Welcome to the fifth issue of Obesity Research Review.

A study from the US analysed cross-sectional data from 13,626 nondiabetic adults and found chocolate consumption was associated with lower markers of adiposity. Another study from the US found young adults who increased plant-centred diet quality had a lower diabetes risk and gained less weight by middle adulthood. A Spanish population-based cohort study showed that a high adherence to Mediterranean diet at the age of 4 is associated with a lower risk of developing overweight, obesity, and abdominal obesity at age 8. An open-label study investigating the effect of a 6-week intervention with liraglutide and found treatment did not affect pancreatic volume, oedema or cellularity in obese men without diabetes.

A 3-year follow-up study found weight loss after bariatric surgery decreases carotid intima-media thickness and cardiovascular risk factors in middle-aged participants with class 3 obesity. A single centre cohort study assessed QoL in patients who underwent laparoscopic sleeve gastrectomy and laparoscopic Roux-en-Y gastric bypass. The authors reported there was a significant increase in total QoL before the operation and 10 years after surgery in the whole study group and for patients who underwent laparoscopic sleeve gastrectomy. However, there was no significant difference for patients who underwent laparoscopic Roux-en-Y gastric bypass. Findings from a cohort study from the five Nordic countries suggest bariatric surgery may decrease overall cancer risk in women within the first five years after surgery, but not in men. The authors note this decrease may be explained by a decreased risk of breast and endometrial cancer and non-Hodgkin lymphoma in women.

I hope you find the research in this issue useful to you in your practice and I look forward to your comments and feedback.

Kind Regards,

Professor Joseph Proietto
joseph.proietto@researchreview.com.au

Chocolate consumption and indicators of adiposity in US adults

Authors: Smith L., et al

Summary: The researchers used cross-sectional data from 13,626 nondiabetic adults (≥20 years) to investigate the association between consumption of chocolate and measures of adiposity. Overall, 11.1% of the population self-reported any chocolate consumption in either of their two 24-hour dietary recalls. Individuals who reported any chocolate consumption had a lower diabetes risk and gained less weight by middle adulthood. A Spanish population-based cohort study showed that a high adherence to Mediterranean diet at the age of 4 is associated with lower markers of adiposity. Another study from the US found young adults who increased plant-centred diet quality had a lower diabetes risk and gained less weight by middle adulthood. A Spanish population-based cohort study showed that a high adherence to Mediterranean diet at the age of 4 is associated with a lower risk of developing overweight, obesity, and abdominal obesity at age 8. An open-label study investigating the effect of a 6-week intervention with liraglutide and found treatment did not affect pancreatic volume, oedema or cellularity in obese men without diabetes.

Comment: This report must bring joy to the hearts of all chocolate lovers around the World. It would not have been a surprise if it had been found that there was no link between chocolate consumption and markers of adiposity. After all, chocolate is usually eaten as a treat and rarely makes up a significant component of total energy intake in a single day. However, this study reports that body weight and waist circumference were lower in chocolate eaters! Does this mean that chocolate causes weight loss? Possibly (Farhat G et al. Dark chocolate: An obesity paradox or a culprit for weight gain? Phytotherapy Research 28:791-797. 2014). Another explanation may be that those individuals who are gaining weight for other reasons avoid chocolate in their efforts to follow a “healthy” diet. More research is needed on this important nutrient.


Abstract

Independent commentary by Professor Joseph Proietto

Joseph Proietto is Professor Emeritus at the University of Melbourne in the Department of Medicine, Austin Health and an endocrinologist specialising in diabetes and obesity. He established the first obesity clinic in Victoria at the Royal Melbourne Hospital and is now Head of the Weight Control Clinic at Austin Health. Professor Proietto was the inaugural Sir Edward Dunlop Medical Research Foundation, Professor of Medicine, and Head of the Metabolic Disorders Research Group in the Department of Medicine, Austin Health. He is currently on the executive of World Obesity and is Chair of the Clinical Care Committee. Professor Proietto has published over 200 articles and several book chapters on obesity and diabetes. He is the Author of “Body Weight Regulation: Essential Knowledge to Lose Weight and Keep It Off”.

