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From the Editor

In a past editor's intro, I talked a bit about how considering a study's PICO (population, intervention, comparisons, and outcomes) can be useful for interpreting studies. PICO doesn't just apply to trials, but also systematic reviews. In this volume, we cover one such systematic review that looks like it could have benefited from more of a focus on PICO.

The systematic review raises a fascinating and important question: does the way farm animals are raised (primarily by changing what they're fed) affect human health when we consume products from those animals? At least, that's what the title suggests. However, when you jump into the full text, you're immediately greeted with a discussion in the intro focusing mainly on the effect of diet on cancer. While cancer is one aspect of health, it's far from the complete picture.

The authors justify the focus on cancer in their introduction by citing a couple of articles that mention that products from grass-fed animals are higher in conjugated linoleic acid (CLA) and omega-3 fatty acids, which may have anticancer properties. That much is true, but both also have many other possible benefits which their citations mention and that they skip over for the most part. Plus, as we discuss in our review, the link between CLA, omega-3's, and cancer isn't completely clear. The authors also report on serum cholesterol markers "for discussion purposes" (i.e., not because it's related to cancer), along with CLA and omega-3 serum levels in humans and some inflammatory cytokines.

If this sounds confusing and unfocused, that may be because it is. Since it raises the question of what the authors' goal in conducting the review actually was. The authors claimed that their review was systematic in their methods section, but, as we mention in our review, PRISMA guidelines weren't followed, and one of the features of following PRISMA is stating key questions that are being addressed by the review using the PICO (plus study design, so technically PICOS) framework.

The authors did make some choices to be applauded, including not forcing a meta-analysis after they discovered that the studies they uncovered were all very different from each other. And there are also quite a few things to be learned from their research. However, there are also some lessons to be learned about the importance of PICO when it comes to systematic reviews as well.

Gregory Lopez, Editor-in-Chief

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Aspartame: It's sweet to eat, but is it a trick or a treat?

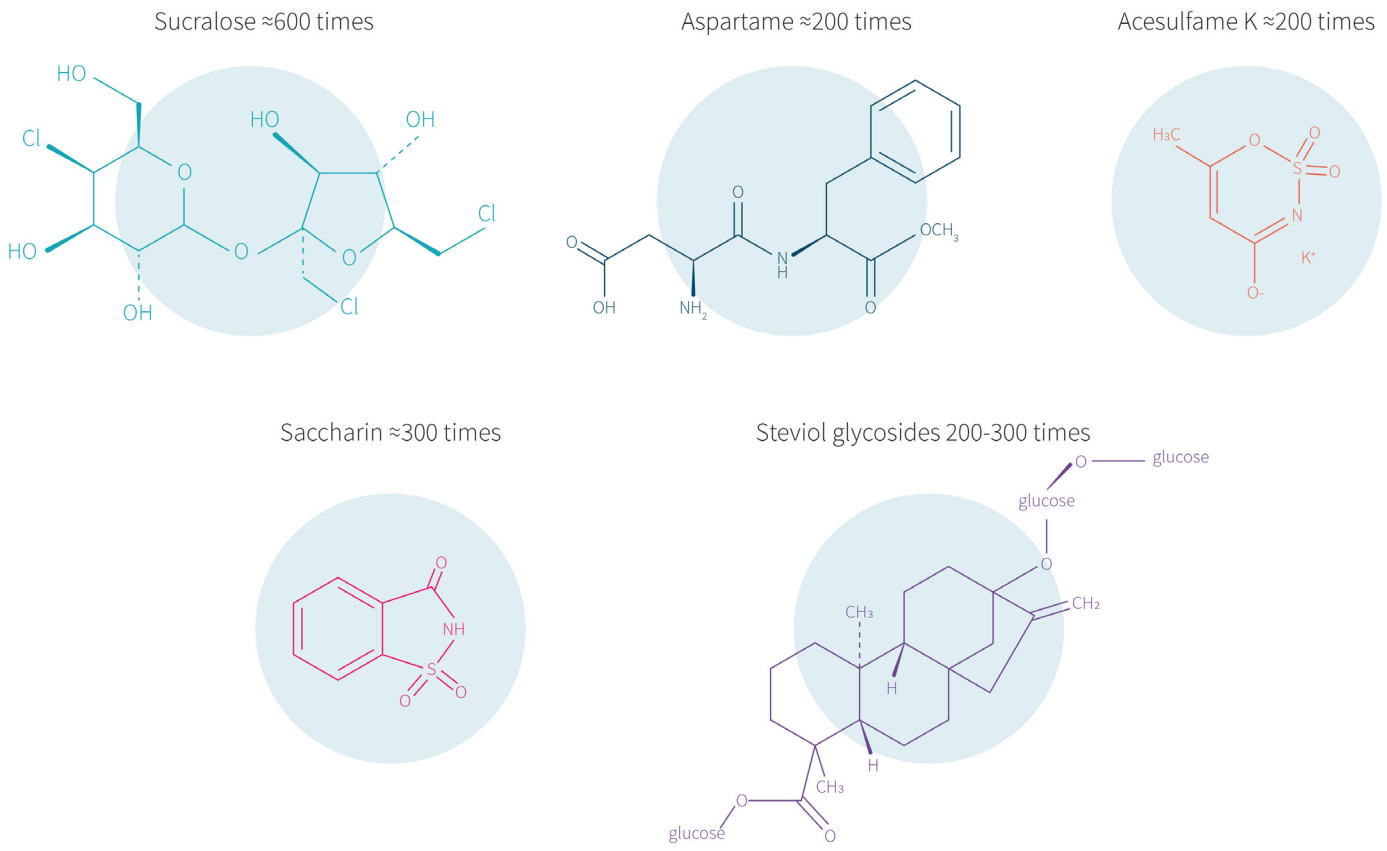
Aspartame Consumption for 12 Weeks Does Not Affect Glycemia, Appetite, or Body Weight of Healthy, Lean Adults in a Randomized Controlled Trial

Introduction

Obesity is a growing problem, not only in the U.S., but increasingly around the world. Recent epidemiological and clinical evidence suggests that sugar consumption can lead to excess calorie intake and therefore promote the development of obesity and metabolic disorders like diabetes. Artificial sweeteners like aspartame have been studied as a potential sugar substitute in foods and beverages.

Aspartame is often referred to as a nonnutritive sweetener, but not because aspartame is lacking in calories. Aspartame is a synthetic conjugation of two amino acids: aspartic acid and phenylalanine (which is also why it is called an "artificial" sweetener). It has an energy value of about four kcals per gram, like protein or sugar. However, as you can see in Figure 1, because aspartame is 200 times more potent than table sugar at triggering the sensation of sweetness, far less is needed when manufacturing sweet-tasting foods or beverages. This means that if you were regularly consuming sugar-sweetened soft drinks that contained 150 kcals each, you could switch to a diet soft drink containing a nonnutritive sweetener like aspartame and ingest less than one kcal. This relatively simple substitution could have implications for people with diabetes and dramatic impacts on the development of obesity.

Figure 1: Relative potency of nonnutritive sweeteners relative to sucrose



However, the research on aspartame is not crystal clear. For example, a paper published in 1988 raised the possibility that aspartame could negatively affect the satiety response and lead to overconsumption. Yet, in 1994, the results of two human trials concluded there was no difference in energy intake for individuals that "preloaded" meals with aspartame and those that did not. This seemed to put an end to the confusion until 1997, when a study claimed that women consuming aspartame-sweetened beverages over-ate the day after consuming the drink compared to women drinking sugary beverages or mineral water.

The back-and-forth continued with a 2006 meta-analysis indicating consumption of aspartame is associated with a significant decrease in energy consumption and weight relative to sugar consumption. In 2010, a new hypothesis was offered that suggested artificial sweeteners do indeed promote feeding behavior if the artificially-sweetened food or beverage does not satisfy our food reward pathways.

To muddy the waters further, evidence concerning whether aspartame or other artificial sweeteners stimulate an insulin response or affect glucose tolerance is seemingly conflicted. A 2016 review of the literature discussed rodent studies that indicated aspartame led to impaired glucose tolerance, while a 2017 review pointed out that human trials to date had observed no effect.

It is unclear how exactly aspartame would have these effects on glucose and insulin, as the proposed mechanisms have not been extensively studied. A popular hypothesis is that aspartame and other sweeteners stimulate a cephalic phase insulin response. That is, the sweet sensation you get from tasting something sweet can stimulate the release of insulin before your food is absorbed. Another hypothesis is that since aspartame is a flexible molecule that can bind to sweet taste receptors, it may also be possible to stimulate signal transduction elsewhere in the body that might alter glucose uptake or insulin release. More recently, scientists have proposed that any changes in insulin sensitivity may be mediated by aspartame's effect on the gut microbiome.

Human studies are needed to further investigate the role artificial sweeteners like aspartame play in our metabolism and feeding patterns. The study under review sought to clarify some of the discord on the subject by examining different levels of aspartame consumption and how it affects glycemia, appetite, and body composition.

