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Energy Distribution, Energy Intake, and Glycaemic Control in Type-2 Diabetes

Chamorro R, Basfi-Fer K, Sepúlveda B, et al. Meal timing across the day modulates daily energy intake in adult patients with type 2 diabetes. *European Journal of Clinical Nutrition*. 2022;10.1038/s41430-022-01128-z.

Background

- The term “meal timing” may in fact encompass several relevant exposures, including the the clock time of eating, the temporal distribution of overall energy, meal frequency, regularity, and the total duration of the eating period
- For glycaemic control in particular, the distribution of energy and the clock timing of that energy intake have emerged as important factors, particular for individuals with impaired glucose tolerance.

The Study

- A cross-sectional analysis of 80 participants with T2D in Santiago, Chile; the study compared HbA1c levels according to energy and macronutrient intake in three time-bins: 06:00 to 11:59 h [“P1”]; 12:00 to 17:59 h [“P2”], and; 18:00 to 00:30 h [“P3”].

Findings, Strengths & Limitations

- The proportion of total daily energy intake [TDEI] in P1, P2, and P3, was 22.8%, 37.5%, and 39.7%, respectively. A higher proportion of energy intake in P3 correlated with greater TDEI. Higher protein and carbohydrate intake in P1 was associated with lower TDEI.
- Greater energy in P3 was associated with higher HbA1c.
- The study had a clearly defined inclusion criteria and a sample of participants with relatively well-controlled T2D. The cross-sectional nature of the design means these data are a snapshot in time, rather than a prospective analysis of associations over time between dietary distribution and metabolic health.

Context

- The findings support prior research showing that more energy intake later in the day is associated with higher TDEI.
- There appear to be two main drivers of this relationship; the first is increasing energy content of eating occasions as the day progresses, and the second is decreasing time between eating occasions.
- This may be due to lower satiety, which is highest in the morning and declines steadily over the course of the day, possibly reflecting the circadian rhythm in hunger peaking in the evening.

Application

- Interventions suggest that Interventions suggest that high energy and high protein/carbohydrate breakfast led to significant weight loss and suppression of the gut-derived appetite hormone, ghrelin.
- The body of evidence for glycaemic control and benefits of earlier temporal distribution of energy are clear.
- However, outcomes like weight loss or energy expenditure are not influenced by the clock times of meals or distribution of energy.

Can Restricting Junk Food Ads on Public Transport Make a Difference?

Yau A, Berger N, Law C, et al. 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: A controlled interrupted time series analysis. *PLoS Medicine*. 2022;19(2):e1003915.

Background

- Of the multiplicity of well-refined strategies that the food industry uses to make people sick, outdoor marketing appears to be one of the most effective.
- Food marketing overwhelmingly emphasises unhealthy foods and commonly uses public transport systems to advertise such foods.
- In 2019, Transport for London [TfL] fully implemented a policy of restricted advertising of high fat, sugar, and salt [HFSS] foods on the underground, overground rail, buses, and at bus stops other outdoor spaces; how did this policy influence intake?

The Study

- The investigators used data on household food and beverage purchases recorded with barcode scanners, to compare purchases of HFSS foods before the policy to another region of the UK where the policy had not been introduced.

Findings, Strengths & Limitations

- Weekly purchases from HFSS products following the introduction of restrictions showed relative decreases of Liver fat decreased by:
 - **Energy:** by 1,001kcal [95% CI 456 to 1,546kcal]
 - **Saturated Fat:** by 26.4g [95% CI 12.5 to 40.4g]
 - **Sugar:** by 80.7g [95% CI 41.4 to 120.1g]
 - **Salt:** 2.2g [95% CI 5.4g to 9.8g]
- The reductions primarily reflected decreases in purchases of chocolates and confectionary.
- This was a large dataset and refined statistical analysis. TfL is the largest transport network in Western Europe, and the findings may thus have wider generalisability that a smaller city/network could lack in an analysis such as this. Differences in transport use between London and the North of England may have influenced the findings.

Context

- The TfL policy still ultimately allowed for a lot of junk to be advertised in sneaky ways.
- This study provides another strand of evidence that mandatory policy interventions targeting the food environment are by orders of magnitude more efficacious than voluntary schemes that leave it up to industry to do the right thing.
- There is scant evidence that public-private partnerships are effective at promoting the public health, even though they are celebrated as an approach.

Application

- There is not necessarily individual-level application of a study like this.
- However, in a field like nutrition which tends to attract a certain demographic, the more that we can understand wider determinants of food intake and the influence of the food environment, the more effective – and empathetic – a field we can be.

Does Folate Lower Stroke Risk?

Yuan S, Mason AM, Carter P, Burgess S, Larsson SC. Homocysteine, B vitamins, and cardiovascular disease: a Mendelian randomization study. BMC Med. 2021 Apr 23;19(1):97.

