watch, and therefore the ability to set alarms for glucose levels. This can be overcome with additional devices, but really we need the later-generation models. What this study shows is that by using alarms, people can achieve better time in range, and also reduce their fear of hypoglycaemia and improve their general treatment satisfaction. It's a no brainer really.

Reference: Acta Diabetol; Published online April 13, 2022
Abstract

Effect of divergent continuous glucose monitoring technologies on glycaemic control in type 1 diabetes mellitus

Authors: Elbalshy M et al.

Summary: This was a systematic review with meta-analysis of data from 15 RCTs investigating adjunctive CGM, five investigating nonadjunctive CGM and two investigating intermittently-scanned CGM, all versus traditional capillary glucose monitoring, in patients with type 1 diabetes. A statistically significant absolute improvement in HbA_{1c} level was seen when data from all three CGM categories were pooled and compared with the comparator (mean difference, –0.22 percentage points [95% CI –0.31, –0.14]), with the strongest effect seen for adjunctive CGM (–0.26% [–0.36, –0.16]). There was also a significant increase in time in target glucose level range of 5.4% for CGM interventions versus the comparator, with the strongest effect seen with nonadjunctive CGM (6.0%).

Comment: This one is for PHARMAC too – the rest of us don't need convincing. The evidence is mounting for the benefits of subcutaneous glucose monitoring in people with type 1 diabetes. This is a systematic review and meta-analysis of RCTs of various forms of CGM versus finger prick capillary glucose level monitoring on glycaemic control. The data are clear that CGM improves glycaemic control as measured by HbA_{1c} level or time in range. What this hides are the other major benefits of CGM, which include satisfaction and quality of life, and reduction in hypoglycaemia. Furthermore, isn't it barbaric that we have a technology available which minimises the need for needles and painful finger pricks in children, avoids the need to wake children overnight and gives parents some sanity, yet we don't fund it.

Reference: Diabet Med 2022;e14854
Abstract

Comparison of insulin dose adjustments made by artificial intelligence based decision support system and by physicians in people with type 1 diabetes using multiple daily injections therapy

Authors: Nimri R et al.

Summary: Twenty physicians from academic centres were surveyed on 17 cases of individuals with type 1 diabetes treated with multiple daily insulin injections with questions on recommended insulin dose adjustments based on glucose level and insulin data; their recommended insulin dose adjustments were compared with an automated decision support system. The automated decision support system was noninferior to the surveyed physicians with respect to agreement and disagreement in the direction of insulin dose adjustment for basal rate, carbohydrate-to insulin ratio and correction factor, although the automated decision support system consistently returned an insulin dose change that was smaller in magnitude to the changes proposed by the physicians.

Comment: We are at risk of becoming redundant and irrelevant! This is an interesting study comparing recommendations for insulin regimen adjustment by expert clinicians across a range of countries with the advice generated by an automated artificial intelligence system. Both were given a set of 17 different sets of data. There was no significant difference in dose adjustments between physicians and the computer, although the computer tended to give more conservative adjustments. We are seeing artificial intelligence at work in the latest pump algorithms for insulin dose adjustments. In that setting, there is a wealth of data input from CGM. However, whether artificial intelligence can be equally effective and safe with fewer and more random datapoints that are typical of people with finger prick capillary monitoring remains unclear. It's all about pattern recognition at the end of the day, but as we know, there are many unpredictable variables that come to play in real people living real lives with type 1 diabetes.

Reference: Diabetes Technol Ther, Published online March 24, 2022
Abstract

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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.

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