Aspartame is an artificial sweetener made from two amino acids that is widely used in foods and beverages to replace sugar while reducing calorie content. However, there is some controversy over how effective aspartame is at controlling glucose, and the present study sought to clarify this.

Who and what was studied?

The study under review was a preregistered randomized controlled trial involving 93 normal weight, young adults with normal fasting blood glucose levels. None of the participants used low-calorie sweeteners more often than once per week.

Participants were randomly assigned to one of three arms for the 12-week trial: a control group consuming no aspartame, a group consuming 350 milligrams of aspartame per day (about the same as two cans of diet soda), and a group consuming 1050 milligrams of aspartame per day (about the same as two liters of diet soda). The control group consumed water and placebo pills, while the aspartame groups consumed aspartame-sweetened fruit-flavored drinks containing 350 milligrams of aspartame with placebo pills (low-dose group) or pills providing an extra 700 milligrams of aspartame (high-dose group).

The primary outcome of interest was a change in oral glucose tolerance measured by an oral glucose tolerance test (OGTT). This test involves drinking a measured amount of glucose and taking blood samples at specific time points following ingestion to assess the body's response. Secondary outcomes were changes in body composition and self-reported appetite. All outcomes were corrected for multiple comparisons. Serum biochemical markers like liver enzymes and cholesterol were also measured, although these were not listed in the study's preregistation.

OGTT measurements were taken at baseline and after twelve weeks, body composition was assessed weekly, and participants were instructed to keep an appetite log via a smartphone app. Urine samples were also collected weekly to estimate compliance with the treatment program.

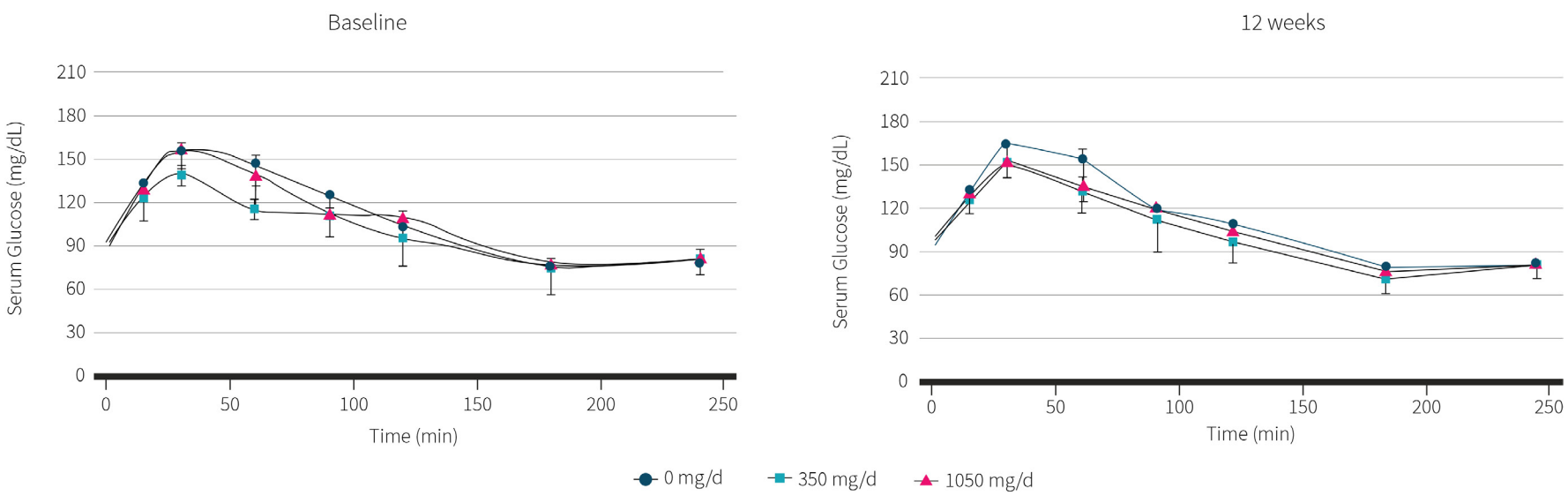
Finally, it is worth noting that the trial was funded by the Ajinomoto Company, a manufacturer of aspartame and other food additives.

This was a randomized controlled trial in which healthy, young adults consumed zero, 350, or 1050 milligrams of aspartame daily for 12 weeks. The primary outcome was glucose tolerance, and secondary outcomes were body composition and appetite ratings.

What were the findings?

There were no significant differences between or within the three groups for changes in glucose tolerance, insulin secretion, body composition, or measures of appetite. You can see the specifics of how the three groups' OGTT results looked at baseline and after 12 weeks in Figure 2. None of the serum markers differed between groups, either. Moreover, no clear trends were apparent in the data.

Figure 2: Aspartame had no effect on glucose tolerance



What does the study really tell us?

This study gives us useful data on a topic that may have seemed obvious, but has nevertheless been viewed as ambiguous because rodent and human studies had not aligned.

The two treatment arms of the trial provide insight into what effect might be observed in casual consumers of aspartame and rather extreme aspartame consumers. To put the doses in perspective, 350 milligrams of aspartame is roughly equivalent to two 12 fl. oz. cans of diet soda, while 1050 milligrams of aspartame can be found in approximately two liters of diet soda. Accordingly, the findings of this study have real-world applicability, unlike many animal trials that use unrealistically high doses of consumption. The results of its primary outcome seems clear: at both low and high doses, aspartame has no discernable effect on glycemic control.

It is worth noting, though, that the authors did not include a power analysis in the report. Power analyses are performed in order to ensure that an adequate population size is used to be able to detect an effect of aspartame, if there really is one. While the population size that the authors used may be sufficient to detect an effect if there is one, this cannot be said for certain; thus, the lack of effect could also be attributable to the study being underpowered. A documented power analysis would have lent additional credence to the findings.

With free-living studies like these, it can be difficult to know how well participants are adhering to their assigned treatments. However, urinary samples were taken to gauge compliance in this study, which turned out to be about 95% using the urinary biomarkers.

Potential limitations of this study include the way appetite and hunger was gauged. The researchers instructed study

participants to record feelings of appetite every waking hour of every day for 12 weeks using a smartphone application. However, no evidence was presented that evaluated the validity of this method, nor was any information given on how consistently the participants performed this task. In this light, it might be worth interpreting the lack of measured effect on appetite with caution.

Additionally, no information on the participants' diets was collected. Bodyweight and composition remained unchanged in all groups, suggesting that changes in dietary habits were small or nonexistent, but it is still possible that changes could have shadowed an effect of aspartame. Ideally, this free-living study would be complemented by a controlled-feeding study using a similar intervention (aspartame dose, participant characteristics, etc.).

The study under review provides pragmatic experimental evidence that consuming even high, but still realistic, doses of aspartame (equivalent to two liters of diet soda) does not cause blood sugar abnormalities or affect body composition or appetite.

The big picture

This study adds to the growing body of evidence that aspartame has little effect on glucose tolerance or body composition in humans.

Recently published human studies on this topic have reached similar conclusions. For example, 24-hour glucose profiles and energy intake did not significantly differ when participants "preloaded" lunch with either sugar or a low-calorie sweetener of stevia, aspartame, or monk fruit. Likewise, a 24-week weight loss trial comparing women who drank water to those who drank diet beverages resulted in equal weight loss, body composition, and fasting blood glucose levels by the end of the weight loss period. At the end of the weight loss period the water group had a slightly lowered fasting insulin level. However, after a 12-month weight maintenance phase following the weight loss, the water group had lost more weight, had a lower BMI, and had lower fasting insulin levels compared to the diet beverage group, although no significant difference remained with fasting glucose between groups. A comparable year-long trial investigating both men and women drinking diet beverages to those drinking water resulted in opposite findings: namely, the diet group experienced greater weight loss than the water group.