Background

- In epidemiological research, elevated homocysteine is a consistent independent risk factor for cardiovascular diseases [CVD], including stroke.
- There remains a lack of clarity on whether homocysteine is a cause or consequence of disease because, while vitamins B6/B9/B12 reliably lower homocysteine levels, there is little to no good evidence that this chain of B-vits>homocysteine lowers CVD risk.
- Many intervention trials of B-vitamins on CVD risk found ‘null’ results; could genetic studies shed more light on the question?

The Study

- The study investigated the effects of genetic predisposition to higher blood levels of homocysteine, folate, B6, and B12, on cardiovascular disease.

Findings, Strengths & Limitations

- Genetically higher homocysteine levels there was 11% higher odds of total stroke, 26% higher odds for subarachnoid haemorrhage, and 11% higher odds for ischaemic stroke.
- Genetically higher B9 levels were associated with 12% lower odds of coronary artery disease and 14% lower odds for total stroke.
- Genetically higher B6 levels were associated with 12% lower odds of ischaemic stroke and 30% higher odds for peripheral artery disease. There were no significant associations for B12 and any CVD outcome.
- A strength was that 8 different genetic studies were utilised to determine genetic associations with CVD endpoints. The main limitations were that the genetic variants identified for the B-vitamins were only associated with a fraction of the variance in levels of B-vitamins, reflecting the fact that genetics don't strongly influence nutritional status.

Context

- For vascular diseases, the strength of evidence now suggests that elevated homocysteine is an antecedent to vascular disease that causally increases risk of stroke. That the present study adjusted for the effects of the selected genetic variants that also influence blood pressure or kidney disease strengthens that causal inference.
- Folic acid supplementation was shown to significantly lower stroke risk by 12% in studies conducted in countries *without* folate food fortification policies; there is no association from studies in countries that had existing folate fortification policies.
- In participants with low baseline folate status, supplementation lowers stroke risk by 21%.
- Folic acid supplementation reliably lower homocysteine levels, and this effect linearly increases relative to baseline HCY levels.

Application

- This is another line of evidence that supports prophylactic supplementation of folic acid in people who don't eat enough greens [i.e., most of the population] and/or women in reproductive life stages.

Sugar and Fatty Liver in Adolescents: the Lower the Better?

Cohen CC, Li KW, Alazraki AL, et al. Dietary sugar restriction reduces hepatic de novo lipogenesis in adolescent boys with fatty liver disease. *Journal of Clinical Investigation*. 2021;131(24):e150996.

Background

- Non-alcoholic fatty liver disease [NAFLD] is now a substantial concern in paediatric populations.
- In general population studies the prevalence of paediatric NAFLD is ~7.6%, however, in childhood obesity clinics the prevalence is 34.1%.
- The relationship with dietary sugars is worth considering given that children and adolescents may be more likely to consume excessive free sugars.

The Study

- 40 adolescent boys aged 11–16 years old with NAFLD completed an 8-week randomised trial comparing a low-sugar intervention diet to participants' usual habitual diet as the control diet. The intervention diet was designed to have <3% added sugars.
- The primary outcome was change in *de novo lipogenesis* [DNL] between diets, and the secondary outcome was change in liver fat levels between diets.

Findings, Strengths & Limitations

- DNL decreased from 34.6% to 24.1% in the intervention group [no change in the control group]; a 10.6% decrease in DNL between groups. The results were similar when adjusted for weight change in both groups.
- Liver fat levels decreased by 6.3% between groups.
- Strengths include the block and stratified randomisation procedure, the high compliance, and measurements of DNL and liver fat using advanced, accurate laboratory methods.
- Limitations include the all-male sample, imbalanced intensity of intervention between groups, and open-label design of the trial.

Context

- The reduction in sugar intake had a moderate positive correlation with change in DNL.
- The fact that the reduction in DNL did not correlate strongly with reductions in liver fat may reflect the fact that DNL is merely one pathway of hepatic fat accumulation.
- The level of sugar reduction achieved in the present study is impressive for a paediatric setting [added sugars intake in the intervention group was estimated at 1.1%], but this required significant intervention by the research team.
- Participants in the present study were 97% Hispanic, and ethnic differences in the role of DNL in fatty liver have been observed. The findings may not extrapolate to other ethnic groups.

Application

- For adolescents, particularly those at higher levels of adiposity, the benefit of earlier risk reduction and improved cardio-metabolic health warrants an emphasis on added sugar reduction to <5% energy.
- For those working with paediatric populations, attention in the present study should be given to the lengths that were taken to facilitate the reduction in added sugars; a whole-family affair could likely provide the best odds to achieve the desired outcome.