Independent commentary by Professor Joseph Proietto
No effects of a 6-week intervention with a glucagon-like peptide-1 receptor agonist on pancreatic volume and oedema in obese men without diabetes

Authors: Svane MS, et al

Summary: The open-label study investigated the effect liraglutide on pancreatic volume, oedema, cellularity and DNA synthesis in 14 obese men without diabetes. Participants were examined at baseline, during titration (week 4) of liraglutide towards 3.0 mg/day, and 2 weeks after steady-state treatment (week 6) of a final dose of liraglutide. The researchers reported plasma amylose (+7 UL, [95% CI 3-11], P < .01) and lipase (+9 UL [7-30], P < .01) increased during liraglutide treatment. However, pancreatic volume did not change from baseline to steady state of treatment and no change in pancreatic cellular infiltration was found. During titration of liraglutide, position emission tomography-based fluorothymidine uptake (DNA synthesis) in pancreatic tissue increased numerically (+0.08 [0.00-0.17], P = .0507).

Comment: This study provides some reassurance about the effects of a GLP-1 agonist on the pancreas. In the 3 mg liraglutide studies there was a modest increase in pancreaticlith in the liraglutide arm of the study. From an evolutionary perspective, GLP-1 has a pedigree as a growth factor for the gut and we must remember that the pancreas is an outgrowth of the gut. The Gila monster, a lizard that lives in the North American desert only eats twice a year. In between meals it’s gut atrophies (you don’t maintain an organ you are not using). When the Gila monster eats again, it releases a cocktail of hormones from it’s saliva that causes the gut to grow quickly. Exenatide was discovered as one of the proteins produced in the salivary gland of the Gila monster. Exenatide was found to have ~ 50% homology to human GLP-1 but is active on the human GLP-1 receptor. Exenatide was marketed for the treatment of type 2 diabetes as Byetta and Bydureon. So GLP-1 has an evolutionary history as a growth factor. The results of this study have to be interpreted with that history in mind.


Childhood BMI and fasting glucose and insulin predict adult type 2 diabetes: The International Childhood Cardiovascular Cohort (i3C) Consortium

Authors: Hu T, et al

Summary: The study cohort included 6,738 participants. Of these, 6.5% reported onset of type 2 diabetes between ages 20 and 59 (mean 40.9 years), and 96% of them reported use of a confirmed antidiabetic medication. The authors reported BMI and glucose (age and sex standardised) were associated with incident type 2 diabetes after adjustment for cohort, country, sex, race, age, and calendar year of measurement. Increasing levels of childhood BMI and glucose were related to an increased risk of type 2 diabetes beginning at age 30 years, beginning at cut points <95th percentile for BMI and <100 mg/dL for glucose. Insulin was positively associated with adult type 2 diabetes after adjustment for BMI and glucose and added to type 2 diabetes discrimination.

Comment: This study finds the unsurprising fact that elevated BMI, fasting glucose and insulin in childhood are predictive of type 2 diabetes. Elevated glucose and elevated insulin together are strange. It is generally agreed that obesity causes insulin resistance, which causes insulin levels to rise to maintain glucose normal. Diabetes comes when the insulin-producing beta cells start to fail and insulin starts reducing then glucose starts rising. So how can we have both insulin and glucose elevated early on in the development of diabetes? Let me tell you a story. When Dr Sof Andrikopoulos wanted to start his studies on the mechanisms of beta cell failure in type 2 diabetes, he obtained a line of DBA/2 mice. These mice have normal glucose tolerance when lean but develop severe diabetes when obese. Sof started his experiments by checking insulin secretory capacity expecting some defect in insulin secretion early on. To everyone’s surprise DBA/2 mice significantly hypersecrete insulin (Xicofrit S et al. Comparison of insulin secretory function in two mouse models with different susceptibility to beta-cell failure. Endocrinology 143:2085-92; 2002). This led to the discovery that the overworking of the beta cell speeds up its demise. (Astor-Mooney K et al. Too much of a good thing: why it is bad to stimulate the beta cell to secrete insulin. Diabetologia 51(4):540-5. 2008.) Thus it is possible to have both elevated glucose and elevated insulin early on in the development of diabetes.

Reference: Diabetes Care. 2020 Sep 1; Online ahead of print Abstract

A shift toward a plant-centered diet from young to middle adulthood and subsequent risk of type 2 diabetes and weight gain: The Coronary Artery Risk Development in Young Adults (CARDIA) study

Authors: Choi Y, et al

Summary: The prospective study from the US enrolled adults aged 18-30 years and analysed the associations between change in plant-centred diet quality over 20 years and diabetes and change in BMI, waist circumference, and weight. The researchers measured plant-centred diet quality using the A Priori Diet Quality Score (APDQS); a higher score favours nutritionally rich plant foods. During a mean follow-up of 9.3 (± 1.7) years, 206 case subjects with incident diabetes were observed. They found participants with the largest increase in APDQS over 20 years had a 48% (95% CI 0.31-0.85; P-trend < 0.001) lower risk of diabetes over the subsequent 10 years compared with participants whose score remained stable. In addition, each 1-SD increment in APDQS over 20 years was associated with lower gains in BMI, waist circumference, and weight during the same period, but not with subsequent changes.