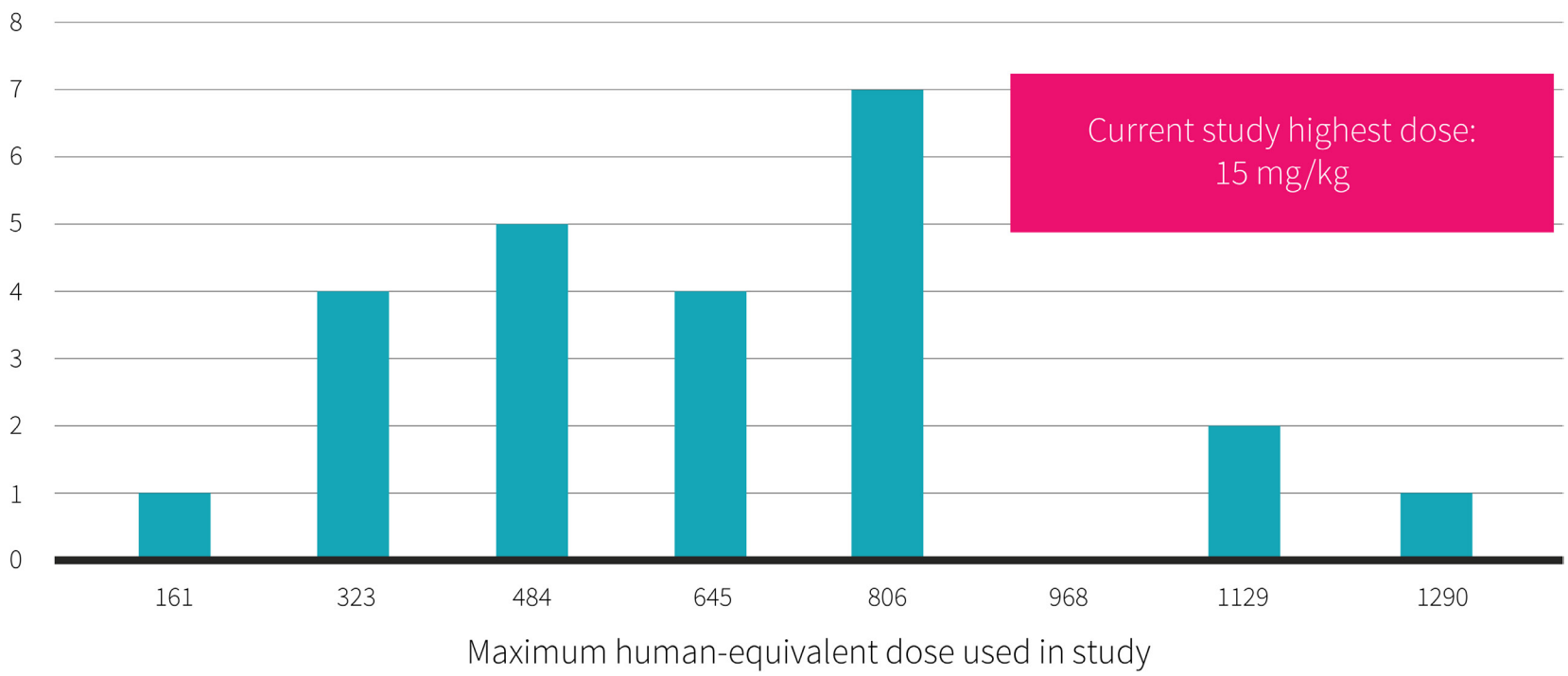
A 2014 meta-analysis of randomized controlled trials indicated that artificial and low-calorie sweeteners modestly reduce body weight and BMI compared with their sugary counterparts.

If we try to examine publications specific to artificial sweeteners and risk of diabetes, we do not find much in the literature. A 1976 trial of patients with type 2 diabetes administered aspartame for 90 days and found no adverse effects. A similar 1989 trial administered aspartame to type 2 diabetics for six weeks and found no differences in glycemic control, glucose tolerance, or insulin. A 1985 trial where aspartame was administered to both type 1 and type 2 diabetics found no changes in plasma glucose. A recent meta-analysis examining these trials of diabetics as well as clinical parameters related to diabetes concluded that, compared to a control such as water, aspartame had little to no effect on blood glucose, insulin, body weight, or energy intake.

While aspartame is not without controversy, the preponderance of evidence suggests that this substance does not have a significant effect on insulin levels, glucose clearance, body weight, or appetite, even in large doses. For those interested in lower-calorie alternatives to sugary foods and beverages, aspartame may be effective way to manage insulin levels and mitigate weight gain.

One point worth mentioning, which is depicted in Figure 3, is that animal studies typically use much higher doses than humans actually consume and in some cases higher doses than humans *can* consume. This is worth remembering when reading studies on aspartame and other artificial sweeteners.

Figure 3: Number of studies using various human-equivalent doses in aspartame toxicology (mg/kg body weight)



Reference: Butchko et al. Regul Toxicol Pharmacol. 2002 Apr.

The lion's share of randomized clinical trials refute negative effects of aspartame and other artificial sweeteners on glycemia and food intake. On the other hand, observational studies have yielded mixed results, with a number of epidemiologists reporting significant associations between artificial sweetener intake and BMI. Whether, and to what extent, this link is mediated by confounding factors should be a topic for future research.

Frequently asked questions

Has sucralose, another popular artificial sweetener, been investigated for its effect on glycemic control?

Studies have shown that sucralose (aka Splenda) has little effect on blood glucose and insulin levels. Indeed, a 1993 German trial tested Ace K, aspartame, cyclamate, and saccharin and found that their influence on insulin levels did not differ significantly from drinking only water. Indeed, a 2017 12-week, double blind placebo-controlled trial concluded that there were no significant differences between sucralose and placebo in several biomarkers of glycemic control that included OGTT, insulin, and HbA1c levels. However, somewhat paradoxically, sucralose has been shown to exacerbate both the glycemic and insulin response when consumed with carbohydrate.

Has aspartame been linked to cancer?

The history of aspartame research is not without controversy. Several rodent studies have been performed over the years suggesting that aspartame is potentially carcinogenic at very high doses. However, other scientific review papers written by authors with financial ties to the industry have downplayed their significance. Other evidence suggests that aspartame can cause oxidative stress and lead to inflammation. Again, this data is largely from rodent studies.

Human studies evaluating the link have been sparse and only observational in nature, relying on prospective cohorts. One cohort study indicated no association with high aspartame intake and hematopoietic and brain cancers. An assessment of the Nurses' Health Study and Health Professionals Follow-Up Study indicated an increased risk in men of non-Hodgkin lymphoma and multiple myeloma who consume greater than one diet beverage per day. However, there was no risk of these cancers in women who consumed diet drinks, and there was no association in men or women with diet beverage consumption and leukemia.

Does aspartame cause migraines?

Dietary triggers of migraine headaches can be difficult to pin down. However, some evidence suggests that aspartame may be involved in inducing migraines in a subset of susceptible individuals. One proposed mechanism for this phenomenon is oxidative stress induced by aspartame. Another possible mechanism suggested by rodent studies is that aspartame can block increase of brain levels of serotonin, and abnormal serotonin levels have been linked to migraines.

It has also been suggested that the products of aspartame metabolism—namely methanol, formaldehyde, and diketopiperazine—may play a role in the development of mental disorders and disrupt the central nervous system.

Are there other known benefits to aspartame?

Aspartame and other low-calorie sweeteners have been shown to reduce the risk of dental caries. This is due to both the displacement of sugar in the diet as well as the bacteriostatic and cariostatic properties. That is, some dental journals have suggested that sweeteners including saccharin, aspartame, and xylitol may actively prevent bacteria from reproducing.

What should I know?

Aspartame is a widely used artificial sweetener that many people use in foods and beverages to reduce their caloric content for weight management purposes and to manage blood glucose and insulin levels. However, some studies have indicated that aspartame may not be as effective at controlling weight or blood glucose as may have been previously thought. This particular study under review attempts to add some clarity to the noise.

This study was a randomized, controlled trial that assigned participants to water, a moderate dose of daily aspartame, and a high dose of daily aspartame for twelve weeks. The main outcome of interest was glucose tolerance, but other outcomes were measured such as body composition and appetite ratings. After the intervention, there was no significant differences in any of these measures between the groups or within the groups compared to baseline ratings. Essentially, aspartame had no effect on these factors.

The results of this study support the majority of publicly available evidence that consumption of aspartame, even in higher than normal doses, has little effect on insulin secretion, glucose tolerance, or body composition. Furthermore, while aspartame's effect on appetite and hunger are still disputed, this study lends credence to its lack of effect. ◆

Do you have some thoughts on aspartame? Should Def Leppard write a new song called "Pour Some Sugar-Substitute on Me"? Discuss it over at the ERD Facebook forum.

ERD Mini: The latest skinny on polyunsaturated fats according to the Cochrane Collaboration

Back in ERD #42, volume 1, we covered a major meta-analysis examining omega-3 fatty acid supplementation's effects on cardiovascular outcomes which found no association with any outcome. In July of 2018, the Cochrane Collaboration released another meta-analysis of omega-3's cardiovascular effects, as well as two other meta-analyses looking at omega-6 and polyunsaturated fatty acid intake as a whole. All three analyses were done by many of the same researchers. Below are some of the main take-aways from these three meta-analyses.

Omega-3 fatty acids (mostly as supplements, but sometimes as dietary advice or ALA-enriched foods; mostly moderate- to high-quality evidence)		
Outcome	Lower bound of 95% CI for relative risk	Upper bound of 95% CI for relative risk
All-cause mortality	0.90	1.03
Cardiovascular mortality	0.87	1.03
Cardiovascular events	0.94	1.04
Authors' main conclusions: Little to no effect on cardiovascular health and mortality, although ALA may slightly reduce risk of cardiovascular disease, arrhythmia, and mortality from coronary heart disease.		

Omega-6 fatty acids (all studies involved linolenic acid (LA) or gamma-LA, usually replacing saturated or monounsaturated fats in the diet; mostly low-quality evidence)		
All-cause mortality	0.88	1.12
Cardiovascular mortality	0.76	1.55
Cardiovascular events	0.81	1.15
Authors' main conclusions: No effects on cardiovascular health besides small decrease in heart attack risk. Also reduces total cholesterol.		

Total polyunsaturated fat intake (mostly as supplements, but sometimes as dietary advice, enriched foods, or a combination; mostly low- to moderate-quality evidence)		
All-cause mortality	0.89	1.07
Cardiovascular mortality	0.82	1.26
Cardiovascular events	0.79	1.01
Authors' main conclusions: No effect on mortality, but slightly reduces risk of cardiovascular disease. Slightly decreases serum triglycerides and total cholesterol, but also may slightly increase weight.		

Note that none of the big outcomes we presented were statistically significant, since the 95% confidence interval overlaps with a relative risk of one, which would indicate no effect. A small handful of statistically significant effects were found, though, some of which we mention in the table.

Also note that we reported these outcomes using 95% confidence intervals instead of point estimates. The reason why is because one way to interpret the 95% confidence interval is as the range of values that the data are consistent with. With that in mind, we'd like to hear your thoughts: given the results of these three meta-analyses, do you interpret these outcomes as largely null, or do you think there's still room for thinking that polyunsaturated fats may be helpful for some aspects of cardiovascular health? See what your peers are saying, and have your own say, over at the ERD Facebook forum!

Does the 16:8 fasting diet boost weight loss and health?

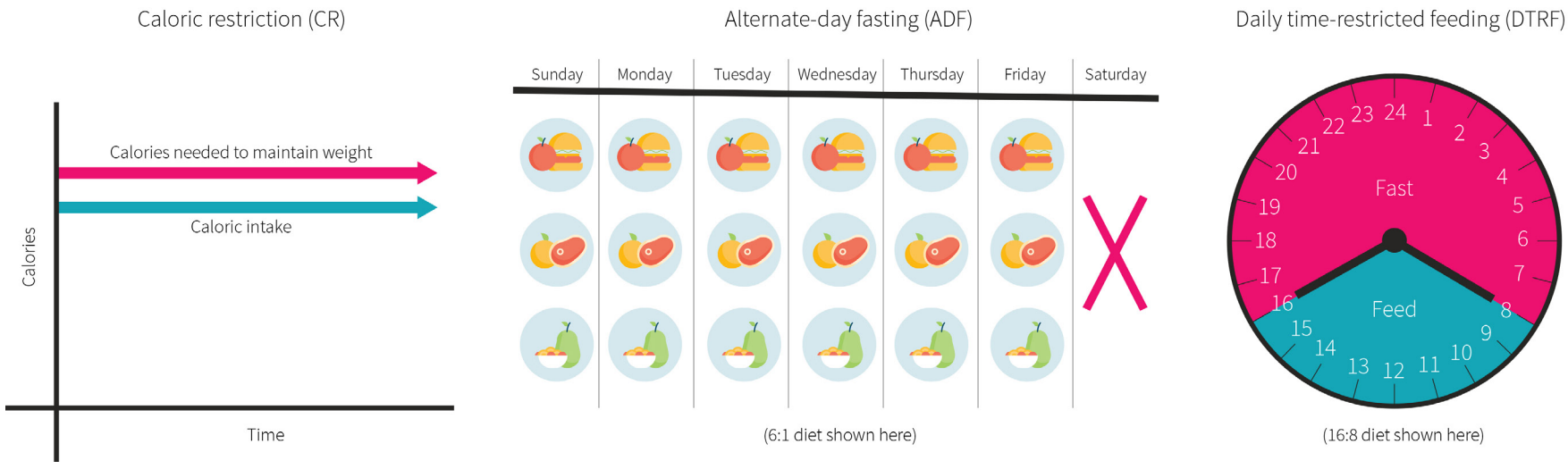
Effects of 8-hour time restricted feeding on body weight and metabolic disease risk factors in obese adults: A pilot study

Introduction

Calorie restriction (CR) is a reduction in calorie intake that does not lead to malnutrition or starvation. Long-term CR has been associated with improved weight management and aging, as well as a reduced risk of diseases related to metabolic health, such as type 2 diabetes, heart disease, and cancer.

Intermittent fasting (IF) is becoming an increasingly popular way of achieving CR, which involves alternating cycles of eating and fasting. Some types of IF are illustrated in comparision to CR in Figure 1. One type of IF, alternate-day fasting (ADF), involves alternating days of fasting and feasting, usually by eating regularly one day and then fasting for 24 hours until dinner on the following day, two to three days per week. Daily time-restricted feeding (DTRF) is another type of IF in which all food is consumed within a three to 12 hour period every day. For example, the 16:8 diet involves consuming all food within an eight-hour window and fasting for the remaining 16 hours of the day. This seems to be the most common type of IF promoted in the fitness industry. Similarly, Islamic fasting during Ramadan involves fasting between dawn and dusk and consuming all food after sunset.

Figure 1: Some different types of diets



Some studies have found that ADF leads to similar levels of weight loss as traditional CR diets. ADF may also lead to improvements in markers of health like cholesterol, blood pressure, and insulin regulation.

A smaller number of studies have investigated the effects of DTRF. Some animal studies have found that DTRF may result in improvements in metabolic health. Human studies have found that DTRF was associated with sustained weight loss in obese participants and improvements in body composition and certain markers of health.

No previous studies have examined whether DTRF is an effective approach to promote weight loss as well as reducing the risk of metabolic problems in obese participants. Therefore, the study under review aimed to explore the effect of an eight-hour time-restricted diet (i.e. a 16:8 diet) in obese adults, in terms of the effect on bodyweight and metabolic health.

Intermittent fasting (IF) is a popular way of achieving a calorie deficit to promote weight loss and health. Research has found that certain types of IF, such as daily time-restricted feeding, are associated with successful weight loss and health improvements. However, no previous studies have directly examined the effect of daily time-restricted feeding (DTRF) in obese participants. This study sought to fill that knowledge gap.

Who and what was studied?

This 12-week pilot study recruited 23 metabolically healthy, obese adults (20 females and three males, majority African American) with an average age of 50 years and an average BMI of 35. These participants were compared to a matched historical control group from a previous weight loss study rather than to a control group within the current study. Beyond metabolic health, participants were excluded if they were pregnant, night shift workers, smokers, or going through menopause.

A two-week baseline weight stabilization period took place before the trial began, where participants were asked to not alter their usual dietary and physical activity habits (which was less than 7,500 steps per day). Participants then followed an eight-hour DTRF intervention for 12 weeks. This involved unrestricted eating between 10:00 am and 6:00 p.m. daily,

with only calorie-free beverages (like water, diet soda, tea, or coffee) between 6:00 pm and 10:00 am. Compliance with this intervention was measured using a self-documented daily adherence log.

Change in bodyweight was the primary outcome of this study, and the authors had calculated that the study would achieve 80% statistical power to detect a 3% difference in body weight if 19 participants completed the trial.

Power calculations are used to determine how many participants are needed in a study to to detect an effect of a certain size, if one exists. If a study doesn't have enough participants, then statistical tests may not be able to pick up on a significant difference between the groups even when an effect exists. To avoid this happening, it is advised that studies should yield statistically significant results in at least 80% of the cases; in other words, the study should have a statistical power of 80%. A study with 95% power is more able to detect significant differences than a study which is 80% powered.

Factors that go into a power calculation include the study's statistical significance threshold (e.g. $p < 0.05$ or < 0.001, sometimes called its alpha level) and how big of an effect you would like to detect. This means that if you want to detect small effects (such as a small change in weight or cholesterol), the study would need more participants. It also means that if no statistically significant effect is found, this could mean an effect exists, but is smaller than the study was able to detect given its power. If the researchers don't do a power calculation, it makes it much more difficult to interpret a lack of statistically significant effects.

The researchers also assessed body composition (via DXA) and other risk factors related to metabolic health as secondary outcomes: blood pressure, heart rate, blood lipids (total cholesterol, direct LDL-C, HDL-C, and triglycerides), fasting glucose and insulin, insulin resistance, and homocysteine.

Participants completed a seven-day food record during the baseline period and at week 12. Rather than weighing food, guidance was provided by a dietitian on how to complete these food diaries using household measures (like cups and spoons). Nutritionist software was then used to calculate the total daily intake of energy, fat, protein, carbohydrate, cholesterol, and fiber.