Comment: This prospective study concludes that the selection of nutritionally rich plant foods in youth protects from both overweight and diabetes. Unfortunately, although the study was prospective it was not randomised. The subjects selected the diet to have. Thus, we cannot be sure that those who had the genetic predisposition to obesity and diabetes selected a different diet to those that did not.

Reference: Diabetes Care. 2020 Aug 26; Online ahead of print Abstract

A factorial experiment to optimize remotely delivered behavioral treatment for obesity: Results of the Opt-IN study

Authors: Spring B, et al

Summary: The Optimization of Remotely Delivered Intensive Lifestyle Treatment for Obesity (Opt-IN) study developed a remotely delivered, technology-supported weight-loss package. Adults (n = 562) with BMI ≥ 25 were randomly assigned to conditions crossing five dichotomous treatment components set to either low/high (12 vs. 24 coaching calls) or offline/primary care provider reports, text messaging, meal replacements, and buddy training. About 84.3% of participants completed the six-month weight loss program and final assessment. The authors reported the treatment package yielding maximum weight loss for <$3500 included 12 coaching calls, buddy training, and primary care provider progress reports. This package produced average weight loss of 6.1 kg, with 57.1% losing ≥5% and 51.6% losing ≥7%, and cost $427 per person.

Comment: As usual, the weight loss was only 6.1 kg, about the weight loss achieved with lifestyle diets. While this amount of loss is fine for people that have mild overweight, it is not enough weight loss for someone with severe obesity. A better approach to weight loss is to do a ketogenic VLED-based diet. It gives rapid weight loss that can match what is achieved with barisric surgery and is safe. (Sumithran P. et al. Safe year-long use of a very-low-calorie diet for the treatment of severe obesity. Med J Aust 188:366-8. 2008; Purcell K. et al. The effect of rate of weight loss on long term weight management: a randomised controlled trial. The Lancet Diabetes & Endocrinology 2:954-962. 2014)

Reference: Obesity (Silver Spring). 2020 Sep;28(9):1652-1662 Abstract

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Bariatric surgery-induced changes in intima-media thickness and cardiovascular risk factors in class 3 obesity: A 3-year follow-up study

Authors: Domenech-Ximénez B, et al

Summary: The study cohort comprised of 87 participants with obesity (BMI 43 [40-47]) and 75 controls; 21 (25%) participants with obesity underwent bariatric surgery. The investigators measured BMI, blood pressure, cholesterol, triglycerides, fasting plasma glucose, C-reactive protein, carotid intima-media thickness (CIMT), and Framingham Risk Score at baseline and at 3-year follow-up. They found after bariatric surgery, BMI decreased from 45.45 to 27.28 (P < 0.001), and mean CIMT decreased from 0.64 mm (0.56-0.75 mm) to 0.54 mm (0.46-0.65 mm) (P < 0.012), equivalent to 0.005 mm/kg of weight lost. Furthermore, at 3-year follow-up, participants who had undergone bariatric surgery had similar CIMT and cardiovascular risk factors to the control group.

Comment: This study gives the good news that significant weight loss reverses cardiovascular risk factors and CIMT. The problem with this paper is the title, which implies that bariatric surgery caused improvement in CIMT. It was actually weight loss. They don’t say how much weight loss medical therapy achieved but it must have been very modest as usual (see above).

Reference: Obesity (Silver Spring). 2020 Sep;28(9):1663-1670

Abstract

The longitudinal relation of childhood height to subsequent obesity in a large electronic health record database

Authors: Freedman DS, et al

Summary: This study explored the longitudinal association of childhood height with adult BMI in an electronic health record database of 2.8 million children. Children were initially examined between the ages of 2 and 13.9 years and, on average, were re-examined 4 years later. There was a cross-sectional correlation between height-for-age z score and BMI that increased from r = -0.06 (age of 2 years) to r = 0.37 (age of 9-10 years). In addition, height-for-age at the first visit was related to subsequent BMI and obesity. It was noted about 40% of this longitudinal association was independent of initial BMI, but its magnitude decreased.

Comment: This study adds to the observation that children that are particularly tall when young (2-14 years) are susceptible to obesity. What could possibly be the cause for the link? Ghrelin, the only hormone that stimulates hunger, is known to stimulate growth hormone release. A good study to do is to see if taller children have a higher ghrelin level.