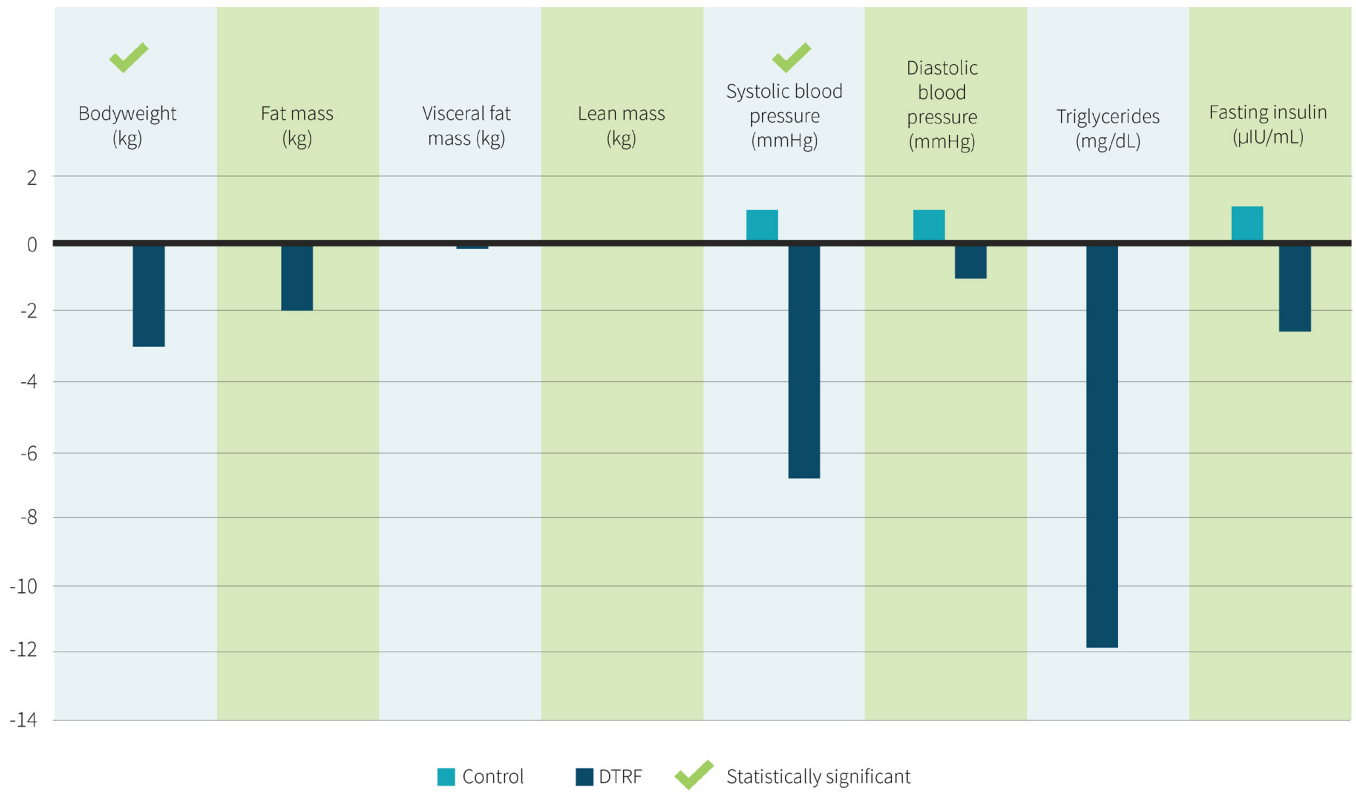
This study was preregistered within two months of the trial beginning, but there are some differences between the outcome measures listed under the study registration and those reported in the study. For example, the inflammatory markers tumor necrosis factor-alpha (TNF) and interleukin-6 (IL-6) are listed as secondary outcome measures in the preregistration but are not reported in this study.

This study assessed how eating all food within an eight-hour window daily for 12 weeks affected the bodyweight, body composition, and metabolic health of 23 obese adults.

What were the findings?

As you can see in Figure 2, bodyweight was significantly reduced by 3.0 kilograms or 2.6% in the DTRF group compared to the control group, which did not lose any weight by week 12.

Figure 2: Changes in select outcomes over 12 weeks

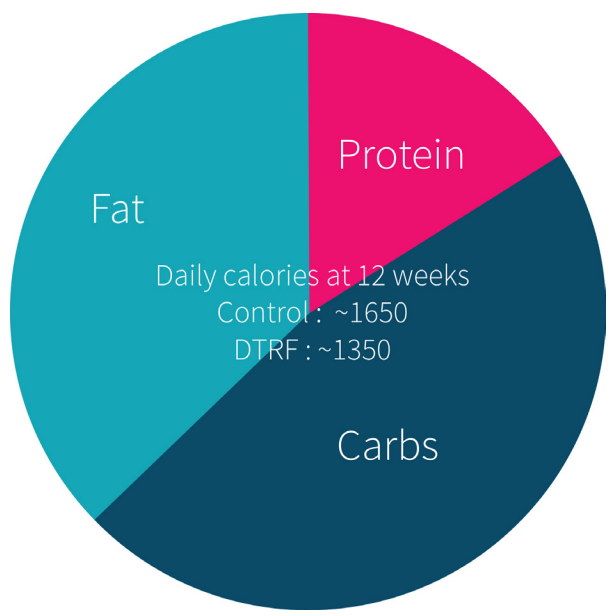


The reduction in bodyweight was accompanied by a significant 1-point reduction in BMI, but changes in total fat mass (-2.0 kilograms) and visceral fat mass (-0.1 kilograms) did not reach statistical significance when compared to the control group. Notably, lean mass was not affected in either group.

With regard to secondary outcomes, systolic blood pressure significantly decreased in the DTRF group by 7.0 mmHg (5.5%) compared to the control group. No between-group differences were observed in other parameters of metabolic health, although the DTRF group did experience significant reductions over time in fasting insulin (-31%), insulin resistance (-37%), triglycerides (-11%), and homocysteine (-9%).

By week 12, according to the second seven-day food log, participant energy intake was significantly reduced in the DTRF group by 341 calories per day on average, whereas the control group's energy intake stayed relatively stable. However, there were no significant differences in activity level or nutrient intake between the DTRF and control group during the trial. The breakdown of macronutrient intake (which was the same for both groups) is shown in Figure 3.

Figure 3: Macronutrient and caloric intake for both groups in this study



In terms of compliance, participants followed the guidelines to eat within an eight-hour window on an average of 5.6 days per week during the trial, and compliance was similar throughout the 12 weeks. The DTRF group's average eating window (eight hours) was significantly less than that of the control group (11 hours). However, only 17 participants (26% dropout rate) completed the intervention.

DTRF lead to a significant decrease in body weight, BMI, systolic blood pressure, and calorie intake compared to the control group. There were no significant changes in nutrient intake, activity level, or other markers of metabolic health.

What does the study really tell us?

This pilot trial of obese adults found that eating all food within an eight-hour window (as compared with the participants' usual 11-hour eating window), for an average of six days per week, resulted in an average weight loss of 3.0 kilograms (2.6%) after 12 weeks. Although this only works out to a weight loss rate of roughly 0.25 kilograms per week, which is below the usual goal of 0.5 - 1.0 kilograms per week, it was the result of simply shortening the eating window without active calorie restriction.

The DTRF group and control group consumed a similar amount of calories per day before the study began, but without counting calories the DTRF group were consuming 341 fewer calories per day on average by the end of the trial. This calorie reduction was significant when compared to the control group, but is still lower than the recommended daily calorie reduction for weight loss, which is 500 - 1000 calories per day, which could explain the suboptimal rate of weight loss.

Body fat was reduced by 2.0 kilograms. Although this was not a significant reduction, it may be related to the fact that the study was small and this was one of many outcomes. This may also explain the lack of statistical significance in the other measures as well, such as insulin resistance and triglycerides; those measures showed significant within-group changes but not between-group differences. The only exception was systolic blood pressure, which was "elevated" on average before the study began, as defined by the ACC/AHA guidelines, and decreased by 7.0 mmHg (5.5%) in the DTRF group.

It is important to note that participants only complied with this DTRF intervention for an average of 5.6 days per week, rather than following it on a daily basis. This may mimic a common eating pattern, which involves eating more freely on the weekend, but may also suggest that it is difficult to stick to this style of eating every day. Similarly, the 26% dropout rate in this study was quite high. However, the authors reported that none of the participants dropped out due to issues with the diet.

This study is of particular interest since it's the first carried out in metabolically healthy obese adults to investigate the effects of eight-hour DTRF. It also had several strengths. For instance, the chosen outcome measures are relevant to the study, and the nutrition analysis software and pedometers used to assess activity are both known to be reliable. Also, the trial was carried out in free-living participants, rather than in a lab setting, which increases the external validity of

the findings. There are no apparent conflicts of interest and the trial was preregistered early on. This suggests that the authors have been transparent about the way the study was carried out, although some of the secondary outcomes differ from those that were pre-registered (e.g. the inflammatory markers which were tested).

A key limitation of this study is that it was a pilot study using historical controls from a previous study whose measurements could have been taken up to five years ago. The gold standard study design for intervention-based studies such as this is a randomized controlled trial. The authors of this study report closely matching participants with the control group based on age, sex and BMI; control participants were recruited from a similar location and the majority of participants in both trials were African American, but there is no mention of whether they were matched in relation to race. Furthermore, the gap in time between when the measurements were taken from DTRF group and the control group could have caused differences to arise which could have affected the overall results. For example, food availability or average health knowledge in society may have changed over the course of five years.

The study under review was also relatively short (12 weeks) so it doesn't show the effects of DTRF in the long term. It also only involved metabolically healthy obese participants, who were mainly female African Americans, so the results of the study may not apply to other population groups. While this study had some limitations, it was labelled accurately as a pilot study, meant to pave the way for future research, not to be the final word on DTFR.

This pilot study found that limiting dietary intake to eight hours for roughly six days per week for 12 weeks resulted in a small daily calorie deficit, a small amount of weight loss, and a slight reduction in systolic blood pressure. As this is the first study to look at the effects of this type of intervention in a group of obese adults, further research is needed to explore the effectiveness of DTFR.

The big picture

A systematic review from 2016 found that IF was as effective as traditional CR for promoting weight loss, but it was not superior to CR. There were also similar dropout rates in the IF and CR groups, and IF was found to not improve metabolic health more than CR diets. However, the current evidence base related to the effects of IF in humans is limited, and most of the studies to date are related to ADF rather than DTRF.

A more recent randomized controlled trial, which investigated the effect of ADF in a group of metabolically healthy obese adults, found that ADF lead to a similar amount of weight loss as a CR diet, but LDL cholesterol levels also increased in the ADF group, whereas this did not happen in the CR group. The results of the metabolic markers in the study under review also did not significantly improve as a result of the DTRF intervention, with the exception of a 5.5% reduction in systolic blood pressure. This reduction in systolic blood pressure was comparable to a study from 2014, which found that a form of ADF that included small meals on the fast day (which totaled 25% of total daily energy requirements) resulted in a 5.9% reduction in systolic blood pressure.

There is evidence from animal studies that DTRF can promote weight loss and metabolic health. A human study from 2016 which examined the effects of a daily eight-hour eating window in resistance trained males also found that DTRF

was associated with reducing fat mass and improving certain markers of metabolic health (including glucose, insulin, and triglycerides), while maintaining strength and muscle mass. Another human study found that restricting dietary intake to a 10-hour feeding window in a group of healthy overweight adults resulted in 4% weight loss that was maintained for 12 months, which is a higher degree of weight loss than the 2.6% weight loss which occured in the study under review. Furthermore, a study which examined the effect of ADF in metabolically healthy adults found reported weight loss of 6.8% after six months. Other studies have found lower levels of weight loss in DTRF groups, which is more similar to the study under review. For example, a study which examined the effects of a four-hour eating window on four days per week resulted in 1.1% weight loss after eight weeks.

The mechanisms behind the benefits of DTRF are not fully established, but a reduction in calorie intake and the knock-on effects of using stored energy while fasting are likely to be a significant factors. It is also thought that the stress that IF places on the body can trigger cellular repair, which can lead to metabolic improvements. Another potential factor is how the timing of eating interacts with our circadian rhythm. For example, a study conducted in mice found that DTRF led to improvements in circadian rhythm and metabolic health. Human studies have also found that eating bigger meals earlier in the day, rather than in the evening, was associated with improved weight loss, which may also be related to our circadian rhythm. We covered some evidence linking metabolic health to circadian rhythms in ERD #44, Volume 2, where we reviewed a study examining early time-restricted feeding. But overall, more research is needed to explore the potential impact of circadian rhythm in the context of IF and health.

There is some evidence that IF diets, including the 16:8 diet, can promote weight loss and a reduction in calorie intake. The evidence is more mixed in terms of metabolic outcomes, and more research is needed.

Frequently asked questions

Beyond weight and metabolic health, have any other benefits of IF been found?

There is some evidence that IF diets may positively affect the aging process. For example, a systematic review of human studies from 2016 found that dietary restriction, including both CR and IF, were associated with reducing inflammation and improving biomarkers related to healthy aging. Similarly, a literature review from 2017 reported that IF may promote cellular repair processes that reduce the risk of developing diseases related to aging.

Some studies have also found that fasting may have a positive effect in terms of mood and cognition. For example, an intervention study which included 32 older men found that IF was associated with improved mood states. However, most of the evidence related to IF is related to weight management and metabolic health, so more studies are needed to investigate the wider effects of IF.

Are there any risks related to fasting diets?

There is mixed evidence about whether fasting damages the liver. Some old animal studies have found that fasting can remove toxins from the liver, while other animal studies have identified that fasting causes the liver to shrink and work less efficiently. Human studies have also found that fasting can impair the liver's ability to remove toxins from the body.

Fasting has also been associated with: increasing insulin resistance, increasing LDL cholesterol, reducing muscle mass and ability to exercise, reducing immunity, and causing headaches. However, some of these studies found that prolonged fasting (e.g. for 24-72 days) is worse than a shorter fast (e.g. for 10 hours), so DTRF may be a less risky option than a longer fast.

A systematic review from 2015 reviewed whether IF was healthy or harmful. This concluded that although there is some evidence that fasting might be beneficial in terms of weight and metabolic health, more humans studies are needed before conclusions can be made about the safety and long-term health effects of IF.

Does fasting get better results with shorter feeding windows?
There isn't enough evidence to answer this question definitively, but the available research has not shown that there is an advantage to a shorter fasting duration. For example, 4% weight loss has been observed with a DTFR window of 10-11 hours, while the current study used an eight-hour DTRF window, which resulted in 2.6% weight loss. Similarly, a four-hour eating window on four days per week resulted in 1.1% weight loss after eight weeks.

What should I know?

Daily time-restricted feeding (DTRF) is a type of intermittent fasting (IF) that involves consuming all food within a set time frame (usually three to 12 hours) every day. This is growing in popularity as a method for reducing calorie intake and promoting health. However, there is limited evidence about the effects of IF on human health, and this is the first study which has investigated the effects of DTRF (the 16:8 diet in particular) in a group of healthy obese adults.

Results showed that restricting dietary intake to an eight-hour window between 10:00 am and 6:00 pm for 12 weeks resulted in 3.0 kilogram weight loss, a reduction in calorie intake, and a slight reduction in systolic blood pressure. Given that this was a pilot study, further randomized controlled trials with a larger sample size, longer trial duration, and that use objective measures of daily eating duration are needed. ◆

Did this study convince you that the 16:8 diet is a healthy way to eat? Head over to the ERD Facebook forum to share your thoughts!

You are what you eat, right?

Meat, eggs, full-fat dairy, and nutritional boogeymen: Does the way in which animals are raised affect health differently in humans?

Introduction

Cancer prevention recommendations vary significantly from different organizations regarding macronutrient composition and food type. Most of these recommendations are based on epidemiologic studies that vary in population, data evaluation, and dietary assessment methods, and have some inherent biases. Advice to consume a low-fat diet and increase fruit and vegetable intake has yielded inconsistent results, with the postulation that there may be a low threshold effect (i.e., benefits are only seen in populations consuming little fruits and vegetables to begin with) or specific nutrients that have benefits.

It appears consumers believe organic food reduces cancer risk and they associate 'organic' with the natural process of food production that incorporates care for the environment, animal welfare, and no use of fertilizers or pesticides. This appears to be a large part of the drive for the need to know a food's origin, from the name of the farmer that tended the crops to the way Paul the pig was raised, slaughtered, and processed.

Whether or not the origins or treatment conditions of foods influence nutrition (beyond normal variation) along with any associated changes in cancer risk, is still being explored. From 1950 to 1999, various garden crops are reported to have decreased levels of some nutrients, conventionally believed to be because of agricultural conditions and/or practice, but the cause is actually suggested to be the selection of cultivars that increase yield. It has also been suggested that soil mineral depletion has not influenced mineral content of fruits and vegetables, with the only contributor to a 'dilution effect' being the adoption of higher yield crop varieties.

The latest buzz on animal foods and cancer risk has to do with some strong evidence that processed and red meat increases cancer risk, according to the World Cancer Research Fund. What if the conditions that animals are raised in have an impact on the relationship of animal foods with cancer risk? One review has reported that organically raised

animals produce meat and cheese with higher conjugated linoleic acid (CLA), and polyunsaturated fatty acids, such as the now famous omega-3 fatty acids. Another study has suggested that meat from pasture-fed animals contain more healthful nutrients than grain-fed animals, such as fatty acids and antioxidants, which are associated with cancer risk prevention. The specifics of some of these differences are shown in FIgure 1.

Figure 1: Select nutrients in grass-fed beef compared to grain-fed

Reference: Daley et al. Nutr J. 2010 Mar

CLA and omega-3 have been associated with various health benefits, and the increased levels of both that are found in products from animals raised in more species-appropriate conditions suggests the raising of animals could impact human health and cancer prevention. The authors of the study under review state that they wanted to address the lack of scientific dialogue regarding differences that pasture-raised animal foods may have on health and cancer prevention. This study aimed to assess the differing effects on CLA and omega-3 and other health biomarkers in humans following the consumption of eggs, butter, cheese, and meat from differently raised animals.