Reference: Obesity (Silver Spring). 2020 Sep;28(9):1742-1749

Abstract

High adherence to a Mediterranean diet at age 4 reduces obesity, overweight and abdominal obesity incidence in children at the age of 8

Authors: Notario-Barandiaran L, et al

Summary: The researchers analysed data from children in the Spanish INMA population-based cohort study who attended follow-up visits at age 4 and 8 years (n = 1801 and n = 1527, respectively). Diet was assessed at the age of 4 using a validated food frequency questionnaire. In cross-sectional analyses at the age of 4 no association was observed between adherence to Mediterranean diet and overweight, obesity, or abdominal obesity. In longitudinal analyses, a high adherence to Mediterranean diet at age 4 was associated with lower incidence of overweight (HR = 0.38; p = 0.001), obesity (HR = 0.16; p = 0.002), and abdominal obesity (HR = 0.30; p = 0.008) at the age of 8.

Comment: This study reports that in the longitudinal study, children who at the age of 4 had a high adherence to the Mediterranean diet had lower risk of developing obesity at age 8. It is interesting to note that this study is on Spanish children. Among these children not having a Mediterranean diet is abnormal. So, the question that must be asked is, why are the parents of children that develop obesity by age 8 prone to be food “rebels” in a Mediterranean country? The protection from obesity may not have anything to do with the Mediterranean diet. How else can you explain the fact that Malta has the highest prevalence of obesity in Europe?


Abstract

Quality of life 10 years after bariatric surgery

Authors: Major P, et al

Summary: This single centre cohort study included 34 patients who underwent laparoscopic sleeve gastrectomy (LSG) and 31 patients who underwent laparoscopic Roux-en-Y gastric bypass (LRYGB). Preoperatively, and after 1 and 10 years, quality of life (QoL) was assessed using SF-36 and MA-QoLII. After 10 years, 72% of patients filled out these questionnaires. The authors reported global QoL score before surgery was 48.3 ± 20.6; at the 1-year follow-up it was 79.7 ± 9.8; at 10-year follow-up it was 65.1 ± 21.4. They found there was a significant increase in total QoL between measurements before the operation and 10 years after surgery in the whole study group (p = 0.001) and for patients who underwent LSG (p = 0.001). However, there was no significant difference between total QoL prior to surgery and 10 years after for patients who underwent LRYGB (p = 0.450).

Comment: This study suggests that quality of life was improved long term in those patients who lost weight with LSG but not in those who lost weight with LRYGB. This was presumably due to more surgical consequences in the LRYGB group. However, while both groups had big increases in both mental and physical quality of life scores at 1 year after surgery in both groups the benefits reduced at 10 years; but reduced more in LRYGB than in LSG groups. So when considering long term quality of life, surgery is not as superior as a method of weight loss as it may seem. It would be interesting to compare the quality of life of those patients who lost significant amount of weight with a medical program and maintained it for 10 years with the help of hunger suppressing medication.


Abstract

Cancer risk after bariatric surgery in a cohort study from the five Nordic countries

Authors: Tao W, et al

Summary: The study cohort included all adults diagnosed with obesity in national patient registries in Denmark, Finland, Iceland, Norway and Sweden from 1980 to 2012. Among 482,572 participants with obesity, 49,096 underwent bariatric surgery. The team concluded bariatric surgery was followed by a decreased overall cancer risk in women (HR 0.86), but not in men (HR 0.98). They noted risk reduction was observed only within the first five post-operative years. Among specific tumours, HRs decreased for breast cancer (HR 0.81), endometrial cancer (HR 0.69) and non-Hodgkin lymphoma (HR 0.64) in female bariatric surgery patients, while the risk of kidney cancer increased in both sexes (HR 1.44).

Comment: This study suggests that significant weight loss with bariatric surgery reduces some cancers in women in the first 5 years after surgery. Strangely this was not the case in men. This could have been influenced by the type of cancers that were impacted (endometrial and breast cancers) which impact only women. However, non-Hodgkin lymphoma was also only significantly reduced in women. The mechanisms by which obesity increases the risk of some cancers are not really known. A search of the literature failed to uncover precise mechanisms. There was vague talk about insulin and insulin-like growth factor -1 (IGF-1). More research is needed. This study also reports an increase in renal cancer in both sexes in those undergoing bariatric surgery, this is really surprising since other studies suggest that obesity increases the risk of renal cancer (Wilson KM, Cho E (2016) Obesity and Kidney Cancer. In: Pischon T, Nimptsch K (eds) Obesity and Cancer. Recent Results in Cancer Research, vol 208. Springer, Cham).


Abstract