Cancer prevention recommendations vary significantly across organizations, whether it be macronutrient composition or food type, but the public seems to believe that the conditions in which the food is grown have an impact on its cancer-preventive potential. It appears that agricultural conditions and practices are not to blame for the reduced nutrient levels of plants, while animals raised alternatively to conventional methods appear to yield animal products with higher nutritive value, such as increased conjugated linoleic acid (CLA) and omega-3 fatty acid. The study under review aimed to assess differences in CLA, omega-3, and other health biomarkers in humans following the consumption of animal products from animals raised through different methods.

Who and what was studied?

This systematic review searched for studies comparing the health effects and nutrient profiles of eggs, meat, butter, and cheese sourced from animals subject to different living conditions. Specifically, the authors looked at effects on inflammatory factors (interleukin-6 (IL-6), IL-8, tumor necrosis factor (TNF), and C-reactive protein (CRP)), blood lipids, CLA, and omega-3 fatty acids (ALA, EPA, and DHA). Ultimately, 29 studies were included for review.

There was no primary outcome declared and the study was not pre-registered. A meta-analysis was attempted but aborted due to differences in study design, participant inclusion criteria, diet composition, physiologic outcomes measured, poor study quality, and limited number of studies. Ten studies focused on CLA and 19 focused on omega-3 fatty acids, with an average of about 30 participants per study and ranging from five to 153.

This was a systematic review of 29 comparative studies assessing the influence of changes in animal diet on measures of lipid metabolism and inflammation. Studies varied in design, inclusion criteria, diet composition, physiologic outcomes measures, and quality, preventing meta-analytic assessment.

What were the findings?

Out of ten studies focused on CLA, seven looked at dairy and three looked at beef. Eight out of ten studies demonstrated a direct increase in serum CLA concentrations or food CLA content in their experimental group versus their control group, but only four reported differences in physiologic markers. However, the experimental groups differed wildly between studies, making comparisons meaningless. For instance, some of the studies focused on adding sunflower seeds to the cattle feed, while others examined traditionally- vs. grass-fed beef. Two studies reported decreases in HDL-C and two others reported reduced inflammatory markers. For the nitty-gritty details, see Figure 2.

Out of 19 studies focused on omega-3, 14 looked at eggs, two looked at cheese, two at beef, and one at eggs, cheese, and different kinds of meat. All demonstrated increases in serum or food omega-3 content, but, just like with studies examining CLA, the differences in the ways the animals were raised and which products were consumed varied wildly, adding everything from marine algae to flaxseed to the animal feed. About half of the studies did not show any changes in measures of lipid or inflammatory markers. Four studies reported decreased triglycerides, while two showed increases. Two studies reported increases in HDL-C and one reported increases in LDL-C. You can check out Figure 2 for more details.

Figure 2: The effects on human disease biomarkers found in this review

Animal product consumed	Animal-raising intervention	Human effects relative to control
Butter	Sunflower seeds added to cow feed	↓ Total cholesterol; ↑ HDL-C
Red Meat	Wild game (kangaroo) vs. conventionally-raised wagyu beef	↓ Inflammatory markers
Cheese	Grass-fed	↓ Inflammatory markers
Red Meat	Grass-fed	↑ HDL-C

Human effects found in studies focused on omega-3 fatty acids

Eggs	Fish oil added to feed	↓ Triglycerides; ↓ Systolic pressure
Eggs	Flaxseed added to feed	↓ Triglycerides (in one study); ↑ Triglycerides (in another study)
Eggs	Flaxseed and sunflower seed added to feed	↑ HDL-C; ↓ Triglycerides
Eggs	Marine algae added to feed	↑ LDL-C
Eggs	Tuna oil added to feed	↓ Triglycerides
Red Meat	Grass-fed	↑ Triglycerides; ↑ HDL-C; ↑ LDL particle size

Almost all studies reported that changes in animal raising led to serum increases in CLA or omega-3 fatty acids when certain animal products were consumed, but changes in lipid and inflammatory markers were reported in less than half of the studies for either nutrient. Furthermore, the animal products examined and the differences between the studies' animal-raising methods make comparison between them meaningless.

What does the study really tell us?

While the interventions uncovered in this systematic review were all over the map, the overall pattern hints that supplementation of animal diet with seeds (sunflower, flax) and/or fish oil, or grass-feeding only appears to increase serum CLA and omega-3 fatty acids in human participants that consume the alternatively-raised animal products. Whether these increases in specific nutritional components lead to beneficial changes in lipid and inflammatory markers and corresponding health effects, let alone cancer, which was barely mentioned, is not clear.

The biomarkers assessed for inflammation may be known cancer biomarkers, but only two out of 29 studies demonstrated decreases and both were associated with CLA level increases. Both studies had small sample sizes of ten participants. One of the two studies assessed differences in cheese from grass-fed animals, while the other compared game meat (kangaroo) to conventional wagyu (a japanese beef cattle breed) beef, meaning it could simply be that kangaroo meat has greater CLA on its own.

With regard to the lipid health biomarker changes resulting from the increased omega-3 fatty acids of alternatively-raised animal products, four studies demonstrated decreases in triglycerides, suggesting a benefit, but triglycerides increased in two other studies, bringing that benefit into question.The omega-3 improved animal products were also associated with increases of HDL. That is in contrast to CLA, which was associated with decreased levels of the "good" cholesterol in two studies.

While two investigators independently selected studies, likely in an attempt to reduce internal bias — a good practice in the context of systematic review methodology — their method of systematizing the review process was unconventional. They did not state that they followed any particular framework for writing a systematic review, such as the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement. The addition of 20 studies, beyond the nine selected via the generally accepted way (from search results according to inclusion criteria), is uncommon. The process of selecting studies from the citations of the nine conventionally-selected studies biases the study selection. It also raises the question of whether their choice of search criteria was appropriate. If those twenty other studies were found without following the search criteria, why were they not found during the initial search?

A review of any kind is only as good as the studies included. The fact that the authors decided against a meta-analysis because of a large variance in study design, participant inclusion criteria, diet composition, physiologic outcomes measured, poor study quality, and limited number of studies casts doubt on whether a systematic review would have much weight either. After all, the average participant number for the studies included was 30, with a low of five and high of 153. These small participant numbers, alone, could explain the inconclusive and diverging results in the existing literature. It is not clear whether the studies considered baseline health of participants either (if participants in some of the

studies were already lacking CLA or omega-3), which could explain why biomarkers demonstrated a slight benefit in some studies, while other studies did not. More research is necessary, preferably with a more systematic and controlled method.

It is important to consider the evidence behind CLA and omega-3 and the biomarkers assessed in these studies, as well as the reason why the supplemented feed leads to increases in CLA and omega-3. Generally, when something is supplemented, unless there are problems with absorption or a complex metabolism, it would make sense that more of the substance in the diet of an animal that one consumes would increase that substance in the consumer. An increase of omega-3 in eggs from chickens fed feed supplemented with flax seeds, which are high in omega-3, simply makes sense. As for the evidence regarding health benefits behind CLA and omega-3, even the authors themselves note that "data in humans is limited" for cancer benefits regarding CLA, and supplementation of omega-3 fatty acids "has yielded mixed results" regarding cancer benefits.

Moreover, the study selection was not oriented toward cancer prevention at all. The word 'cancer', or any other related terms, were not used in the search criteria or inclusion criteria. The authors state that their focus was on cancer, but their real focus seems to be on various health markers and nutrients that themselves have weak connections to cancer prevention.

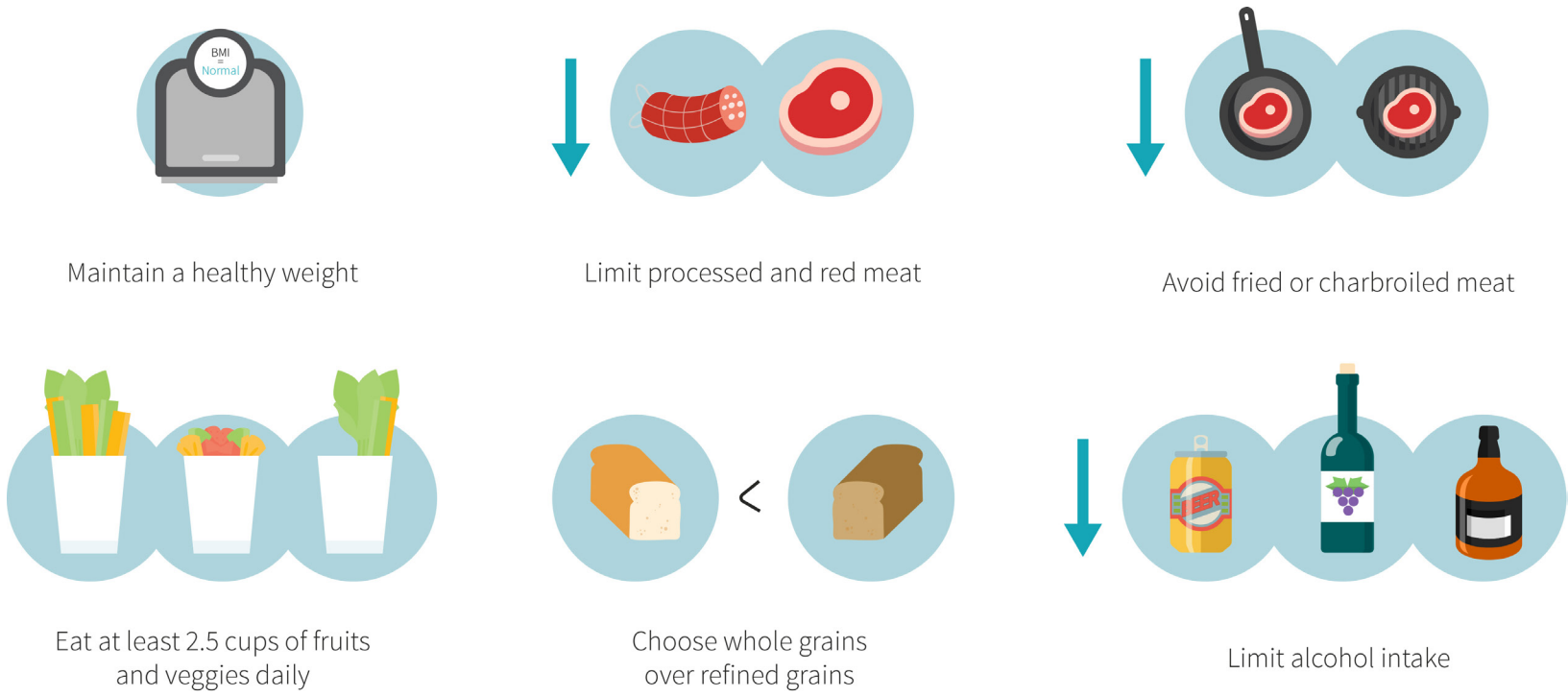
The current systematic review suggests that conventional grain animal diet supplementation with seeds, fish oil, or grass, increase serum CLA and omega-3 fatty acids in human participants consuming products from alternatively-raised animals. It is unclear whether these changes are beneficial for health, as the results were inconsistent with each other. With its non-standardized, unconventional approach to study selection, the review is at increased risk of bias. Moreover, the methodological differences, as well as the presence of claims that the authors themselves suggested to have limited evidence, restrict the strength of the results.

The big picture

The American Cancer Society's dietary guidelines for cancer risk prevention, shown in Figure 3, suggest moderation: careful monitoring of calorie consumption (not to go overboard, but not to starve either), an emphasis on plant foods and whole grains, and avoidance of alcohol and (recently) processed and red meats. Other guidelines are very similar, but, as the authors of this study indicate, none of these guidelines distinguish between natural and/or organically vs. conventionally-raised foods.

Anticancer activity driven by CLA has been suggested to work through its apoptotic (programmed cell death) activity as well as interruption of cancer cell growth in vitro and in vivo. However, as mentioned by the authors of this study, human studies are limited to epidemiological studies, with no clinical studies relating CLA intake and incidence of cancer. The few epidemiological studies available have not been able to find a protective effect of CLA against breast or kidney cancer, but there appears to be some protective influence against colorectal cancer. The conflicting data make it hard to determine any clear influence of CLA on cancer risk prevention, but it does not appear to have much potential from the data at hand.

Figure 3: ACS nutritional guidelines



Omega-3 fatty acids' anticancer effects are also controversial. A comprehensive review of omega-3 and its health benefits cites four clinical studies that reported reduced cancer risk, three with increasing fish intake and one with omega-3 intake. One of the six studies reported an increased risk of basal cell melanoma with increased omega-3 intake, while another reported no relationship between fish intake and breast cancer risk. Recently, the emphasis has been on achieving a proper ratio of omega-3 to omega-6 fatty acids for optimal health, with a suggested one to four times greater ratio of omega-6 fatty acids than omega-3 fatty acids.

Changes in cultivation or raising practices surrounding food production are bound to have small impacts here and there, with climate change being a large factor, but it appears some differences may not make a large enough change to substantially influence nutrient content beyond normal variations. Even though the nutritive value of fruits and vegetables has declined over the years, the decline is likely due to changes in cultivars, such as the adoption of semi-dwarf grains for greater yields. It is suggested that fruit and vegetable consumption at recommended amounts will still allow people to meet their nutrient requirements, with the beneficial trade-off of greater yields.

An increase in specific nutrients, such as CLA and omega-3, can be achieved by changing the diet of livestock. Beef (100 grams) has been reported to vary from 14.3 to 16.1 milligrams of CLA and 14.9 to 32.4 milligrams of omega-3s. The amounts achieved by different feeding practices may not reach sufficient levels to deserve to be labeled as a significant source of a particular nutrient. To give you an idea, the adequate levels of omega-3 fatty acid intake for the average adult male is 1.6 grams per day. With the average American consuming 128 grams of meat per day, only about 0.04 grams of omega-3 fatty acids come from beef. That is about 2.5% of the recommended daily intake, in comparison to about 1.2% if consuming conventionally raised beef. When looking at the big picture, the difference is minimal.

Variations in particular nutrients, such as polyunsaturated fats, may also simply be due to differences between animal species/meat types, similar to different fruit and vegetable cultivars. There is also such a thing as too much supplementation, as high levels of flaxseed have demonstrated increased oxidation in beef when compared to more moderate levels. Another aspect that could be considered is crop-livestock integration, producing a synergy between farm plants

and animals with its own benefits (i.e. soil fertility) along with naturally improving the variety of animal diets, rather than simply increasing one nutrient. Because of the large amount of variables present in animal and produce production, plenty more research is necessary to begin to answer the questions at hand.

While there is some controversial evidence for the anti-carcinogenic effects of omega-3s, the lack of evidence of beneficial effects of CLA and the often small downstream effects of feed supplements on the agricultural end-products make it unrealistic to expect huge health benefits from the overall marginal increases in omega-3s and CLA in animal food products.

Frequently asked questions

How much antibiotics, hormones, pesticides, etc. used in conventional agriculture get into food products?

Significant levels of contaminants can cause consumer illness, such as allergy, immunosuppression, cancers, and more, but this is why food products are monitored and regulated. Maximum residue values and restrictions vary by country, which can lead to problems with imported/exported products, but there is research and regulation to ensure these compounds do not reach harmful levels.

Take hormones, for example: the Joint FAO/WHO Expert Committee on Food Additives concluded that hormones used on cattle are incapable of exerting hormonal effects on humans through consumption of the cattle's meat due to low bioavailability and, even if absorbed, presence in an inactive form. Reports demonstrate that hormone levels in meat are several times below the amount endogenously produced by humans. On the other hand, while antibiotics have not demonstrated any substantial data demonstrating any threat to consumer health, there are potential mechanisms that are still being explored to ensure no harm is being done.

How much omega-3 do people consume?

According to the American Heart Association, one should consume a serving of fatty fish about two times per week to achieve recommended levels of omega-3 fatty acids. The Food and Agricultural Organization of the United Nations recently reported that global per capita fish consumption is above 20 kilograms per year. With a serving of fish measuring out to about four ounces (about 0.114 kilograms) according to the United States Food and Drug Administration, that means per capita fish consumption is above two servings of fish per week. Nonetheless, only fatty fish is really high in omega-3s and the average westerner may simply be eating fried fish sticks or fish and chips. Having omega-3 fatty acids in eggs (or other animal products) is an added benefit simply by providing another source of the nutrient in the diet, making it more available to those who may have limited access to fatty fish or allergies to seafood. It would not cover the need for omega-3 levels as easily as fatty fish can (omega-3 eggs could not replace fish), but it's another source!

How much CLA do people consume?

While there is no official recommendation for CLA intake, the average American is estimated to consume between 151 to 212 milligrams per day. A serving of milk or beef is estimated to have between 0.3 to 81 milligrams of CLA, generally depending on the fat content of the food (hence the large range); skim milk is reported to have 1.8 milligrams of CLA per gram of fat, while 2% milk is estimated to have 5.0 milligrams.

What should I know?

This systematic review suggests that increases in serum CLA and omega-3 fatty acids can be seen when humans consume animal products from livestock whose diets are supplemented with seeds, fish oil, or grass. CLA does not have substantial evidence to clearly state any anti-cancer influence, while omega-3 fatty acids have some potential (along with other health benefits) but the relationship is still controversial. Some studies found by this review suggest that these animal products also could influence disease biomarkers in humans. However, drawing any strong conclusions from this isn't possible due to the large variance of conditions across the included studies, along with unconventional search criteria and methodology that could introduce bias into the review. Changes in animal-raising practices may improve nutrient quantity and variety, but the health implications of these changes are still far from clear. ◆

Visit the ERD Facebook forum for discussion around this issue!

Credits

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